The rapidly changing nature of the pandemic requires not only that CDC act swiftly, but also deftly to ensure that its actions are commensurate with the threat. This necessarily involves assessing evolving conditions that inform CDC's determinations.

The conditions that existed on September 4, 2020 have only worsened. As of January 21, 2021, there have been over 24,400,000 cases and over 400,000 deaths. Data collected by Princeton University show that eviction filings are occurring; it is therefore expected that large numbers of evictions would be processed if the Order were to expire. [*https://evictionlab.org/eviction-tracking*]. Without this Order, there is every reason to expect that evictions will increase significantly, resulting in further spread of COVID–19. It is imperative is to act quickly to protect the public health, and it would be impracticable and contrary to the public interest to delay the issuance and effective date of the Order pending notice-and-comment rulemaking.

Similarly, if this Order qualifies as a rule under the APA, the Office of Information and Regulatory Affairs (OIRA) has determined that it would be a major rule under the Congressional Review Act (CRA). But there would not be a delay in its effective date. The agency has determined that for the same reasons, there would be good cause under the CRA to make the requirements herein effective immediately

If any provision of this Order, or the application of any provision to any persons, entities, or circumstances, shall be held invalid, the remainder of the provisions, or the application of such provisions to any persons, entities, or circumstances other than those to which it is held invalid, shall remain valid and in effect.

This Order shall be enforced by federal authorities and cooperating state and local authorities through the provisions of 18 U.S.C. 3559, 3571; 42 U.S.C. 243, 268, 271; and 42 CFR 70.18. However, this Order has no effect on the contractual obligations of renters to pay rent and shall not preclude charging or collecting fees, penalties, or interest as a result of the failure to pay rent or other housing payment on a timely basis, under the terms of any applicable contract.

Criminal Penalties

Under 18 U.S.C. 3559, 3571; 42 U.S.C. 271; and 42 CFR 70.18, a person violating this Order may be subject to a fine of no more than $100,000 if the violation does not result in a death, or a fine of no more than $250,000 if the violation results in a death, or as otherwise provided by law. An organization violating this Order may be subject to a fine of no more than $200,000 per event if the violation does not result in a death or $500,000 per event if the violation results in a death or as otherwise provided by law. The U.S. Department of Justice may initiate criminal proceedings as appropriate seeking imposition of these criminal penalties.

Notice to Cooperating State and Local Officials

Under 42 U.S.C. 243, the U.S. Department of Health and Human Services is authorized to cooperate with and aid state and local authorities in the enforcement of their quarantine and other health regulations and to accept state and local assistance in the enforcement of Federal quarantine rules and regulations, including in the enforcement of this Order.

Notice of Available Federal Resources

While this Order to prevent eviction is effectuated to protect the public health, the states and units of local government are reminded that the Federal Government has deployed unprecedented resources to address the pandemic, including housing assistance.

The Department of Housing and Urban Development (HUD) has informed CDC that all HUD grantees—states, cities, communities, and nonprofits—who received Emergency Solutions Grants (ESG) or Community Development Block Grant (CDBG) funds under the CARES Act may use these funds to provide temporary rental assistance, homelessness prevention, or other aid to individuals who are experiencing financial hardship because of the pandemic and are at risk of being evicted, consistent with applicable laws, regulations, and guidance.

HUD has further informed CDC that:

HUD's grantees and partners play a critical role in prioritizing efforts to support this goal. As grantees decide how to deploy CDBG–CV and ESG–CV funds provided by the CARES Act, all communities should assess what resources have already been allocated to prevent evictions and homelessness through temporary rental assistance and homelessness prevention, particularly to the most vulnerable households.

HUD stands at the ready to support American communities take these steps to reduce the spread of COVID–19 and maintain economic prosperity. Where gaps are identified, grantees should coordinate across available Federal, non-Federal, and philanthropic funds to ensure these critical needs are sufficiently addressed and utilize HUD 's technical assistance to design and implement programs to support a coordinated response to eviction prevention needs. For program support, including technical assistance, please visit *www.hudexchange.info/program-support*. For further information on HUD resources, tools, and guidance available to respond to the COVID–19 pandemic, state and local officials are directed to visit *https://www.hud.gov/coronavirus*. These tools include toolkits for Public Housing Authorities and Housing Choice Voucher landlords related to housing stability and eviction prevention, as well as similar guidance for owners and renters in HUD-assisted multifamily properties.

Similarly, the Department of the Treasury has informed CDC that the funds allocated through the Coronavirus Relief Fund and the Emergency Rental Assistance Program may be used to fund rental assistance programs to prevent eviction. Visit *https://home.treasury.gov/policy-issues/cares/state-and-local-governments* for more information about the Coronavirus Relief Fund and *https://home.treasury.gov/policy-issues/cares/emergency-rental-assistance-program* for more information about the Emergency Rental Assistance Program..

Effective Date

This Order is effective on January 31, 2021 and will remain in effect, unless extended, modified, or rescinded, through March 31, 2021.

Authority

The authority for this Order is Section 361 of the Public Health Service Act (42 U.S.C. 264) and 42 CFR 70.2.

Dated: January 29, 2021.

Sherri Berger

Acting Chief of Staff, Centers for Disease Control and Prevention.

[FR Doc. 2021–02243 Filed 1–29–21; 4:15 pm]

BILLING CODE 4163–18–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Centers for Disease Control and Prevention

Requirement for Persons To Wear Masks While on Conveyances and at Transportation Hubs

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Notice of Agency Order.

SUMMARY: The Centers for Disease Control and Prevention (CDC), a component of the U.S. Department of Health and Human Services (HHS), announces an Agency Order requiring persons to wear masks over the mouth and nose when traveling on any conveyance (*e.g.,* airplanes, trains, subways, buses, taxis, ride-shares, ferries, ships, trolleys, and cable cars) into or within the United States. A person must also wear a mask on any conveyance departing from the United States until the conveyance reaches its foreign destination. Additionally, a person must wear a mask while at any transportation hub within the United States (*e.g.,* airport, bus terminal, marina, train station, seaport or other port, subway station, or any other area that provides transportation within the United States). Furthermore, operators of conveyances and transportation hubs must use best efforts to ensure that persons wear masks as required by this Order.

DATES: This Order takes effect at 11:59 p.m. Monday February 1, 2021.

FOR FURTHER INFORMATION CONTACT: Jennifer Buigut, Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, 1600 Clifton Road NE, MS H16–4, Atlanta, GA 30329. Email: *dgmqpolicyoffice@cdc.gov*.

SUPPLEMENTARY INFORMATION: The virus that causes COVID–19 spreads very easily and sustainably between people who are in close contact with one another (within about 6 feet) mainly through respiratory droplets produced when an infected person coughs, sneezes, or talks. These droplets can land in the mouths, eyes, or noses of people who are nearby and possibly be inhaled into the lungs. Some people without symptoms also spread the virus. In general, the more closely a person interacts with others and the longer that interaction, the higher the risk of COVID–19 spread.

This Order is issued to preserve human life; maintain a safe and operating transportation system; mitigate the further introduction, transmission, and spread of COVID–19 into the United States and from one state or territory into any other state or territory; and support response efforts to COVID–19 at the Federal, state, local, territorial, and tribal level.

Appropriately worn masks reduce the spread of COVID–19—particularly given the evidence of pre-symptomatic and asymptomatic transmission of COVID–19. Masks are most likely to reduce the spread of COVID–19 when they are widely used by people in public settings. Using masks along with other preventive measures, including social distancing, frequent handwashing, and cleaning and disinfecting frequently touched surfaces, is one of the most effective strategies available for reducing COVID–19 transmission.

This Order will remain in effect unless modified or rescinded based on specific public health or other considerations, or until the Secretary of Health and Human Services rescinds the determination under section 319 of the Public Health Service Act (42 U.S.C. 247d) that a public health emergency exists.

A copy of the Order is provided below and a copy of the signed order can be found at *https://www.cdc.gov/quarantine/masks/mask-travel-guidance.html*

CENTERS FOR DISEASE CONTROL AND PREVENTION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

ORDER UNDER SECTION 361

OF THE PUBLIC HEALTH SERVICE ACT (42 U.S.C. 264)

AND 42 CODE OF FEDERAL REGULATIONS 70.2, 71.31(b), 71.32(b)

REQUIREMENT FOR PERSONS TO WEAR MASKS

WHILE ON CONVEYANCES AND AT TRANSPORTATION HUBS

SUMMARY:

Notice and Order; and subject to the limitations under ''Applicability,'' pursuant to 42 U.S.C. 264(a) and 42 CFR 70.2, 71.31(b), and 71.32(b):

(1) Persons [1] must wear [2] masks over the mouth and nose when traveling on conveyances into and within the United States. Persons must also wear masks at transportation hubs as defined in this Order.

(2) A conveyance operator transporting persons into and within the United States [3] must require all persons onboard to wear masks for the duration of travel.

(3) A conveyance operators operating a conveyance arriving at or departing from a U.S. port of entry must require all persons on board to wear masks for the duration of travel as a condition of controlled free pratique.[4]

(4) Conveyance operators must use best efforts to ensure that any person on the conveyance wears a mask when boarding, disembarking, and for the duration of travel. Best efforts include:

- Boarding only those persons who wear masks;
- instructing persons that Federal law requires wearing a mask on the conveyance and failure to comply constitutes a violation of Federal law;
- monitoring persons onboard the conveyance for anyone who is not wearing a mask and seeking compliance from such persons;
- at the earliest opportunity, disembarking any person who refuses to comply; and
- providing persons with prominent and adequate notice to facilitate awareness and compliance of the requirement of this Order to wear a mask; best practices may include, if feasible, advance notifications on digital platforms, such as on apps, websites, or email; posted signage in multiple languages with illustrations; printing the requirement on transit tickets; or other methods as appropriate.

(5) Operators of transportation hubs must use best efforts to ensure that any person entering or on the premises of the transportation hub wears a mask. Best efforts include:

- Allowing entry only to those persons who wear masks;
- instructing persons that Federal law requires wearing a mask in the transportation hub and failure to comply constitutes a violation of Federal law;
- monitoring persons on the premises of the transportation hub for anyone who is not wearing a mask and seeking compliance from such persons;
- at the earliest opportunity, removing any person who refuses to comply from the premises of the transportation hub; and
- providing persons with prominent and adequate notice to facilitate awareness and compliance with the requirement of this Order to wear a mask; best practices may include, if feasible, advance notifications on digital platforms, such as on apps, websites, or

[1] As used in this Order, ''persons'' includes travelers (*i.e.,* passengers and crew), conveyance operators, and any workers or service providers in the transportation hub.

[2] To ''wear a mask'' means to wear a mask over the nose and mouth.

[3] This includes international, interstate, or intrastate waterways, subject to the jurisdiction of the United States.

[4] As a condition of this controlled free pratique to commence or continue operations in the United States, conveyance operators must additionally require all persons to wear masks on board conveyances departing from the United States and for the duration of their travel until the conveyance arrives at the foreign destination if at any time any of the persons on the conveyance (passengers, crew, or conveyance operators) will return to the United States while this Order remains in effect. This precaution must be followed regardless of scheduled itinerary.

email; posted signage in multiple languages with illustrations; printing the requirement on transit tickets; or other methods as appropriate.

DEFINITIONS:

Controlled free pratique shall have the same definition as under 42 CFR 71.1, meaning ''permission for a carrier to enter a U.S. port, disembark, and begin operation under certain stipulated conditions.''

Conveyance shall have the same definition as under 42 CFR 70.1, meaning ''an aircraft, train, road vehicle,[5] vessel . . . or other means of transport, including military.'' Included in the definition of ''conveyance'' is the term ''carrier'' which under 42 CFR 71.1 has the same definition as conveyance under 42 CFR 70.1.

Conveyance operator means an individual operating a conveyance and an individual or organization causing or authorizing the operation of a conveyance.

Mask means a material covering the nose and mouth of the wearer, excluding face shields.[6]

Interstate traffic shall have the same definition as under 42 CFR 70.1, meaning

''(1):

(i) The movement of any conveyance or the transportation of persons or property, including any portion of such movement or transportation that is entirely within a state or possession—

(ii) From a point of origin in any state or possession to a point of destination in any other state or possession; or

(iii) Between a point of origin and a point of destination in the same state or possession but through any other state, possession, or contiguous foreign country.

(2) Interstate traffic does not include the following:

(i) The movement of any conveyance which is solely for the purpose of unloading persons or property transported from a foreign country or loading persons or property for transportation to a foreign country.

(ii) The movement of any conveyance which is solely for the purpose of effecting its repair, reconstruction, rehabilitation, or storage.''

Intrastate traffic means the movement of any conveyance or the transportation or movement of persons occurring solely within the boundaries of a state or territory, or on tribal land.

Possession shall have the same definition as under 42 CFR 70.1 and 71.1, meaning a ''U.S. territory.''

State shall have the same definition as under 42 CFR 70.1, meaning ''any of the 50 states, plus the District of Columbia.''

Territory shall have the same definition as ''U.S. territory'' under 42 CFR 70.1 and 71.1, meaning ''any territory (also known as possessions) of the United States, including American Samoa, Guam, the [Commonwealth of the] Northern Mariana Islands, the Commonwealth of Puerto Rico, and the U.S. Virgin Islands.''

Transportation hub means any airport, bus terminal, marina, seaport or other port, subway station, terminal (including any fixed facility at which passengers are picked-up or discharged), train station, U.S. port of entry, or any other location that provides transportation subject to the jurisdiction of the United States.

Transportation hub operator means an individual operating a transportation hub and an individual or organization causing or authorizing the operation of a transportation hub.

U.S. port shall have the same definition as under 42 CFR 71.1, meaning any ''seaport, airport, or border crossing point under the control of the United States.''

STATEMENT OF INTENT:

This Order shall be interpreted and implemented in a manner as to achieve the following objectives:

- Preservation of human life;
- Maintaining a safe and secure operating transportation system;
- Mitigating the further introduction, transmission, and spread of COVID–19 into the United States and from one state or territory into any other state or territory; and
- Supporting response efforts to COVID–19 at the Federal, state, local, territorial, and tribal levels.

APPLICABILITY:

This Order shall not apply within any state, locality, territory, or area under the jurisdiction of a Tribe that (1) requires a person to wear a mask on conveyances; (2) requires a person to wear a mask at transportation hubs; and (3) requires conveyances to transport only persons wearing masks. Such requirements must provide the same level of public health protection as—or greater protection than—the requirements listed herein.

In addition, the requirement to wear a mask shall not apply under the following circumstances:

- While eating, drinking, or taking medication, for brief periods;
- While communicating with a person who is hearing impaired when the ability to see the mouth is essential for communication;
- If, on an aircraft, wearing of oxygen masks is needed because of loss of cabin pressure or other event affecting aircraft ventilation;
- If unconscious (for reasons other than sleeping), incapacitated, unable to be awakened, or otherwise unable to remove the mask without assistance;[7] or
- When necessary to temporarily remove the mask to verify one's identity such as during Transportation Security Administration screening or when asked to do so by the ticket or gate agent or any law enforcement official.

This Order exempts the following categories of persons:[8]

- A child under the age of 2 years;
- A person with a disability who cannot wear a mask, or cannot safely wear a mask, because of the disability as defined by the Americans with Disabilities Act (42 U.S.C. 12101 *et seq.*).[9]

[5] This includes rideshares meaning arrangements where passengers travel in a privately owned road vehicle driven by its owner in connection with a fee or service.

[6] A properly worn mask completely covers the nose and mouth of the wearer. A mask should be secured to the head, including with ties or ear loops. A mask should fit snugly but comfortably against the side of the face. Masks do not include face shields. Masks can be either manufactured or homemade and should be a solid piece of material without slits, exhalation valves, or punctures. Medical masks and N–95 respirators fulfill the requirements of this Order. CDC guidance for attributes of acceptable masks in the context of this Order is available at: *https://www.cdc.gov/quarantine/masks/mask-travel-guidance.html.*

[7] Persons who are experiencing difficulty breathing or shortness of breath or are feeling winded may remove the mask temporarily until able to resume normal breathing with the mask. Persons who are vomiting should remove the mask until vomiting ceases. Persons with acute illness may remove the mask if it interferes with necessary medical care such as supplemental oxygen administered via an oxygen mask.

[8] Operators of conveyances or transportation hubs may impose requirements, or conditions for carriage, on persons requesting an exemption from the requirement to wear a mask, including medical consultation by a third party, medical documentation by a licensed medical provider, and/or other information as determined by the operator, as well as require evidence that the person does not have COVID–19 such as a negative result from a SARS–CoV–2 viral test or documentation of recovery from COVID–19. CDC definitions for SARS-CoV–2 viral test and documentation of recovery are available in the Frequently Asked Questions at: *https://www.cdc.gov/coronavirus/2019-ncov/travelers/testing-international-air-travelers.html.* Operators may also impose additional protective measures that improve the ability of a person eligible for exemption to maintain social distance (separation from others by 6 feet), such as scheduling travel at less crowded times or on less crowded conveyances, or seating or otherwise situating the individual in a less crowded section of the conveyance or transportation hub. Operators may further require that persons seeking exemption from the requirement to wear a mask request an accommodation in advance.

[9] This is a narrow exception that includes a person with a disability who cannot wear a mask

Continued

• A person for whom wearing a mask would create a risk to workplace health, safety, or job duty as determined by the relevant workplace safety guidelines or federal regulations.

This Order exempts the following categories of conveyances, including persons on board such conveyances:

• Private conveyances operated solely for personal, non-commercial use;

• Commercial motor vehicles or trucks as these terms are defined in 49 CFR 390.5, if the driver is the sole occupant of the vehicle or truck;

• Conveyances operated or chartered by the U.S. military services provided that such conveyance operators observe Department of Defense precautions to prevent the transmission of COVID–19 that are equivalent to the precautions in this Order.

This Order applies to persons on conveyances and at transportation hubs directly operated by U.S. state, local, territorial, or tribal government authorities, as well as the operators themselves. U.S. state, local, territorial, or tribal government authorities directly operating conveyances and transportation hubs may be subject to additional federal authorities or actions, and are encouraged to implement additional measures enforcing the provisions of this Order regarding persons traveling onboard conveyances and at transportation hubs operated by these government entities.

To the extent permitted by law, and consistent with President Biden's Executive Order of January 21, 2021 (Promoting COVID–19 Safety in Domestic and International Travel),[10] Federal agencies are required to implement additional measures enforcing the provisions of this Order.

BACKGROUND:

There is currently a pandemic of respiratory disease (coronavirus disease 2019 or ''COVID–19'') caused by a novel coronavirus (SARS–COV–2). As of January 27, 2021, there have been 99,638,507 confirmed cases of COVID–19 globally, resulting in more than 2,141,000 deaths. As of January 27, 2021, there have been over 25,000,000 cases identified in the United States and over 415,000 deaths due to the disease. New SARS–CoV–2 variants have emerged in recent weeks, including at least one with evidence of increased transmissibility.[11]

The virus that causes COVID–19 spreads very easily and sustainably between people who are in close contact with one another (within about 6 feet) mainly through respiratory droplets produced when an infected person coughs, sneezes, or talks. These droplets can land in the mouths, eyes, or noses of people who are nearby and possibly be inhaled into the lungs. Infected people without symptoms (asymptomatic) and those in whom symptoms have not yet developed (pre-symptomatic) can also spread the virus. In general, the more closely an infected person interacts with others and the longer those interactions, the higher the risk of COVID–19 spread. COVID–19 may be transmitted by touching surfaces or objects that have the virus on them and then touching one's own or another person's eyes, nose, or mouth.

Masks help prevent people who have COVID–19, including those who are pre-symptomatic or asymptomatic, from spreading the virus to others.[12] Masks are primarily intended to reduce the emission of virus-laden droplets, *i.e.,* they act as source control by blocking exhaled virus.[13] This is especially relevant for asymptomatic or pre-symptomatic infected wearers who feel well and may be unaware of their infectiousness to others, and who are estimated to account for more than 50% of transmissions.[14] [15] Masks also provide personal protection to the wearer by reducing inhalation of these droplets, *i.e.,* they reduce wearers' exposure through filtration.[16] The community benefit of wearing masks for SARS–CoV–2 control is due to the combination of these effects; individual prevention benefit increases with increasing numbers of people using masks consistently and correctly.

Appropriately worn masks reduce the spread of COVID–19—particularly given the evidence of pre-symptomatic and asymptomatic transmission of COVID–19. Seven studies have confirmed the benefit of universal masking in community level analyses: in a unified hospital system,[17] a German city,[18] a U.S. State,[19] a panel of 15 U.S. States and Washington, DC,[20] [21] as well as both Canada [22] and the United States [23] nationally. Each analysis demonstrated that, following directives from organizational and political leadership for universal masking, new infections fell significantly. Two of these studies [24] [25] and an additional analysis of data from 200 countries that included localities within the United States [26] also demonstrated reductions in

for reasons related to the disability. CDC will issue additional guidance regarding persons who cannot wear a mask under this exemption. *https://www.cdc.gov/quarantine/masks/mask-travel-guidance.html.*

[10] *https://www.whitehouse.gov/briefing-room/presidential-actions/2021/01/21/executive-order-promoting-covid-19-safety-in-domestic-and-international-travel/.*

[11] *https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/scientific-brief-emerging-variants.html.*

[12] *https://www.cdc.gov/coronavirus/2019-ncov/more/masking-science-sars-cov2.html.*

[13] Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine.* 2020;26(5):676–680.*https://dx.doi.org/10.1038/s41591-020-0843-2.*

[14] Moghadas SM, Fitzpatrick MC, Sah P, et al. The implications of silent transmission for the control of COVID–19 outbreaks. *Proc Natl Acad Sci U S A.* 2020;117(30):17513–17515.10.1073/pnas.2008373117. *https://www.ncbi.nlm.nih.gov/pubmed/32632012.*

[15] Johansson MA, Quandelacy TM, Kada S, et al. SARS–CoV–2 Transmission From People Without COVID–19 Symptoms. Johansson MA, et al. JAMA Netw Open. 2021 Jan 4;4(1):e2035057. doi: 10.1001/jamanetworkopen.2020.35057.

[16] Ueki H, Furusawa Y, Iwatsuki-Horimoto K, et al. Effectiveness of Face Masks in Preventing Airborne Transmission of SARS–CoV–2. *mSphere.* 2020;5(5).10.1128/mSphere.00637–20. *https://www.ncbi.nlm.nih.gov/pubmed/33087517.*

[17] Wang X, Ferro EG, Zhou G, Hashimoto D, Bhatt DL. Association Between Universal Masking in a Health Care System and SARS–CoV–2 Positivity Among Health Care Workers. *JAMA.* 2020.10.1001/jama.2020.12897. *https://www.ncbi.nlm.nih.gov/pubmed/32663246.*

[18] Mitze T., Kosfeld R., Rode J., Wälde K. *Face Masks Considerably Reduce COVID–19 Cases in Germany: A Synthetic Control Method Approach.* IZA—Institute of Labor Economics (Germany);2020.ISSN: 2365–9793, DP No. 13319. *http://ftp.iza.org/dp13319.pdf.*

[19] Gallaway MS, Rigler J, Robinson S, et al. Trends in COVID–19 Incidence After Implementation of Mitigation Measures—Arizona, January 22-August 7, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(40):1460–1463.10.15585/mmwr.mm6940e3. *https://www.ncbi.nlm.nih.gov/pubmed/33031366.*

[20] Lyu W, Wehby GL. Community Use Of Face Masks And COVID–19: Evidence From A Natural Experiment Of State Mandates In The US. *Health Aff (Millwood).* 2020;39(8):1419–1425.10.1377/hlthaff.2020.00818. *https://www.ncbi.nlm.nih.gov/pubmed/32543923.*

[21] Hatzius J, Struyven D, Rosenberg I. Face Masks and GDP. *Goldman Sachs Research https://www.goldmansachs.com/insights/pages/face-masks-and-gdp.html.* Accessed January 20, 2021.

[22] Karaivanov A., Lu SE, Shigeoka H., Chen C., Pamplona S. *Face Masks, Public Policies and Slowing the Spread of Covid–19: Evidence from Canada* National Bureau of Economic Research 2020. Working Paper 27891. *http://www.nber.org/papers/w27891.*

[23] Chernozhukov V, Kasahara H, Schrimpf P. Causal Impact of Masks, Policies, Behavior on Early Covid–19 Pandemic in the U.S. J Econom. 2021 Jan;220(1):23–62. doi: 10.1016/j.jeconom.2020.09.003. Epub 2020 Oct 17.

[24] Hatzius J, Struyven D, Rosenberg I. Face Masks and GDP. *Goldman Sachs Research https://www.goldmansachs.com/insights/pages/face-masks-and-gdp.html.* Accessed January 20, 2021.

[25] Chernozhukov V, Kasahara H, Schrimpf P. Causal Impact of Masks, Policies, Behavior on Early Covid–19 Pandemic in the U.S. J Econom. 2021 Jan;220(1):23–62. doi: 10.1016/j.jeconom.2020.09.003. Epub 2020 Oct 17.

[26] Leffler CT, Ing EB, Lykins JD, Hogan MC, McKeown CA, Grzybowski A. Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks. Am J Trop Med Hyg. 2020 Dec;103(6):2400–2411. doi: 10.4269/ajtmh.20–1015. Epub 2020 Oct 26.

mortality. An economic analysis using U.S. data found that, given these effects, increasing universal masking by 15% could prevent the need for lockdowns and reduce associated losses of up to $1 trillion or about 5% of gross domestic product.[27]

Wearing a mask especially helps protect those at increased risk of severe illness from COVID–19[28] and workers who frequently come into close contact with other people (*e.g.,* at transportation hubs). Masks are most likely to reduce the spread of COVID–19 when they are widely used by people in public settings. Using masks along with other preventive measures, including social distancing, frequent handwashing, and cleaning and disinfecting frequently touched surfaces, is one of the most effective strategies available for reducing COVID–19 transmission.

Traveling on multi-person conveyances increases a person's risk of getting and spreading COVID–19 by bringing persons in close contact with others, often for prolonged periods, and exposing them to frequently touched surfaces. Air travel often requires spending time in security lines and crowded airport terminals. Social distancing may be difficult if not impossible on flights. People may not be able to distance themselves by the recommended 6 feet from individuals seated nearby or those standing in or passing through the aircraft's aisles. Travel by bus, train, vessel, and other conveyances used for international, interstate, or intrastate transportation pose similar challenges.

Intrastate transmission of the virus has led to—and continues to lead to—interstate and international spread of the virus, particularly on public conveyances and in travel hubs, where passengers who may themselves be traveling only within their state or territory commonly interact with others traveling between states or territories or internationally. Some states, territories, Tribes, and local public health authorities have imposed mask-wearing requirements within their jurisdictional boundaries to protect public health.[29] Any state or territory without sufficient mask-wearing requirements for transportation systems within its jurisdiction has not taken adequate measures to prevent the spread of COVID–19 from such state or territory to any other state or territory. That determination is based on, *inter alia,* the rapid and continuing transmission of the virus across all states and territories and across most of the world. Furthermore, given how interconnected most transportation systems are across the nation and the world, local transmission can grow even more quickly into interstate and international transmission when infected persons travel on non-personal conveyances without wearing a mask and with others who are not wearing masks.

Therefore, I have determined that the mask-wearing requirements in this Order are reasonably necessary to prevent the further introduction, transmission, or spread of COVID–19 into the United States and among the states and territories. Individuals traveling into or departing from the United States, traveling interstate, or traveling entirely intrastate, conveyance operators that transport such individuals, and transportation hub operators that facilitate such transportation, must comply with the mask-wearing requirements set forth in this Order.

America's transportation systems are essential. Not only are they essential for public health, they are also essential for America's economy and other bedrocks of American life. Those transportation systems carry life-saving medical supplies and medical providers into and across the nation to our hospitals, nursing homes, and physicians' offices. Trains, planes, ships, and automobiles bring food and other essentials to our communities and to our homes. Buses bring America's children and teachers to school. Buses, trains, and subways, bring America's workforce to their jobs.

Requiring masks on our transportation systems will protect Americans and provide confidence that we can once again travel safely even during this pandemic. Therefore, requiring masks will help us control this pandemic and aid in re-opening America's economy.

The United States and countries around the world are currently embarking on efforts to vaccinate their populations, starting with healthcare personnel and other essential workers at increased risk of exposure to SARS–CoV–2 and people at increased risk for severe illness from the virus. While vaccines are highly effective at preventing severe or symptomatic COVID–19, at this time there is limited information on how much the available COVID–19 vaccines may reduce transmission in the general population and how long protection lasts.[30] Therefore, this mask requirement, as well as CDC recommendations to prevent spread of COVID–19,[31] additionally apply to vaccinated persons. Similarly, CDC recommends that people who have recovered from COVID–19 continue to take precautions to protect themselves and others, including wearing masks; [32] therefore, this mask requirement also applies to people who have recovered from COVID–19.

ACTION:

Until further notice, under 42 U.S.C. 264(a) and 42 CFR 70.2, 71.31(b), and 71.32(b), unless excluded or exempted as set forth in this Order, a person must wear a mask while boarding, disembarking, and traveling on any conveyance into or within the United States. A person must also wear a mask at any transportation hub that provides transportation within the United States.

Conveyance operators traveling into or within the United States may transport only persons wearing masks and must use best efforts to ensure that masks are worn when embarking, disembarking, and throughout the duration of travel. Operators of transportation hubs must use best efforts to ensure that any person entering or on the premises of the transportation hub wears a mask.

As a condition of receiving controlled free pratique under 42 CFR 71.31(b) to enter a U.S. port, disembark passengers, and begin operations at any U.S. port of entry, conveyances arriving into the United States must require persons to wear masks while boarding, disembarking, and for the duration of travel. Conveyance operators must also require all persons to wear masks while boarding and for the duration of their travel on board conveyances departing from the United States until the conveyance arrives at the foreign destination, if at any time any of the persons onboard (passengers, crew, or conveyance operators) will return to the United States while this Order remains in effect. These travel conditions are

[27] Hatzius J, Struyven D, Rosenberg I. Face Masks and GDP. *Goldman Sachs Research https://www.goldmansachs.com/insights/pages/face-masks-and-gdp.html.* Accessed January 20, 2021.

[28] *https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/index.html.*

[29] Based on internet sources, 37 states plus DC and Puerto Rico mandate the wearing of masks in public. Among the jurisdictions that have imposed mask mandates, variations in requirements exist. For example, exemptions for children range in cutoff age from 2 to 12, but masks are generally required in indoor public spaces such as restaurants and stores, on public transit and ride-hailing services, and outdoors when unable to maintain 6 feet of distance from others. *See https://www.aarp.org/health/healthy-living/info-2020/states-mask-mandates-coronavirus.html* (accessed January 28, 2021).

[30] *https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html.*

[31] *https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html.*

[32] *https://www.cdc.gov/coronavirus/2019-ncov/hcp/duration-isolation.html.*

necessary to mitigate the harm of further introduction of COVID–19 into the United States.

Requiring a properly worn mask is a reasonable and necessary measure to prevent the introduction, transmission and spread of COVID–19 into the United States and among the states and territories under 42 U.S.C. 264(a) and 42 CFR 71.32(b). Among other benefits, masks help prevent dispersal of an infected person's respiratory droplets that carry the virus. That precaution helps prevent droplets from landing in the eye, mouth, or nose or possibly being inhaled into the lungs of an uninfected person, or from landing on a surface or object that an uninfected person may then touch and then touch his or her own or another's eyes, nose, or mouth. Masks also provide some protection to the wearer by helping reduce inhalation of respiratory droplets.

This Order shall not apply within any state, locality, territory, or area under the jurisdiction of a Tribe, where the controlling governmental authority: (1) Requires a person to wear a mask on conveyances; (2) requires a person to wear a mask at transportation hubs; and (3) requires conveyances to transport only persons wearing masks. Those requirements must provide the same level of public health protection as—or greater protection than—the requirements listed herein.

In accordance with 42 U.S.C. 264(e), state, local, territorial, and tribal authorities may impose additional requirements that provide greater public health protection and are more restrictive than the requirements in this Order. Consistent with other federal, state, or local legal requirements, this Order does not preclude operators of conveyances or transportation hubs from imposing additional requirements, or conditions for carriage, that provide greater public health protection and are more restrictive than the requirements in this Order (*e.g.,* requiring a negative result from a SARS–CoV–2 viral test or documentation of recovery from COVID–19 or imposing requirements for social distancing or other recommended protective measures).

This Order is not a rule within the meaning of the Administrative Procedure Act (''APA'') but rather is an emergency action taken under the existing authority of 42 U.S.C. 264(a) and 42 CFR 70.2, 71.31(b), 71.32(b). In the event that a court determines this Order qualifies as a rule under the APA, notice and comment and a delay in effective date are not required because there is good cause to dispense with prior public notice and comment and the opportunity to comment on this Order and the delay in effective date. Considering the public health emergency caused by COVID–19, it would be impracticable and contrary to the public's health, and by extension the public's interest, to delay the issuance and effective date of this Order. Similarly, the Office of Information and Regulatory Affairs has determined that if this Order were a rule, it would be a major rule under the Congressional Review Act, but there would not be a delay in its effective date as the agency has determined that there would be good cause to make the requirements herein effective immediately under the APA.

This order is also an economically significant regulatory action under Executive Order 12866 and has therefore been reviewed by the Office of Information and Regulatory Affairs of the Office of Management and Budget. The agency is proceeding without the complete analysis required by Executive Order 12866 under the emergency provisions of 6(a)(3)(D) of that Order.

If any provision of this Order, or the application of any provision to any carriers, conveyances, persons, or circumstances, shall be held invalid, the remainder of the provisions, or the application of such provisions to any carriers, conveyances, persons, or circumstances other than those to which it is held invalid, shall remain valid and in effect.

To address the COVID–19 public health threat to transportation security, this Order shall be enforced by the Transportation Security Administration under appropriate statutory and regulatory authorities including the provisions of 49 U.S.C. 106, 114, 44902, 44903, and 46301; and 49 CFR part 1503, 1540.105, 1542.303, 1544.305 and 1546.105.

This Order shall be further enforced by other federal authorities and may be enforced by cooperating state and local authorities through the provisions of 18 U.S.C. 3559, 3571; 42 U.S.C. 243, 268, 271; and 42 CFR 70.18 and 71.2.[33]

EFFECTIVE DATE:

This Order shall enter into effect on February 1, 2021, at 11:59 p.m. and will remain in effect unless modified or rescinded based on specific public health or other considerations, or until the Secretary of Health and Human Services rescinds the determination under section 319 of the Public Health Service Act (42 U.S.C. 247d) that a public health emergency exists.

Dated: February 1, 2021.

Sherri Berger,

Acting Chief of Staff, Centers for Disease Control and Prevention.

[FR Doc. 2021–02340 Filed 2–1–21; 4:15 pm]

BILLING CODE 4163–18–P

[33] While this Order may be enforced and CDC reserves the right to enforce through criminal penalties, CDC does not intend to rely primarily on these criminal penalties but instead strongly encourages and anticipates widespread voluntary compliance as well as support from other federal agencies in implementing additional civil measures enforcing the provisions of this Order, to the extent permitted by law and consistent with President Biden's Executive Order of January 21, 2021 (Promoting COVID–19 Safety in Domestic and International Travel).

DEPARTMENT OF THE INTERIOR

Geological Survey

[GX20EG31DW50100; OMB Control Number 1028-New]

Agency Information Collection Activities; Hydrography Addressing tool

AGENCY: U.S. Geological Survey, Interior.

ACTION: Notice of Information Collection; request for comment.

SUMMARY: In accordance with the Paperwork Reduction Act of 1995, we, the U.S. Geological Survey (USGS) are proposing a new information collection.

DATES: Interested persons are invited to submit comments on or before April 5, 2021.

ADDRESSES: Send your comments on this information collection request (ICR) by mail to U.S. Geological Survey, Information Collections Officer, 12201 Sunrise Valley Drive MS 159, Reston, VA 20192; or by email to *gs-info_collections@usgs.gov*. Please reference OMB Control Number 1028–xxxx in the subject line of your comments.

FOR FURTHER INFORMATION CONTACT: To request additional information about this ICR, contact Michael Tinker by email at *mdtinker@usgs.gov* or by telephone at 303–202–4476.

SUPPLEMENTARY INFORMATION: In accordance with the Paperwork Reduction Act of 1995, we provide the general public and other Federal agencies with an opportunity to comment on new, proposed, revised, and continuing collections of information. This helps us assess the impact of our information collection requirements and minimize the public's reporting burden. It also helps the public understand our information collection requirements and provide the requested data in the desired format.

We are soliciting comments on the proposed ICR that is described below.

BRIEFING ROOM

Executive Order on Promoting COVID-19 Safety in Domestic and International Travel

JANUARY 21, 2021 • PRESIDENTIAL ACTIONS

By the authority vested in me as President by the Constitution and the laws of the United States of America, it is hereby ordered as follows:

Section 1. Policy. Science-based public health measures are critical to preventing the spread of coronavirus disease 2019 (COVID-19) by travelers within the United States and those who enter the country from abroad. The Centers for Disease Control and Prevention (CDC), the Surgeon General, and the National Institutes of Health have concluded that mask-wearing, physical distancing, appropriate ventilation, and timely testing can mitigate the risk of travelers spreading COVID-19. Accordingly, to save lives and allow all Americans, including the millions of people employed in the transportation industry, to travel and work safely, it is the policy of my Administration to implement these public health measures consistent with CDC guidelines on public modes of transportation and at ports of entry to the United States.

Sec. 2. Immediate Action to Require Mask-Wearing on Certain Domestic Modes of Transportation.

(a) Mask Requirement. The Secretary of Labor, the Secretary of Health and Human Services (HHS), the Secretary of Transportation (including through the Administrator of the Federal Aviation Administration (FAA)), the Secretary of Homeland Security (including through the Administrator of the Transportation Security Administration (TSA) and the Commandant of the United States Coast Guard), and the heads of any other executive departments and agencies (agencies) that have relevant regulatory authority (heads of agencies) shall immediately take action, to the extent appropriate and consistent with applicable law, to require masks to be worn in compliance with CDC guidelines in or on:

(i) airports;

(ii) commercial aircraft;

(iii) trains;

(iv) public maritime vessels, including ferries;

(v) intercity bus services; and

(vi) all forms of public transportation as defined in section 5302 of title 49, United States Code.

(b) Consultation. In implementing this section, the heads of agencies shall consult, as appropriate, with interested parties, including State, local, Tribal, and territorial officials; industry and union representatives from the transportation sector; and consumer representatives.

(c) Exceptions. The heads of agencies may make categorical or case-by-case exceptions to policies developed under this section, consistent with applicable law, to the extent that doing so is necessary or required by law. If the heads of agencies do make exceptions, they shall require alternative and appropriate safeguards, and shall document all exceptions in writing.

(d) Preemption. To the extent permitted by applicable law, the heads of agencies shall ensure that any action taken to implement this section does not preempt State, local, Tribal, and territorial laws or rules imposing public health measures that are more protective of public health than those required by the heads of agencies.

(e) Coordination. The Coordinator of the COVID-19 Response and Counselor to the President (COVID-19 Response Coordinator) shall coordinate the implementation of this section. The heads of agencies shall update the COVID-19 Response Coordinator on their progress in implementing this section, including any categorical exceptions established under subsection (c) of this section, within 7 days of the date of this order and regularly thereafter. The heads of agencies are encouraged to bring to the attention of the COVID-19 Response Coordinator any questions regarding the scope or implementation of this section.

Sec. 3. Action to Implement Additional Public Health Measures for Domestic Travel.

(a) Recommendations. The Secretary of Transportation (including through the Administrator of the FAA) and the Secretary of Homeland Security (including through the Administrator of the TSA and the Commandant of the Coast Guard), in consultation with the Director of CDC, shall promptly provide to the COVID-19 Response Coordinator recommendations concerning how their respective agencies may impose additional public health measures for domestic travel.

(b) Consultation. In implementing this section, the Secretary of Transportation and the Secretary of Homeland Security shall engage with interested parties, including State, local,

Tribal, and territorial officials; industry and union representatives from the transportation sector; and consumer representatives.

Sec. 4. Support for State, Local, Tribal, and Territorial Authorities. The COVID-19 Response Coordinator, in coordination with the Secretary of Transportation and the heads of any other relevant agencies, shall promptly identify and inform agencies of options to incentivize, support, and encourage widespread mask-wearing and physical distancing on public modes of transportation, consistent with CDC guidelines and applicable law.

Sec. 5. International Travel.

(a) Policy. It is the policy of my Administration that, to the extent feasible, travelers seeking to enter the United States from a foreign country shall be:

(i) required to produce proof of a recent negative COVID-19 test prior to entry; and

(ii) required to comply with other applicable CDC guidelines concerning international travel, including recommended periods of self-quarantine or self-isolation after entry into the United States.

(b) Air Travel.

(i) The Secretary of HHS, including through the Director of CDC, and in coordination with the Secretary of Transportation (including through the Administrator of the FAA) and the Secretary of Homeland Security (including through the Administrator of the TSA), shall, within 14 days of the date of this order, assess the CDC order of January 12, 2021, regarding the requirement of a negative COVID-19 test result for airline passengers traveling into the United States, in light of subsection (a) of this section. Based on such assessment, the Secretary of HHS and the Secretary of Homeland Security shall take any further appropriate regulatory action, to the extent feasible and consistent with CDC guidelines and applicable law. Such assessment and regulatory action shall include consideration of:

(A) the timing and types of COVID-19 tests that should satisfy the negative test requirement, including consideration of additional testing immediately prior to departure;
(B) the proof of test results that travelers should be required to provide;
(C) the feasibility of implementing alternative and sufficiently protective public health measures, such as testing, self-quarantine, and self-isolation on arrival, for travelers entering the United States from countries where COVID-19 tests are inaccessible, particularly where such inaccessibility of tests would affect the ability of United States citizens and lawful

permanent residents to return to the United States; and
(D) measures to prevent fraud.

(ii) The Secretary of HHS, in coordination with the Secretary of Transportation (including through the Administrator of the FAA) and the Secretary of Homeland Security (including through the Administrator of the TSA), shall promptly provide to the President, through the COVID-19 Response Coordinator, a plan for how the Secretary and other Federal Government actors could implement the policy stated in subsection (a) of this section with respect to CDC-recommended periods of self-quarantine or self-isolation after a flight to the United States from a foreign country, as he deems appropriate and consistent with applicable law. The plan shall identify agencies' tools and mechanisms to assist travelers in complying with such policy.

(iii) The Secretary of State, in consultation with the Secretary of HHS (including through the Director of CDC), the Secretary of Transportation (including through the Administrator of the FAA), and the Secretary of Homeland Security, shall seek to consult with foreign governments, the World Health Organization, the International Civil Aviation Organization, the International Air Transport Association, and any other relevant stakeholders to establish guidelines for public health measures associated with safe international travel, including on aircraft and at ports of entry. Any such guidelines should address quarantine, testing, COVID-19 vaccination, follow-up testing and symptom-monitoring, air filtration requirements, environmental decontamination standards, and contact tracing.

(c) Land Travel. The Secretary of State, in consultation with the Secretary of HHS, the Secretary of Transportation, the Secretary of Homeland Security, and the Director of CDC, shall immediately commence diplomatic outreach to the governments of Canada and Mexico regarding public health protocols for land ports of entry. Based on this diplomatic engagement, within 14 days of the date of this order, the Secretary of HHS (including through the Director of CDC), the Secretary of Transportation, and the Secretary of Homeland Security shall submit to the President a plan to implement appropriate public health measures at land ports of entry. The plan should implement CDC guidelines, consistent with applicable law, and take into account the operational considerations relevant to the different populations who enter the United States by land.

(d) Sea Travel. The Secretary of Homeland Security, through the Commandant of the Coast Guard and in consultation with the Secretary of HHS and the Director of CDC, shall, within 14 days of the date of this order, submit to the President a plan to implement appropriate public health measures at sea ports. The plan should implement CDC guidelines, consistent with applicable law, and take into account operational considerations.

(e) International Certificates of Vaccination or Prophylaxis. Consistent with applicable law, the Secretary of State, the Secretary of HHS, and the Secretary of Homeland Security (including through the Administrator of the TSA), in coordination with any relevant international organizations, shall assess the feasibility of linking COVID-19 vaccination to International Certificates of Vaccination or Prophylaxis (ICVP) and producing electronic versions of ICVPs.

(f) Coordination. The COVID-19 Response Coordinator, in consultation with the Assistant to the President for National Security Affairs and the Assistant to the President for Domestic Policy, shall coordinate the implementation of this section. The Secretary of State, the Secretary of HHS, the Secretary of Transportation, and the Secretary of Homeland Security shall update the COVID-19 Response Coordinator on their progress in implementing this section within 7 days of the date of this order and regularly thereafter. The heads of all agencies are encouraged to bring to the attention of the COVID-19 Response Coordinator any questions regarding the scope or implementation of this section.

Sec. 6. General Provisions. (a) Nothing in this order shall be construed to impair or otherwise affect:

(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

JOSEPH R. BIDEN JR.

THE WHITE HOUSE,
January 21, 2021.

Centers for Disease Control and Prevention

COVID-19

Emerging SARS-CoV-2 Variants

Updated Jan. 28, 2021 Print

Multiple SARS-CoV-2 variants are circulating globally. Several new variants emerged in the fall of 2020, most notably:

Previous update: Dec. 29, 2020

US COVID-19 Cases Caused by Variants

View a map showing the number of confirmed cases in each state.

In the United Kingdom (UK), a new variant of SARS-CoV-2 (known as 20I/501Y.V1, VOC 202012/01, or B.1.1.7) emerged with a large number of mutations. This variant has since been detected in numerous countries around the world, including the United States (US). In January 2021, scientists from UK reported evidence[1] that suggests the B.1.1.7 variant may be associated with an increased risk of death compared with other variants. More studies are needed to confirm this finding. This variant was reported in the US at the end of December 2020.

- In South Africa, another variant of SARS-CoV-2 (known as 20H/501Y.V2 or B.1.351) emerged independently of B.1.1.7. This variant shares some mutations with B.1.1.7. Cases attributed to this variant have been detected in multiple countries outside of South Africa. This variant was reported in the US at the end of January 2021.
- In Brazil, a variant of SARS-CoV-2 (known as P.1) emerged that was first was identified in four travelers from Brazil, who were tested during routine screening at Haneda airport outside Tokyo, Japan. This variant has 17 unique mutations,

including three in the receptor binding domain of the spike protein. This variant was detected in the US at the end of January 2021.

Scientists are working to learn more about these variants to better understand how easily they might be transmitted and the effectiveness of currently authorized vaccines against them. New information about the virologic, epidemiologic, and clinical characteristics of these variants is rapidly emerging.

CDC, in collaboration with other public health agencies, is monitoring the situation closely. CDC is working to detect and characterize emerging viral variants. Furthermore, CDC has staff available to provide technical support to investigate the epidemiologic and clinical characteristics of SARS-CoV-2 variant infections. CDC will communicate new information as it becomes available.

Emerging Variants

B.1.1.7 lineage (a.k.a. 20I/501Y.V1 Variant of Concern (VOC) 202012/01)

- This variant has a mutation in the receptor binding domain (RBD) of the spike protein at position 501, where the amino acid asparagine (N) has been replaced with tyrosine (Y). The shorthand for this mutation is N501Y. This variant also has several other mutations, including:
  - 69/70 deletion: occurred spontaneously many times and likely leads to a conformational change in the spike protein
  - P681H: near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. This mutation has also emerged spontaneously multiple times.
- This variant is estimated to have first emerged in the UK during September 2020.
- Since December 20, 2020, several countries have reported cases of the B.1.1.7 lineage, including the United States.
- This variant is associated with increased transmissibility (i.e., more efficient and rapid transmission).
- In January 2021, scientists from UK reported evidence[1] that suggests the B.1.1.7 variant may be associated with an increased risk of death compared with other variants.
- Early reports found no evidence to suggest that the variant has any impact on the severity of disease or vaccine efficacy.[2],[3],[4]

B.1.351 lineage (a.k.a. 20H/501Y.V2)

- This variant has multiple mutations in the spike protein, including K417N, E484K, N501Y. Unlike the B.1.1.7 lineage detected in the UK, this variant does not contain the deletion at 69/70.
- This variant was first identified in Nelson Mandela Bay, South Africa, in samples dating back to the beginning of October 2020, and cases have since been detected outside of South Africa, including the United States
- The variant also was identified in Zambia in late December 2020, at which time it appeared to be the predominant variant in the country.
- Currently there is no evidence to suggest that this variant has any impact on disease severity.
- There is some evidence to indicate that one of the spike protein mutations, E484K, may affect neutralization by some polyclonal and monoclonal antibodies.[4],[5]

P.1 lineage (a.k.a. 20J/501Y.V3)

- The P.1 variant is a branch off the B.1.1.28 lineage that was first reported by the National Institute of Infectious Diseases (NIID) in Japan in four travelers from Brazil, sampled during routine screening at Haneda airport outside Tokyo.
- The P.1 lineage contains three mutations in the spike protein receptor binding domain: K417T, E484K, and N501Y.
- There is evidence to suggest that some of the mutations in the P.1 variant may affect its transmissibility and antigenic profile, which may affect the ability of antibodies generated through a previous natural infection or through vaccination to recognize and neutralize the virus.
  - A recent study reported on a cluster of cases in Manaus, the largest city in the Amazon region, in which the P.1 variant was identified in 42% of the specimens sequenced from late December.[5] In this region, it is estimated that approximately 75% of the population had been infected with SARS-CoV2 as of October 2020. However, since mid-

approximately 79% of the population had been infected with SARS-CoV-2 as of October 2020. However, since mid-December the region has observed a surge in cases. The emergence of this variant raises concerns of a potential increase in transmissibility or propensity for SARS-CoV-2 re-infection of individuals.

- This variant was identified in the United States at the end of January 2021.

Why Strain Surveillance is Important for Public Health

CDC has been conducting SARS-CoV-2 strain surveillance to build a collection of SARS-CoV-2 specimens and sequences to support public health response. Routine analysis of the available genetic sequence data will enable CDC and its public health partners to identify variant viruses for further characterization.

Viruses generally acquire mutations over time, giving rise to new variants. For instance, another variant recently emerged in Nigeria.[1] CDC also is monitoring this strain but, at this time, it has shown no concerning characteristics to public health experts.

Some of the potential consequences of emerging variants are the following:

- **Ability to spread more quickly in people.** There is already evidence that one mutation, D614G, confers increased ability to spread more quickly than the wild-type[2] SARS-CoV-2. In the laboratory, 614G variants propagate more quickly in human respiratory epithelial cells, outcompeting 614D viruses. There also is epidemiologic evidence that the 614G variant spreads more quickly than viruses without the mutation.
- **Ability to cause either milder or more severe disease in people.** In January 2021, experts in the UK reported that B.1.1.7 variant may be associated with an increased risk of death compared to other variants. More studies are needed to confirm this finding.
- **Ability to evade detection by specific viral diagnostic tests.** Most commercial reverse-transcription polymerase chain reaction (RT-PCR)-based tests have multiple targets to detect the virus, such that even if a mutation impacts one of the targets, the other RT-PCR targets will still work.
- **Decreased susceptibility to therapeutic agents such as monoclonal antibodies.**
- **Ability to evade natural or vaccine-induced immunity.** Both vaccination against and natural infection with SARS-CoV-2 produce a "polyclonal" response that targets several parts of the spike protein. The virus would likely need to accumulate multiple mutations in the spike protein to evade immunity induced by vaccines or by natural infection.

Among these possibilities, the last—the ability to evade vaccine-induced immunity—would likely be the most concerning because once a large proportion of the population is vaccinated, there will be immune pressure that could favor and accelerate emergence of such variants by selecting for "escape mutants." There is no evidence that this is occurring, and most experts believe escape mutants are unlikely to emerge because of the nature of the virus.

[1] Analysis of sequences from the African Centre of Excellence for Genomics of Infectious Diseases (ACEGID), Redeemer's University, Nigeria, identified two SARS-CoV-2 sequences belonging to the B.1.1.207 lineage. These sequences share one non-synonymous mutation in the spike protein (P681H) in common with the B.1.1.7 lineage but does not share any of the other 22 unique mutations of B.1.1.7 lineage. The P681H residue is near the S1/S2 furin cleavage site, a site with high variability in coronaviruses. At this time, it is unknown when this variant may have first emerged. Currently there is no evidence to indicate this variant has any impact on disease severity or is contributing to increased transmission of SARS-CoV-2 in Nigeria.

[2] "Wild-type" refers to the strain of virus – or background strain – that contains no major mutations.

Strain Surveillance in the US

In the United States, sequence-based strain surveillance has been ramping up with the following components:

- **National SARS-CoV-2 Strain Surveillance ("NS3"):** Since November 2020, state health departments and other public health agencies have been regularly sending SARS-CoV-2 samples to CDC for sequencing and further characterization. This system is now being scaled to process 750 samples nationally per week. One strength of this system is that it allows for characterization of viruses beyond what sequencing alone can provide.

- **Surveillance in partnership with commercial diagnostic laboratories:** CDC is contracting with large national reference labs to provide sequence data from across the United States. As of mid-January, CDC has commitments from these laboratories to sequence 6,000 samples per week and is exploring options to increase this number.
- **Contracts with universities:** CDC has contracts with seven universities to conduct genomic surveillance in collaboration with public health agencies.
- **Sequencing within state and local health departments:** Since 2014, CDC's Advanced Molecular Detection Program has been integrating next-generation sequencing and bioinformatics capabilities into the US public health system. Several state and local health departments have been applying these resources as part of their response to COVID-19. To further support these efforts, CDC released $15 million in funding, with COVID supplemental funds, through the Epidemiology and Laboratory Capacity Program on December 18, 2020.
- **The SPHERES consortium:** Since early in the pandemic, CDC has led a national consortium of laboratories sequencing SARS-CoV-2 (SPHERES) to coordinate US sequencing efforts outside of CDC. The SPHERES consortium consists of more than 160 institutions, including academic centers, industry, non-governmental organizations, and public health agencies.

Through these efforts, anonymous genomic data are made available through public databases for use by public health professionals, researchers, and industry.

References

[1]Horby P, Huntley C, Davies N, et al. NERVTAG note on B.1.1.7 severity . SAGE meeting report. January 21, 2021.

[2]Wu K, Werner AP, Moliva JI, et al. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. *bioRxiv*. Posted January 25, 2021.

[3]Xie X, Zou J, Fontes-Garfias CR, et al. Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera . *bioRxiv*. Posted January 7, 2021. Greaney AJ, Loes AN, Crawford KHD, et al. Comprehensive mapping of mutations to the SARS-CoV-2 receptor-binding domain that affect recognition by polyclonal human serum antibodies . bioRxiv. [Preprint posted online January 4, 2021]

[4]Weisblum Y, Schmidt F, Zhang F, et al. Escape from neutralizing antibodies by SARS-CoV-2 spike protein variantsexternal icon . eLife 2020;9:e61312.

[5]Resende PC, Bezerra JF, de Vasconcelos RHT, at al. Spike E484K mutation in the first SARS-CoV-2 reinfection case confirmed in Brazil, 2020 . [Posted on www.virological.org on January 10, 2021]

Last Updated Jan. 28, 2021

CDC Centers for Disease Control and Prevention

COVID-19

Scientific Brief: Community Use of Cloth Masks to Control the Spread of SARS-CoV-2

Updated Nov. 20, 2020 Print

Background

SARS-CoV-2 infection is transmitted predominately by respiratory droplets generated when people cough, sneeze, sing, talk, or breathe. CDC recommends community use of masks, specifically non-valved multi-layer cloth masks, to prevent transmission of SARS-CoV-2. Masks are primarily intended to reduce the emission of virus-laden droplets ("source control"), which is especially relevant for asymptomatic or presymptomatic infected wearers who feel well and may be unaware of their infectiousness to others, and who are estimated to account for more than 50% of transmissions.[1,2] Masks also help reduce inhalation of these droplets by the wearer ("filtration for personal protection"). The community benefit of masking for SARS-CoV-2 control is due to the combination of these effects; individual prevention benefit increases with increasing numbers of people using masks consistently and correctly.

Source Control to Block Exhaled Virus

Multi-layer cloth masks block release of exhaled respiratory particles into the environment,[3-6] along with the microorganisms these particles carry.[7,8] Cloth masks not only effectively block most large droplets (i.e., 20-30 microns and larger)[9] but they can also block the exhalation of fine droplets and particles (also often referred to as aerosols) smaller than 10 microns ;[3,5] which increase in number with the volume of speech[10-12] and specific types of phonation.[13] Multi-layer cloth masks can both block up to 50-70% of these fine droplets and particles[3,14] and limit the forward spread of those that are not captured.[5,6,15,16] Upwards of 80% blockage has been achieved in human experiments that have measured blocking of all respiratory droplets,[4] with cloth masks in some studies performing on par with surgical masks as barriers for source control.[3,9,14]

Filtration for Personal Protection

Studies demonstrate that cloth mask materials can also reduce wearers' exposure to infectious droplets through filtration, including filtration of fine droplets and particles less than 10 microns. The relative filtration effectiveness of various masks has varied widely across studies, in large part due to variation in experimental design and particle sizes analyzed. Multiple layers of cloth with higher thread counts have demonstrated superior performance compared to single layers of cloth with lower thread counts, in some cases filtering nearly 50% of fine particles less than 1 micron .[14,17-29] Some materials (e.g., polypropylene) may enhance filtering effectiveness by generating triboelectric charge (a form of static electricity) that enhances capture of charged particles[18,30] while others (e.g., silk) may help repel moist droplets[31] and reduce fabric wetting and thus maintain breathability and comfort.

Human Studies of Masking and SARS-CoV-2 Transmission

Data regarding the "real-world" effectiveness of community masking are limited to observational and epidemiological studies.

- An investigation of a high-exposure event, in which 2 symptomatically ill hair stylists interacted for an average of 15 minutes with each of 139 clients during an 8-day period, found that none of the 67 clients who subsequently consented to an interview and testing developed infection. The stylists and all clients universally wore masks in the salon as required by local ordinance and company policy at the time.[32]

- In a study of 124 Beijing households with ≥ 1 laboratory-confirmed case of SARS-CoV-2 infection, mask use by the index patient and family contacts before the index patient developed symptoms reduced secondary transmission within the households by 79%.[33]
- A retrospective case-control study from Thailand documented that, among more than 1,000 persons interviewed as part of contact tracing investigations, those who reported having always worn a mask during high-risk exposures experienced a greater than 70% reduced risk of acquiring infection compared with persons who did not wear masks under these circumstances.[34]
- A study of an outbreak aboard the USS Theodore Roosevelt, an environment notable for congregate living quarters and close working environments, found that use of face coverings on-board was associated with a 70% reduced risk.[35]
- Investigations involving infected passengers aboard flights longer than 10 hours strongly suggest that masking prevented in-flight transmissions, as demonstrated by the absence of infection developing in other passengers and crew in the 14 days following exposure.[36,37]

Seven studies have confirmed the benefit of universal masking in community level analyses: in a unified hospital system,[38] a German city,[39] a U.S. state,[40] a panel of 15 U.S. states and Washington, D.C.,[41,42] as well as both Canada[43] and the U.S.[44] nationally. Each analysis demonstrated that, following directives from organizational and political leadership for universal masking, new infections fell significantly. Two of these studies[42,44] and an additional analysis of data from 200 countries that included the U.S.[45] also demonstrated reductions in mortality. An economic analysis using U.S. data found that, given these effects, increasing universal masking by 15% could prevent the need for lockdowns and reduce associated losses of up to $1 trillion or about 5% of gross domestic product.[42]

Conclusions

Experimental and epidemiological data support community masking to reduce the spread of SARS-CoV-2. The prevention benefit of masking is derived from the combination of source control and personal protection for the mask wearer. The relationship between source control and personal protection is likely complementary and possibly synergistic[14], so that individual benefit increases with increasing community mask use. Further research is needed to expand the evidence base for the protective effect of cloth masks and in particular to identify the combinations of materials that maximize both their blocking and filtering effectiveness, as well as fit, comfort, durability, and consumer appeal. Adopting universal masking policies can help avert future lockdowns, especially if combined with other non-pharmaceutical interventions such as social distancing, hand hygiene, and adequate ventilation.

References

1. Moghadas SM, Fitzpatrick MC, Sah P, et al. The implications of silent transmission for the control of COVID-19 outbreaks. *Proc Natl Acad Sci U S A.* 2020;117(30):17513-17515.10.1073/pnas.2008373117. https://www.ncbi.nlm.nih.gov/pubmed/32632012 .
2. Johansson MA, Quandelacy TM, Kada S, et al. Controlling COVID-19 requires preventing SARS-CoV-2 transmission from people without symptoms. *submitted.* 2020.
3. Lindsley WG, Blachere FM, Law BF, Beezhold DH, Noti JD. Efficacy of face masks, neck gaiters and face shields for reducing the expulsion of simulated cough-generated aerosols. *medRxiv.* 2020. https://doi.org/10.1101/2020.10.05.20207241 .
4. Fischer EP, Fischer MC, Grass D, Henrion I, Warren WS, Westman E. Low-cost measurement of face mask efficacy for filtering expelled droplets during speech. *Sci Adv.* 2020;6(36).10.1126/sciadv.abd3083. https://www.ncbi.nlm.nih.gov/pubmed/32917603 .
5. Verma S, Dhanak M, Frankenfield J. Visualizing the effectiveness of face masks in obstructing respiratory jets. *Phys Fluids (1994).* 2020;32(6):061708.10.1063/5.0016018. https://www.ncbi.nlm.nih.gov/pubmed/32624649 .
6. Bahl P, Bhattacharjee S, de Silva C, Chughtai AA, Doolan C, MacIntyre CR. Face coverings and mask to minimise droplet dispersion and aerosolisation: a video case study. *Thorax.* 2020;75(11):1024-1025.10.1136/thoraxjnl-2020-215748. https://www.ncbi.nlm.nih.gov/pubmed/32709611 .
7. Davies A, Thompson KA, Giri K, Kafatos G, Walker J, Bennett A. Testing the efficacy of homemade masks: would they protect in an influenza pandemic? *Disaster Med Public Health Prep.* 2013;7(4):413-418.10.1017/dmp.2013.43. https://www.ncbi.nlm.nih.gov/pubmed/24229526 .
8. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nature Medicine.* 2020;26(5):676-680.https://dx.doi.org/10.1038/s41591-020-0843-2 .

9. Bandiera L., Pavar G., Pisetta G., et al. Face coverings and respiratory tract droplet dispersion. *medRxiv.* 2020.10.1101/2020.08.11.20145086. https://doi.org/10.1101/2020.08.11.20145086 .
10. Alsved M, Matamis A, Bohlin R, et al. Exhaled respiratory particles during singing and talking. *Aerosol Sci Technol.* 2020.10.1080/02786826.2020.1812502.
11. Asadi S, Wexler AS, Cappa CD, Barreda S, Bouvier NM, Ristenpart WD. Aerosol emission and superemission during human speech increase with voice loudness. *Sci Rep.* 2019;9(1):2348.10.1038/s41598-019-38808-z. https://www.ncbi.nlm.nih.gov/pubmed/30787335 .
12. Morawska L., Johnson GR, Ristovski ZD, et al. Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *Aerosol Sci.* 2009;40(3):256-269. https://www.sciencedirect.com/science/article/pii/S0021850208002036 .
13. Abkarian M, Mendez S, Xue N, Yang F, Stone HA. Speech can produce jet-like transport relevant to asymptomatic spreading of virus. *Proc Natl Acad Sci U S A.* 2020;117(41):25237-25245.10.1073/pnas.2012156117. https://www.ncbi.nlm.nih.gov/pubmed/32978297 .
14. Ueki H, Furusawa Y, Iwatsuki-Horimoto K, et al. Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2. *mSphere.* 2020;5(5).10.1128/mSphere.00637-20. https://www.ncbi.nlm.nih.gov/pubmed/33087517 .
15. Rodriguez-Palacios A, Cominelli F, Basson AR, Pizarro TT, Ilic S. Textile Masks and Surface Covers-A Spray Simulation Method and a "Universal Droplet Reduction Model" Against Respiratory Pandemics. *Front Med (Lausanne).* 2020;7:260.10.3389/fmed.2020.00260. https://www.ncbi.nlm.nih.gov/pubmed/32574342 .
16. Viola I.M., Peterson B., Pisetta G., et al. *Face coverings, aerosol dispersion and mitigation of virus transmission risk.* 2020. https://arxiv.org/abs/2005.10720 .
17. Rengasamy S, Eimer B, Shaffer RE. Simple respiratory protection–evaluation of the filtration performance of cloth masks and common fabric materials against 20-1000 nm size particles. *Ann Occup Hyg.* 2010;54(7):789-798.10.1093/annhyg/meq044. https://www.ncbi.nlm.nih.gov/pubmed/20584862 .
18. Konda A, Prakash A, Moss GA, Schmoldt M, Grant GD, Guha S. Aerosol Filtration Efficiency of Common Fabrics Used in Respiratory Cloth Masks. *ACS Nano.* 2020;14(5):6339-6347.10.1021/acsnano.0c03252. https://www.ncbi.nlm.nih.gov/pubmed/32329337 .
19. Long KD, Woodburn EV, Berg IC, Chen V, Scott WS. Measurement of filtration efficiencies of healthcare and consumer materials using modified respirator fit tester setup. *PLoS One.* 2020;15(10):e0240499.10.1371/journal.pone.0240499. https://www.ncbi.nlm.nih.gov/pubmed/33048980 .
20. O'Kelly E, Pirog S, Ward J, Clarkson PJ. Ability of fabric face mask materials to filter ultrafine particles at coughing velocity. *BMJ Open.* 2020;10(9):e039424.10.1136/bmjopen-2020-039424. https://www.ncbi.nlm.nih.gov/pubmed/32963071 .
21. Aydin O, Emon B, Cheng S, Hong L, Chamorro LP, Saif MTA. Performance of fabrics for home-made masks against the spread of COVID-19 through droplets: A quantitative mechanistic study. *Extreme Mech Lett.* 2020;40:100924.10.1016/j.eml.2020.100924. https://www.ncbi.nlm.nih.gov/pubmed/32835043 .
22. Bhattacharjee S, Bahl P, Chughtai AA, MacIntyre CR. Last-resort strategies during mask shortages: optimal design features of cloth masks and decontamination of disposable masks during the COVID-19 pandemic. *BMJ Open Respir Res.* 2020;7(1).10.1136/bmjresp-2020-000698. https://www.ncbi.nlm.nih.gov/pubmed/32913005 .
23. Maurer L, Peris D, Kerl J, Guenther F, Koehler D, Dellweg D. Community Masks During the SARS-CoV-2 Pandemic: Filtration Efficacy and Air Resistance. *J Aerosol Med Pulm Drug Deliv.* 2020.10.1089/jamp.2020.1635. https://www.ncbi.nlm.nih.gov/pubmed/32975460 .
24. Hill WC, Hull MS, MacCuspie RI. 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. *Nano Lett.* 2020;20(10):7642-7647.10.1021/acs.nanolett.0c03182. https://www.ncbi.nlm.nih.gov/pubmed/32986441 .
25. Whiley H, Keerthirathne TP, Nisar MA, White MAF, Ross KE. Viral Filtration Efficiency of Fabric Masks Compared with Surgical and N95 Masks. *Pathogens.* 2020;9(9).10.3390/pathogens9090762. https://www.ncbi.nlm.nih.gov/pubmed/32957638 .
26. Hao W, Parasch A, Williams S, et al. Filtration performances of non-medical materials as candidates for manufacturing facemasks and respirators. *Int J Hyg Environ Health.* 2020;229:113582.10.1016/j.ijheh.2020.113582. https://www.ncbi.nlm.nih.gov/pubmed/32917368 .
27. van der Sande M, Teunis P, Sabel R. Professional and home-made face masks reduce exposure to respiratory infections among the general population. *PLoS One.* 2008;3(7):e2618.10.1371/journal.pone.0002618. https://www.ncbi.nlm.nih.gov/pubmed/18612429 .
28. Chu DK, Akl EA, Duda S, 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. *Lancet.* 2020.10.1016/S0140-

6736(20)31142-9. https://doi.org/10.1016/S0140-6736(20)31142-9 .

29. Clase CM, Fu EL, Ashur A, et al. Forgotten Technology in the COVID-19 Pandemic: Filtration Properties of Cloth and Cloth Masks-A Narrative Review. *Mayo Clin Proc.* 2020;95(10):2204-2224.10.1016/j.mayocp.2020.07.020. https://www.ncbi.nlm.nih.gov/pubmed/33012350 .
30. Zhao M, Liao L, Xiao W, et al. Household Materials Selection for Homemade Cloth Face Coverings and Their Filtration Efficiency Enhancement with Triboelectric Charging. *Nano Lett.* 2020;20(7):5544-5552.10.1021/acs.nanolett.0c02211. https://www.ncbi.nlm.nih.gov/pubmed/32484683 .
31. Parlin AF, Stratton SM, Culley TM, Guerra PA. A laboratory-based study examining the properties of silk fabric to evaluate its potential as a protective barrier for personal protective equipment and as a functional material for face coverings during the COVID-19 pandemic. *PLoS One.* 2020;15(9):e0239531.10.1371/journal.pone.0239531. https://www.ncbi.nlm.nih.gov/pubmed/32946526 .
32. Hendrix MJ, Walde C, Findley K, Trotman R. 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. *MMWR Morb Mortal Wkly Rep.* 2020;69(28):930-932.10.15585/mmwr.mm6928e2. https://www.ncbi.nlm.nih.gov/pubmed/32673300 .
33. Wang Y, Tian H, Zhang L, 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. *BMJ Glob Health.* 2020;5(5).10.1136/bmjgh-2020-002794. https://www.ncbi.nlm.nih.gov/pubmed/32467353 .
34. Doung-Ngern P, Suphanchaimat R, Panjangampatthana A, et al. Case-Control Study of Use of Personal Protective Measures and Risk for Severe Acute Respiratory Syndrome Coronavirus 2 Infection, Thailand. *Emerg Infect Dis.* 2020;26(11).10.3201/eid2611.203003. https://www.ncbi.nlm.nih.gov/pubmed/32931726 .
35. Payne DC, Smith-Jeffcoat SE, Nowak G, et al. SARS-CoV-2 Infections and Serologic Responses from a Sample of U.S. Navy Service Members – USS Theodore Roosevelt, April 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(23):714-721.10.15585/mmwr.mm6923e4. https://www.ncbi.nlm.nih.gov/pubmed/32525850 .
36. Schwartz KL, Murti M, Finkelstein M, et al. Lack of COVID-19 transmission on an international flight. *Cmaj.* 2020;192(15):E410.10.1503/cmaj.75015. https://www.ncbi.nlm.nih.gov/pubmed/32392504 .
37. Freedman DO, Wilder-Smith A. In-flight Transmission of SARS-CoV-2: a review of the attack rates and available data on the efficacy of face masks. *J Travel Med.* 2020.10.1093/jtm/taaa178. https://www.ncbi.nlm.nih.gov/pubmed/32975554 .
38. Wang X, Ferro EG, Zhou G, Hashimoto D, Bhatt DL. Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers. *JAMA.* 2020.10.1001/jama.2020.12897. https://www.ncbi.nlm.nih.gov/pubmed/32663246 .
39. Mitze T., Kosfeld R., Rode J., Wälde K. *Face Masks Considerably Reduce COVID-19 Cases in Germany: A Synthetic Control Method Approach.* IZA – Institute of Labor Economics (Germany);2020.ISSN: 2365-9793, DP No. 13319. http://ftp.iza.org/dp13319.pdf .
40. Gallaway MS, Rigler J, Robinson S, et al. Trends in COVID-19 Incidence After Implementation of Mitigation Measures – Arizona, January 22-August 7, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(40):1460-1463.10.15585/mmwr.mm6940e3. https://www.ncbi.nlm.nih.gov/pubmed/33031366 .
41. Lyu W, Wehby GL. Community Use Of Face Masks And COVID-19: Evidence From A Natural Experiment Of State Mandates In The US. *Health Aff (Millwood).* 2020;39(8):1419-1425.10.1377/hlthaff.2020.00818. https://www.ncbi.nlm.nih.gov/pubmed/32543923 .
42. Hatzius J, Struyven D, Rosenberg I. Face Masks and GDP. *Goldman Sachs Research* https://www.goldmansachs.com/insights/pages/face-masks-and-gdp.html . Accessed July 8, 2020.
43. Karaivanov A., Lu S.E., Shigeoka H., Chen C., Pamplona S. *Face Masks, Public Policies And Slowing The Spread Of Covid-19: Evidence from Canada* National Bureau Of Economic Research 2020.Working Paper 27891. http://www.nber.org/papers/w27891 .
44. Chernozhukov V, Kasahara H, Schrimpf P. Causal Impact of Masks, Policies, Behavior on Early Covid-19 Pandemic in the U.S. *medRxiv.* 2020.10.1101/2020.05.27.20115139. http://medrxiv.org/content/early/2020/05/29/2020.05.27.20115139.abstract .
45. Leffler CT, Ing EB, Lykins JD, Hogan MC, McKeown CA, Grzybowski A. Association of country-wide coronavirus mortality with demographics, testing, lockdowns, and public wearing of masks (updated August 4, 2020). *medRxiv.* 2020.10.1101/2020.05.22.20109231. http://medrxiv.org/content/early/2020/05/25/2020.05.22.20109231.abstract .

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The Science of Masking to Control COVID-19 [PDF – 28 slides]

The Science of Masking to Control COVID-19 (Abbreviated) [PDF – 7 slides]

Last Updated Nov. 20, 2020

BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-020-0843-2
nature medicine

Respiratory virus shedding in exhaled breath and efficacy of face masks

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We identified seasonal human coronaviruses, influenza viruses and rhinoviruses in exhaled breath and coughs of children and adults with acute respiratory illness. Surgical face masks significantly reduced detection of influenza virus RNA in respiratory droplets and coronavirus RNA in aerosols, with a trend toward reduced detection of coronavirus RNA in respiratory droplets. Our results indicate that surgical face masks could prevent transmission of human coronaviruses and influenza viruses from symptomatic individuals.

Respiratory virus infections cause a broad and overlapping spectrum of symptoms collectively referred to as acute respiratory virus illnesses (ARIs) or more commonly the 'common cold'. Although mostly mild, these ARIs can sometimes cause severe disease and death[1]. These viruses spread between humans through direct or indirect contact, respiratory droplets (including larger droplets that fall rapidly near the source as well as coarse aerosols with aerodynamic diameter >5 µm) and fine-particle aerosols (droplets and droplet nuclei with aerodynamic diameter ≤5 µm)[2,3]. Although hand hygiene and use of face masks, primarily targeting contact and respiratory droplet transmission, have been suggested as important mitigation strategies against influenza virus transmission[4], little is known about the relative importance of these modes in the transmission of other common respiratory viruses[2,3,5]. Uncertainties similarly apply to the modes of transmission of COVID-19 (refs. [6,7]).

Some health authorities recommend that masks be worn by ill individuals to prevent onward transmission (source control)[4,8]. Surgical face masks were originally introduced to protect patients from wound infection and contamination from surgeons (the wearer) during surgical procedures, and were later adopted to protect healthcare workers against acquiring infection from their patients. However, most of the existing evidence on the filtering efficacy of face masks and respirators comes from in vitro experiments with nonbiological particles[9,10], which may not be generalizable to infectious respiratory virus droplets. There is little information on the efficacy of face masks in filtering respiratory viruses and reducing viral release from an individual with respiratory infections[8], and most research has focused on influenza[11,12].

Here we aimed to explore the importance of respiratory droplet and aerosol routes of transmission with a particular focus on coronaviruses, influenza viruses and rhinoviruses, by quantifying the amount of respiratory virus in exhaled breath of participants with medically attended ARIs and determining the potential efficacy of surgical face masks to prevent respiratory virus transmission.

Results

We screened 3,363 individuals in two study phases, ultimately enrolling 246 individuals who provided exhaled breath samples (Extended Data Fig. 1). Among these 246 participants, 122 (50%) participants were randomized to not wearing a face mask during the first exhaled breath collection and 124 (50%) participants were randomized to wearing a face mask. Overall, 49 (20%) voluntarily provided a second exhaled breath collection of the alternate type.

Infections by at least one respiratory virus were confirmed by reverse transcription PCR (RT–PCR) in 123 of 246 (50%) participants. Of these 123 participants, 111 (90%) were infected by human (seasonal) coronavirus ($n=17$), influenza virus ($n=43$) or rhinovirus ($n=54$) (Extended Data Figs. 1 and 2), including one participant co-infected by both coronavirus and influenza virus and another two participants co-infected by both rhinovirus and influenza virus. These 111 participants were the focus of our analyses.

There were some minor differences in characteristics of the 111 participants with the different viruses (Table 1a). Overall, 24% of participants had a measured fever ≥37.8 °C, with patients with influenza more than twice as likely than patients infected with coronavirus and rhinovirus to have a measured fever. Coronavirus-infected participants coughed the most with an average of 17 (s.d. = 30) coughs during the 30-min exhaled breath collection. The profiles of the participants randomized to with-mask versus without-mask groups were similar (Supplementary Table 1).

We tested viral shedding (in terms of viral copies per sample) in nasal swabs, throat swabs, respiratory droplet samples and aerosol samples and compared the latter two between samples collected with or without a face mask (Fig. 1). On average, viral shedding was higher in nasal swabs than in throat swabs for each of coronavirus (median 8.1 $\log_{10}$ virus copies per sample versus 3.9), influenza virus (6.7 versus 4.0) and rhinovirus (6.8 versus 3.3), respectively. Viral RNA was identified from respiratory droplets and aerosols for all three viruses, including 30%, 26% and 28% of respiratory droplets and 40%, 35% and 56% of aerosols collected while not wearing a face mask, from coronavirus, influenza virus and rhinovirus-infected participants, respectively (Table 1b). In particular for coronavirus, we identified OC43 and HKU1 from both respiratory

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Table 1a | Characteristics of individuals with symptomatic coronavirus, influenza virus or rhinovirus infection

	All who provided exhaled breath	Coronavirus	Influenza virus	Rhinovirus
	(*n* = 246)	(*n* = 17)	(*n* = 43)	(*n* = 54)
	n (%)	*n* (%)	*n* (%)	*n* (%)
Female	144 (59)	13 (76)	22 (51)	30 (56)
Age group, years				
11–17	12 (5)	0 (0)	8 (19)	4 (7)
18–34	114 (46)	10 (59)	11 (26)	24 (44)
35–50	79 (32)	2 (12)	16 (37)	18 (33)
51–64	35 (14)	4 (24)	8 (19)	5 (9)
≥ 65	6 (2)	1 (6)	0 (0)	3 (6)
Chronic medical conditions				
Any	49 (20)	5 (29)	5 (12)	10 (19)
Respiratory	18 (7)	0 (0)	4 (9)	3 (6)
Influenza vaccination				
Ever	94 (38)	6 (35)	15 (35)	20 (37)
Current season	23 (9)	2 (12)	1 (2)	4 (7)
Previous season only	71 (29)	4 (24)	14 (33)	16 (30)
Ever smoker	31 (13)	1 (6)	6 (14)	6 (11)
Time since illness onset, h				
<24	22 (9)	0 (0)	5 (12)	2 (4)
24–48	100 (41)	9 (53)	13 (30)	25 (46)
48–72	85 (35)	8 (47)	18 (42)	20 (37)
72–96	39 (16)	0 (0)	7 (16)	7 (13)
History of measured fever ≥37.8 °C	58 (24)	3 (18)	17 (40)	8 (15)
Measured fever ≥37.8 °C at presentation	36 (15)	2 (12)	18 (42)	2 (4)
Measured body temperature (°C) at enrollment (mean, s.d.)	36.8 (0.8)	36.9 (0.8)	37.4 (0.9)	36.6 (0.7)
Symptoms at presentation				
Fever	111 (45)	10 (59)	27 (63)	16 (30)
Cough	198 (80)	15 (88)	40 (93)	44 (81)
Sore throat	211 (86)	15 (88)	31 (72)	49 (91)
Runny nose	200 (81)	17 (100)	36 (84)	48 (89)
Headache	186 (76)	13 (76)	30 (70)	38 (70)
Myalgia	176 (72)	12 (71)	31 (72)	34 (63)
Phlegm	176 (72)	9 (53)	34 (79)	41 (76)
Chest tightness	64 (26)	3 (18)	12 (28)	9 (17)
Shortness of breath	103 (42)	6 (35)	14 (33)	25 (46)
Chills	100 (41)	8 (47)	29 (67)	16 (30)
Sweating	95 (39)	5 (29)	18 (42)	20 (37)
Fatigue	218 (89)	16 (94)	38 (88)	48 (89)
Vomiting	19 (8)	2 (12)	5 (12)	2 (4)
Diarrhea	17 (7)	2 (12)	1 (2)	6 (11)
Number of coughs during exhaled breath collection (mean, s.d.)	8 (14)	17 (30)	8 (11)	5 (9)

Seasonal coronavirus (*n* = 17), seasonal influenza virus (*n* = 43) and rhinovirus (*n* = 54) infections were confirmed in individuals with acute respiratory symptoms by RT–PCR in any samples (nasal swab, throat swab, respiratory droplets and aerosols) collected.

droplets and aerosols, but only identified NL63 from aerosols and not from respiratory droplets (Supplementary Table 2 and Extended Data Fig. 3).

We detected coronavirus in respiratory droplets and aerosols in 3 of 10 (30%) and 4 of 10 (40%) of the samples collected without face masks, respectively, but did not detect any virus in respiratory droplets or aerosols collected from participants wearing face masks, this difference was significant in aerosols and showed a trend toward reduced detection in respiratory droplets (Table 1b). For influenza virus, we detected virus in 6 of 23 (26%) and 8 of 23 (35%) of the

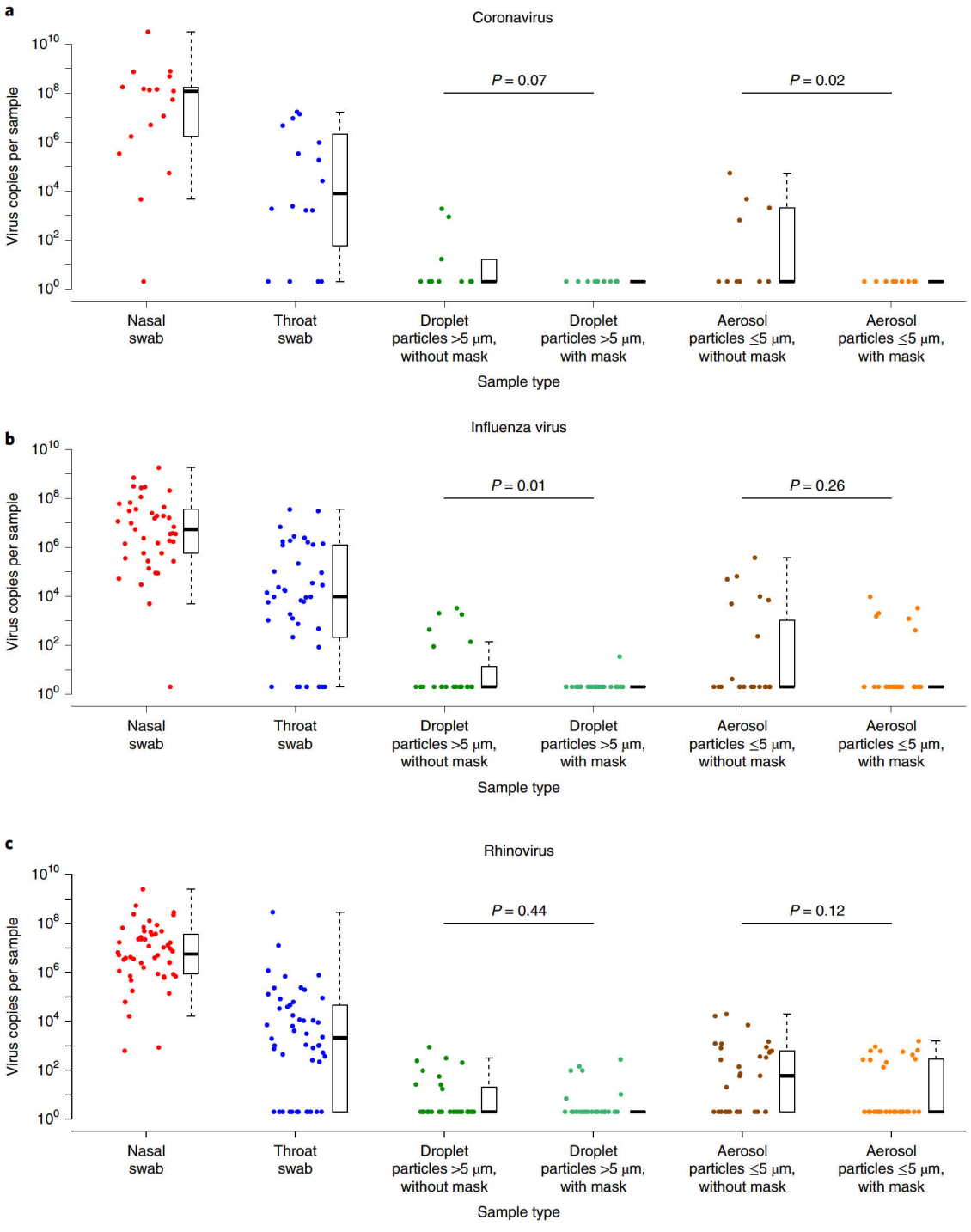

Fig. 1 | Efficacy of surgical face masks in reducing respiratory virus shedding in respiratory droplets and aerosols of symptomatic individuals with coronavirus, influenza virus or rhinovirus infection. a–c, Virus copies per sample collected in nasal swab (red), throat swab (blue) and respiratory droplets collected for 30min while not wearing (dark green) or wearing (light green) a surgical face mask, and aerosols collected for 30min while not wearing (brown) or wearing (orange) a face mask, collected from individuals with acute respiratory symptoms who were positive for coronavirus (**a**), influenza virus (**b**) and rhinovirus (**c**), as determined by RT–PCR in any samples. *P* values for mask intervention as predictor of $\log_{10}$ virus copies per sample in an unadjusted univariate Tobit regression model which allowed for censoring at the lower limit of detection of the RT–PCR assay are shown, with significant differences in bold. For nasal swabs and throat swabs, all infected individuals were included (coronavirus, *n*=17; influenza virus, *n*=43; rhinovirus, *n*=54). For respiratory droplets and aerosols, numbers of infected individuals who provided exhaled breath samples while not wearing or wearing a surgical face mask, respectively were: coronavirus (*n*=10 and 11), influenza virus (*n*=23 and 28) and rhinovirus (*n*=36 and 32). A subset of participants provided exhaled breath samples for both mask interventions (coronavirus, *n*=4; influenza virus, *n*=8; rhinovirus, *n*=14). The box plots indicate the median with the interquartile range (lower and upper hinge) and ±1.5×interquartile range from the first and third quartile (lower and upper whiskers).

Table 1b | Efficacy of surgical face masks in reducing respiratory virus frequency of detection and viral shedding in respiratory droplets and aerosols of symptomatic individuals with coronavirus, influenza virus or rhinovirus infection

	Droplet particles >5 µm			Aerosol particles ≤5 µm		
Virus type	Without surgical face mask	With surgical face mask	*P*	Without surgical face mask	With surgical face mask	*P*
	Detection of virus					
	No. positive/no. total (%)	No. positive/no. total (%)		No. positive/no. total (%)	No. positive/no. total (%)	
Coronavirus	3 of 10 (30)	0 of 11 (0)	0.09	**4 of 10 (40)**	**0 of 11 (0)**	**0.04**
Influenza virus	**6 of 23 (26)**	**1 of 27 (4)**	**0.04**	8 of 23 (35)	6 of 27 (22)	0.36
Rhinovirus	9 of 32 (28)	6 of 27 (22)	0.77	19 of 34 (56)	12 of 32 (38)	0.15
	Viral load (log_{10} virus copies per sample)					
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)	
Coronavirus	0.3 (0.3, 1.2)	0.3 (0.3, 0.3)	0.07	**0.3 (0.3, 3.3)**	**0.3 (0.3, 0.3)**	**0.02**
Influenza virus	**0.3 (0.3, 1.1)**	**0.3 (0.3, 0.3)**	**0.01**	0.3 (0.3, 3.0)	0.3 (0.3, 0.3)	0.26
Rhinovirus	0.3 (0.3, 1.3)	0.3 (0.3, 0.3)	0.44	1.8 (0.3, 2.8)	0.3 (0.3, 2.4)	0.12

P values for comparing the frequency of respiratory virus detection between the mask intervention were obtained by two-sided Fisher's exact test and (two-sided) *P* values for mask intervention as predictor of log_{10} virus copies per sample were obtained by an unadjusted univariate Tobit regression model, which allowed for censoring at the lower limit of detection of the RT-PCR assay, with significant differences in bold. Undetectable values were imputed as 0.3 log_{10} virus copies per sample. IQR, interquartile range.

respiratory droplet and aerosol samples collected without face masks, respectively. There was a significant reduction by wearing face masks to 1 of 27 (4%) in detection of influenza virus in respiratory droplets, but no significant reduction in detection in aerosols (Table 1b). Moreover, among the eight participants who had influenza virus detected by RT–PCR from without-mask aerosols, five were tested by viral culture and four were culture-positive. Among the six participants who had influenza virus detected by RT–PCR from with-mask aerosols, four were tested by viral culture and two were culture-positive. For rhinovirus, there were no significant differences between detection of virus with or without face masks, both in respiratory droplets and in aerosols (Table 1b). Conclusions were similar in comparisons of viral shedding (Table 1b). In addition, we found a significant reduction in viral shedding (Supplementary Table 2) in respiratory droplets for OC43 (Extended Data Fig. 4) and influenza B virus (Extended Data Fig. 5) and in aerosols for NL63 (Extended Data Fig. 4).

We identified correlations between viral loads in different samples (Extended Data Figs. 6–8) and some evidence of declines in viral shedding by time since onset for influenza virus but not for coronavirus or rhinovirus (Extended Data Fig. 9). In univariable analyses of factors associated with detection of respiratory viruses in various sample types, we did not identify significant association in viral shedding with days since symptom onset (Supplementary Table 3) for respiratory droplets or aerosols (Supplementary Tables 4–6).

A subset of participants (72 of 246, 29%) did not cough at all during at least one exhaled breath collection, including 37 of 147 (25%) during the without-mask and 42 of 148 (28%) during the with-mask breath collection. In the subset for coronavirus ($n=4$), we did not detect any virus in respiratory droplets or aerosols from any participants. In the subset for influenza virus ($n=9$), we detected virus in aerosols but not respiratory droplets from one participant. In the subset for rhinovirus ($n=17$), we detected virus in respiratory droplets from three participants, and we detected virus in aerosols in five participants.

Discussion

Our results indicate that aerosol transmission is a potential mode of transmission for coronaviruses as well as influenza viruses and rhinoviruses. Published studies detected respiratory viruses[13,14] such as influenza[12,15] and rhinovirus[16] from exhaled breath, and the detection of SARS-CoV[17] and MERS-CoV[18] from air samples (without size fractionation) collected from hospitals treating patients with severe acute respiratory syndrome and Middle East respiratory syndrome, but ours demonstrates detection of human seasonal coronaviruses in exhaled breath, including the detection of OC43 and HKU1 from respiratory droplets and NL63, OC43 and HKU1 from aerosols.

Our findings indicate that surgical masks can efficaciously reduce the emission of influenza virus particles into the environment in respiratory droplets, but not in aerosols[12]. Both the previous and current study used a bioaerosol collecting device, the Gesundheit-II (G-II)[12,15,19], to capture exhaled breath particles and differentiated them into two size fractions, where exhaled breath coarse particles >5 µm (respiratory droplets) were collected by impaction with a 5-µm slit inertial Teflon impactor and the remaining fine particles ≤5 µm (aerosols) were collected by condensation in buffer. We also demonstrated the efficacy of surgical masks to reduce coronavirus detection and viral copies in large respiratory droplets and in aerosols (Table 1b). This has important implications for control of COVID-19, suggesting that surgical face masks could be used by ill people to reduce onward transmission.

Among the samples collected without a face mask, we found that the majority of participants with influenza virus and coronavirus infection did not shed detectable virus in respiratory droplets or aerosols, whereas for rhinovirus we detected virus in aerosols in 19 of 34 (56%) participants (compared to 4 of 10 (40%) for coronavirus and 8 of 23 (35%) for influenza). For those who did shed virus in respiratory droplets and aerosols, viral load in both tended to be low (Fig. 1). Given the high collection efficiency of the G-II (ref. [19]) and given that each exhaled breath collection was conducted for 30 min, this might imply that prolonged close contact would be required for transmission to occur, even if transmission was primarily via aerosols, as has been described for rhinovirus colds[20]. Our results also indicate that there could be considerable heterogeneity in contagiousness of individuals with coronavirus and influenza virus infections.

The major limitation of our study was the large proportion of participants with undetectable viral shedding in exhaled breath for each of the viruses studied. We could have increased the sampling duration beyond 30 min to increase the viral shedding being captured, at the cost of acceptability in some participants. An alternative approach would be to invite participants to perform forced coughs during exhaled breath collection[12]. However, it was the aim of our present study to focus on recovering respiratory

virus in exhaled breath in a real-life situation and we expected that some individuals during an acute respiratory illness would not cough much or at all. Indeed, we identified virus RNA in a small number of participants who did not cough at all during the 30-min exhaled breath collection, which would suggest droplet and aerosol routes of transmission are possible from individuals with no obvious signs or symptoms. Another limitation is that we did not confirm the infectivity of coronavirus or rhinovirus detected in exhaled breath. While the G-II was designed to preserve viability of viruses in aerosols, and in the present study we were able to identify infectious influenza virus in aerosols, we did not attempt to culture coronavirus or rhinovirus from the corresponding aerosol samples.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41591-020-0843-2.

Received: 2 March 2020; Accepted: 20 March 2020;
Published online: 3 April 2020

References

1. Nichols, W. G., Peck Campbell, A. J. & Boeckh, M. Respiratory viruses other than influenza virus: impact and therapeutic advances. *Clin. Microbiol. Rev.* **21**, 274–290 (2008).
2. Shiu, E. Y. C., Leung, N. H. L. & Cowling, B. J. Controversy around airborne versus droplet transmission of respiratory viruses: implication for infection prevention. *Curr. Opin. Infect. Dis.* **32**, 372–379 (2019).
3. Tellier, R., Li, Y., Cowling, B. J. & Tang, J. W. Recognition of aerosol transmission of infectious agents: a commentary. *BMC Infect. Dis.* **19**, 101 (2019).
4. Xiao, J. et al. Nonpharmaceutical measures for pandemic influenza in nonhealthcare settings-personal protective and environmental measures. *Emerg. Infect. Dis.* https://doi.org/10.3201/eid2605.190994 (2020).
5. Kutter, J. S., Spronken, M. I., Fraaij, P. L., Fouchier, R. A. M. & Herfst, S. Transmission routes of respiratory viruses among humans. *Curr. Opin. Virol.* **28**, 142–151 (2018).
6. Cowling, B. J. & Leung, G. M. Epidemiological research priorities for public health control of the ongoing global novel coronavirus (2019-nCoV) outbreak. *Euro Surveill.* https://doi.org/10.2807/1560-7917.ES.2020.25.6.2000110 (2020).
7. Han, Q., Lin, Q., Ni, Z. & You, L. Uncertainties about the transmission routes of 2019 novel coronavirus. *Influenza Other Respir. Viruses* https://doi.org/10.1111/irv.12735 (2020).
8. MacIntyre, C. R. & Chughtai, A. A. Facemasks for the prevention of infection in healthcare and community settings. *BMJ* **350**, h694 (2015).
9. Ha'eri, G. B. & Wiley, A. M. The efficacy of standard surgical face masks: an investigation using "tracer particles". *Clin. Orthop. Relat. Res.* **148**, 160–162 (1980).
10. Patel, R. B., Skaria, S. D., Mansour, M. M. & Smaldone, G. C. Respiratory source control using a surgical mask: an in vitro study. *J. Occup. Environ. Hyg.* **13**, 569–576 (2016).
11. Johnson, D. F., Druce, J. D., Birch, C. & Grayson, M. L. A quantitative assessment of the efficacy of surgical and N95 masks to filter influenza virus in patients with acute influenza infection. *Clin. Infect. Dis.* **49**, 275–277 (2009).
12. Milton, D. K., Fabian, M. P., Cowling, B. J., Grantham, M. L. & McDevitt, J. J. Influenza virus aerosols in human exhaled breath: particle size, culturability, and effect of surgical masks. *PLoS Pathog.* **9**, e1003205 (2013).
13. Huynh, K. N., Oliver, B. G., Stelzer, S., Rawlinson, W. D. & Tovey, E. R. A new method for sampling and detection of exhaled respiratory virus aerosols. *Clin. Infect. Dis.* **46**, 93–95 (2008).
14. Stelzer-Braid, S. et al. Exhalation of respiratory viruses by breathing, coughing and talking. *J. Med. Virol.* **81**, 1674–1679 (2009).
15. Yan, J. et al. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc. Natl Acad. Sci. USA* **115**, 1081–1086 (2018).
16. Tovey, E. R. et al. Rhinoviruses significantly affect day-to-day respiratory symptoms of children with asthma. *J. Allergy Clin. Immunol.* **135**, 663–669 (2015).
17. Booth, T. F. et al. Detection of airborne severe acute respiratory syndrome (SARS) coronavirus and environmental contamination in SARS outbreak units. *J. Infect. Dis.* **191**, 1472–1477 (2005).
18. Kim, S. H. et al. Extensive viable Middle East respiratory syndrome (MERS) coronavirus contamination in air and surrounding environment in MERS isolation wards. *Clin. Infect. Dis.* **63**, 363–369 (2016).
19. McDevitt, J. J. et al. Development and performance evaluation of an exhaled-breath bioaerosol collector for influenza virus. *Aerosol Sci. Technol.* **47**, 444–451 (2013).
20. Jennings, L. C. & Dick, E. C. Transmission and control of rhinovirus colds. *Eur. J. Epidemiol.* **3**, 327–335 (1987).

Methods

Study design. Participants were recruited year-round from March 2013 through May 2016 in a general outpatient clinic of a private hospital in Hong Kong. As routine practice, clinic staff screened all individuals attending the clinics for respiratory and any other symptoms regardless of the purpose of the visit at triage. Study staff then approached immediately those who reported at least one of the following symptoms of ARI for further screening: fever ≥37.8 °C, cough, sore throat, runny nose, headache, myalgia and phlegm. Individuals who reported ≥2 ARI symptoms, within 3 d of illness onset and ≥11 years of age were eligible to participate. After explaining the study to and obtaining informed consent from the participants, a rapid influenza diagnostic test, the Sofia Influenza A + B Fluorescent Immunoassay Analyzer (cat. no. 20218, Quidel), was used to identify influenza A or B virus infection as an incentive to participate. All participants provided a nasal swab for the rapid test and an additional nasal swab and a separate throat swab for subsequent virologic confirmation at the laboratory. All participants also completed a questionnaire to record basic information including age, sex, symptom severity, medication, medical conditions and smoking history. In the first phase of the study from March 2013 to February 2014 ('Influenza Study'), the result of the rapid test was used to determine eligibility for further participation in the study and exhaled breath collection, whereas in the second phase of the study from March 2014 to May 2016 ('Respiratory Virus Study'), the rapid test did not affect eligibility. Eligible participants were then invited to provide an exhaled breath sample for 30 min in the same clinic visit.

Before exhaled breath collection, each participant was randomly allocated in a 1:1 ratio to either wearing a surgical face mask (cat. no. 62356, Kimberly-Clark) or not during the collection. To mimic the real-life situation, under observation by the study staff, participants were asked to attach the surgical mask themselves, but instruction on how to wear the mask properly was given when the participant wore the mask incorrectly. Participants were instructed to breathe as normal during the collection, but (natural) coughing was allowed and the number of coughs was recorded by study staff. Participants were then invited to provide a second exhaled breath sample of the alternate type (for example if the participant was first assigned to wearing a mask they would then provide a second sample without a mask), but most participants did not agree to stay for a second measurement because of time constraints. Participants were compensated for each 30-min exhaled breath collection with a supermarket coupon worth approximately US$30 and all participants were gifted a tympanic thermometer worth approximately US$20.

Ethical approval. Written informed consent was obtained from all participants ≥18 years of age and written informed consent was obtained from parents or legal guardians of participants 11–17 years of age in addition to their own written informed consent. The study protocol was approved by the Institutional Review Board of The University of Hong Kong and the Clinical and Research Ethics Committee of Hong Kong Baptist Hospital.

Collection of swabs and exhaled breath particles. Nasal swabs and throat swabs were collected separately, placed in virus transport medium, stored and transported to the laboratory at 2–8 °C and the virus transport medium was aliquoted and stored at −70 °C until further analysis. Exhaled breath particles were captured and differentiated into two size fractions, the coarse fraction containing particles with aerodynamic diameter >5 µm (referred to here as 'respiratory droplets'), which included droplets up to approximately 100 µm in diameter and the fine fraction with particles ≤5 µm (referred to here as 'aerosols') by the G-II bioaerosol collecting device[12,15,19]. In the G-II device, exhaled breath coarse particles >5 µm were collected by a 5-µm slit inertial Teflon impactor and the remaining fine particles ≤5 µm were condensed and collected into approximately 170 ml of 0.1% BSA/PBS. Both the impactor and the condensate were stored and transported to the laboratory at 2–8 °C. The virus on the impactor was recovered into 1 ml and the condensate was concentrated into 2 ml of 0.1% BSA/PBS, aliquoted and stored at −70 °C until further analysis. In a validation study, the G-II was able to recover over 85% of fine particles >0.05 µm in size and had comparable collection efficiency of influenza virus as the SKC BioSampler[19].

Laboratory testing. Samples collected from the two studies were tested at the same time. Nasal swab samples were first tested by a diagnostic-use viral panel, xTAG Respiratory Viral Panel (Abbott Molecular) to qualitatively detect 12 common respiratory viruses and subtypes including coronaviruses (NL63, OC43, 229E and HKU1), influenza A (nonspecific, H1 and H3) and B viruses, respiratory syncytial virus, parainfluenza virus (types 1–4), adenovirus, human metapneumovirus and enterovirus/rhinovirus. After one or more of the candidate respiratory viruses was detected by the viral panel from the nasal swab, all the samples from the same participant (nasal swab, throat swab, respiratory droplets and aerosols) were then tested with RT–PCR specific for the candidate virus(es) for determination of virus concentration in the samples. Infectious influenza virus was identified by viral culture using MDCK cells as described previously[21], whereas viral culture was not performed for coronavirus and rhinovirus.

Statistical analyses. The primary outcome of the study was virus generation rate in tidal breathing of participants infected by different respiratory viruses and the efficacy of face masks in preventing virus dissemination in exhaled breath, separately considering the respiratory droplets and aerosols. The secondary outcomes were correlation between viral shedding in nose swabs, throat swabs, respiratory droplets and aerosols and factors affecting viral shedding in respiratory droplets and aerosols.

We identified three groups of respiratory viruses with the highest frequency of infection as identified by RT–PCR, namely coronavirus (including NL63, OC43, HKU1 and 229E), influenza virus and rhinovirus, for further statistical analyses. We defined viral shedding as $\log_{10}$ virus copies per sample and plotted viral shedding in each sample (nasal swab, throat swab, respiratory droplets and aerosols); the latter two were stratified by mask intervention. As a proxy for the efficacy of face masks in preventing transmission of respiratory viruses via respiratory droplet and aerosol routes, we compared the respiratory virus viral shedding in respiratory droplet and aerosol samples between participants wearing face masks or not, by comparing the frequency of detection with a two-sided Fisher's exact test and by comparing viral load (defined as $\log_{10}$ virus copies per sample) by an unadjusted univariate Tobit regression model, which allowed for censoring at the lower limit of detection of the RT–PCR assay. We also used the unadjusted univariate Tobit regression to investigate factors affecting viral shedding in respiratory droplets and aerosols without mask use, for example age, days since symptom onset, previous influenza vaccination, current medication and number of coughs during exhaled breath collection. We investigated correlations between viral shedding in nasal swab, throat swab, respiratory droplets and aerosols with scatter-plots and calculated the Spearman's rank correlation coefficient between any two types of samples. We imputed 0.3 $\log_{10}$ virus copies ml^{-1} for undetectable values before transformation to $\log_{10}$ virus copies per sample. All analyses were conducted with R v.3.6.0 (ref. [22]) and the VGAM package v.1.1.1 (ref. [23]).

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

Anonymized raw data and R syntax to reproduce all the analyses, figures, tables and supplementary tables in the published article are available at: https://doi.org/10.5061/dryad.w9ghx3fkt.

References

21. Chan, K. H., Peiris, J. S., Lim, W., Nicholls, J. M. & Chiu, S. S. Comparison of nasopharyngeal flocked swabs and aspirates for rapid diagnosis of respiratory viruses in children. *J. Clin. Virol.* **42**, 65–69 (2008).
22. R: a language and environment for statistical computing (R Foundation for Statistical Computing, Vienna, Austria, 2019).
23. Yee, T. W. *Vector Generalized Linear and Additive Models: with an Implementation in R* (Springer, 2016).

Acknowledgements

This work was supported by the General Research Fund of the University Grants Committee (grant no. 765811), the Health and Medical Research Fund (grant no. 13120592) and a commissioned grant of the Food and Health Bureau and the Theme-based Research Scheme (project no. T11-705/14-N) of the Research Grants Council of the Hong Kong SAR Government. We acknowledge colleagues including R. O. P. Fung, A. K. W. Li, T. W. Y. Ng, T. H. C. So, P. Wu and Y. Xie for technical support in preparing and conducting this study and enrolling participants; J. K. M. Chan, S. Y. Ho, Y. Z. Liu and A. Yu for laboratory support; S. Ferguson, W. K. Leung, J. Pantelic, J. Wei and M. Wolfson for technical support in constructing and maintaining the G-II device; V. J. Fang, L. M. Ho and T. T. K. Lui for setting up the database; and C. W. Y. Cheung, L. F. K. Cheung, P. T. Y. Ching, A. C. H. Lai, D. W. Y. Lam, S. S. Y. Lo, A. S. K. Luk and other colleagues at the Outpatient Center and Infection Control Team of Hong Kong Baptist Hospital for facilitating this study.

Author contributions

All authors meet the International Committee of Medical Journal Editors criteria for authorship. The study protocol was drafted by N.H.L.L. and B.J.C. Data were collected by N.H.L.L., E.Y.C.S. and B.J.P.H. Laboratory testing was performed by D.K.W.C. and K.-H.C. Statistical analyses were conducted by N.H.L.L. N.H.L.L. and B.J.C. wrote the first draft of the manuscript, and all authors provided critical review and revision of the text and approved the final version.

Competing interests

B.J.C. consults for Roche and Sanofi Pasteur. The authors declare no other competing interests.

Additional information

Extended data is available for this paper at https://doi.org/10.1038/s41591-020-0843-2.

Supplementary information is available for this paper at https://doi.org/10.1038/s41591-020-0843-2.

Correspondence and requests for materials should be addressed to B.J.C.

Peer review information Alison Farrell was the primary editor on this article and managed its editorial process and peer review in collaboration with the rest of the editorial team.

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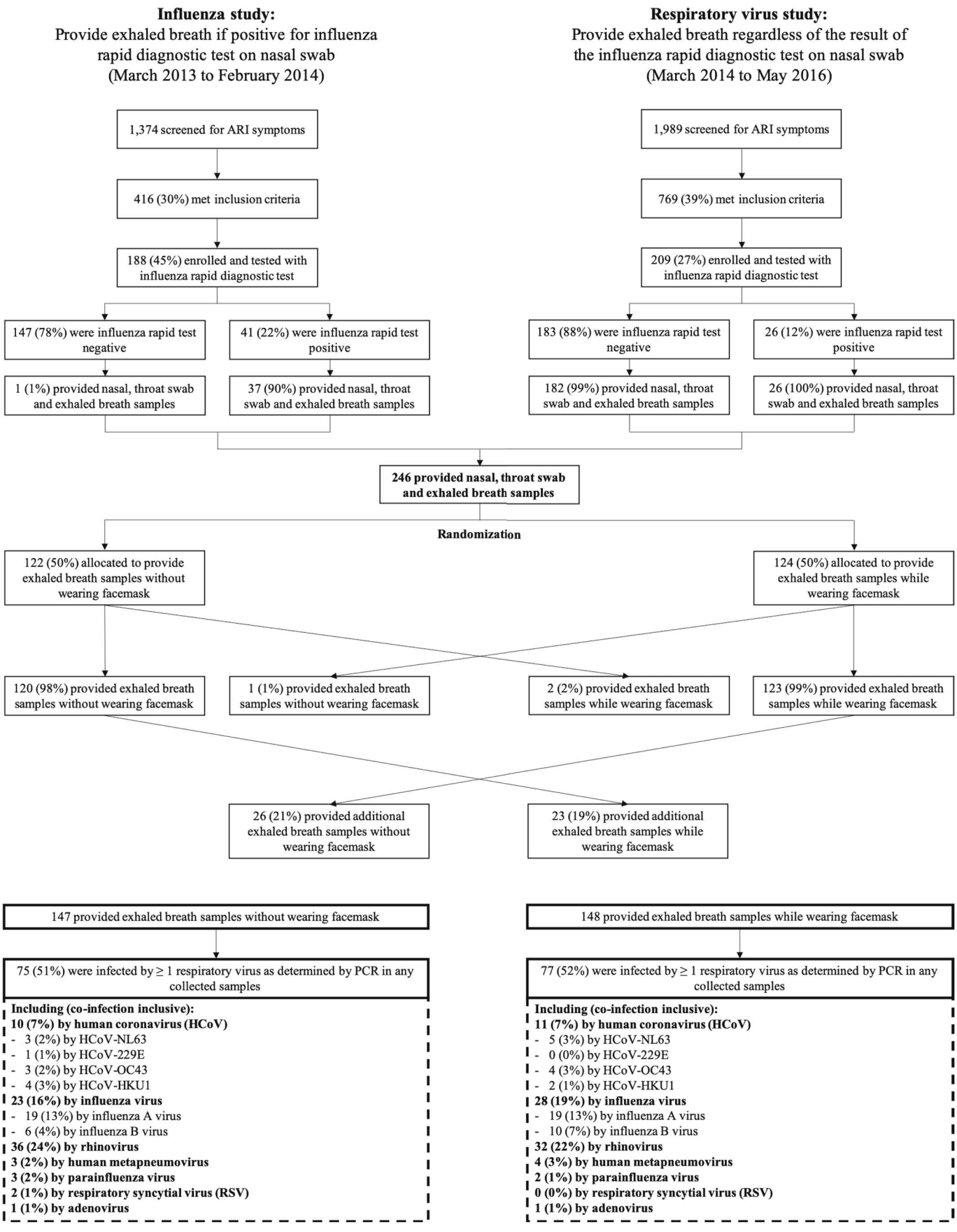
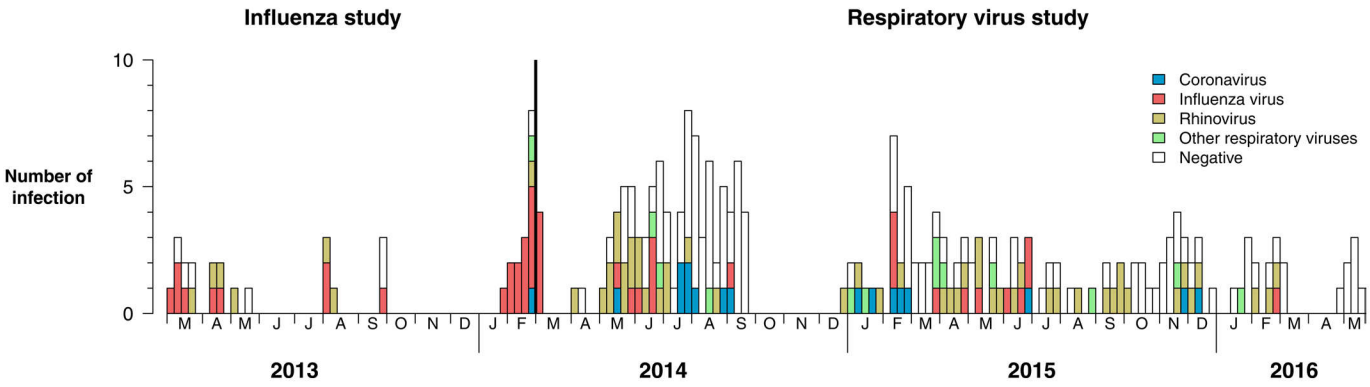
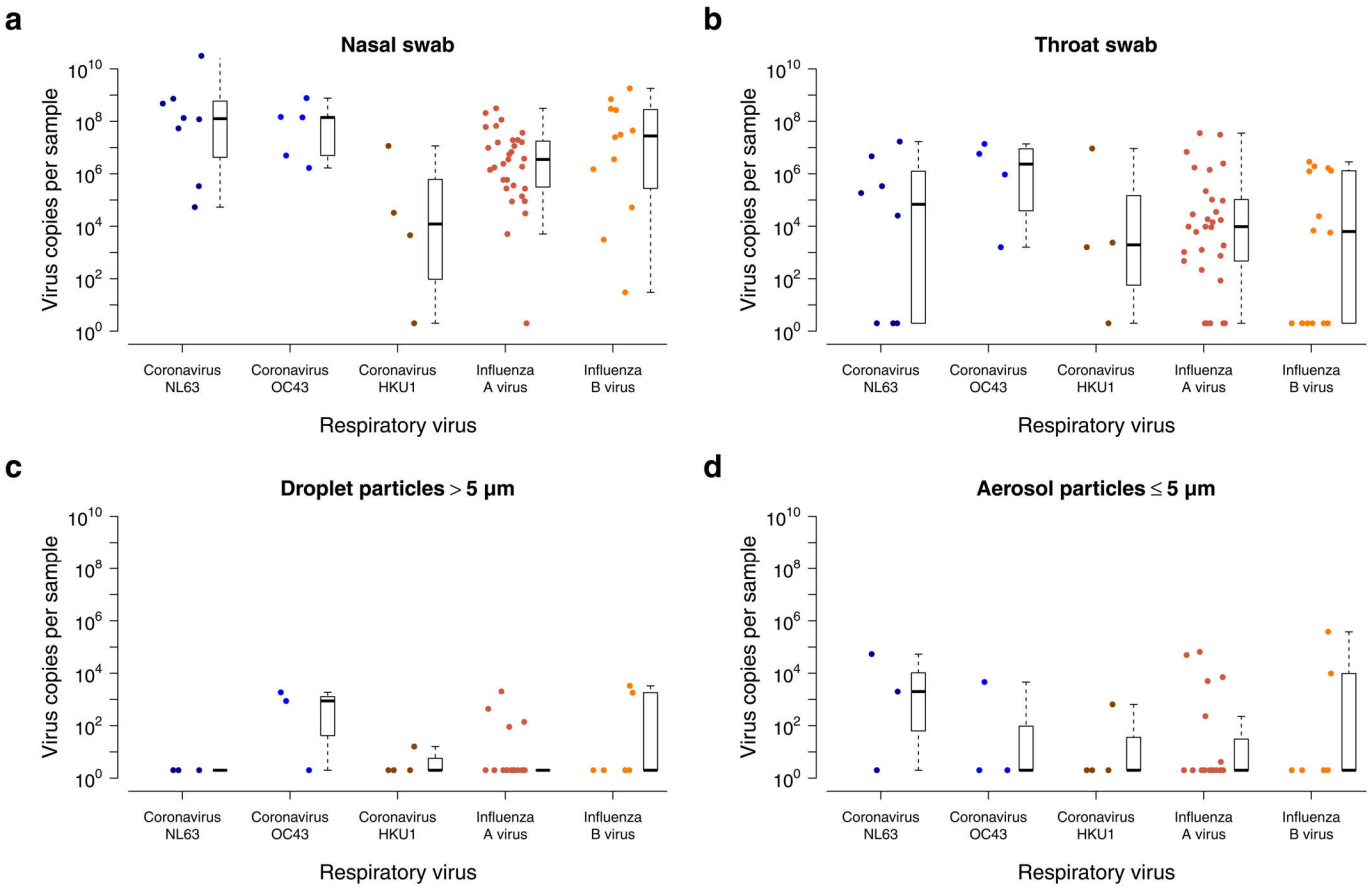


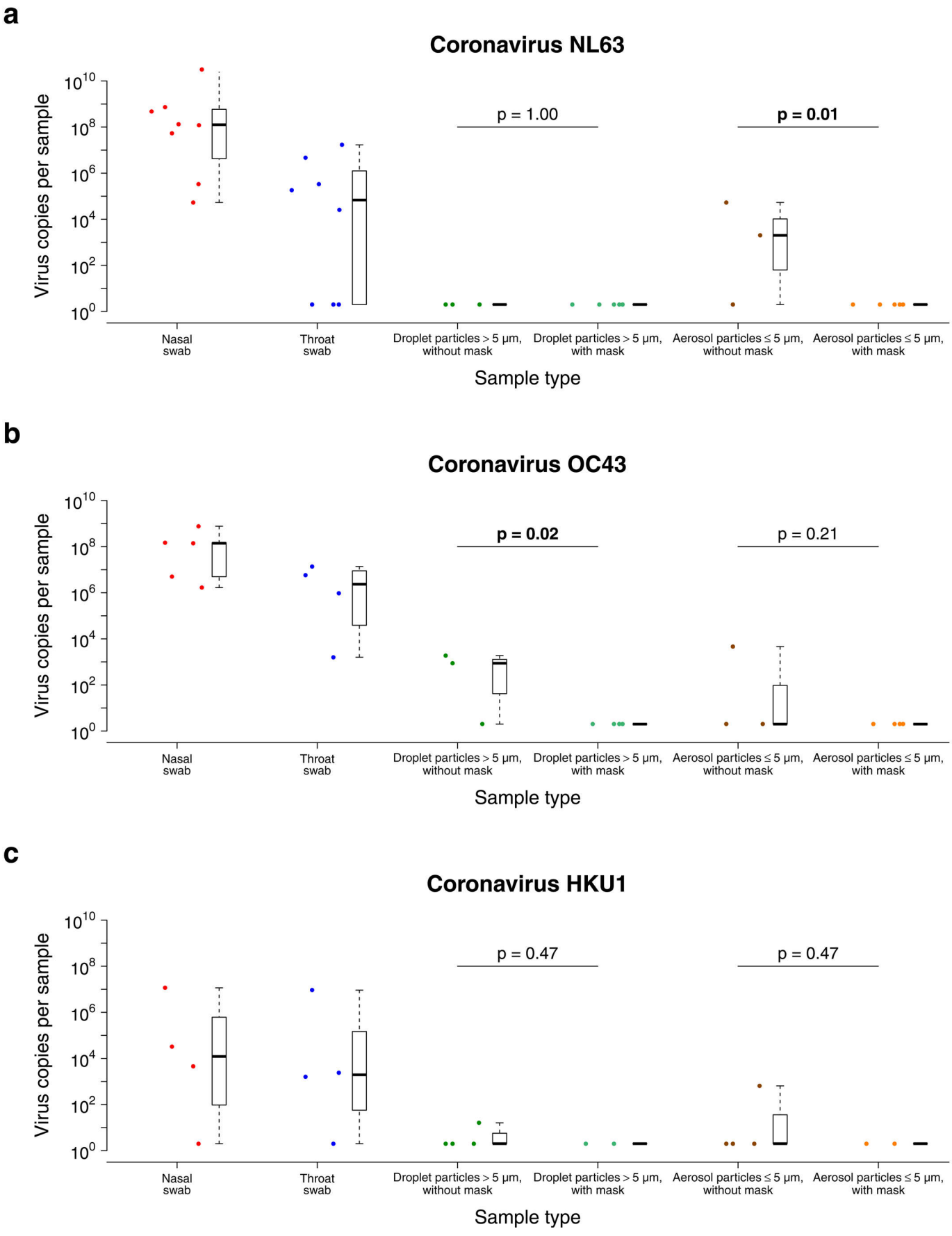
Extended Data Fig. 1 | Participant enrolment, randomization of mask intervention and identification of respiratory virus infection.



Extended Data Fig. 2 | Weekly number of respiratory virus infections identified by RT-PCR in symptomatic individuals who had provided exhaled breath samples (respiratory droplets and aerosols) during the study period. Blue, coronavirus; red, influenza virus; yellow, rhinovirus; green, other respiratory viruses including human metapneumovirus, parainfluenza virus, respiratory syncytial virus and adenovirus; white, no respiratory virus infection identified.

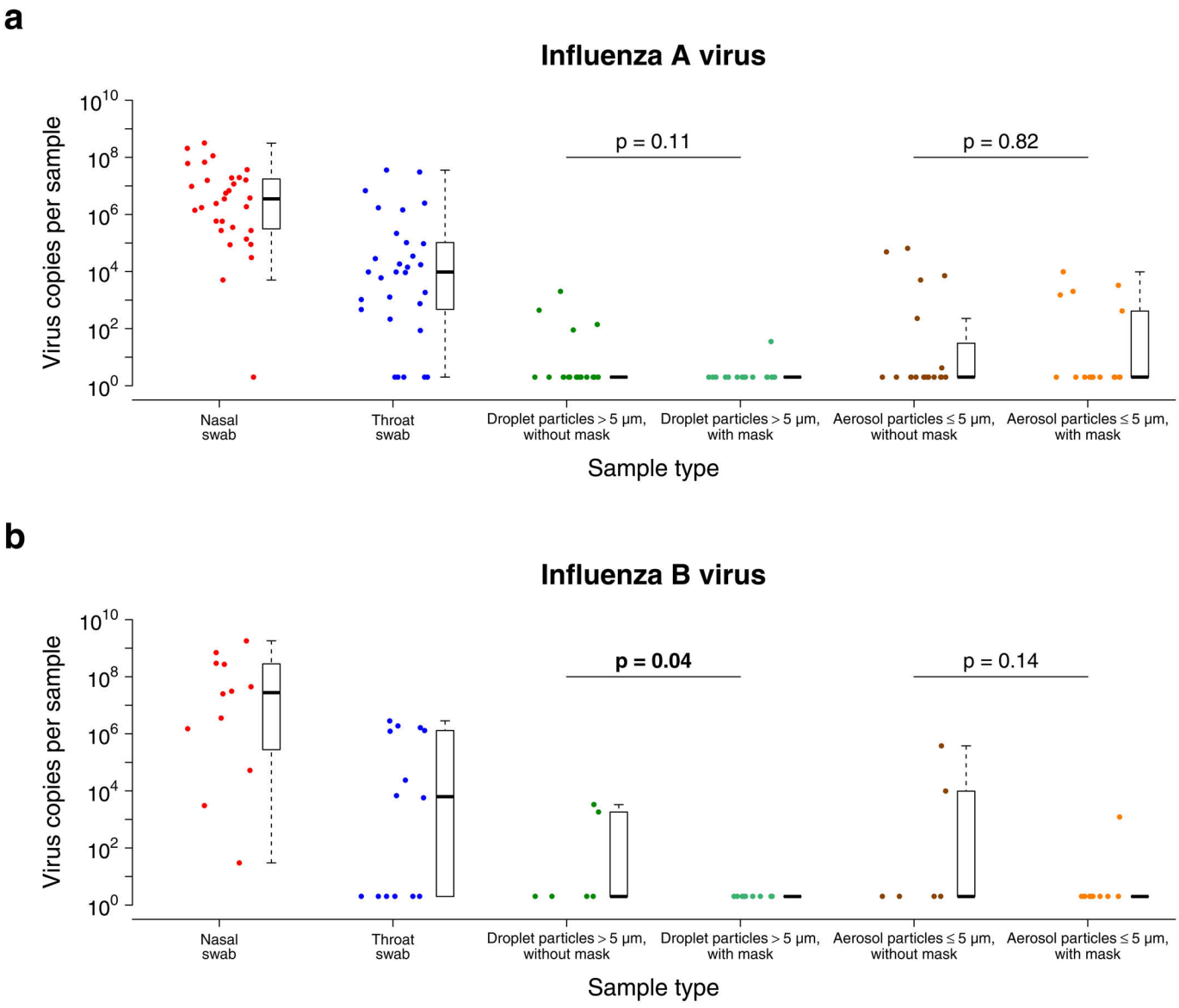


Extended Data Fig. 3 | Respiratory virus shedding in (a) nasal swab, (b) throat swab, (c) respiratory droplets and (d) aerosols in symptomatic individuals with coronavirus NL63, coronavirus OC43, coronavirus HKU1, influenza A and influenza B virus infection. For nasal swabs and throat swabs, all infected individuals identified by RT-PCR in any collected samples were included: coronavirus NL63 (n = 8), coronavirus OC43 (n = 5), coronavirus HKU1 (n = 4), influenza A virus (n = 31) and influenza B virus (n = 14). For respiratory droplets and aerosols, only infected individuals who provided exhaled breath samples while not wearing a surgical face mask were included: coronavirus NL63 (n = 3), coronavirus OC43 (n = 3), coronavirus HKU1 (n = 4), influenza A virus (n = 19) and influenza B virus (n = 6). The box plots indicate the median with the interquartile range (lower and upper hinge) and ±1.5 × interquartile range from the first and third quartile (lower and upper whisker). Dark blue, coronavirus NL63; light blue, coronavirus OC43; brown, coronavirus HKU1; red, influenza A virus; orange, influenza B virus.

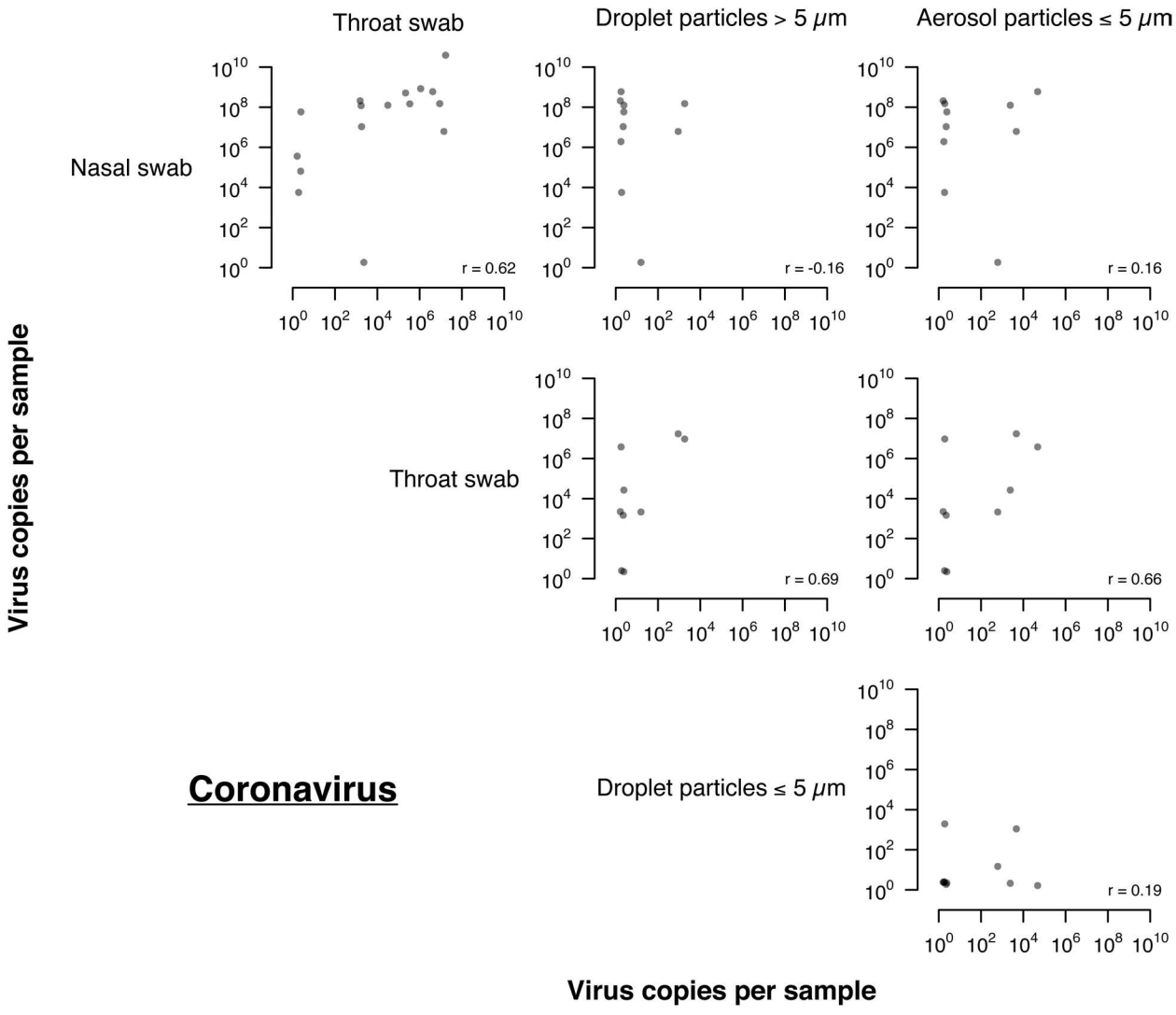


Extended Data Fig. 4 | See next page for caption.

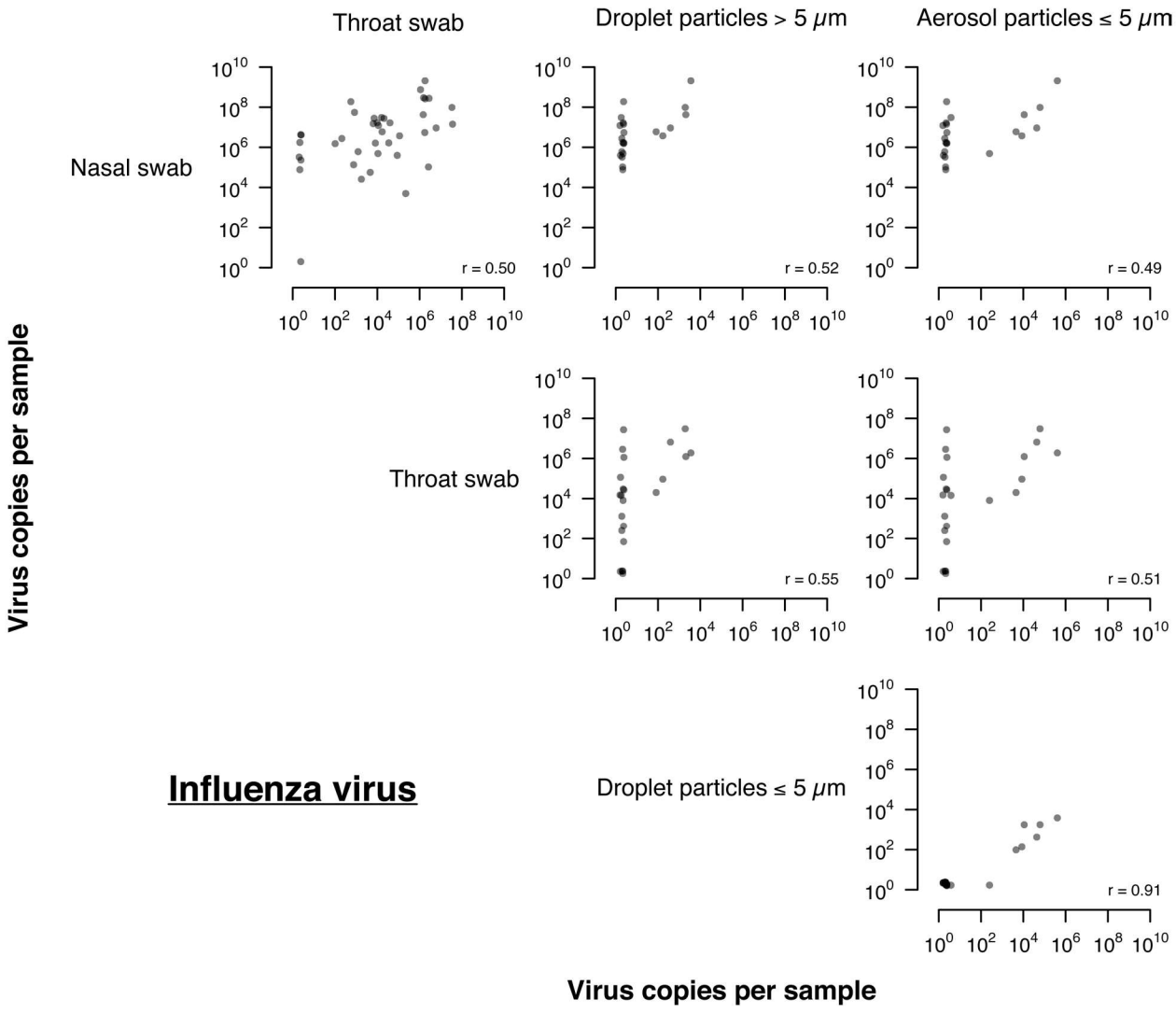
Extended Data Fig. 4 | Efficacy of surgical face masks in reducing respiratory virus shedding in respiratory droplets and aerosols of symptomatic individuals with seasonal coronaviruses including (a) coronavirus NL63, (b) coronavirus OC43 and (c) coronavirus HKU1. The figure shows the virus copies per sample collected in nasal swab (red), throat swab (blue), respiratory droplets collected for 30 min while not wearing (dark green) or wearing (light green) a surgical face mask and aerosols collected for 30 min while not wearing (brown) or wearing (orange) a face mask, collected from individuals with acute respiratory symptoms who were positive for coronavirus NL63, coronavirus OC43 and coronavirus HKU1 as determined by RT-PCR in any samples. *P* values for mask intervention as predictor of $\log_{10}$ virus copies per sample in an unadjusted univariate Tobit regression model which allowed for censoring at the lower limit of detection of the RT-PCR assay are shown, with significant differences in bold. For nasal swabs and throat swabs, all infected individuals were included (coronavirus NL63, n = 8; coronavirus OC43, n = 5; coronavirus HKU1, n = 4). For respiratory droplets and aerosols, numbers of infected individuals who provided exhaled breath samples while not wearing or wearing a surgical face mask, respectively were: coronavirus NL63 (n = 3 and 5), coronavirus OC43 (n = 3 and 4), coronavirus HKU1 (n = 4 and 2). A subset of participants provided exhaled breath samples for both mask interventions (coronavirus NL63, n = 0; coronavirus OC43, n = 2; coronavirus HKU1, n = 2).



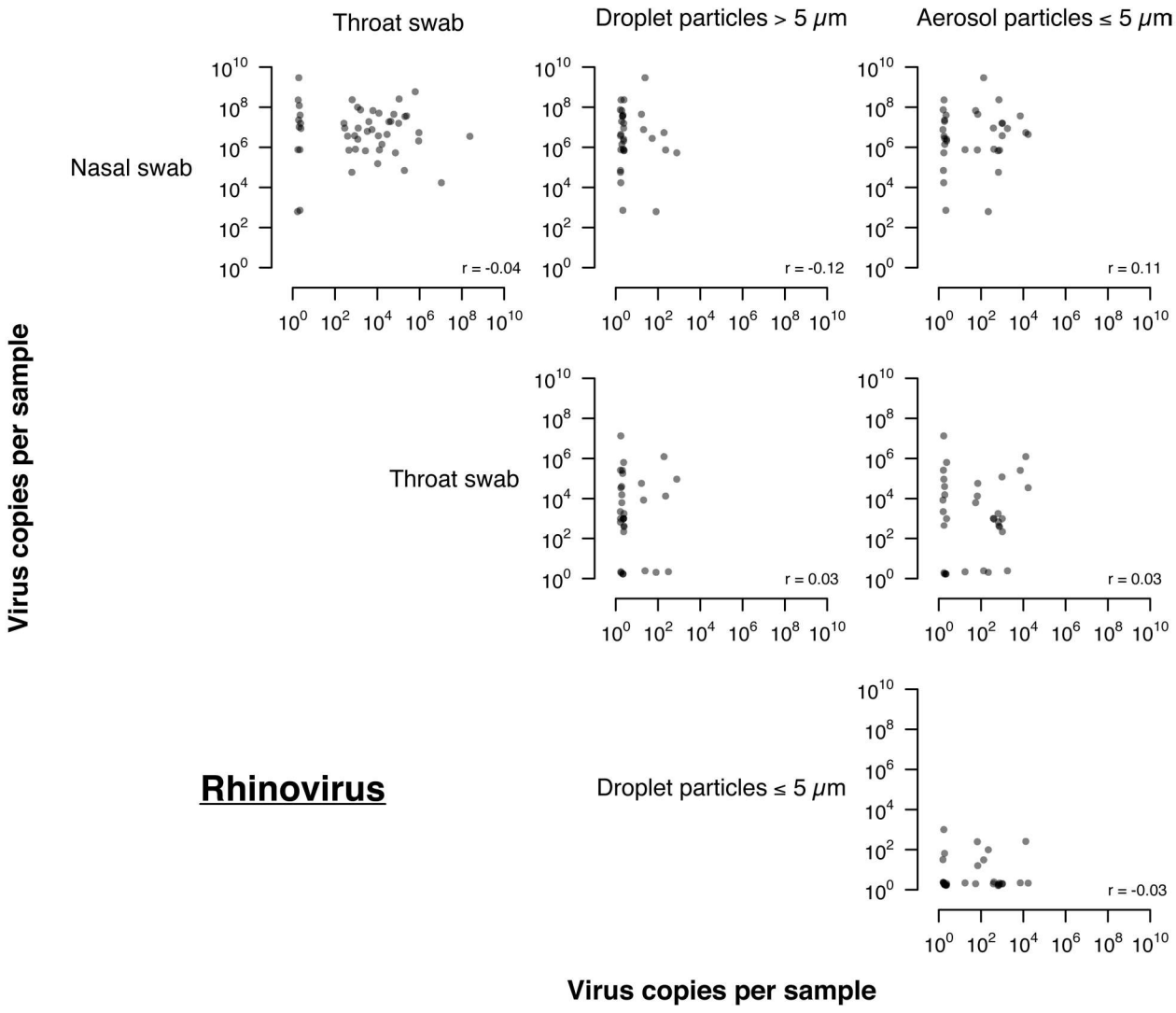
Extended Data Fig. 5 | Efficacy of surgical face masks in reducing respiratory virus shedding in respiratory droplets and aerosols of symptomatic individuals with seasonal influenza viruses including (a) influenza A and (b) influenza B virus. The figure shows the virus copies per sample collected in nasal swab (red), throat swab (blue), respiratory droplets collected for 30 min while not wearing (dark green) or wearing (light green) a surgical face mask and aerosols collected for 30 min while not wearing (brown) or wearing (orange) a face mask, collected from individuals with acute respiratory symptoms who were positive for influenza A and influenza B virus as determined by RT-PCR in any samples. *P* values for mask intervention as predictor of $\log_{10}$ virus copies per sample in an unadjusted univariate Tobit regression model which allowed for censoring at the lower limit of detection of the RT-PCR assay are shown, with significant differences in bold. For nasal swabs and throat swabs, all infected individuals were included (influenza A virus, n = 31; influenza B virus, n = 14). For respiratory droplets and aerosols, numbers of infected individuals who provided exhaled breath samples while not wearing or wearing a surgical face mask, respectively were: influenza A virus (n = 19 and 19), influenza B virus (n = 6 and 10). A subset of participants provided exhaled breath samples for both mask interventions (influenza A virus, n = 7; influenza B virus, n = 2).



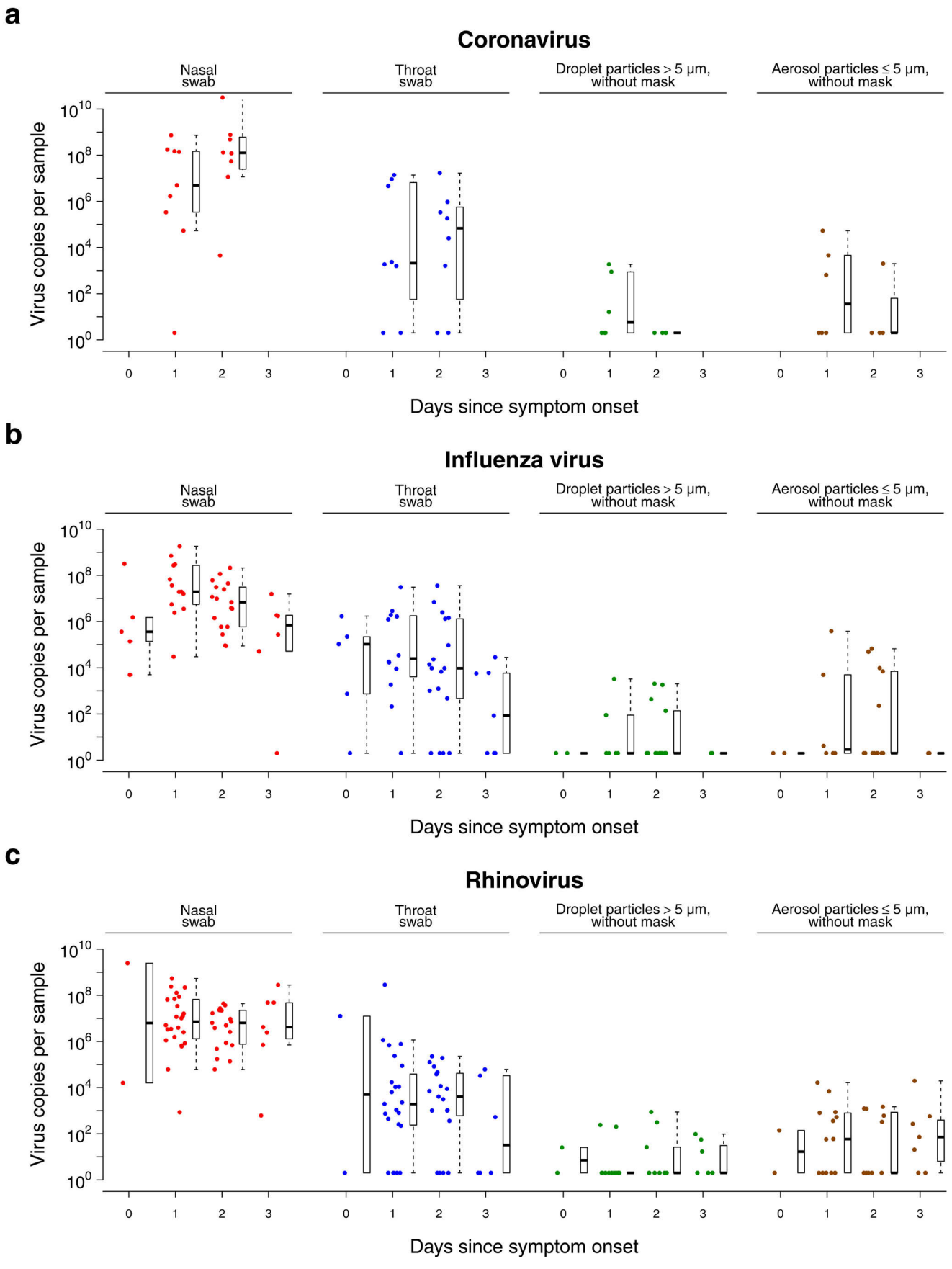
Extended Data Fig. 6 | Correlation of coronavirus viral shedding between different samples (nasal swab, throat swab, respiratory droplets and aerosols) in symptomatic individuals with seasonal coronavirus infection. For nasal swabs and throat swabs, all infected individuals were included (n = 17). For respiratory droplets and aerosols, only infected individuals who provided exhaled breath samples while not wearing a surgical face mask were included (n = 10). r, the Spearman's rank correlation coefficient.



Extended Data Fig. 7 | Correlation of influenza viral shedding between different samples (nasal swab, throat swab, respiratory droplets and aerosols) in symptomatic individuals with seasonal influenza infection. For nasal swabs and throat swabs, all infected individuals were included (n = 43). For respiratory droplets and aerosols, only infected individuals who provided exhaled breath samples while not wearing a surgical face mask were included (n = 23). r, the Spearman's rank correlation coefficient.



Extended Data Fig. 8 | Correlation of rhinovirus viral shedding between different samples (nasal swab, throat swab, respiratory droplets and aerosols) in symptomatic individuals with rhinovirus infection. For nasal swabs and throat swabs, all infected individuals were included (n = 54). For respiratory droplets and aerosols, only infected individuals who provided exhaled breath samples while not wearing a surgical face mask were included (n = 36). r, the Spearman's rank correlation coefficient.



Extended Data Fig. 9 | See next page for caption.

Extended Data Fig. 9 | Respiratory virus shedding in respiratory droplets and aerosols stratified by days from symptom onset for (a) coronavirus, (b) influenza virus or (c) rhinovirus. The figures shows the virus copies per sample collected in nasal swab (red), throat swab (blue), respiratory droplets (dark green) and aerosols (brown) collected for 30 min while not wearing a surgical face mask, stratified by the number of days from symptom onset on which the respiratory droplets and aerosols were collected. For nasal swabs and throat swabs, all infected individuals were included (coronavirus, n = 17; influenza virus, n = 43; rhinovirus, n = 54). For respiratory droplets and aerosols, numbers of infected individuals who provided exhaled breath samples while not wearing or wearing a surgical face mask, respectively were: coronavirus (n = 10 and 11), influenza virus (n = 23 and 28), rhinovirus (n = 36 and 32). A subset of participants provided exhaled breath samples for both mask interventions (coronavirus, n = 4; influenza virus, n = 8; rhinovirus, n = 14). The box plots indicate the median with the interquartile range (lower and upper hinge) and ± 1.5 × interquartile range from the first and third quartile (lower and upper whisker).

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Last updated by author(s): Mar 4, 2020

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☐	☒	A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
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☐	☒	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
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Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No software was used.
Data analysis	All analyses were conducted with R version 3.6.0 and the VGAM package 1.1.1.

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Life sciences study design

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Sample size	We estimated a priori the sample size to be 300 participants. The primary outcome of the study was the reduction in the exhaled virus concentration of normal tidal breathing by wearing face mask in terms of total virus by RT-PCR as a proxy for infectious virus particle. We expected that a 1-log reduction in exhaled virus particle by face mask intervention would have a clinically relevant effect in reducing the probability of transmission. Except for influenza, there was no quantitative data available from exhaled breath samples from respiratory virus-infected individuals before the present study. If the standard deviation of exhaled virus concentration was 1 log copies/ml (Milton et al., PLoS Pathog 2013), we would detect a difference of >1 log copies/ml in the mask vs control group as long as we have >15 participants with a specific respiratory virus. For example, if our study included 23 participants with rhinovirus detectable in exhaled breath without a mask, we will have 80% power and 0.05 significance level to identify differences in viral shedding in aerosols of 1.28 log10 copies associated with the use of face masks, assuming a standard deviation of 1.54 log10 copies based on data from nasal and throat swab (Lu et al., J Clin Microbiol 2008). We expected from 300 individuals with ARI, at least 150 to have a respiratory virus, and at least 20-30 to have each of rhinovirus, coronavirus, adenovirus and parainfluenza plus small numbers of other respiratory viruses, assuming the Viral Panel would detect respiratory viruses in 60% of participants including 10% by influenza (since we partly recruited during the influenza seasons) and the other 50% made up of rhinovirus, coronavirus, adenovirus and parainfluenza virus.
Data exclusions	As described in the Results section and Supplementary Figure 1, only participants who provided exhaled breath samples and randomized to mask intervention were included; and final analyses were performed only for participants with either coronavirus, influenza virus or rhinovirus infection, which had sufficient sample size for comparison between mask intervention.
Replication	Samples from a subset of participants identified with a coronavirus, influenza or rhinovirus infection were re-tested by RT-PCR with consistent results. R syntax is available to reproduce all the analyses, figures, tables and supplementary tables in the published article.
Randomization	Prior to the exhaled breath collection, each participant was randomly allocated in a 1:1 ratio to either wearing a surgical face mask or not during the exhaled breath collection using a computer-generated sequence. The allocation was concealed to the study stuff performing the exhaled breath collection before allocation of the mask intervention.
Blinding	Blinding to the participant and the study stuff for the mask intervention was not possible. The study staff performing the statistical analyses was also involved in the data collection. We expected there would be minimal bias due to unblinding since data collection for questionnaires was done before randomization to mask intervention, and viral load from a sample measured by RT-PCR is an objective measurement.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☐	☒ Clinical data

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Madin-Darby Canine Kidney (MDCK) cells
Authentication	European Collection of Authenticated Cell Cultures.
Mycoplasma contamination	We confirm that all cell lines tested negative for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	Nil

Human research participants

Policy information about studies involving human research participants

Population characteristics	As described in the Results section, Table 1a and Supplementary Table 1, there were some differences in characteristics of participants with the different viruses. Overall, most participants were younger adults and 5% were age 11-17 years, but there were more children with influenza virus and no children in the subgroup with coronavirus infection. Overall, 59% were female, but there were more females among the subgroup with coronavirus infection. The majority of participants did not have underlying medical conditions and overall 9% had received influenza vaccination for the current season but only 2% among those with influenza virus infection. The majority of participants were sampled within 24–48 or 48–72 hours of illness onset. 24% of participants had a measured fever ≥37.8ºC, with influenza patients more than twice as likely than coronavirus and rhinovirus-infected patients to have a measured fever. Coronavirus-infected participants coughed the most with an average of 17 (SD 30) coughs during the 30-minute exhaled breath collection. The profile of the participants randomized to with-mask vs without-mask groups were similar.
Recruitment	As described in the Methods section, participants were recruited year-round from March 2013 through May 2016 in a general outpatient clinic of a private hospital in Hong Kong. As routine practice, clinic staff screened all individuals attending the clinics for respiratory and any other symptoms regardless of the purpose of the visit at the triage. Study staff then approached immediately those who reported at least one of the following symptoms of acute respiratory illness (ARI) for further screening: fever≥37.8ºC, cough, sore throat, runny nose, headache, myalgia and phlegm. Individuals who reported ≥2 ARI symptoms, within 3 days of illness onset and ≥11 years of age were eligible to participate.
Ethics oversight	As described in the Methods section, the study protocol was approved by the Institutional Review Board of The University of Hong Kong and the Clinical and Research Ethics Committee of Hong Kong Baptist Hospital.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Clinical data

Policy information about clinical studies

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Clinical trial registration	The present study was not registered in clinical trials registries, as it was a laboratory-based study of detection of viruses in exhaled breath and the effect of wearing surgical facemasks on virus detection. It was not a Phase II/III clinical trial.
Study protocol	Not available in clinical trials registries (as above). Study protocol will be made available to editors and peer reviewers if requested.
Data collection	As described in the Methods section, participants were recruited year-round from March 2013 through March 2016 in a general outpatient clinic of a private hospital in Hong Kong. Data collection for questionnaires and exhaled breath sample collection was done face-to-face with the participant by trained study staff at the same clinic on the day of participant enrolment.
Outcomes	As pre-specified in the study protocol, the primary outcomes of the study were the virus generation rate in the tidal breathing of participants infected by different respiratory viruses, and the efficacy of face mask in preventing virus dissemination in exhaled breath especially at the aerosol fraction. As pre-specified in the study protocol, one of the secondary outcomes was to provide indirect evidence for relative importance of different transmission routes of influenza and other respiratory viruses. In this regard, in the present manuscript we examined the correlation between viral shedding in nose swabs, throat swabs, respiratory droplets and aerosols, and factors affecting viral shedding in respiratory droplets and aerosols. As described in the Discussion section in the present manuscript about the limitation of our study, there was large proportion of participants with undetectable viral shedding in exhaled breath for each of the viruses studied, and therefore we were unable to examine the exhaled respiratory virus reduction proportion by chi-squared test, nor the exhaled respiratory virus reduction volume (i.e. viral load) by t-test and linear regression as pre-specified in the study protocol. Instead, we have used Fisher's exact test and Tobit regression for the same purposes respectively.

The implications of silent transmission for the control of COVID-19 outbreaks

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Edited by Mary E. Power, University of California, Berkeley, CA, and approved June 23, 2020 (received for review April 30, 2020)

Since the emergence of coronavirus disease 2019 (COVID-19), unprecedented movement restrictions and social distancing measures have been implemented worldwide. The socioeconomic repercussions have fueled calls to lift these measures. In the absence of population-wide restrictions, isolation of infected individuals is key to curtailing transmission. However, the effectiveness of symptom-based isolation in preventing a resurgence depends on the extent of presymptomatic and asymptomatic transmission. We evaluate the contribution of presymptomatic and asymptomatic transmission based on recent individual-level data regarding infectiousness prior to symptom onset and the asymptomatic proportion among all infections. We found that the majority of incidences may be attributable to silent transmission from a combination of the presymptomatic stage and asymptomatic infections. Consequently, even if all symptomatic cases are isolated, a vast outbreak may nonetheless unfold. We further quantified the effect of isolating silent infections in addition to symptomatic cases, finding that over one-third of silent infections must be isolated to suppress a future outbreak below 1% of the population. Our results indicate that symptom-based isolation must be supplemented by rapid contact tracing and testing that identifies asymptomatic and presymptomatic cases, in order to safely lift current restrictions and minimize the risk of resurgence.

COVID-19 | contact tracing | case isolation

Many countries, including the United States, are struggling to control coronavirus disease 2019 (COVID-19) outbreaks. Understanding how silent infections that are in the presymptomatic phase or asymptomatic contribute to transmission will be fundamental to the success of postlockdown control strategies. The effectiveness of symptom-based interventions depends on the fraction of infections that are asymptomatic, the infectiousness of those asymptomatic cases, and the duration and infectiousness of the presymptomatic phase. Empirical studies have indicated that individuals may be most infectious during the presymptomatic phase (1), an unusual characteristic for a respiratory infection.

To quantify the population-level contribution of silent transmission to COVID-19 spread, we extended our previous model (2, 3) to include asymptomatic infections and the presymptomatic stage, parameterized with data regarding the trajectory of symptom onset and the proportion of secondary cases generated in each stage of infection (1, 4). As empirical studies indicate that asymptomatic infections account for 17.9 to 30.8% of all infections (5, 6), for both of these values, we quantified the proportion of the attack rate attributable to transmission during presymptomatic, asymptomatic, and symptomatic stages. Furthermore, this quantification was combined with a series of scenario analyses to identify the level of isolation required for symptomatic or silently infected individuals, to suppress the attack rate below 1%. Our results highlight the role of silent transmission as the primary driver of COVID-19 outbreaks and underscore the need for mitigation strategies, such as contact tracing, that detect and isolate infectious individuals prior to the onset of symptoms.

Results

Translating clinical data on infectiousness and symptoms (1) to population-level epidemiological impact, our results indicate that the majority of transmission is attributable to people who are not exhibiting symptoms, either because they are still in the presymptomatic stage or the infection is asymptomatic (Fig. 1). Specifically, if 17.9% of infections are asymptomatic (5), we found that the presymptomatic stage and asymptomatic infections account for 48% and 3.4% of transmission, respectively (Fig. 1*A*). Considering a greater asymptomatic proportion of 30.8% reported in another empirical study (6), the presymptomatic phase and asymptomatic infections account for 47% and 6.6% of transmission, respectively (Fig. 1*B*). Consequently, even immediate isolation of all symptomatic cases is insufficient to achieve control (Fig. 1). Specifically, mean attack rates remain above 25% of the population when 17.9% of infections are asymptomatic and above 28% when 30.8% of infectious are asymptomatic.

Given the inadequacy of symptom-based isolation to control COVID-19 outbreaks, we considered the synergistic impact of isolation for presymptomatic and asymptomatic infections. Combined with case isolation, our results indicate that 33% and 42% detection and isolation of silent infections would be needed to suppress the attack rate below 1%, for asymptomatic proportions of 17.9% and 30.8%, respectively (Fig. 1*C*).

Discussion

Our results indicate that silent disease transmission during the presymptomatic and asymptomatic stages are responsible for more than 50% of the overall attack rate in COVID-19 outbreaks. Furthermore, such silent transmission alone can sustain outbreaks even if all symptomatic cases are immediately isolated. The results corroborate recent contact tracing studies indicating a substantial role of presymptomatic transmission among 243 COVID-19 cases in Singapore (7) and 468 COVID-19 cases in China (8).

Our findings highlight the urgent need to scale up testing of suspected cases without symptoms as noted in revised guidelines by Centers for Disease Control and Prevention (9). Furthermore, symptom-based surveillance must be supplemented by rapid contact-based surveillance that can identify exposed individuals prior to their infectious period (10). Specifically, our estimation for isolation of silently infected individuals is a lower bound, as

Author contributions: S.M.M. and A.P.G. designed research; S.M.M., M.C.F., P.S., A.P., A.S., B.H.S., and A.P.G. performed research; S.M.M., M.C.F., P.S., A.P., A.S., B.H.S., and A.P.G. analyzed data; and S.M.M., M.C.F., P.S., A.P., B.H.S., and A.P.G. wrote the paper.

The authors declare no competing interest.

Data deposition: The model code, computational system, and parameters are available in GitHub at https://github.com/ABM-Lab/covid19abm.jl.

[1]S.M.M. and M.C.F. contributed equally to this work.

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First published July 6, 2020.

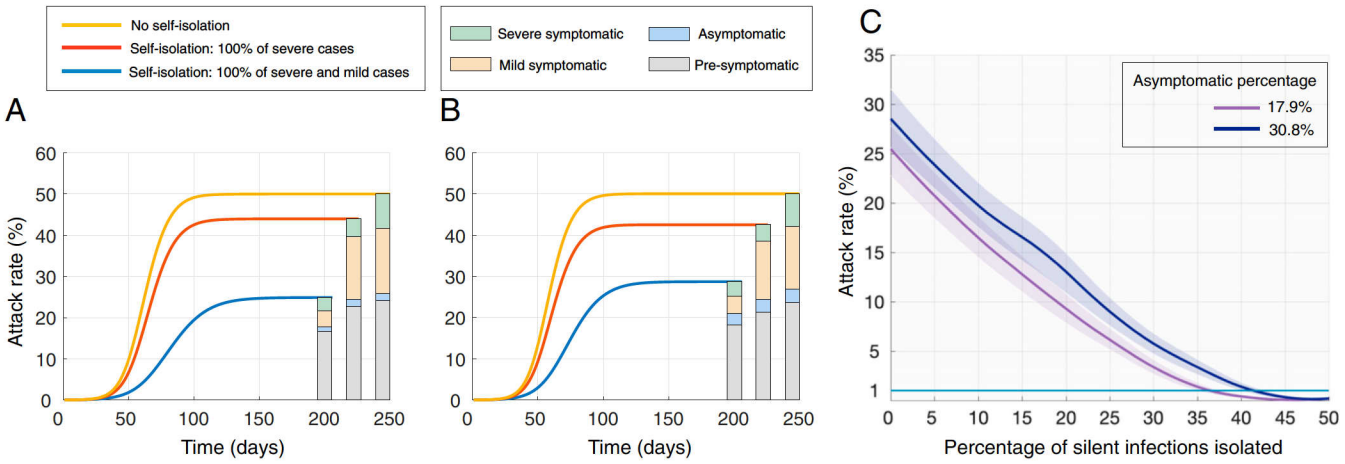

Fig. 1. Attack rates when the proportion of infections that are asymptomatic is (*A*) 17.9% and (*B*) 30.8%, for scenarios of case isolation including none (yellow), all severe cases (red), and all symptomatic cases (blue). Bars indicate the proportion of attack rate attributable to transmission in different stages of infections. (*C*) Attack rate when a percentage of silent (i.e., presymptomatic and asymptomatic) infections are detected and isolated in addition to immediate isolation of both mild and severe symptomatic cases.

inevitable imperfections in isolation of symptomatic cases translates to a greater need to prevent silent transmission. Delays in contact tracing increase the risk of onward transmission, especially since those without symptoms are generally unaware of their infection risk to others, and therefore are less likely to curtail social interactions. Therefore, our estimates of the realized transmission from a silently infected individual, and their relative contribution to transmission under status quo, is likely to be conservative. These dangers are particularly salient in the context of deliberations about lifting social distancing restrictions.

Complicating future surveillance and control efforts of COVID-19 is the possibility that the seasonal drivers of influenza might comparably intensify transmission of COVID-19, such that a resurgence of COVID-19 would coincide with the next influenza season in the Northern Hemisphere. Similarities in symptoms between the two diseases may further erode the effectiveness of measures that rely on symptoms. As plans are being implemented for lifting mitigation measures, the benefits of contact-based surveillance should be evaluated to ensure adequate resources are deployed to suppress ongoing outbreaks, prevent rebound, and minimize the impact of future COVID-19 waves.

Materials and Methods

We extended our agent-based COVID-19 transmission model (3) to include the presymptomatic phase and asymptomatic infections based on recent

Table 1. Model parameters and their distributions

Description	Age group					Source
	0 y to 4 y	5 y to 19 y	20 y to 49 y	50 y to 64 y	≥65 y	
Transmission probability per contact during presymptomatic stage	0.0575, 0.0698	0.0575, 0.0698	0.0575, 0.0698	0.0575, 0.0698	0.0575, 0.0698	Calibrated to $R_0 = 2.5$
Incubation period (days)	Log-normal (mean: 5.2, SD: 0.1)	Log-normal (mean: 5.2, SD: 0.1)	Log-normal (mean: 5.2, SD: 0.1)	Log-normal (mean: 5.2, SD: 0.1)	Log-normal (mean: 5.2, SD: 0.1)	(13)
Asymptomatic period (days)	Gamma (shape: 5, scale: 1)	Gamma (shape: 5, scale: 1)	Gamma (shape: 5, scale: 1)	Gamma (shape: 5, scale: 1)	Gamma (shape: 5, scale: 1)	Derived from ref. 12
Presymptomatic period (days)	Gamma (shape: 1.058, scale: 2.174)	Gamma (shape: 1.058, scale: 2.174)	Gamma (shape: 1.058, scale: 2.174)	Gamma (shape: 1.058, scale: 2.174)	Gamma (shape: 1.058, scale: 2.174)	Derived from ref. 1
Infectious period from onset of symptoms (days)	Gamma (shape: 2.768, scale: 1.1563)	Gamma (shape: 2.768, scale: 1.1563)	Gamma (shape: 2.768, scale: 1.1563)	Gamma (shape: 2.768, scale: 1.1563)	Gamma (shape: 2.768, scale: 1.1563)	Derived from ref. 14
Proportion of symptomatic cases with mild symptoms	0.95	0.9	0.85	0.60	0.20	(2, 3)

empirical evidence (1, 4). Each individual had an associated epidemiological status: susceptible, infected and incubating, presymptomatic, asymptomatic, symptomatic with either mild or severe illness, recovered, or dead. The daily number of contacts for each individual was sampled from an age-specific negative-binomial distribution based on an empirically determined contact matrix (11). In the absence of case isolation, each individual has 10.21 (SD: 7.65), 16.79 (SD: 11.72), 13.79 (SD: 10.50), 11.26 (SD: 9.59), and 8.00 (SD: 6.96) daily contacts in age groups 0 y to 4 y, 5 y to 19 y, 20 y to 49 y, 50 y to 64 y, and 65+ y, respectively.

Transmission was implemented probabilistically for contacts between susceptible and infectious individuals in the presymptomatic, asymptomatic, or symptomatic stages (Table 1). A proportion of infected individuals remained asymptomatic through recovery (5, 6), with an average infectious period of 5.0 d (12). The remaining proportion of infected individuals developed symptoms after an average incubation period of 5.2 d, which was sampled from a log-normal distribution (13). For symptomatic cases, the incubation period included a highly infectious presymptomatic stage prior to the onset of symptoms (1). The duration of the presymptomatic stage was sampled from a Gamma distribution with a mean of 2.3 d (1). Infectious period for symptomatic cases after the onset of symptoms was sampled from a Gamma distribution with a mean of 3.2 d (14). Among symptomatic cases, we applied an age-dependent probability of mild or severe illness (2, 3). Taking into account that infectiousness is estimated to peak 0.7 d before symptom onset (1), we calculated the transmissibility within each phase relative to the presymptomatic phase. These relative transmissibilities were estimated as 11%, 44%, and 89%, calculated using R_0 components of asymptomatic, mild symptomatic, and severe symptomatic phases (4). To account for empirical uncertainty in these parameters, we sampled these values from a uniform distribution in the ranges of 0.05 to 0.16, 0.39 to 0.49, and 0.84 to 0.94, for asymptomatic, mild symptomatic, and severe symptomatic, respectively.

In the base case scenario, individuals are not isolated at any stage of infection. In order to test whether silent transmission is truly a driver of COVID-19 outbreaks, we then modeled symptom-based case isolation in which symptomatic cases were isolated immediately upon symptom onset and would remain isolated until recovery; thus, one can only transmit the disease during the presymptomatic stage. Case isolation was implemented by reducing the number of daily interactions to a maximum of three contacts, in acknowledgment that household or hospital transmission may still occur despite isolation efforts (2, 3). To identify whether outbreak control (defined as <1% cumulative incidence) could be achieved by curtailing silent transmission, we further considered isolation of presymptomatic and asymptomatic infections. We therefore simulated scenarios in which a proportion (in the range 0 to 50%) of presymptomatic and asymptomatic individuals were isolated, in addition to all symptomatic cases. The model was populated with 10,000 individuals reproducing demography for New York City. For both 17.9% and 30.8% as the asymptomatic proportion (5, 6), we calibrated the model to a reproduction number $R_0 = 2.5$ in the absence of control measures (13). Simulations were seeded with an initial infection, and daily incidence of infection was averaged over 500 independent realizations. Model code is available at https://github.com/ABM-Lab/covid19abm.jl.

Data Availability. The computational system and parameters are available at https://github.com/ABM-Lab/covid19abm.jl.

ACKNOWLEDGMENTS. S.M.M. acknowledges Canadian Institutes of Health Research Grant OV4 – 170643 and Natural Sciences and Engineering Research Council of Canada. A.P.G. acknowledges NIH 1RO1AI151176-01, NSF RAPID 2027755, and NSF CCF-1918784. M.C.F. acknowledges NIH Health 1K01AI141576-01.

1. X. He *et al.*, Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat. Med.* **26**, 672–675 (2020).
2. S. M. Moghadas *et al.*, Projecting hospital utilization during the COVID-19 outbreaks in the United States. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 9122–9126 (2020).
3. A. Shoukat *et al.*, Projecting demand for critical care beds during COVID-19 outbreaks in Canada. *CMAJ* **192**, E489–E496 (2020).
4. L. Ferretti *et al.*, Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing. *Science* **368**, eabb6936 (2020).
5. K. Mizumoto, K. Kagaya, A. Zarebski, G. Chowell, Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. *Euro Surveill.* **25**, 2000180 (2020).
6. H. Nishiura *et al.*, Estimation of the asymptomatic ratio of novel coronavirus infections (COVID-19). *Int. J. Infect. Dis.* **94**, 154–155 (2020).
7. W. E. Wei *et al.*, Presymptomatic transmission of SARS-CoV-2–Singapore, January 23-March 16, 2020. *MMWR Morb. Mortal. Wkly. Rep.* **69**, 411–415 (2020).
8. Z. Du *et al.*, Serial interval of COVID-19 among publicly reported confirmed cases. *Emerg. Infect. Dis.* **26**, 1341–1343 (2020).
9. Centers for Disease Control and Prevention, Overview of testing for SARS-CoV-2. https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fhcp%2Fclinical-criteria.html#changes, Accessed 20 June 2020.
10. C. M. Wolfe *et al.*, Ebola virus disease contact tracing activities, lessons learned and best practices during the Duport Road outbreak in Monrovia, Liberia, November 2015. *PLoS Negl. Trop. Dis.* **11**, e0005597 (2017).
11. J. Mossong *et al.*, Social contacts and mixing patterns relevant to the spread of infectious diseases. *PLoS Med.* **5**, e74 (2008).
12. M. Gatto *et al.*, Spread and dynamics of the COVID-19 epidemic in Italy: Effects of emergency containment measures. *Proc. Natl. Acad. Sci. U.S.A.* **117**, 10484–10491 (2020).
13. Q. Li *et al.*, Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* **382**, 1199–1207 (2020).
14. R. Li *et al.*, Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2). *Science* **368**, 489–493 (2020).

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Effectiveness of Face Masks in Preventing Airborne Transmission of SARS-CoV-2

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ABSTRACT Guidelines from the CDC and the WHO recommend the wearing of face masks to prevent the spread of coronavirus (CoV) disease 2019 (COVID-19); however, the protective efficiency of such masks against airborne transmission of infectious severe acute respiratory syndrome CoV-2 (SARS-CoV-2) droplets/aerosols is unknown. Here, we developed an airborne transmission simulator of infectious SARS-CoV-2-containing droplets/aerosols produced by human respiration and coughs and assessed the transmissibility of the infectious droplets/aerosols and the ability of various types of face masks to block the transmission. We found that cotton masks, surgical masks, and N95 masks all have a protective effect with respect to the transmission of infective droplets/aerosols of SARS-CoV-2 and that the protective efficiency was higher when masks were worn by a virus spreader. Importantly, medical masks (surgical masks and even N95 masks) were not able to completely block the transmission of virus droplets/aerosols even when completely sealed. Our data will help medical workers understand the proper use and performance of masks and determine whether they need additional equipment to protect themselves from infected patients.

IMPORTANCE Airborne simulation experiments showed that cotton masks, surgical masks, and N95 masks provide some protection from the transmission of infective SARS-CoV-2 droplets/aerosols; however, medical masks (surgical masks and even N95 masks) could not completely block the transmission of virus droplets/aerosols even when sealed.

KEYWORDS COVID-19, N95 masks, SARS-CoV-2, aerosols, droplets, face masks

The potential for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission via infective droplets and aerosols (1), coupled with guidelines from the CDC (https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/diy-cloth-face-coverings.html) and WHO (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks) recommending the wearing of face masks to prevent the spread of CoV disease 2019 (COVID-19), prompted us to evaluate the protective efficiency of face masks against airborne transmission of infectious SARS-CoV-2 droplets/aerosols.

We developed an airborne transmission simulator of infectious droplets/aerosols produced by human respiration and coughs and assessed the transmissibility of the infectious droplets/aerosols produced and the ability of various types of face masks to block the transmission (Fig. 1, and see the Methods section in Text S1 in the supplemental material for additional details). A test chamber for airborne transmission exper-

Citation Ueki H, Furusawa Y, Iwatsuki-Horimoto K, Imai M, Kabata H, Nishimura H, Kawaoka Y. 2020. Effectiveness of face masks in preventing airborne transmission of SARS-CoV-2. mSphere 5:e00637-20. https://doi.org/10.1128/mSphere.00637-20.

Editor Michael J. Imperiale, University of Michigan–Ann Arbor

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Received 25 June 2020
Accepted 1 October 2020
Published 21 October 2020

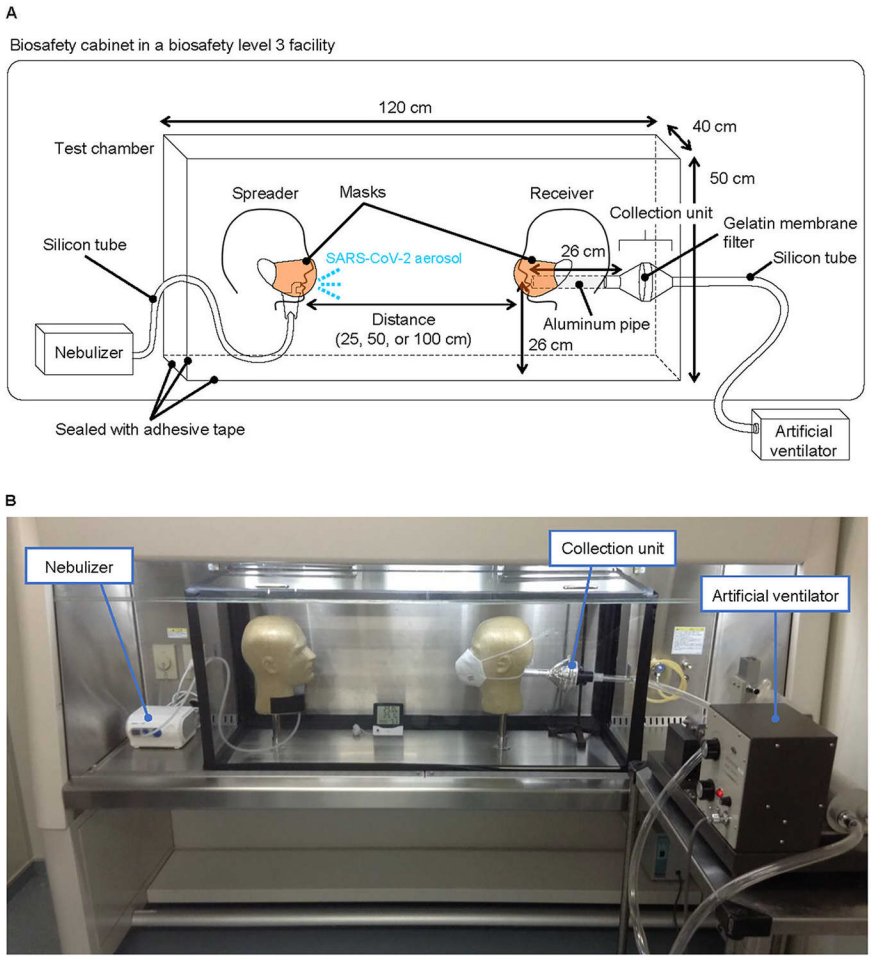

FIG 1 Simulation system for airborne transmission of virus droplets/aerosols. Schematic image (A) and a photograph (B) of the system. A test chamber for airborne transmission experiments was constructed in a BSL3 facility, and two mannequin heads were placed facing each other. One mannequin head was connected to a customized compressor nebulizer and exhaled a mist of virus suspension through its mouth to mimic a viral spreader. The other mannequin head was connected to an artificial ventilator through a virus particle collection unit. Tidal breathing, conducted by the artificial ventilator, was set to a lung ventilation rate representative of a steady state in adults (i.e., 0.5 liter of tidal volume, a respiratory rate of 18 breaths/min, and a 50% gas exchange rate). Face masks were attached to the mannequin heads according to each manufacturer's instructions.

iments was constructed in a biosafety level 3 (BSL3) facility, and two mannequin heads were placed facing each other. One mannequin head was connected to a customized compressor nebulizer and exhaled a mist of virus suspension through its mouth, mimicking a virus spreader. The nebulizer was charged with 6 ml of virus suspension at the viral doses in culture medium indicated in Fig. 2 (without fetal calf serum) or diluted in phosphate-buffered saline to generate droplets/aerosols, and the respiration was exhaled continuously, simulating a mild cough at a flow speed of 2 m/s (2) for 20 min. Although the initial particle size exhaled was 5.5 ± 0.2 μm in mass median diameter (particle size percentages were as follows: <3 μm, 20%; 3 to 5 μm, 40%; >5 to 8 μm, 40% [3]), some of the droplets likely gradually evaporated and changed to aerosols. Therefore, both droplets and aerosols were likely present in the chamber. The other mannequin head was connected to an artificial ventilator through a virus particle collection unit. Tidal breathing, conducted by the artificial ventilator, was set to a lung ventilation rate representative of a steady state in adults. Face masks were attached to the mannequin heads, and the viral loads and infective virus that passed through the masks were measured by use of a plaque assay and quantitative real-time reverse transcription PCR (qRT-PCR), respectively.

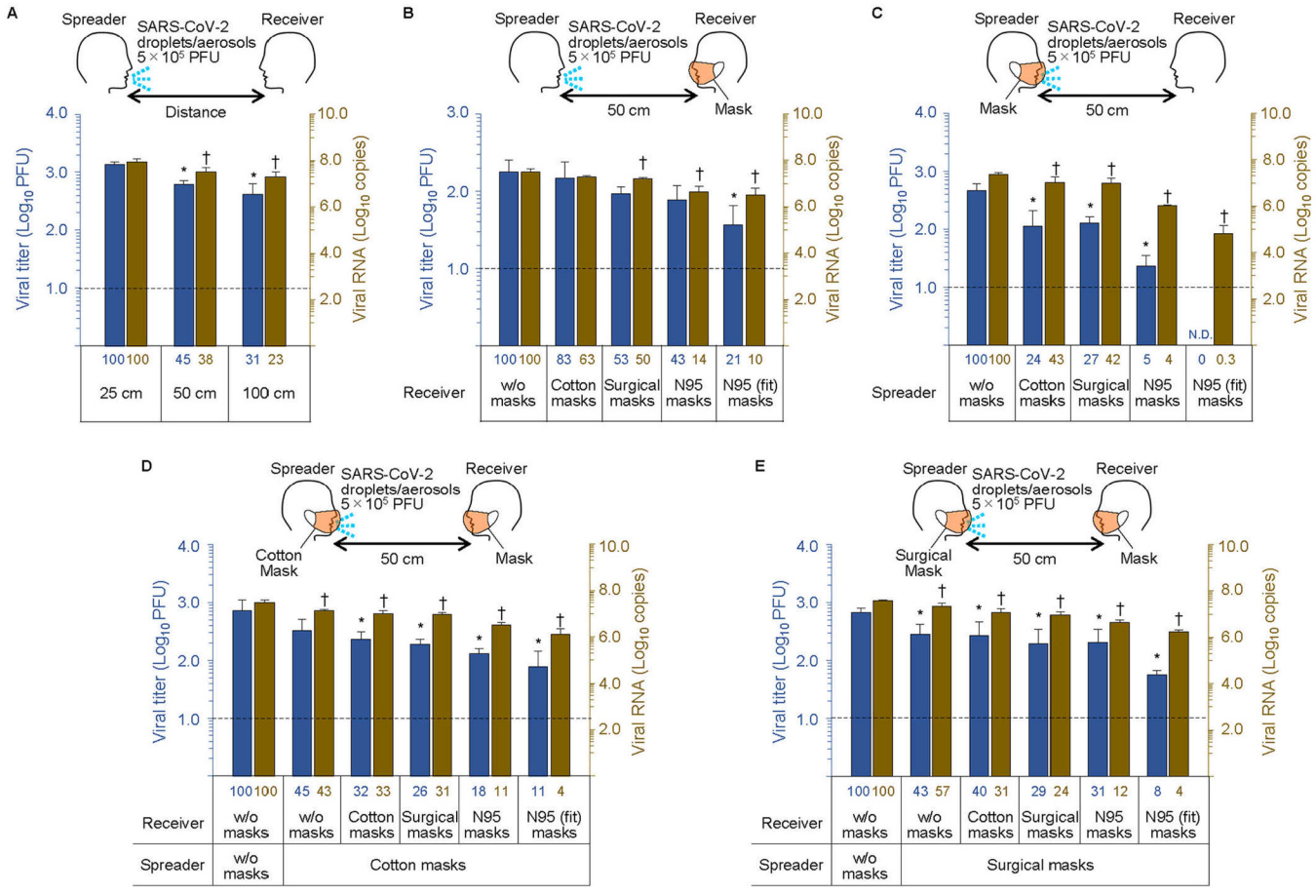

FIG 2 Mask protective efficiency against SARS-CoV-2 droplets/aerosols. The nebulizer was charged with virus suspension (5×10^5 PFU [A to E], 1×10^8 PFU [F and G], 1×10^5 PFU [H], and 1×10^4 PFU [I]) to generate droplets/aerosols and exhaled continuously to simulate a mild cough at a flow speed of 2 m/s for 20 min. Face masks were attached to the mannequin heads, and the viral loads and infective virus that passed through the masks were measured by use of a plaque assay and quantitative real-time reverse transcription PCR (qRT-PCR), respectively. The N95 masks were evaluated using the following two conditions: the mask fit naturally along the contours of the mannequin's head, or the edges of the N95 masks were sealed with adhesive tape. The blue bars and dots and the *y* axis on the left show virus titers. The brown bars and dots and the *y* axis on the right show the copy numbers of viral RNA. The numbers below the bars show the percentages relative to the leftmost control bar values. Triangles in panel I indicate that the value was below the detection limit. Data are presented as means ± standard deviations (SD). ND, none detected; w/o, without. The experiments were repeated three times ($n = 3$). * and † indicate significant differences from values for the control group (the leftmost column) ($P < 0.05$).

Viral loads in the inhalation droplets/aerosols were inversely proportional to the distance between the virus spreader and the virus receiver; however, infectious virus was detected even 1 m away (Fig. 2A). The blue bars and the brown bars in the figures show the viral titers and viral RNA copy numbers, respectively. The numbers below each bar show the percentages relative to the leftmost control column values. When a mannequin exposed to the virus was equipped with various masks (cotton mask, surgical mask, or N95 mask), the uptake of the virus droplets/aerosols was reduced. A cotton mask led to an approximately 20% to 40% reduction in virus uptake compared to no mask (Fig. 2B). The N95 mask had the highest protective efficacy (approximately 80% to 90% reduction) of the various masks examined; however, infectious virus penetration was measurable even when the N95 mask was completely fitted to the face with adhesive tape (Fig. 2B). In contrast, when a mask was attached to the mannequin that released virus, cotton and surgical masks blocked more than 50% of the virus transmission, whereas the N95 mask showed considerable protective efficacy (Fig. 2C). There was a synergistic effect when both the virus receiver and virus spreader wore masks (cotton masks or surgical masks) to prevent the transmission of infective droplets/aerosols (Fig. 2D and E).

We next tested the protective efficacy of masks when the amount of exhaled virus

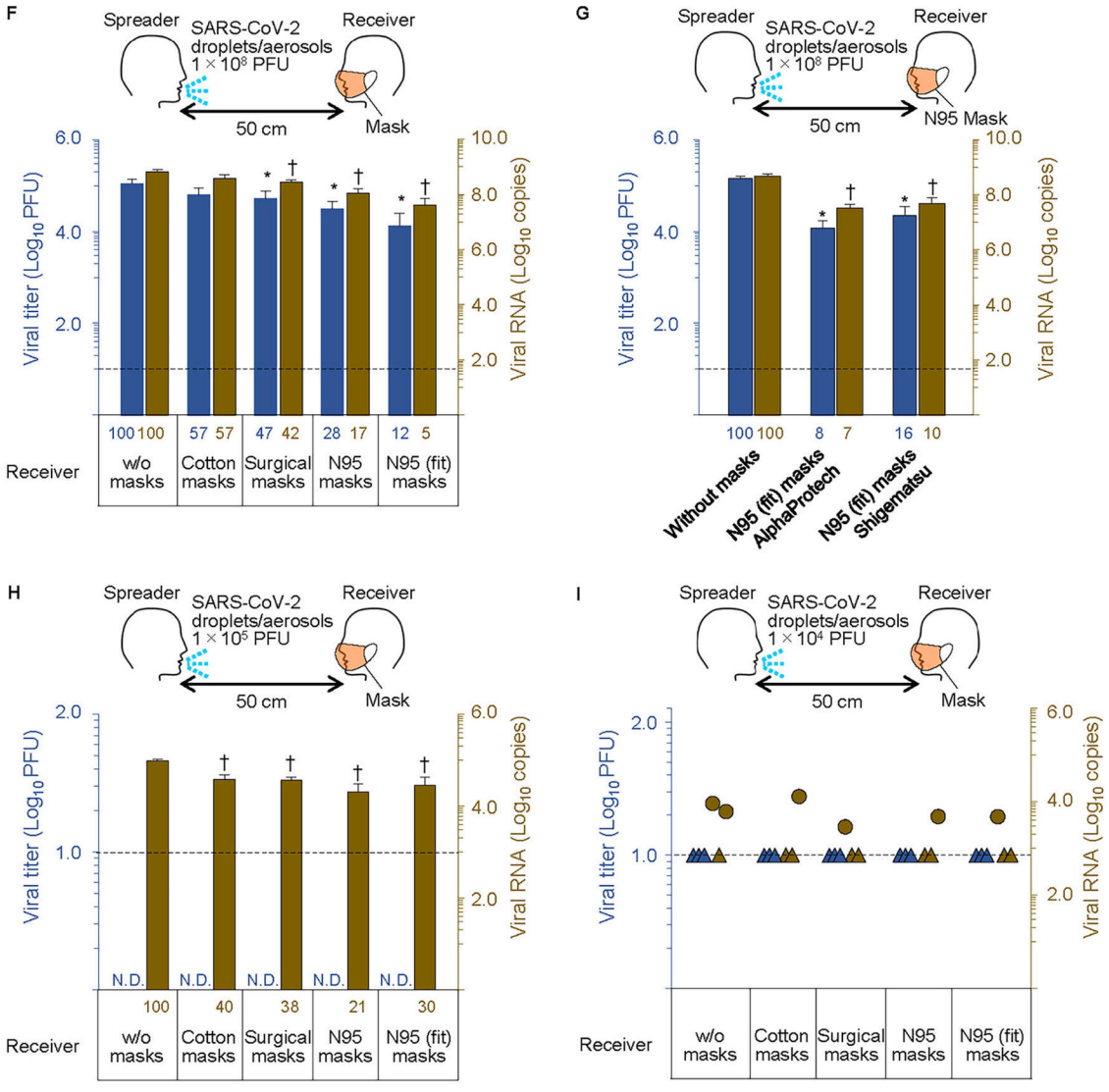

FIG 2 (Continued)

was increased. The viral load was augmented to 10^8 PFU and exhaled by the spreader; then the uptake of the virus droplets/aerosols was measured when various types of masks were attached to the receiver. As with the lower viral load (5×10^5 PFU) shown in Fig. 2B, the N95 mask sealed with adhesive tape showed approximately 90% protective efficacy (see Fig. 2F and G for a comparison of two N95 products). When the amount of exhaled virus was reduced to 10^5 PFU or 10^4 PFU, infectious viruses were not detected, even in the samples from the unmasked receiver (Fig. 2H and I). Viral RNA was detected in all samples; however, due to the quantitative decrease, there was no difference in protective efficacy among all of the masks, including the sealed N95 masks.

Our airborne simulation experiments showed that cotton masks, surgical masks, and N95 masks had a protective effect with respect to the transmission of infective droplets/aerosols and that the protective efficiency was higher when masks were worn by the virus spreader. Considerable viral loads have been detected in the nasal and throat swabs of asymptomatic and minimally symptomatic patients, as well as those of symptomatic patients, which suggests transmission potential (4). Accordingly, it is desirable for individuals to wear masks in public spaces. Importantly, medical masks (surgical masks and even N95 masks) were not able to completely block the transmis-

sion of virus droplets/aerosols even when fully sealed under the conditions that we tested. In this study, infectious SARS-CoV-2 was exhaled as droplets/aerosols and mask efficacy was examined. To allow quantification, we conducted our studies by using a relatively high dose of virus, and under these conditions, it is possible that the protective capacity of the masks was exceeded. Although the efficiency of detecting infectious virus was reduced when the amount of exhaled virus was reduced, viral RNA was detected regardless of the type of mask used. These results indicate that it is difficult to completely block this virus even with a properly fitted N95 mask. However, it remains unknown whether the small amount of virus that was able to pass through the N95 masks would result in illness.

It has been reported that the stability of the virus in the air changes depending on the droplet/aerosol components, such as inorganics, proteins, and surfactants, suggesting that the permeation efficiency of masks is also affected by the components of viral droplets/aerosols (5, 6). In our experiments, the virus was suspended in culture supernatant without fetal calf serum or was diluted with phosphate-buffered saline. Further detailed analysis will be required to reveal the precise relationship between the protective efficiency of masks and the components of viral droplets/aerosols.

Our data will help medical workers understand the proper use and performance of masks (e.g., the importance of fitting masks and avoiding their reuse) and to determine whether they need additional protective equipment (e.g., a negative-pressure room or positive-pressure masks) to protect themselves from infected patients.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

TEXT S1, DOCX file, 0.05 MB.

ACKNOWLEDGMENTS

We thank S. Watson for editing the manuscript. We also thank M. Ito, M. Okuda, and J. Murakami (University of Tokyo) for technical assistance.

This research was supported by Japan Program for Infectious Diseases Research and Infrastructure from the Japan Agency for Medical Research and Development (AMED) (grant JP20wm0125002), by the Japan Initiative for Global Research Network on Infectious Diseases (J-GRID) from AMED (grant JP19fm0108006), and by the NIAID-funded Center for Research on Influenza Pathogenesis (CRIP; grant HHSN272201400008C).

REFERENCES

1. Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, Sun L, Duan Y, Cai J, Westerdahl D, Liu X, Xu K, Ho K-F, Kan H, Fu Q, Lan K. 2020. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. Nature 582:557–560. https://doi.org/10.1038/s41586-020-2271-3.
2. Nishimura H, Sakata S and Kaga A. 2013. A new methodology for studying dynamics of aerosol particles in sneeze and cough using a digital high-vision, high-speed video system and vector analyses. PLoS One 8:e80244. https://doi.org/10.1371/journal.pone.0080244.
3. Berg EB, Picard RJ. 2009. *In vitro* delivery of budesonide from 30 jet nebulizer/compressor combinations using infant and child breathing patterns. Respir Care 54:1671–1678.
4. Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q, Song T, He J, Yen H-L, Peiris M, Wu J. 2020. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. N Engl J Med 382:1177–1179. https://doi.org/10.1056/NEJMc2001737.
5. Kormuth KA, Lin K, Prussin AJ, Vejerano EP, Tiwari AJ, Cox SS, Myerburg MM, Lakdawala SS, Marr LC. 2018. Influenza virus infectivity is retained in aerosols and droplets independent of relative humidity. J Infect Dis 218:739–747. https://doi.org/10.1093/infdis/jiy221.
6. Smither SJ, Eastaugh LS, Findlay JS, Lever MS. 2020. Experimental aerosol survival of SARS-CoV-2 in artificial saliva and tissue culture media at medium and high humidity. Emerg Microbes Infect 9:1415–1417. https://doi.org/10.1080/22221751.2020.1777906.

JAMA

View Article

JAMA. 2020 Aug 18; 324(7): 703–704.
Published online 2020 Jul 14. doi: 10.1001/jama.2020.12897: 10.1001/jama.2020.12897

PMCID: PMC7362190
PMID: 32663246

Association Between Universal Masking in a Health Care System and SARS-CoV-2 Positivity Among Health Care Workers

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Accepted for Publication: July 1, 2020.

Published Online: July 14, 2020. doi:10.1001/jama.2020.12897

Author Contributions: Dr Bhatt had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Wang and Ferro contributed equally to this article.

Concept and design: Wang, Ferro, Hashimoto, Bhatt.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Wang, Ferro.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Wang, Zhou.

Administrative, technical, or material support: Wang, Ferro, Hashimoto.

Supervision: Hashimoto, Bhatt.

Conflict of Interest Disclosures: Dr Bhatt discloses the following relationships: advisory board: Cardax, CellProthera, Cereno Scientific, Elsevier Practice Update Cardiology, Level Ex, Medscape Cardiology, PhaseBio, PLx Pharma, Regado Biosciences; board of directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; chair: American Heart Association Quality Oversight Committee, NCDR-ACTION Registry Steering Committee, VA CART Research and Publications Committee; data monitoring committees: Baim Institute for Clinical Research, Cleveland Clinic, Contego Medical, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine, Population Health Research Institute; honoraria: American College of Cardiology, Baim Institute for Clinical Research, Belvoir Publications, Duke Clinical Research Institute, HMP Global, *Journal of the American College of Cardiology*, K2P, Level Ex, Medtelligence/ReachMD, MJH Life Sciences, Population Health Research Institute, Slack Publications, Society of Cardiovascular Patient Care, WebMD; deputy editorship: *Clinical Cardiology*; research funding: Abbott, Afimmune, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim,

Bristol-Myers Squibb, Cardax, Chiesi, CSL Behring, Eisai, Ethicon, Ferring Pharmaceuticals, Forest Laboratories, Fractyl, Idorsia, Ironwood, Ischemix, Lexicon, Lilly, Medtronic, Pfizer, PhaseBio, PLx Pharma, Regeneron, Roche, Sanofi Aventis, Synaptic, The Medicines Company; royalties: Elsevier; site coinvestigator: Biotronik, Boston Scientific, CSI, St Jude Medical, Svelte; trustee: American College of Cardiology; unfunded research: FlowCo, Merck, Novo Nordisk, Takeda. No other disclosures were reported.

Additional Contributions: We thank Stacey A. Duey, MT(ASCP), MCHP, Mass General Brigham, for assistance in extracting data from the Research Patient Data Registry, and Karen Hopcia, ScD, ANP-BC, Mass General Brigham, for assistance in extracting data from Occupational Health Services. No compensation was received for their roles.

Received 2020 May 20; Accepted 2020 Jul 1.

This study describes SARS-CoV-2 PCR test positivity among health care workers before, during, and after implementation of a policy requiring universal masking of all health care workers and patients in a large health care system in Massachusetts.

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has severely affected health care workers (HCWs).[1] As a result, hospital systems began testing HCWs[2] and implementing infection control measures to mitigate workforce depletion and prevent disease spread.[3] Mass General Brigham (MGB) is the largest health care system in Massachusetts, with 12 hospitals and more than 75 000 employees. In March 2020, MGB implemented a multipronged infection reduction strategy involving systematic testing of symptomatic HCWs and universal masking of all HCWs and patients with surgical masks.[4] This study assessed the association of hospital masking policies with the SARS-CoV-2 infection rate among HCWs.

Methods

The institutional review board of MGB approved the study and waived informed consent. Using electronic medical records, we identified HCWs providing direct and indirect patient care who were tested for SARS-CoV-2 with reverse transcriptase–polymerase chain reaction between March 1 and April 30, 2020. The primary criterion for testing HCWs in our health care system was having symptoms consistent with SARS-CoV-2 infection. Information on the job description of each HCW was obtained by linking their record to the MGB Occupational Health Services and Human Resources databases.

We identified 3 phases during the study period: a preintervention period before implementation of universal masking of HCWs (March 1-24, 2020); a transition period until implementation of universal masking of patients (March 25–April 5, 2020) plus an additional lag period to allow for manifestations of symptoms (April 6-10, 2020), as previously defined[5]; and an intervention period (April 11-30, 2020). Positivity rates included the first positive test result for all HCWs in the numerator and HCWs who never tested positive plus those who tested positive that day in the denominator. For each HCW, any tests subsequent to their first positive test result were excluded. Using weighted nonlinear regression, we fit the best curve for the preintervention and intervention periods (based on R^2 value). The number of daily tests was used as the weight such that days with more tests had more weight in determining the curve. The overall slope of each period was calculated using linear regression to estimate the mean trend, regardless of curve shape. The change in overall slope between the preintervention and intervention periods was compared to determine any statistically significant change in mean trend, using a 2-sided $\alpha = .05$. The analysis was conducted using R version 4.0 (R Foundation).

Results

Of 9850 tested HCWs, 1271 (12.9%) had positive results for SARS-CoV-2 (median age, 39 years; 73% female; 7.4% physicians or trainees, 26.5% nurses or physician assistants, 17.8% technologists or nursing support, and 48.3% other). During the preintervention period, the SARS-CoV-2 positivity rate increased exponentially from 0% to 21.32%, with a weighted mean increase of 1.16% per day and a case doubling time of 3.6 days (95% CI, 3.0-4.5 days). During the intervention period, the positivity rate decreased linearly from 14.65% to 11.46%, with a weighted mean decline of 0.49% per day and a net slope change of 1.65% (95% CI, 1.13%-2.15%; $P < .001$) more decline per day compared with the preintervention period (Figure).

Discussion

Universal masking at MGB was associated with a significantly lower rate of SARS-CoV-2 positivity among HCWs. This association may be related to a decrease in transmission between patients and HCWs and among HCWs. The decrease in HCW infections could be confounded by other interventions inside and outside of the health care system (Figure), such as restrictions on elective procedures, social distancing measures, and increased masking in public spaces, which are limitations of this study. Despite these local and statewide measures, the case number continued to increase in Massachusetts throughout the study period,[6] suggesting that the decrease in the SARS-CoV-2 positivity rate in MGB HCWs took place before the decrease in the general public. Randomized trials of universal masking of HCWs during a pandemic are likely not feasible. Nonetheless, these results support universal masking as part of a multipronged infection reduction strategy in health care settings.

Notes

Section Editor: Jody W. Zylke, MD, Deputy Editor.

References

1. Adams JG, Walls RM. Supporting the health care workforce during the COVID-19 global epidemic. *JAMA*. 2020;323(15):1439-1440. doi:10.1001/jama.2020.3972 [PubMed: 32163102] [CrossRef: 10.1001/jama.2020.3972]

2. Hunter E, Price DA, Murphy E, et al. . First experience of COVID-19 screening of health-care workers in England. *Lancet*. 2020;395(10234):e77-e78. doi:10.1016/S0140-6736(20)30970-3 [PMCID: PMC7176380] [PubMed: 32333843] [CrossRef: 10.1016/S0140-6736(20)30970-3]

3. Black JRM, Bailey C, Przewrocka J, Dijkstra KK, Swanton C. COVID-19: the case for health-care worker screening to prevent hospital transmission. *Lancet*. 2020;395(10234):1418-1420. doi:10.1016/S0140-6736(20)30917-X [PMCID: PMC7162624] [PubMed: 32305073] [CrossRef: 10.1016/S0140-6736(20)30917-X]

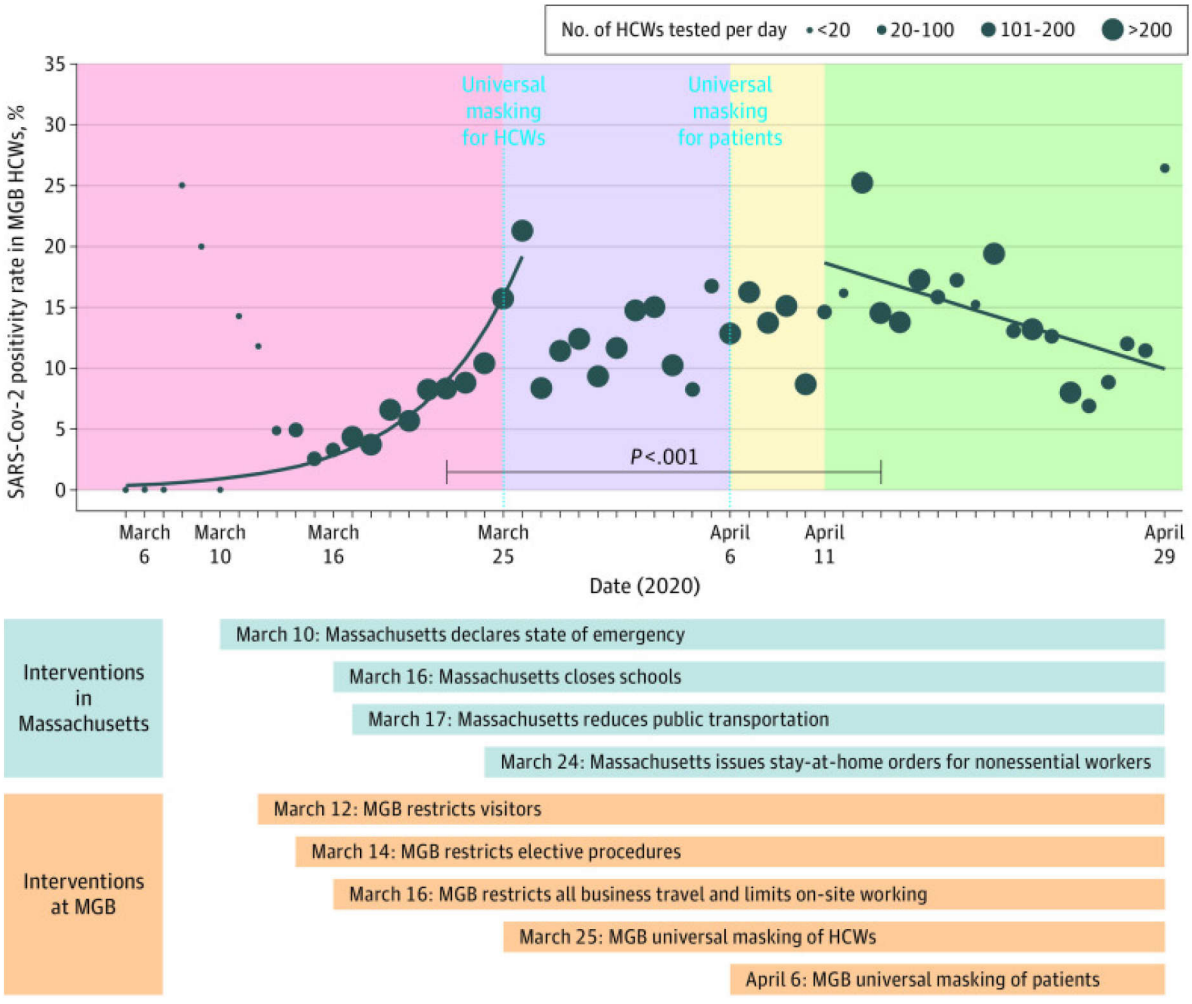
4. Klompas M, Morris CA, Sinclair J, Pearson M, Shenoy ES. Universal masking in hospitals in the Covid-19 era. *N Engl J Med*. 2020;382(21):e63. doi:10.1056/NEJMp2006372 [PubMed: 32237672] [CrossRef: 10.1056/NEJMp2006372]

5. Sen S, Karaca-Mandic P, Georgiou A. Association of stay-at-home orders with COVID-19 hospitalizations in 4 states. *JAMA*. 2020;323(24):2522-2524. doi:10.1001/jama.2020.9176 [PMCID: PMC7254451] [PubMed: 32459287] [CrossRef: 10.1001/jama.2020.9176]

6. Massachusetts Department of Public Health COVID-19 dashboard—April 30, 2020. Accessed June 27, 2020. https://www.mass.gov/doc/covid-19-dashboard-april-30-2020/download

Figures and Tables

Figure.



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Temporal Trend in Percentage Positivity of SARS-CoV-2 Testing Among HCWs

HCW indicates health care worker; MGB, Mass General Brigham; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. All dates given are for the year 2020. The size of each data marker is proportional to the total number of SARS-CoV-2 tests performed each day over the time of the study period (x-axis), while the position of each data marker along the y-axis shows the percentage of daily test results that were positive among HCWs. The horizontal bars below the x-axis represent the timing of key interventions implemented in the state of Massachusetts and at MGB. The dotted lines represent the implementation dates of hospital policies. The study period is divided into 3 phases: a preintervention period before implementation of universal masking of HCWs (pink), which includes March 26, the day after implementation of universal masking for HCWs, to account for HCWs who became symptomatic after business hours on March 25 and were tested on March 26; a transition period until implementation of universal masking of patients (purple) plus an additional lag period (yellow); and the intervention period (green). For the preintervention and intervention periods, daily tests were fitted by weighted nonlinear regression (curves). The change in overall slope was compared between the 2 curves to determine any statistically significant changes in trend (as shown by the *P* value).

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Face Masks Considerably Reduce COVID-19 Cases in Germany: A Synthetic Control Method Approach

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ISSN: 2365-9793

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IZA DP No. 13319 JUNE 2020

ABSTRACT

Face Masks Considerably Reduce COVID-19 Cases in Germany: A Synthetic Control Method Approach[1]

We use the synthetic control method to analyze the effect of face masks on the spread of Covid-19 in Germany. Our identification approach exploits regional variation in the point in time when face masks became compulsory. Depending on the region we analyse, we find that face masks reduced the cumulative number of registered Covid-19 cases between 2.3% and 13% over a period of 10 days after they became compulsory. Assessing the credibility of the various estimates, we conclude that face masks reduce the daily growth rate of reported infections by around 40%.

JEL Classification: I18, C23

Keywords: COVID-19, public health measures, face masks, synthetic control method, Germany

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1 Introduction

Many countries have experimented with several public health measures to mitigate the spread of Covid-19. One particular measure that has been introduced are face masks. It is of obvious interest to understand the contribution made by such a measure to reducing infections.

The effect of face masks on the spread of infections has been studied for a long time. The usefulness in the clinical context is beyond dispute. There is also considerable evidence that they helped in mitigating the spread of epidemics such as SARS 2003 or influenza (see below). The effect of face masks worn in public on the spread of Covid-19 has not been systematically analyzed so far. This is the objective of this paper.

There is a general perception in Germany that public wearing of face masks reduces incidences considerably. This perception comes mainly from the city of Jena. After face masks were introduced on 6 April 2020, the number of new infections fell almost to zero. Jena is not the only city or region in Germany, however, that introduced face masks. Face masks became compulsory in all federal states between 20 April and 29 April 2020. Six regions made masks compulsory before the introduction at the federal level. These dates lay between 6 April and 25 April (see appendix A and Kleyer et al., 2020, for a detailed overview of regulations in Germany). This leads to a lag between individual regions and the corresponding federal states of between two and 18 days.

We derive findings by employing synthetic control methods (SCM, Abadie and Gardeazabal, 2003, Abadie et al., 2010, Abadie, 2019). Our identification approach exploits the previously mentioned regional variation in the point in time when face masks became compulsory in public transport and sales shops. We use data for 401 German regions to estimate the effect of this public health measure on the development of registered infections with Covid-19. We consider the timing of mandatory face masks as an exogenous event to the local population. Masks were imposed by local authorities and were not the outcome of some process in which the population was involved.[2] We compare the Covid-19 development in various regions to their synthetic counterparts. The latter are constructed as a weighted average of control regions that are similar to the regions of interest. Structural dimensions taken into account include prior Covid-19 cases, their demographic structure and the local health care system.

We indeed find strong and convincing statistical support for the general perception that public wearing of face masks in Jena strongly reduced the number of incidences. We obtain a synthetic control group that closely follows the Covid-19 trend before introduction of mandatory masks in Jena and the difference between Jena and this group is very large after 6 April. Our findings indicate that the early introduction of face masks in Jena has resulted in a reduction of almost 25% in the cumulative number of reported Covid-19 cases after 20 days. The drop is greatest, larger than 50%, for the age group 60 years and above. Our results are robust when we conduct sensitivity checks and apply several placebo tests, e.g. tests for pseudo-treatment effects in similarly sized cities in the federal state of Thuringia and for pseudo-treatment effects in Jena before the treatment actually started. We also test for announcement effects.

Constructing control groups for other single regions is not always as straightforward as for Jena. As a consequence, it is harder to identify the effect of face masks in these regions. When we

[2] This is similar to the setup in Abadie et al. (2010), who study the effect of an increase in the tobacco tax in California. The tobacco tax was decided upon by the state government.

move from single to multiple treatment effects, we find smaller effects. They are still sufficiently large, however, to support our point that wearing face masks is a very cost-efficient measure for fighting Covid-19. When we summarize all of our findings in one single measure (we compare all measures in appendix B.4), we conclude that the daily growth rate of Covid-19 cases in the synthetic control group falls by around 40% due to mandatory mask-wearing relative to the control group.[3]

Concerning the literature (see appendix D for a more detailed overview), the effects of face masks have been surveyed by Howard et al. (2020) and Greenhalgh et al. (2020). Greenhalgh et al. (2020) mainly presents evidence on the effect of face masks during non-Covid epidemics (influenza and SARS). Marasinghe (2020) reports that they "*did not find any studies that investigated the effectiveness of face mask use in limiting the spread of COVID-19 among those who are not medically diagnosed with COVID-19 to support current public health recommendations*".

In addition to medical aspects (like transmission characteristics of Covid-19 and filtering capabilities of masks), Howard et al. (2020) survey evidence on mask efficiency and on the effect of a population. They first stress that "*no randomized control trials on the use of masks <…> has been published*". The study which is "*the most relevant paper*" for Howard et al. (2020) is one that analyzed *"exhaled breath and coughs of children and adults with acute respiratory illness*" (Leung et al., 2020, p. 676), i.e. used a clinical setting. Concerning the effect of masks on community transmissions, the survey needs to rely on pre-Covid-19 studies. We conclude from this literature review that our paper is the first analysis that provides field evidence on the effect of masks on mitigating the spread of Covid-19.

2 Identification, data and implementation

Identification. Our identification approach exploits the regional variation in the point in time when face masks became mandatory in public transport and sales shops. Given the federal structure of Germany, decisions are made by municipal districts (regions in what follows) and federal states. We can exploit differences by, first, identifying six regions (equivalent to the EU nomenclature of territorial units for statistics, NUTS, level 3) which made wearing face masks compulsory before their respective federal states. For all other regions, mandatory mask-wearing followed the decision of the corresponding federal state. Second, as Figure 1 shows, variation across federal states also implies variations across regions.

To identify possible treatment effects from introducing face masks, we apply SCM for single and multiple treated units. Our methodical choice is motivated as follows: First, the original goal of SCM to "*estimate the effects of <…> interventions that are implemented at an aggregate level affecting a small number of large units (such as cities, regions, or countries)*" (Abadie, 2019, p.3) clearly matches with our empirical setup. Compared to standard regression analyses, SCM is particularly well suited for comparative case study analyses with only one treated unit or a very small number thereof (Abadie and Gardeazabal, 2003, Becker et al., 2018). Second, the method is flexible, transparent and has become a widely utilized tool in the policy evaluation literature (Athey and Imbens, 2017) and for causal analyses in related disciplines

[3] The main channel through which masks reduce transmission of SARS-CoV-2 is the reduction in aerosols and droplets, as argued by Prather et al. (2020).

(see, e.g., Kreif et al., 2015, for an overview of SCM in health economics, Pieters et al., 2017, for a biomedical application).[4]

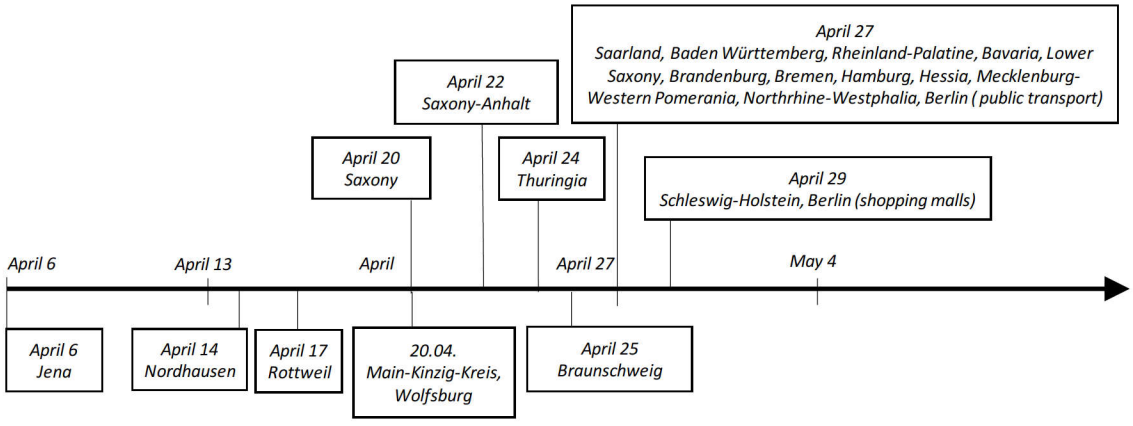

Figure 1: The timing of mandatory mask wearing in federal states (top) and individual regions (below)

SCM identifies synthetic control groups for the treated unit(s) to build a counterfactual. In our case, we need to find a group of regions that have followed the same Covid-19 trend as treated units before mandatory masks in the latter. This control group would then most likely have had the same behavior as treated unit(s) in the absence of the mask obligation. We can then use this group to 'synthesize' the treated unit and conduct causal inference. The synthetic control group is thereby constructed as an estimated weighted average of all regions in which masks did not become compulsory earlier on. Historical realizations of the outcome variable and several other predictor variables that are relevant in determining outcome levels allow us to generate the associated weights, which result from minimizing a pre-treatment prediction error function (see Abadie and Gardeazabal, 2003, Abadie et al., 2010 and Abadie, 2019 for methodical details).

Data. We use the official German statistics on reported Covid-19 cases from the Robert Koch Institute (RKI, 2020). The RKI collects the data from local health authorities and provides updates on a daily basis. Using these data (available via API), we build a balanced panel for 401 NUTS Level 3 regions and 95 days spanning the period from January 28 to May 1, 2020 (38,095 observations). We use the cumulative number of registered Covid-19 cases in each district as main outcome variable.[5] We estimate overall effects for this variable together with disaggregated effects by age groups (persons aged 15-34 years, 35-59 years and 60+ years). As an alternative outcome variable, we also use the cumulative incidence rate. Table 1 shows summary statistics for both variables for our sample period.

Table 1 also presents our other predictor variables. We focus on factors that are likely to describe the regional number and dynamics of reported Covid-19 cases. Obviously, past values

[4] Friedson et al. (2020) employ the SCM to estimate the effect of the shelter-in-place order for California in the development of Covid-19. The authors find *inter alia* that around 1600 deaths from Covid-19 were avoided by this measure during the first four weeks.

[5] We are aware of the existence of hidden infections. As it appears plausible to assume that they are proportional to observed infections across regions, we do not believe that they affect our results. We chose the date of reporting (as opposed to date of infections) because not all reported infections include information about the date of infection.

of (newly) registered Covid-19 cases are important to predict the regional evolution of Covid-19 cases over time in an autoregressive manner. In addition, we argue that a region's demographic structure, such as the overall population density and age structure, and its basic health care system, such as the regional endowment with physicians and pharmacies per population, are important factors for characterizing the local context of Covid-19. Predictor variables are obtained from the INKAR online database of the Federal Institute for Research on Building, Urban Affairs and Spatial Development. We use the latest year available in the database (2017). We consider it likely that regional demographic structures only gradually vary over time such that they can be used to measure regional differences during the spread of Covid-19 in early 2020.

Table 1: Summary Statistics of Covid-19 indicators (outcome variables) and predictors characterizing the regional demographic structure and basic health care system

	Mean	S.D.	Min.	Max.
PANEL A: Data on registered Covid-19 cases				
[1] Newly registered cases per day	4.13	10.66	0	310
[2] Cumulative number of cases	120.86	289.07	0	5795
[3] Cum. cases [2] per 100,000 inhabitants	59.87	106.80	0	1,530.32
PANEL B: Regional demographic structure and local health care system				
Population density (inhabitants/km^2)	534.79	702.40	36.13	4,686.17
Population share of highly educated* individuals (in %)	13.07	6.20	5.59	42.93
Share of females in population (in %)	50.59	0.64	48.39	52.74
Average age of females in population (in years)	45.86	2.11	40.70	52.12
Average age of males in population (in years)	43.17	1.83	38.80	48.20
Old-age dependency ratio (persons aged 65 years and above per 100 of population age 15-64)	34.34	5.46	22.40	53.98
Young-age dependency ratio (persons aged 14 years and below per 100 of population age 15-64)	20.54	1.44	15.08	24.68
Physicians per 10,000 of population	14.58	4.41	7.33	30.48
Pharmacies per 100,000 of population	27.01	4.90	18.15	51.68
Settlement type (categorial variable$^{\$}$)	2.59	1.04	1	4

Notes: * = International Standard Classification of Education (ISCED) Level 6 and above; $ = categories are based on population shares and comprise 1) district-free cities *(kreisfreie Großstädte)*, 2) urban districts *(städtische Kreise)*, 3) rural districts *(ländliche Kreise mit Verdichtungsansätzen)*, 4) sparsely populated rural districts *(dünn besiedelte ländliche Kreise)*.

Implementation. The implementation of the SCM is organized as follows: As baseline analysis, we focus on the single treatment case for the city of Jena for three reasons. First, as shown in Figure 1, Jena was the first region to introduce face masks in public transport and sales shops on April 6. This results in a lead time of 18 days relative to mandatory face masks in the surrounding federal state Thuringia on April 24. By April 29, all German regions had introduced face masks (exact dates are provided in appendix A). A sufficiently long lag between mandatory face masks in the treated unit vis-à-vis the sample of control regions is important for effect identification.

Second, the timing of the introduction of face masks in Jena is -by and large- not affected by other overlapping public health measures related to the Covid-19 spread. Since March 22 the German economy had been in a general "lock down" coordinated among all federal states. Only from April 20 onwards has the economy been gradually reopening. Third, Jena is in various ways a representative case for studying the Covid-19 development: On April 5, which is one day before face masks became compulsory in Jena, the cumulative number of registered Covid-19 cases in Jena was 144. This is very close to the median of 155 for Germany. Similarly, the cumulative number of Covid-19 incidences per 100,000 inhabitants was 126.9 in Jena compared to a mean of 119.3 in Germany (compare Figure A1).

In our baseline configuration of the SCM, we construct the synthetic Jena by including the number of cumulative Covid-19 cases (measured one and seven days before the start of the treatment) and the number of newly registered Covid-19 cases (in the last seven days prior to the start of the treatment) as autoregressive predictor variables. The chosen period shall ensure that the highly non-linear short-run dynamics of regional Covid-19 cases are properly captured. We use cross-validation tests to check the sensitivity of the SCM results when we allow for a shorter training period in the pre-treatment phase by imposing longer lags. The autoregressive predictors are complemented by the cross-sectional data on the region's demographic and basic health care structure.

Although the case study of Jena can be framed in a clear identification strategy, the Covid-19 spread in a single municipality may still be driven by certain particularities and random events that may prevent a generalization of estimated effects. We therefore also test for treatment effect in districts that introduced face masks after Jena but still before they became compulsory in the corresponding federal state. More importantly, however, we apply a multiple treatment approach that takes all regions as treated units which introduced face masks by April 22. This results in 32 regions from Saxony and Saxony-Anhalt. All other regions apart from Thuringia introduced face masks on April 27. We employ this delay to study the effects of mandatory masks up to May 1st. We end on May 1st as we would expect that differences across treated and non-treated regions should disappear 5-7 days after April 27. This delay results from a median incubation time of 5.2 days (Linton et al., 2020 and Lauer et al., 2020) and around 2 days accounting for reporting to authorities (as assumed e.g. in Donsimoni et al., 2020a, b).

Although SCM appears to be a natural choice for our empirical identification strategy, we are well aware of the fact that its validity crucially depends on important practical requirements including the availability of a proper comparison group, the absence of early anticipation effects or interference from other events (Cavallo et al., 2013, Abadie, 2019). In the implementation of the single and multiple treatment SCM we check for these pitfalls through sensitivity and placebo tests. We deal with these issues in our baseline case study for Jena as follows:

1. We have screened the introduction and easing of public health measures, as documented in Kleyer et al. (2020), to ensure that no interference takes place during our period of study. This is the case at least until April 20 when exit strategies from public health measures started.
2. We make sure that the regions used to create the synthetic control, i.e. the donor pool, are not affected by the treatment (Campos et al., 2015). We eliminate the two immediate geographical neighbors of Jena from the donor pool to rule out spillover effects. We also exclude those regions for which anticipation effects may have taken place because face masks became compulsory in quick succession to Jena.

3. We account for early anticipation effects in Jena. Specifically, we take the announcement that face masks will become compulsory one week before their introduction as an alternative start of the treatment period.
4. We apply cross-validation tests to check for sensitivities related to changes in historical values in the outcome variables used as predictors. We also run placebo-in-time tests to check whether effects actually occurred even before the start of the treatment.
5. We test for the sensitivity of the results when changing the donor pool and run comprehensive placebo-in-space tests as a mode of inference in the SCM framework.

Inference thereby relies on permutation tests and follows the procedures suggested by Cavallo et al. (2013) and applied, for example, by Eliason and Lutz (2018) or Hu et al. (2018). For both the single and multiple treatment applications we estimate placebo-treatment effects for each district in which masks did not become compulsory early on. These placebo treatments should be small, relative to the treated regions. We calculate significance levels for the test of the hypothesis that the mask obligation did not significantly affect reported Covid-19 cases. This provides us with *p*–values for each day, which capture the estimated treatment effect on reported Covid-19 cases from placebo regions. The *p*-values are derived from a ranking of the actual treatment effect within the distribution of placebo treatment effects. We follow the suggestion in Galiani and Quistorff (2017) and compute adjusted *p*-values taking the pre-treatment match quality of the placebo treatments into account.[6]

3 The effects of face masks on Covid-19

Baseline results for Jena. Panel A in Figure 2 shows the SCM results for the introduction of face masks in Jena on April 6. The visual inspection of the development of cumulative Covid-19 cases shows that the fit of the synthetic control group is very similar to Jena before the treatment.[7] The difference in the cumulated registered Covid-19 cases between Jena and its corresponding synthetic control unit after the start of the treatment can be interpreted as the treatment effect on the treated.

The figure clearly shows a gradually widening gap in the cumulative number of Covid-19 cases between Jena and the synthetic control unit. The size of the effect 20 days after the start of the treatment (April 26) amounts to a decrease in the number of cumulative Covid-19 cases of 23%. For the first 10 days, the decrease amounts to 13%. Expressed differently, the daily growth rate of the number of infections decreases by 1.32 percentage points per day (see appendix B.4 for computational details and an overview of all measures). If we look at the estimated differences by age groups, Table A2 in the appendix indicates that the largest effects are due to the age group of persons aged 60 years and above. Here the reduction in the number of registered cases is even larger than 50%. For the other two age groups we find a decrease between 10 and 20%.

[6] We conduct all estimations in STATA using "Synth" and "Synth Runner" packages (Abadie at al., 2020, Galiani and Quistorff, 2017). Data and estimation files can be obtained from the authors upon request.

[7] The pre-treatment root mean square prediction error (RMSPE) of 3.145 is significantly below a benchmark RMSPE of 6.669, which has been calculated as the average RMSPE for all 401 regions in the pre-treatment period until April 6. This points to the relatively good fit of the synthetic control group for Jena in this period.

If we consider a median incubation of 5.2 days plus a potential testing and reporting lag of 2-3 days, the occurrence of a gradually widening gap between Jena and its synthetic control three to four days after the mandatory face masks seems fast. One might conjecture that an announcement effect played a role. As shown in appendix B.7, online searches for (purchasing) face masks peaked on April 22, when it was announced that face masks would become compulsory in all German federal states.[8] A smaller peak (70% of the April 22 peak) of online searches appeared on March 31. This is one day after Jena announced that masks would become compulsory on April 6. The announcement was accompanied by a campaign "Jena zeigt Maske" to communicate the necessity to wear face masks in public[9] and was widely discussed all over Germany.

Panel B in Figure 2 therefore plots the results when we set the start of the treatment period to the day of the announcement on 30 March. The visual inspection of the figure shows the existence of a small anticipation effect (which is mainly driven by the relative development of Covid-19 age group 15-34 years (Panel B in Figure A2). Yet, the gap to the synthetic control significantly widens only approximately 10 days after the announcement. As this temporal transmission channel appears plausible against the background of incubation times and given that no other intervention took place around this time in Jena or the regions in the synthetic control group, we take this as first evidence for a face mask-effect in the reduction of Covid-19 infections. Appendix B.6 shows similar SCM results for the incidence rate (overall and by age groups). We find a reduction of approximately 30 cases per 100,000 of population.

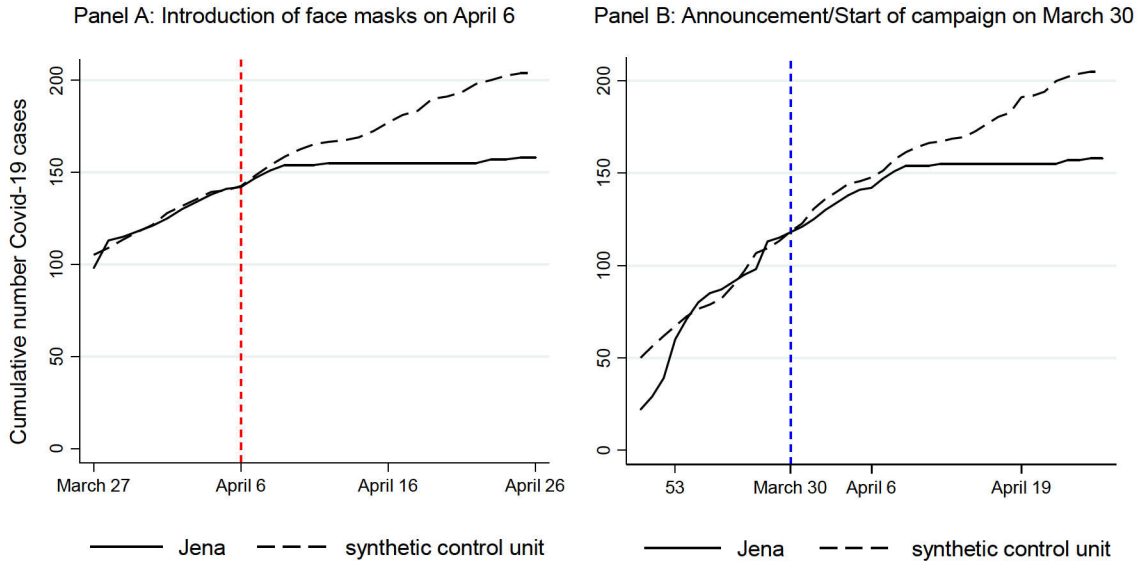

Figure 2: Treatment effects of mandatory face masks in Jena on April 6 and start of campaign on March 30 (see Table A3 and appendix B.2 for details)

[8] See https://www.tagesschau.de/inland/corona-maskenpflicht-103.html. Last accessed May 05, 2020.

[9] See https://www.jenaer-nachrichten.de/stadtleben/13069-jena-zeigt-maske-kampagne-f%C3%BCr-mund-schutz-startet. Last accessed May 05, 2020.

Obviously, the estimated differences in the development of Jena vis-à-vis the synthetic Jena is only consistently estimated if our SCM approach delivers robust results. Accordingly, we have applied several tests to check for the sensitivity of our findings.

Cross-validation and placebo-in-time test. One important factor is that our results are not sensitive to changes in predictor variables. We therefore perform cross-validation checks by modifying the length of the training and validation periods before the start of the treatment. Panel A in Figure 3 shows that lagging the autoregressive predictor variables further in time only slightly changes our results. Importantly, we do not find a systematic downward bias of our baseline specification (cumulative number of reported Covid-19 cases: one and seven days before start of treatment; number of newly registered Covid-19 cases: last seven days before start of treatment) compared to an alternative specification. The latter trains the synthetic control on the basis of information on cumulative Covid-19 cases 7 and 14 days prior to the treatment together with the development of newly register cases between day 7 and 14 prior to the treatment. Given that regional Covid-19 cases developed very dynamically and non-linearly in this period, this is an important finding in terms of the robustness of our results.

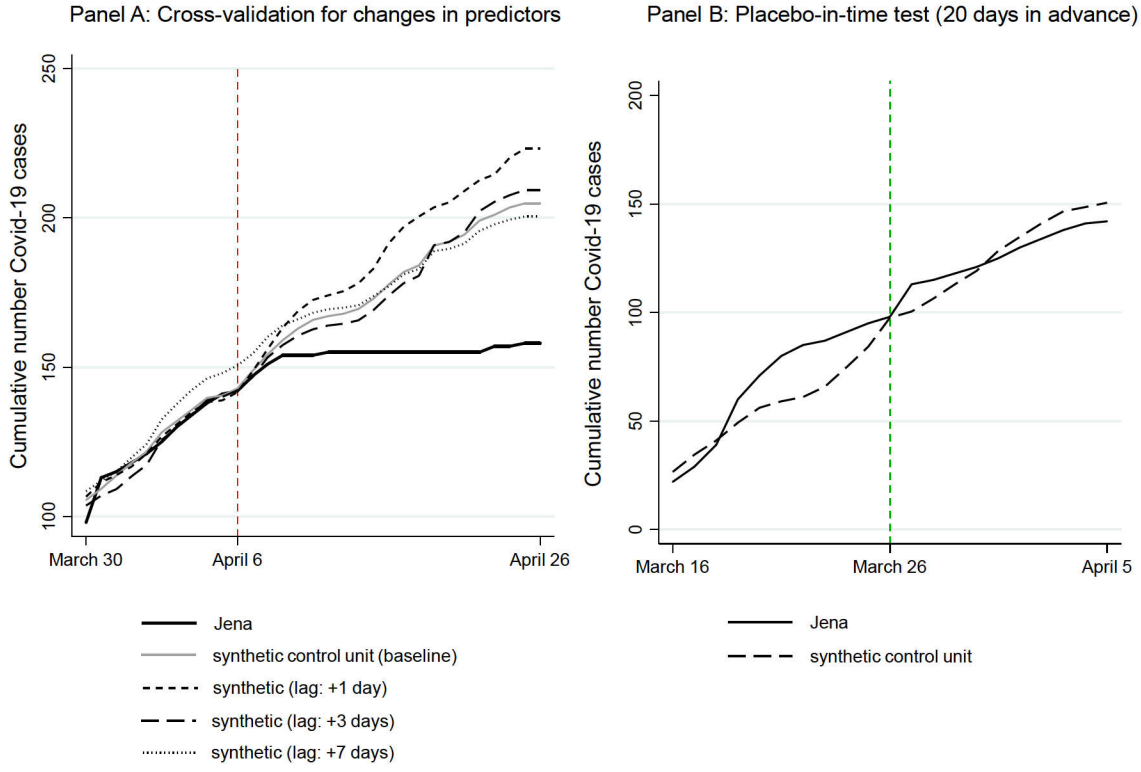

Figure 3: Cross-validation for changes in predictor variables and placebo-in-time test

Notes: In Panel A the baseline specification for the synthetic control group uses historical values of the outcome variable in the following way: i) number of cumulative Covid-19 cases (measured one and seven days before the start of the treatment), ii) the number of newly registered Covid-19 cases (in the last seven days prior to the start of the treatment); the alternative specifications lag these values by 1, 3 and 7 days.

Another important factor for the validity of the results is that we do not observe an anticipation effect for Jena prior to the announcement day. We test for a pseudo-treatment in Jena over a period of 20 days before the introduction of face masks. This period is equally split into a pre-

and pseudo post-treatment period. As Panel B in Figure 3 shows, there is no strong deviation from the path of the synthetic control group. This result needs to be interpreted with some care as the regional variation of Covid-19 cases in Germany is very heterogeneous the longer we go back in time. This is indicated by the generally lower fit of the synthetic control group in matching the development in Jena in mid-March when the absolute number of Covid-19 cases was still low.

Changing the donor pool. In addition, we also check for the sensitivity of the results when changing the donor pool. This may be important as our baseline specification includes the region of Heinsberg in the donor pool used to construct the synthetic Jena (with a weight of 4.6%; compare Table A3). As Heinsberg is one of the German regions which was significantly affected by the Covid-19 pandemic during the Carnival season, this may lead to an overestimation of the effects of face masks. Accordingly, appendix B.8 presents estimates for alternative donor pools. Again, we do not find evidence for a significant bias in our baseline specification. By tendency, the treatment effect becomes larger, particularly if we compare Jena only to other regions in Thuringia (to rule out macro-regional trends) and to a subsample of larger cities (*kreisfreie Städte*). Both subsamples exclude Heinsberg. We also run SCM for subsamples excluding Thuringia (to rule out spillover effects) and for East and West Germany (again in search for specific macro regional trends). Generally, these sensitivity tests underline the robustness of the estimated treatment effect for Jena.

Placebo-in-space tests. A placebo test in space checks whether other cities that did not introduce face masks on April 6 have nonetheless experienced a decline in the number of registered Covid-19 cases. If this had been the case, the treatment effect may be driven by other latent factors rather than face masks. Such latent factors may, for instance, be related to the macro-regional dynamics of Covid-19 in Germany. Therefore, appendix B.9 reports pseudo-treatment effects for similarly sized cities in Thuringia assuming that they have introduced face masks on April 6 although –in fact– they did not. As the figure shows, these cities show either a significantly higher or similar development of registered Covid-19 compared to their synthetic controls. This result provides further empirical support for a relevant effect in the case of Jena.

As a more comprehensive test, we also ran placebo-in-space tests for all other regions that did not introduce face masks on April 6 or closely afterwards. Again, we estimate the same model on each untreated region, assuming it was treated at the same time as Jena. The empirical results in Figure 4 indicate that the reduction in the reported number of Covid-19 cases in Jena clearly exceeds the trend in most other regions – both for the overall sample in Panel A and the subsample of large cities (*kreisfreie Städte*) in Panel B.

As outlined above, one advantage of this type of placebo-in-space-test is allows us to conduct inference. Accordingly, Panel C and Panel D report adjusted *p*-values that indicate the probability if the treatment effect for Jena was observed by chance given the distribution of pseudo-treatment effects in the other German regions (see Galiani and Quistorff, 2017). For both samples, the reported *p*-values indicate that the reduction in the number of Covid-19 cases in Jena did not happen by chance but can be attributed to the introduction of face masks, at the latest - roughly two weeks after the start of the treatment. This timing is again in line with our above argument that a sufficiently long incubation time and testing lags need to be considered in the evaluation of treatment effects.

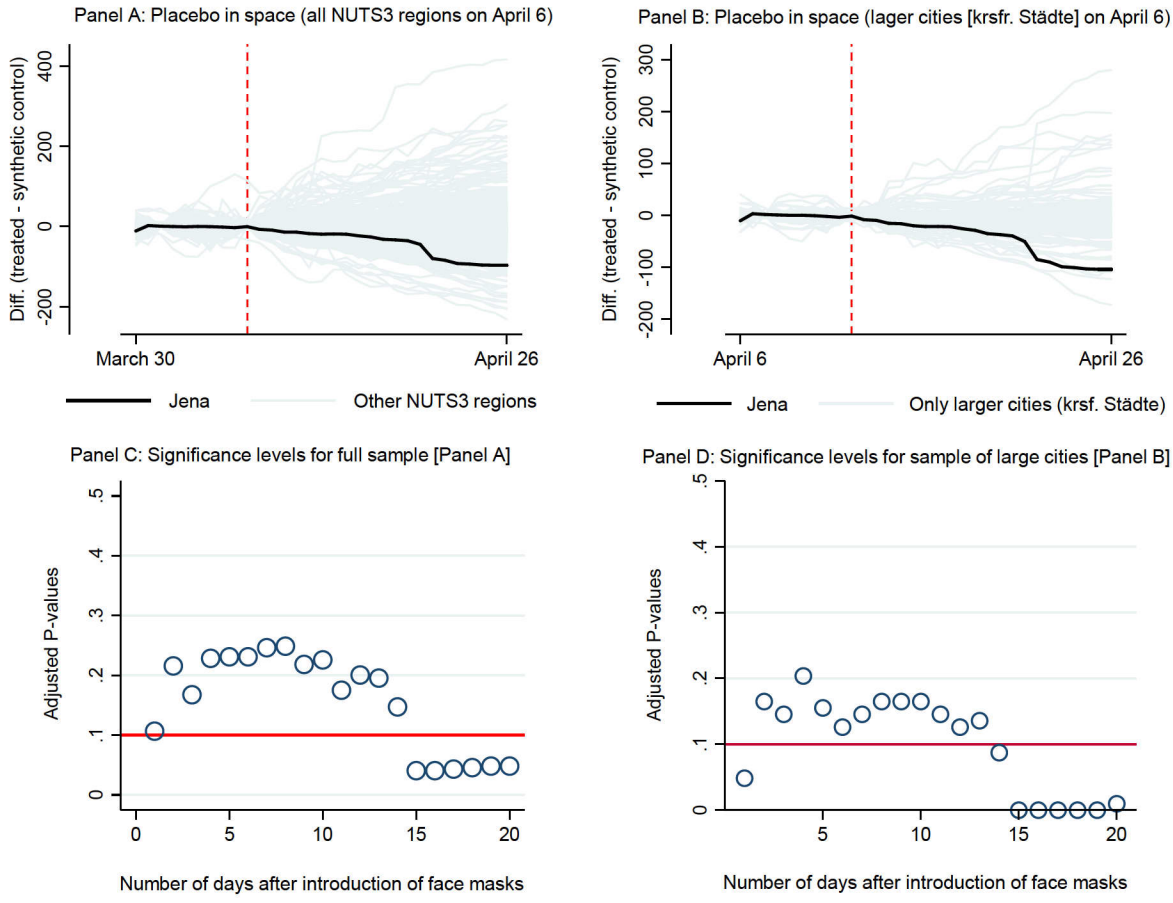

Figure 4: Comprehensive placebo-in-space tests for the effect of face masks on Covid-19 cases

Notes: Graphs exclude the following regions with a very large number of registered Covid-19 cases: Hamburg (2000), Berlin (11000), Munich (9162), Cologne (5315) and Heinsberg (5370). In line with Abadie et al. (2010), we only include placebo effects in the pool for inference if the match quality (pre-treatment RMSPE) of the specific control regions is smaller than 20 times the match quality of the treated unit. *P*-values are adjusted for the quality of the pre-treatment matches (see Galiani and Quistorff, 2017).

Treatment in other districts. Jena may be a unique case. We therefore also study treatment effects for other regions that have antedated the general introduction of face masks in Germany. Further single unit treatment analyses are shown in appendix C. Multiple unit treatments are studied in two ways. The first sample covers all 401 regions and 32 treated units. The second focused on the subsample of 105 larger cities (*kreisfreie Städte*), of which 8 are treated units. Treated regions introduced face masks by April 22. The multiple treatment approach, visible in Figure 5, points to a significant face mask-effect in the reduction of Covid-19 infections. The adjusted *p*-values indicate that the estimated treatment effects are not random.

Face masks may have made a particular difference in the spread of Covid-19, particularly in larger cities with higher population density and accordingly higher intensity of social interaction.[10] Over a period of 10 days, we observe an average reduction of 12.3 cases between treated and control regions. Relative to the average number of cumulative Covid-19 cases on May 1 in control regions (295.6), this amounts to a reduction of 4.2% of cases. The daily growth

[10] This is perfectly in line with Prather et al. (2020) given the reduction in aerosols and droplets via using masks.

rate of the number of infections correspondingly shrinks by 0.42 percentage points. For the entire sample, the reduction in the daily growth rate is estimated to be 0.23 percentage points (see again appendix B.4 for an overview of all measures).

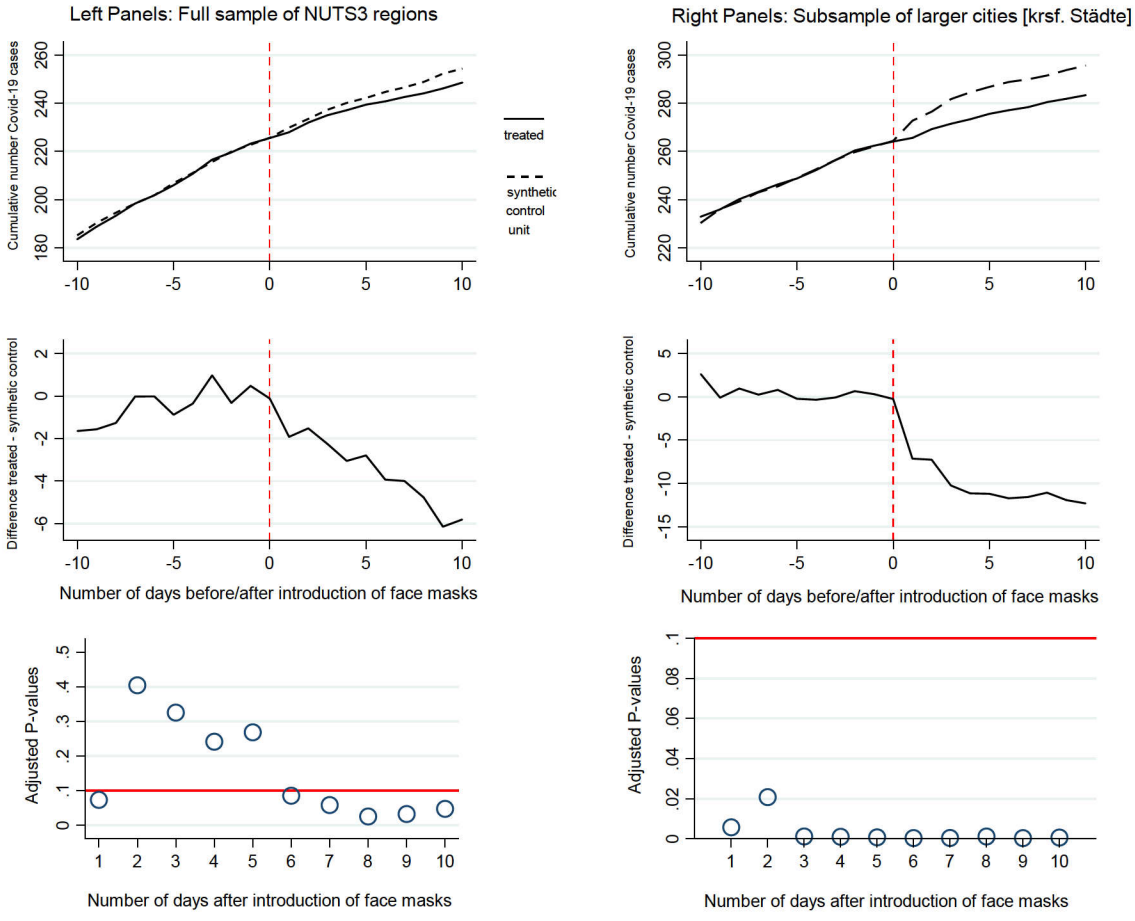

Figure 5: Average treatment effects for introduction of face masks (multiple treated units)

Notes Statistical inference for adjusted *p*-values has been conducted on the basis of a random sample of 1,000,000 placebo averages.

4 Conclusion

We set out by analyzing the city of Jena. The introduction of face masks on 6 April reduced the number of new infections over the next 20 days by almost 25% relative to the synthetic control group. This corresponds to a reduction in the average daily growth rate of the total number of reported infections by 1.32 percentage points. Comparing the daily growth rate in the synthetic control group with the observed daily growth rate in Jena, the latter shrinks by around 60% due to the introduction of face masks. This is a sizeable effect. Wearing face masks apparently helped considerably in reducing the spread of Covid-19. Looking at single treatment effects for all other regions puts this result in some perspective. The reduction in the growth rate of infections amounts to 20% only. By contrast, when we take the multiple treatment effect for larger cities into account, we find a reduction in the growth rate of infections by around 40%.

What would we reply if we were asked what the effect of introducing face masks would have been if they had been made compulsory all over Germany? The answer depends, first, on which of the three percentage measures we found above is the most convincing and, second, on the point in time when face masks are made compulsory. The second aspect is definitely not only of academic interest but would play a major role in the case of a second wave.

We believe that the reduction in the growth rates of infections by 40% to 60% is our best estimate of the effects of face masks. The most convincing argument stresses that Jena introduced face masks before any other region did so. It announced face masks as the first region in Germany while in our post-treatment period no other public health measures were introduced or eased. Hence, it provides the most clear-cut experiment of its effects. Second, as stated above, Jena is a fairly representative region of Germany in terms of Covid-19 cases. Third, the smaller effects observed in the multiple treatment analysis may also result from the fact that –by the time that other regions followed the example of Jena– behavioral adjustments in Germany's population had also taken place. Wearing face masks gradually became more common and more and more people started to adopt their usage even when it was not yet required.

We should also stress that 40 to 60% might still be a lower bound. The daily growth rates in the number of infections when face masks were introduced was around 2 to 3%. These are very low growth rates compared to the early days of the epidemic in Germany, where daily growth rates also lay above 50% (Wälde, 2020). One might therefore conjecture that the effects might have been even greater if masks had been introduced earlier.

We simultaneously stress the need for more detailed analyses. First, Germany is only one country. Different norms or climatic conditions might change the picture for other countries. Second, we have ignored spatial dependencies in the epidemic diffusion of Covid-19. This might play a role. Third, there are various types of face masks. We cannot identify differential effects since mask regulations in German regions do not require a certain type. This calls for further systematic causal analyses of the different health measure implemented to fight the spread of Covid-19. Our results provide some initial empirical evidence on this important matter.

References

Abadie A. (2019), Using Synthetic Controls: Feasibility, Data Requirements, and Methodological Aspects. Article prepared for the *Journal of Economic Literature*. https://economics.mit.edu/files/17847

Abadie A., & Gardeazabal J. (2003), The Economic Costs of Conflict: A Case Study of the Basque Country. *American Economic Review*, 93(1): 113–132. https://www.aeaweb.org/articles?id=10.1257/000282803321455188

Abadie A., A. Diamond, & J. Hainmueller (2010), Synthetic Control Methods for Comparative Case Studies: Estimating the Effect of California's Tobacco Control Program. *Journal of the American Statistical Association*, 105(490): 493–505. https://doi.org/10.1198/jasa.2009.ap08746

Abadie, A., Diamond, A., & Hainmueller, J. (2020), Synth: Stata module to implement synthetic control methods for comparative case studies. Revised version 2020-05-09. https://econpapers.repec.org/software/bocbocode/s457334.htm

Becker S., Heblich S., & Sturm D. (2018), The Impact of Public Employment: Evidence from Bonn, CESifo Working Paper Series 6841, CESifo Group Munich. http://ftp.iza.org/dp11255.pdf

Campos N., Coricelli F., & Moretti L. (2019), Institutional integration and economic growth in Europe. *Journal of Monetary Economics*, 103: 88–104. https://doi.org/10.1016/j.jmoneco.2018.08.001

Donsimoni, J. R., R. Glawion, B. Plachter & K. Wälde (2020a), Projecting the Spread of COVID-19 for Germany, *German Economic Review*, 21: 181-216 https://www.iza.org/publications/dp/13094

Donsimoni, J. R., R. Glawion, B. Plachter, K. Wälde & C. Weiser (2020), Should Contact Bans Be Lifted in Germany? A Quantitative Prediction of Its Effects, *CESifo Economic Studies, forthcoming.* https://idw-online.de/de/attachmentdata79709.pdf

Friedson, A., D. McNichols, J.J. Sabia & D. Dave (2020), Did California's Shelter-In-Place Order Work? Early Coronavirus-Related Public Health Effects, IZA DP No 13160. https://www.iza.org/publications/dp/13160

Galiani, S., & B. Quistorff (2017), The synth_runner package: Utilities to automate synthetic control estimation using synth. *The Stata Journal*, 17(4), 834–849. https://doi.org/10.1177%2F1536867X1801700404

Greenhalgh, T., M. B. Schmid, T. Czypionka, D. Bassler & L. Gruer (2020), Face masks for the public during the covid-19 crisis, *BMJ* 2020;369:m1435. https://doi.org/10.1136/bmj.m1435

Howard, J., A. Huang, Z. Li, Z. Tufekci, V. Zdimal, H-M. v.d. Westhuizen, A. v. Delft, A. Price, L. Fridman, L-H. Tang, V. Tang, G. L. Watson, C.E. Bax, R. Shaikh, F. Questier, D. Hernandez, L.F. Chu, C.M. Ramirez & A. W. Rimoin (2020), Face Masks Against COVID-19: An Evidence Review, Preprints 2020, 2020040203. https://www.doi.org/10.20944/preprints202004.0203.v1

Hu L., R. Kaestner, B. Mazumder, S. Miller & A. Wong (2018), The effect of the affordable care act Medicaid expansions on financial wellbeing, *Journal of Public Economics* 163:99-112. https://doi.org/10.1016/j.jpubeco.2018.04.009.

Kleyer, C., R. Kosfeld, T. Mitze & K. Wälde (2020), Public health measures concerning Covid-19 in Germany: a systematic overview, *mimeo.*

Kreif, N., R. Grieve, D. Hangartner, A. J. Turner, S. Nikolova, & M. Sutton (2016). Examina-tion of the synthetic control method for evaluating health policies with multiple treated units. *Health Economics* 25(12): 1514–1528. https://doi.org/10.1002/hec.3258

Lauer, S.A., K.H. Grantz, Q. Bi, F.K. Jones, Q. Zheng, H.R. Meredith, A.S. Azman, N.G. Reich & J. Lessler (2020), The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application, *Annals of Internal Medicine* 172: 577–582. https://doi.org/10.7326/M20-0504

Leung, N. H. L., D. K. W. Chu, E. Y. C. Shiu, K-H. Chan, J. J. McDevitt, B. J. P. Hau, H-L. Yen, Y. Li, D. K. M. Ip, J. S. M. Peiris, W-H. Seto, G. M. Leung, D. K. Milton & B. J. Cowling (2020) Respiratory virus shedding in exhaled breath and efficacy of face masks, Nat Med 26, 676–680. https://doi.org/10.1038/s41591-020-0843-2

Linton, N.M., T. Kobayashi, Y. Yang, K. Hayashi, A.R. Akhmetzhanov, S.-M. Jung, B. Yuan, R. Kinoshita & H. Nishiura (2020), Incubation period and other epidemiological characteristics of 2019 novel Coronavirus infections with right truncation: A statistical analysis of publicly available case data. *Journal of Clinical Medicine*, 9(2): 538. https://doi.org/10.3390/jcm9020538

Marasinghe, K.M. (2020), Concerns around public health recommendations on face mask use among individuals who are not medically diagnosed with COVID-19 supported by a systematic review search for evidence., *PREPRINT (Version 3) available at Research Square* https://doi.org/10.21203/rs.3.rs-16701/v3.

Pieters, H., R. Curzi, A. Olper & J. Swinnen (2017). Effect of democratic reforms on child mortality: A synthetic control Analysis. *The Lancet Global Health*, 4: e627-e632. https://doi.org/10.1016/S2214-109X(16)30104-8

Prather, K. A., C.C. Wang and R. T. Schooley, 2020, Reducing transmission of SARS-CoV-2, *Science* https://doi.org/10.1126/science.abc6197

Robert Koch Institute (2020): Covid-19 Infektionen, General Website (NPGEO Corona Hub): https://npgeo-corona-npgeo-de.hub.arcgis.com/

Wälde, K. (2020), Corona-Blog, Einschätzung vom Freitag, 20. März 2020, https://www.macro.economics.uni-mainz.de/2020/03/20/einschatzung-vom-freitag-20-marz/

Supplementary Appendix for

Face Masks Considerably Reduce Covid-19 Cases in Germany

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A synthetic control method approach

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A. Timing of introduction of mandatory face masks

Table A1: Overview of dates when masks became compulsory in federal states and districts

Federal State	Public transport	Sales shops	Individual NUTS3 region	Introduction of face masks	Difference in days to state
Baden-Wurttemberg	27.04.2020	27.04.2020	LK Rottweil	17.04.2020	10
Bavaria	27.04.2020	27.04.2020			
Berlin	27.04.2020	29.04.2020			
Brandenburg	27.04.2020	27.04.2020			
Bremen	27.04.2020	27.04.2020			
Hamburg	27.04.2020	27.04.2020			
Hesse	27.04.2020	27.04.2020	Main-Kinzig-Kreis	20.04.2020	7
Mecklenburg-West Pomer.	27.04.2020	27.04.2020			
Lower Saxony	27.04.2020	27.04.2020	Wolfsburg	20.04.2020	7
			Braunschweig	25.04.2020	2
North Rhine-Westphalia	27.04.2020	27.04.2020			
Rheinland-Pfalz	27.04.2020	27.04.2020			
Saarland	27.04.2020	27.04.2020			
Saxony	20.04.2020	20.04.2020			
Saxony-Anhalt	22.04.2020	22.04.2020			
Schleswig-Holstein	29.04.2020	29.04.2020			
Thuringia	24.04.2020	24.04.2020	Jena	06.04.2020	18
			Nordhausen	14.04.2020	10

Notes: A comprehensive overview of all public health measures introduced in German federal states and individual regions is given in Kleyer et al. (2020).