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# Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers

FREE

## A Randomized Controlled Trial

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Author, Article and Disclosure Information

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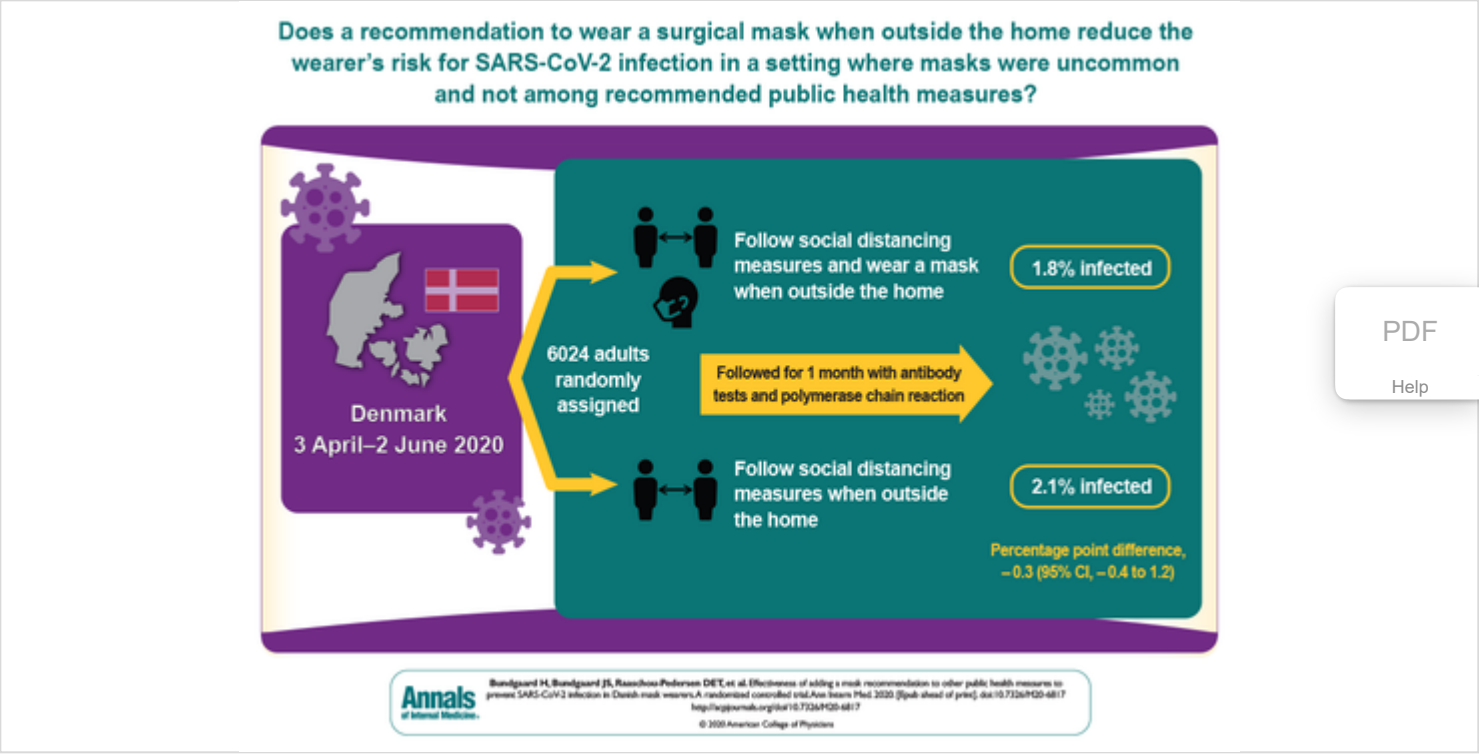


Visual Abstract. Effectiveness of Mask Recommendation for Preventing SARS-CoV-2 Infection

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Help

Observational evidence suggests that mask wearing mitigates SARS-CoV-2 transmission. It is uncertain if this observed association arises through protection of uninfected wearers (protective effect), via reduced transmission from infected mask wearers (source control), or both. This randomized controlled trial investigates whether recommending surgical mask use when outside the home reduces wearers' risk for SARS-CoV-2 infection in a setting where masks were uncommon and not among recommended public health measures.

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## Abstract


### Background:

Observational evidence suggests that mask wearing mitigates transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is uncertain if this observed association arises through protection of uninfected wearers (protective effect), via reduced transmission from infected mask wearers (source control), or both.

### Objective:

To assess whether recommending surgical mask use outside the home reduces wearers' risk for SARS-CoV-2 infection in a setting where masks were uncommon and not among recommended public health measures.

### Design:

Randomized controlled trial (DANMASK-19 [Danish Study to Assess Face Masks for the Protection Against COVID-19 Infection]). (ClinicalTrials.gov: NCT04337541)

### Setting:

Denmark, April and May 2020.

**Participants:**

Adults spending more than 3 hours per day outside the home without occupational mask use.

**Intervention:**

Encouragement to follow social distancing measures for coronavirus disease 2019, plus either no mask recommendation or a recommendation to wear a mask when outside the home among other persons together with a supply of 50 surgical masks and instructions for proper use.

**Measurements:**

The primary outcome was SARS-CoV-2 infection in the mask wearer at 1 month by antibody testing, polymerase chain reaction (PCR), or hospital diagnosis. The secondary outcome was PCR positivity for other respiratory viruses.

**Results:**

A total of 3030 participants were randomly assigned to the recommendation to wear masks, and 2994 were assigned to control; 4862 completed the Infection with SARS-CoV-2 occurred in 42 participants recommended masks (1.8%) and 53 control participants (2.1%). The between-group difference was −0.3 percentage point (95% CI, −1.2 to 0.4 percentage point; $P = 0.38$) (odds ratio, 0.82 [CI, 0.54 to 1.23]; $P = 0.33$). Multiple imputation accounting for loss to follow-up yielded similar results. Although the difference observed was not statistically significant, the 95% CIs are compatible with a 46% reduction to a 23% increase in infection.

**Limitation:**

Inconclusive results, missing data, variable adherence, patient-reported findings on home tests, no blinding, and no assessment of whether masks could decrease disease transmission from mask wearers to others.

**Conclusion:**

The recommendation to wear surgical masks to supplement other public health measures did not reduce the SARS-CoV-2 infection rate among wearers by more than 50% in a community with modest infection rates, some degree of social distancing, and uncommon general mask use. The data were compatible with lesser degrees of self-protection.

**Primary Funding Source:**

The Salling Foundations.

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), has infected more than 54 million persons (1, 2). Measures to impede transmission in health care and community settings are essential (3). The virus is transmitted person-to-person, primarily through the mouth, nose, or eyes via respiratory droplets, aerosols, or fomites (4, 5). It can survive on surfaces for up to 72 hours (6), and touching a contaminated surface followed by face touching is another possible route of transmission (7). Face masks are a plausible means to reduce transmission of respiratory viruses by minimizing the risk that respiratory droplets will reach wearers' nasal or oral mucosa. Face masks are

also hypothesized to reduce face touching (8, 9), but frequent face and mask touching has been reported among health care personnel (10). Observational evidence supports the efficacy of face masks in health care settings (11, 12) and as source control in patients infected with SARS-CoV-2 or other coronaviruses (13).

An increasing number of localities recommend masks in community settings on the basis of this observational evidence, but recommendations vary and controversy exists (14). The World Health Organization (WHO) and the U.S. Centers for Disease Control and Prevention (15) strongly recommend that persons with symptoms or known infection wear masks to prevent transmission of SARS-CoV-2 to others (source control) (16). However, WHO acknowledges that we lack evidence that wearing a mask protects healthy persons from SARS-CoV-2 (prevention) (17). A systematic review of observational studies reported that mask use reduced risk for SARS, Middle East respiratory syndrome, and COVID-19 by 66% overall, 70% in health care workers, and 44% in the community (12). However, surgical and cloth masks were grouped in preventive studies, and none of the 3 included non–health care studies related directly to COVID-19. Another systematic review ( American College of Physicians recommendations (19) concluded that evidence on mask effectiveness for respiratory infection prevention is stronger in health care than community settings.



Observational evidence suggests that mask wearing mitigates SARS-CoV-2 transmission, but whether this observed association arises because masks protect uninfected wearers (protective effect) or because transmission is

reduced from infected mask wearers (source control) is uncertain. Here, we report a randomized controlled trial (20) that assessed whether a recommendation to wear a surgical mask when outside the home among others reduced wearers' risk for SARS-CoV-2 infection in a setting where public health measures were in effect but community mask wearing was uncommon and not recommended.

## Methods

### Trial Design and Oversight

DANMASK-19 (Danish Study to Assess Face Masks for the Protection Against COVID-19 Infection) was an investigator-initiated, nationwide, unblinded, randomized controlled trial (ClinicalTrials.gov: NCT04337541). The trial protocol was registered with the Danish Data Protection Agency (P-2020-311) (Part 10 of the Supplement) and published (21). The researchers presented the protocol to the independent regional scientific ethics committee of the Capital Region of Denmark, which did not require ethics approval (H-20023709) in accordance with Danish legislation (Parts 11 and 12 of the Supplement). The trial was done in accordance with the principles of the Declaration of Helsinki.



### Participants and Study Period

During the study period (3 April to 2 June 2020), Danish authorities did not recommend use of masks in the community and mask use was uncommon

(<5%) outside hospitals (22). Recommended public health measures included quarantining persons with SARS-CoV-2 infection, social distancing (including in shops and public transportation, which remained open), limiting the number of persons seen, frequent hand hygiene and cleaning, and limiting visitors to hospitals and nursing homes (23, 24). Cafés and restaurants were closed during the study until 18 May 2020.

Eligible persons were community-dwelling adults aged 18 years or older without current or prior symptoms or diagnosis of COVID-19 who reported being outside the home among others for at least 3 hours per day and who did not wear masks during their daily work. Recruitment involved media advertisements and contacting private companies and public organizations. Interested citizens had internet access to detailed study information and to research staff for questions (Part 3 of the Supplement). At baseline, participants completed a demographic survey and provided consent for researchers to access their national registry data (Parts 4 and 5 of the Supplement). Recruitment occurred from 3 through 24 April 2020. Half of participants were randomly assigned to a group on 12 April and half on 24 April.



## Intervention

Participants were enrolled and data registered using Research Electronic Data Capture (REDCap) software (25). Eligible participants were randomly assigned 1:1 to the mask or control group using a computer algorithm and were stratified by the 5 regions of Denmark (Supplement Table 1).

Participants were notified of allocation by e-mail, and study packages were sent by courier (Part 7 of the Supplement). Participants in the mask group were instructed to wear a mask when outside the home during the next month. They received 50 three-layer, disposable, surgical face masks with ear loops (TYPE II EN 14683 [Abena]; filtration rate, 98%; made in China). Participants in both groups received materials and instructions for antibody testing on receipt and at 1 month. They also received materials and instructions for collecting an oropharyngeal/nasal swab sample for polymerase chain reaction (PCR) testing at 1 month and whenever symptoms compatible with COVID-19 occurred during follow-up. If symptomatic, participants were strongly encouraged to seek medical care. They registered symptoms and results of the antibody test in the online REDCap system. Participants returned the test material by prepaid express courier.

Written instructions and instructional videos guided antibody testing, oropharyngeal/nasal swabbing, and proper use of masks (Part 8 of the Supplement), and a help line was available to participants. In accordance with WHO recommendations for health care settings at that time, participants were instructed to change the mask if outside the home f more than 8 hours. At baseline and in weekly follow-up e-mails, participants in both groups were encouraged to follow current COVID-19 recommendations from the Danish authorities.



## Antibody and Viral PCR Testing

Participants tested for SARS-CoV-2 IgM and IgG antibodies in whole blood using a point-of-care test (Lateral Flow test [Zhuhai Livzon Diagnostics]) according to the manufacturer's recommendations and as previously described (26). After puncturing a fingertip with a lancet, they withdrew blood into a capillary tube and placed 1 drop of blood followed by 2 drops of saline in the test chamber in each of the 2 test plates (IgM and IgG). Participants reported IgM and IgG results separately as "1 line present" (negative), "2 lines present" (positive), or "I am not sure, or I could not perform the test" (treated as a negative result). Participants were categorized as seropositive if they had developed IgM, IgG, or both. The manufacturer reported that sensitivity was 90.2% and specificity 99.2%. A previously reported internal validation using 651 samples from blood donors before November 2019 and 155 patients with PCR-confirmed SARS-CoV-2 infection estimated a sensitivity of 82.5% (95% CI, 75.3% to 88.4%) and specificity of 99.5% (CI, 98.7% to 99.9%) (26). We (27) and others (28) have reported that oropharyngeal/nasal swab sampling for SARS-CoV-2 by participants, as opposed to health care workers, is clinically useful. Descriptions of RNA extraction, primer and probe used, reverse transcription, preamplifica… and microfluidic quantitative PCR are detailed in Part 6 of the Supple…



## Data Collection

Participants received 4 follow-up surveys (Parts 4 and 5 of the Supplement) by e-mail to collect information on antibody test results, adherence to recommendations on time spent outside the home among others,

development of symptoms, COVID-19 diagnosis based on PCR testing done in public hospitals, and known COVID-19 exposures.

## Outcomes

The primary outcome was SARS-CoV-2 infection, defined as a positive result on an oropharyngeal/nasal swab test for SARS-CoV-2, development of a positive SARS-CoV-2 antibody test result (IgM or IgG) during the study period, or a hospital-based diagnosis of SARS-CoV-2 infection or COVID-19. Secondary end points included PCR evidence of infection with other respiratory viruses (Supplement Table 2).

## Sample Size Calculations

The sample size was determined to provide adequate power for assessment of the combined composite primary outcome in the intention-to-treat analysis. Authorities estimated an incidence of SARS-CoV-2 infection of at least 2% during the study period. Assuming that wearing a face mask halves risk for infection, we estimated that a sample of 4636 participants wou provide the trial with 80% power at a significance level of 5% (2-sided $\alpha$ level). Anticipating 20% loss to follow-up in this community-based study, we aimed to assign at least 6000 participants.



## Statistical Analysis

Participants with a positive result on an antibody test at baseline were excluded from the analyses. We calculated CIs of proportions assuming binomial distribution (Clopper–Pearson).

The primary composite outcome (intention-to-treat) was compared between groups using the $\chi^2$ test. Odds ratios and confidence limits were calculated using logistic regression. We did a per protocol analysis that included only participants reporting complete or predominant use of face masks as instructed. A conservative sensitivity analysis assumed that participants with a positive result on an antibody test at the end of the study who had not provided antibody test results at study entrance had had a positive result at entrance. To further examine the uncertainty of loss to follow-up, we did (post hoc) 200 imputations using the R package smcfcs, version 1.4.1 (29), to impute missing values of outcome. We included sex, age, type of work, time out of home, and outcome in this calculation.

Prespecified subgroups were compared by logistic regression analysis. In a post hoc analysis, we explored whether there was a subgroup defined by a constellation of participant characteristics for which a recommendati wear masks seemed to be effective. We included sex, age, type of work, out of home, and outcome in this calculation.

Two-sided *P* values less than 0.05 were considered statistically significant. Analyses were done using R, version 3.6.1 (R Foundation).



## Role of the Funding Source

An unrestricted grant from the Salling Foundations supported the study, and the BESTSELLER Foundation donated the Livzon tests. The funders did not influence study design, conduct, or reporting.

## Results

### Participants

A total of 17 258 Danish citizens responded to recruitment, and 6024 completed the baseline survey and fulfilled eligibility criteria. The first participants (group 1; $n = 2995$) were randomly assigned on 12 April 2020 and were followed from 14 to 16 April through 15 May 2020. Remaining participants (group 2; $n = 3029$) were randomly assigned on 24 April 2020 and were followed from 2 to 4 May through 2 June 2020. A total of 3030 participants were randomly assigned to the recommendation to wear face masks, and 2994 were assigned not to wear face masks (Figure); 4862 participants (80.7%) completed the study. Table 1 shows baseline characteristics, which were well balanced between groups. Participants reported having spent a median of 4.5 hours per day outside the home



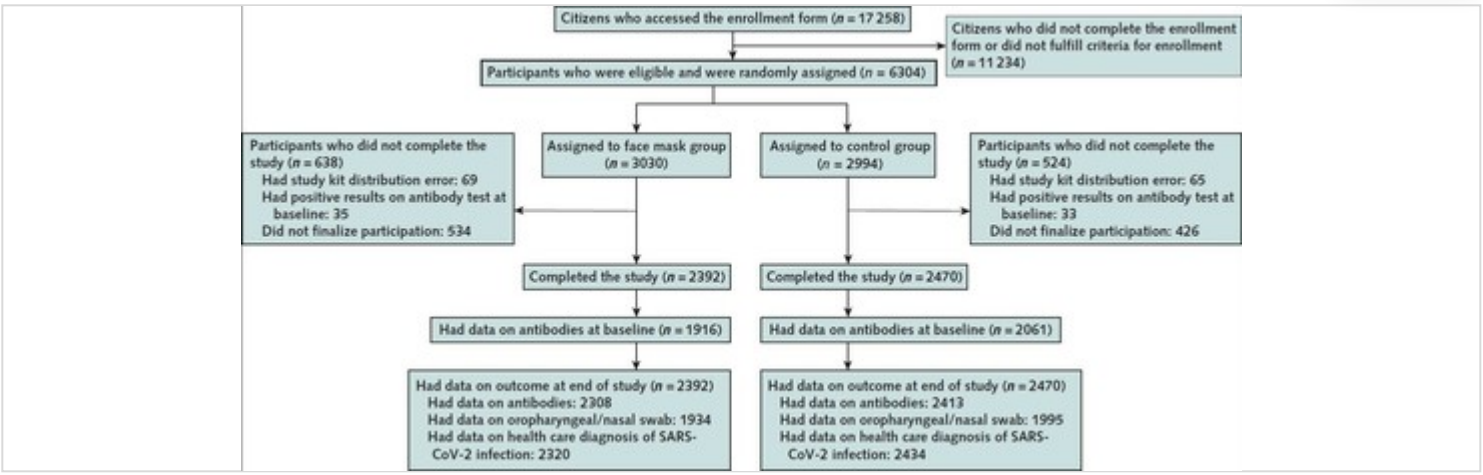

**Figure. Study flow diagram.**

Inclusion and exclusion criteria are described in the Methods section, and criteria for completion of the study are given in the Supplement. SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

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Table 1. Characteristics of Participants Completing the Study

*Table 1.* Characteristics of Participants Completing the Study

| Characteristic | Face Mask Group (*n* = 2392) | Control Group (*n* = 2470) |
|---|---|---|
| Mean age (SD), *y* | 47.4 (14) | 47.0 (13) |
| Female sex, *n* (%) | 1545 (64.6) | 1571 (63.6) |
| Smoker, *n* (%) | 478 (20.0) | 499 (20.2) |
| Wears eyeglasses daily, *n* (%) | 956 (40.0) | 929 (37.6) |
| Capital Region resident, *n* (%)* | 1220 (51.0) | 1289 (52.2) |
| Provided antibody test results at baseline, *n* (%) | 1916 (80.1) | 2061 (83.4) |
| Occupation, *n* (%) | | |
| Shop employee | 108 (4.5) | 85 (3.4) |
| Cashier | 101 (4.2) | 96 (3.9) |
| Craftsperson | 110 (4.6) | 103 (4.2) |
| Office employee | 265 (11.1) | 312 (12.6) |
| Manager | 111 (4.6) | 108 (4.4) |
| Transportation employee | 617 (25.8) | 625 (25.3) |
| Service employee | 107 (4.5) | 104 (4.2) |
| Home care/nursing home employee | 197 (8.2) | 229 (9.3) |
| Early childhood care staff | 89 (3.7) | 88 (3.6) |
| Salesperson | 37 (1.5) | 47 (1.9) |
| Other | 650 (27.2) | 673 (27.2) |

* According to national authority data, the Capital Region had a higher frequency of coronavirus disease 2019 than other Danish regions; see subgroup analyses in **Supplement Figure 2** (available at Annals.org).

## Adherence

Based on the lowest adherence reported in the mask group during follow-up, 46% of participants wore the mask as recommended, 47% predominantly as recommended, and 7% not as recommended.



## Primary Outcome

The primary outcome occurred in 42 participants (1.8%) in the mask group and 53 (2.1%) in the control group. In an intention-to-treat analysis, the between-group difference was −0.3 percentage point (CI, −1.2 to 0.4 percentage point; $P = 0.38$) (odds ratio [OR], 0.82 [CI, 0.54 to 1.23]; $P = 0.33$) in

favor of the mask group (Supplement Figure 1). When this analysis was repeated with multiple imputation for missing data due to loss to follow-up, it yielded similar results (OR, 0.81 [CI, 0.53 to 1.23]; $P = 0.32$). Table 2 provides data on the components of the primary end point, which were similar between groups.

Table 2. Distribution of the Components of the Composite Primary Outcome

*Table 2.* Distribution of the Components of the Composite Primary Outcome

| Outcome Component | Face Mask Group ($n = 2392$), $n$ (%) | Control Group ($n = 2470$), $n$ (%) | Odds Ratio (95% CI)* |
|---|---|---|---|
| Primary composite end point | 42 (1.8) | 53 (2.1) | 0.82 (0.54–1.23) |
| Positive antibody test result† | | | |
| IgM | 31 (1.3) | 37 (1.5) | 0.87 (0.54–1.41) |
| IgG | 33 (1.4) | 32 (1.3) | 1.07 (0.66–1.75) |
| Positive SARS-CoV-2 RT-PCR | 0 (0) | 5 (0.2) | – |
| Health care–diagnosed SARS-CoV-2 or COVID-19 | 5 (0.2) | 10 (0.4) | 0.52 (0.18–1.53) |

COVID-19 = coronavirus disease 2019; RT-PCR = reverse transcriptase polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
* Calculated using logistic regression. The between-group differences in frequencies of positive SARS-CoV-2 RT-PCR were not statistically significant ($P = 0.079$).
† 124 participants in the mask group and 140 in the control group registered "not done" or unclear results of the antibody test—i.e., they were included in the analysis because they sent an oropharyngeal swab for PCR.

In a per protocol analysis that excluded participants in the mask group who reported nonadherence (7%), SARS-CoV-2 infection occurred in 40 participants (1.8%) in the mask group and 53 (2.1%) in the control group (between-group difference, −0.4 percentage point [CI, −1.2 to 0.5 percentage point]; $P = 0.40$) (OR, 0.84 [CI, 0.55 to 1.26]; $P = 0.40$). Supplement Figure 2 provides results of the prespecified subgroup analyses of the primary composite end point. No statistically significant interactions were ide



In the preplanned sensitivity analysis, those who had a positive result on an antibody test at 1 month but had not provided antibody results at baseline were considered to have had positive results at baseline ($n = 18$)—that is, they were excluded from the analysis. In this analysis, the primary outcome occurred in 33 participants (1.4%) in the face mask group and 44 (1.8%) in

the control group (between-group difference, −0.4 percentage point [CI, −1.1 to 0.4 percentage point]; $P = 0.22$) (OR, 0.77 [CI, 0.49 to 1.22]; $P = 0.26$).

Three post hoc (not preplanned) analyses were done. In the first, which included only participants reporting wearing face masks "exactly as instructed," infection (the primary outcome) occurred in 22 participants (2.0%) in the face mask group and 53 (2.1%) in the control group (between-group difference, −0.2 percentage point [CI, −1.3 to 0.9 percentage point]; $P = 0.82$) (OR, 0.93 [CI, 0.56 to 1.54]; $P = 0.78$). The second post hoc analysis excluded participants who did not provide antibody test results at baseline; infection occurred in 33 participants (1.7%) in the face mask group and 44 (2.1%) in the control group (between-group difference, −0.4 percentage point [CI, −1.4 to 0.4 percentage point]; $P = 0.33$) (OR, 0.80 [CI, 0.51 to 1.27]; $P = 0.35$). In the third post hoc analysis, which investigated constellations of patient characteristics, we did not find a subgroup where face masks were effective at conventional levels of statistical significance (data not shown).

A total of 52 participants in the mask group and 39 control participants reported COVID-19 in their household. Of these, 2 participants in the [illegible] mask group and 1 in the control group developed SARS-CoV-2 infection, suggesting that the source of most observed infections was outside the home. Reported symptoms did not differ between groups during the study period (Supplement Table 3).



## Secondary Outcomes

In the mask group, 9 participants (0.5%) were positive for 1 or more of the 11 respiratory viruses other than SARS-CoV-2, compared with 11 participants (0.6%) in the control group (between-group difference, −0.1 percentage point [CI, −0.6 to 0.4 percentage point]; $P = 0.87$) (OR, 0.84 [CI, 0.35 to 2.04]; $P = 0.71$). Positivity for any virus, including SARS-CoV-2, occurred in 9 mask participants (0.5%) versus 16 control participants (0.8%) (between-group difference, −0.3 percentage point [CI, −0.9 to 0.2 percentage point]; $P = 0.26$) (OR, 0.58 [CI, 0.25 to 1.31]; $P = 0.19$).

## Discussion

In this community-based, randomized controlled trial conducted in a setting where mask wearing was uncommon and was not among other recommended public health measures related to COVID-19, a recommendation to wear a surgical mask when outside the home among others did not reduce, at conventional levels of statistical significance, incident SARS-CoV-2 infection compared with no mask recommendation. We designed the study to detect a reduction in infection rate from 2% to 1%. Although no statistically significant difference in SARS-CoV-2 incidenc observed, the 95% CIs are compatible with a possible 46% reduction to 23% increase in infection among mask wearers. These findings do offer evidence about the degree of protection mask wearers can anticipate in a setting where others are not wearing masks and where other public health measures, including social distancing, are in effect. The findings, however, should not be used to conclude that a recommendation for everyone to wear masks in the community would not be effective in reducing SARS-CoV-2

infections, because the trial did not test the role of masks in source control of SARS-CoV-2 infection. During the study period, authorities did not recommend face mask use outside hospital settings and mask use was rare in community settings (22). This means that study participants' exposure was overwhelmingly to persons not wearing masks.

The observed infection rate was similar to that reported in other large Danish studies during the study period (26, 30). Of note, the observed incidence of SARS-CoV-2 infection was higher than we had estimated when planning a sample size that would ensure more than 80% power to detect a 50% decrease in infection. The intervention lasted only 1 month and was carried out during a period when Danish authorities recommended quarantine of diagnosed patients, physical distancing, and hand hygiene as general protective means against SARS-CoV-2 transmission (23). Cafés and restaurants were closed through 18 May, but follow-up of the second randomized group continued through 2 June.

The first randomized group was followed while the Danish society was under lockdown. Reopening occurred (18 May 2020) during follow-up of the group of participants, but it was not reflected in the outcome because infection rates were similar between groups (Supplement Figure 2). The relative infection rate between mask wearers and those not wearing masks would most likely be affected by changes in applied protective means or in the virulence of SARS-CoV-2, whereas the rate difference between the 2 groups would probably not be affected solely by a higher—or lower—number of infected citizens.

Although we saw no statistically significant difference in presence of other respiratory viruses, the study was not sufficiently powered to draw definite conclusions about the protective effect of masks for other viral infections. Likewise, the study had limited power for any of the subgroup analyses.

The primary outcome was mainly defined by antibodies against SARS-CoV-2. This definition was chosen because the viral load of infected patients may be only transiently detectable (31, 32) and because approximately half of persons infected with SARS-CoV-2 are asymptomatic (33, 26). Masks have been hypothesized to reduce inoculum size (34) and could increase the likelihood that infected mask users are asymptomatic, but this hypothesis has been challenged (35). For these reasons, we did not rely solely on identification of SARS-CoV-2 in oropharyngeal/nasal swab samples. As mentioned in the Methods section, an internal validation study estimated that the point-of-care test has 82.5% sensitivity and 99.5% specificity (26).

The observed rate of incident SARS-CoV-2 infection was similar to what was estimated during trial design. These rates were based on thorough screening of all participants using antibody measurements combined with PCR, whereas the observed official infection rates relied solely on PCR test–estimates during the period. In addition, authorities tested only a small subset of primarily symptomatic citizens of the entire population, yielding low incidence rates. On this basis, the infection rates we report here are not comparable with the official SARS-CoV-2 infection rates in the Danish population. The eligibility requirement of at least 3 hours of exposure to other persons outside the home would add to this difference. Between 6

April and 9 May 2020, we found a similar seroprevalence of SARS-CoV-2 of 1.9% (CI, 0.8% to 2.3%) in Danish blood donors using the Livzon point-of-care test and assessed by laboratory technicians (36). Testing at the end of follow-up, however, may not have captured any infections contracted during the last part of the study period, but this would have been true in both the mask and control groups and was not expected to influence the overall findings.

The face masks provided to participants were high-quality surgical masks with a filtration rate of 98% (37). A published meta-analysis found no statistically significant difference in preventing influenza in health care workers between respirators (N95 [American standard] or FFP2 [European standard]) and surgical face masks (38). Adherence to mask use may be higher than observed in this study in settings where mask use is common. Some mask group participants (14%) reported adverse reactions from other citizens (Supplement Table 4). Although adherence may influence the protective effect of masks, sensitivity analyses had similar results across reported adherence.



How SARS-CoV-2 is transmitted—via respiratory droplets, aerosols, or (to a lesser extent) fomites—is not firmly established. Droplets are larger and rapidly fall to the ground, whereas aerosols are smaller (≤5 μm) and may evaporate and remain in the air for hours (39). Transmission of SARS-CoV-2 may take place through multiple routes. It has been argued that for the primary route of SARS-CoV-2 spread—that is, via droplets—face masks would be considered effective, whereas masks would not be effective against spread

via aerosols, which might penetrate or circumnavigate a face mask (37, 39). Thus, spread of SARS-CoV-2 via aerosols would at least partially explain the present findings. Lack of eye protection may also have been of importance, and use of face shields also covering the eyes (rather than face masks only) has been advocated to halt the conjunctival route of transmission (40, 41). We observed no statistically significant interaction between wearers and nonwearers of eyeglasses (Supplement Figure 2). Recent reports indicate that transmission of SARS-CoV-2 via fomites is unusual (42), but masks may alter behavior and potentially affect fomite transmission.

The present findings are compatible with the findings of a review of randomized controlled trials of the efficacy of face masks for prevention (as personal protective equipment) against influenza virus (18). A recent meta-analysis that suggested a protective effect of face masks in the non–health care setting was based on 3 observational studies that included a total of 725 participants and focused on transmission of SARS-CoV-1 rather than SARS-CoV-2 (12). Of 725 participants, 138 (19%) were infected, so the transmission rate seems to be higher than for SARS-CoV-2. Further, these studies focused on prevention of infection in healthy mask wearers from patients with known, diagnosed infection rather than prevention of transmission from persons in their surroundings in general. In addition, identified comparators (control participants) not wearing masks may also have missed other protective means. Recent observational studies that indicate a protective association between mandated mask use in the community and SARS-CoV-2 transmission are limited by study design and simultaneous introduction of other public health interventions (14, 43).

Several challenges regarding wearing disposable face masks in the community exist. These include practical aspects, such as potential incorrect wearing, reduced adherence, reduced durability of the mask depending on type of mask and occupation, and weather. Such circumstances may necessitate the use of multiple face masks during the day. In our study, participants used a mean of 1.7 masks per weekday and 1.3 per weekend day (Supplement Table 4). Wearing a face mask may be physically unpleasant, and psychological barriers and other side effects have been described (44). "Face mask policing" between citizens might reinforce use of masks but may be challenging. In addition, the wearer of a face mask may change to a less cautious behavior because of a false sense of security, as pointed out by WHO (17); accordingly, our face mask group seemed less worried (Supplement Table 4), which may explain their increased willingness to wear face masks in the future (Supplement Table 5). These challenges, including costs and availability, may reduce the efficacy of face masks to prevent SARS-CoV-2 infection.

The potential benefits of a community-wide recommendation to wear masks include combined prevention and source control for symptomatic and asymptomatic persons, improved attention, and reduced potential stigmatization of persons wearing masks to prevent infection of others (17). Although masks may also have served as source control in SARS-CoV-2–infected participants, the study was not designed to determine the effectiveness of source control.

The most important limitation is that the findings are inconclusive, with CIs compatible with a 46% decrease to a 23% increase in infection. Other limitations include the following. Participants may have been more cautious and focused on hygiene than the general population; however, the observed infection rate was similar to findings of other studies in Denmark (26, 30). Loss to follow-up was 19%, but results of multiple imputation accounting for missing data were similar to the main results. In addition, we relied on patient-reported findings on home antibody tests, and blinding to the intervention was not possible. Finally, a randomized controlled trial provides high-level evidence for treatment effects but can be prone to reduced external validity.

Our results suggest that the recommendation to wear a surgical mask when outside the home among others did not reduce, at conventional levels of statistical significance, the incidence of SARS-CoV-2 infection in mask wearers in a setting where social distancing and other public health measures were in effect, mask recommendations were not among those measures, and community use of masks was uncommon. Yet, the findings were inconclusive and cannot definitively exclude a 46% reduction to increase in infection of mask wearers in such a setting. It is important to emphasize that this trial did not address the effects of masks as source control or as protection in settings where social distancing and other public health measures are not in effect.



Reduction in release of virus from infected persons into the environment may be the mechanism for mitigation of transmission in communities where

mask use is common or mandated, as noted in observational studies. Thus, these findings do not provide data on the effectiveness of widespread mask wearing in the community in reducing SARS-CoV-2 infections. They do, however, offer evidence about the degree of protection mask wearers can anticipate in a setting where others are not wearing masks and where other public health measures, including social distancing, are in effect. The findings also suggest that persons should not abandon other COVID-19 safety measures regardless of the use of masks. While we await additional data to inform mask recommendations, communities must balance the seriousness of COVID-19, uncertainty about the degree of source control and protective effect, and the absence of data suggesting serious adverse effects of masks (45).

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## Comments

**19 Comments**

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Farmacologiche M.Negri, Milano, Italia • 26 November 2020

### Evidence from randomised controlled trials on the surgical masks' effect on the spread of respiratory infections in the community

Dear Editor:

In the Bundgaard et al. randomized controlled trial (RCT)[1], face mask use supplementing other public health measures did not significantly reduce SARS-CoV2 infection in people wearing the mask, albeit the results cannot exclude a 46% reduction or a 23% increase in infection among mask wearers. These findings seem to confirm the notion that recommendations on the public use of respiratory devices to prevent SARS-CoV-2 infection have low certainty evidence.[2]

Indirect supportive data can come from studies dealing with the protection offered by surgical masks in influenza-like illness (ILI). We conducted a systematic review and meta-analysis of RCTs (PROSPERO ID: CRD42020178913) on the use of surgical masks in the community as a mean to prevent the spreading of ILI. The population included students and households' members of any age and sex. The main outcome was the risk of ILI among mask users vs non-users. Eligible studies included RCTs published between January 1, 2005 and April 7, 2020 in English language. Two blinded reviewers independently screened the papers identified through a search strategy including umbrella and traditional reviews, based on PubMed/Medline and Embase libraries.[3]

Out of 422 papers, 11 RCTs assessed the role of wearing versus not wearing surgical masks on ILI prevention. Overall, the studies enrolled a total of 7469 subjects. The pooled random effect relative risk (RR) for face mask protection was 0·92 (95% CI:0·81-1·04), suggesting that wearing surgical masks in the community confer no significant protection against ILI in mask wearers. It should be noted that most studies in our meta-analysis were underpowered, and that 73% of them reported a poor adherence of participants to mask use. A sub-analysis of few high compliance studies showed a RR of 0·67, 95% CI:0·46-0·99.

Notably, the type of mask and the securing system may largely influence the filtering effectiveness of face masks, with surgical or procedural masks secured with elastic ear lobes showing the least filtration efficiency.[4]

At variance with observational studies, randomised trials have failed, up to now, to clearly document the utility of wearing masks to prevent SARS-CoV2 infection. A public health intervention promoting face mask use, is usually implemented at units larger than that of individuals. Hence, we suggest that a convenient study design would be a cluster randomised trial assessing, in a factorial way, the impact of promoting the combination of different components of individual protection on the prevention of SARS-CoV2 spreading.

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ANTONIO C BANDEIRA • Director, Brazilian Society of Infectious Diseases • 25 November 2020

## Multiple bias towards the Null

Any study to evaluate the effectiveness of wearing masks should be done with a very careful methodological approach in order to avoid multiple sources of error. We have learned so far that the risk of SARS-CoV-2 infection through the respiratory route is very high specially at home, at lunch and coffee-break times, where nobody uses any mask protection. In this randomized open trial, there was no control over these sources of infection. Besides, only 46% of participants wore the mask as recommended, a very low adherence level. With that in mind, I would expect the results to be biased towards no association between the use of masks and the risk of SARS-CoV-2 infection as the authors stated

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Tuan Nguyen • Garvan Institute of Medical Research • 23 November 2020

## A Bayesian interpretation of the effect of face mask on SARS-Cov-2 infection

Dear Editor:

I would like to offer an alternative interpretation of the DANMASK-19's data [1]. My interpretation centers on the question: *what is the probability that face mask wearing reduces the risk of SARS-Cov-2 infection*. This question can only be answered by a Bayesian approach that updates our pre-existing knowledge with new evidence [2].

Our pre-existing knowledge is informed by a recent meta-analysis which shows that surgical face mask is associated with a 13% reduction in the risk of acute respiratory infection (risk ratio [RR], 0.87; 95% confidence interval [CI], 0.74 to 1.04) [3]. Note that the average risk reduction reported in this meta-analysis is statistically comparable with that observed in the DANMASK-19 study (i.e., 18% risk reduction; RR, 0.82; 95% CI, 0.54 to 1.23).

When the distribution of relative risks obtained from the meta-analysis [3] is updated by the DANMASK-19's relative risk [1] by the Bayesian theorem [4], the new relative risk is 0.85, with 95% credible interval ranging from 0.72 to 0.99. Moreover, the probability that face mask wearing reduces the risk of SARS-Cov-2 infection by at least 50% is zero. Nevertheless, there is a 93% chance that face mask wearing reduces the risk of SARS-Cov-2 infection by at least 5%.



Thus, in settings with moderate Covid-19 infection (such as Denmark) the updated evidence suggests that wearing face mask may modestly protect the wearers from infection with SARS-Cov-2.

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[4] R codes available here: https://github.com/tuanvnguyen/Bayesian-analysis/blob/main/Normal-Normal%20model

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Constantine Manthous • Yale New Haven Health • 21 November 2020

## Masks didn't work? Not so fast

In the November 18 issue of *Annals,* Bundgaard et al conclude: “The recommendation to wear surgical masks to supplement other public health measures did not reduce the SARS-CoV-2 infection rate among wearers . . . (1)“ Not so quick. Study subjects were not required to wear masks at home. Their family members/visitors were neither taxed to wear masks in public nor were they tested for asymptomatic Covid, which is often spread in homes (2). Accordingly, it is plausible, if not likely, that some study subjects caught Covid in their own homes. This critical design flaw prevents any conclusion about the efficacy of masks for preventing Covid; a nuance that will be lost on non-scientists. Nonetheless, the erroneous conclusion was immediately trumpeted, using the *imprimatur* of *Annals,* to challenge mask-wearing. The effect – albeit inadvertent – is almost certain to be greater morbidity and mortality.

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Hadi Ali, MS , Gunce Kaya, MPhil [1], Khameinei Ali, MD, MBA [2][3] • [1] Ferkauf Graduate School of Psychology: Yeshiva University [2] Northwell Health [3] Zucker School of Medicine at Hofstra/ Northwell • 22 November 2020

## Regarding "Effectiveness of Adding a Mask Recommendation to Other Public Health Measures to Prevent SARS-CoV-2 Infection in Danish Mask Wearers"

We commend the authors of the study on broaching a much-debated subject in the current environment. The trial was designed to obtain the most power to detect a difference. Unfortunately, there were confounding variables that were unaccounted for and unmeasured.

There is a flaw in primary outcome ascertainment. False-negative rate and false positive rate of antibody testing, PCR, and diagnosis all vary widely. For example, sensitivity (IgM and IgG) of the antibody kit in this study (86.7% and 66.7%, respectively) is equivalent to a 64.6% PPV with a 5.0% prevalence [1]. This is even more pertinent in the low prevalence (1.2%) Danish population [2], [3].

Individuals who could not correctly perform the test were assumed negative, which would further skew the data. Additionally, the intention group attrition was higher than the control group (638 vs. 524). The characteristics of the study participants' households would heavily affect the data set as well. If family or house members were COVID-19 positive, mask-wearing outside of their homes would not protect them from their highest risk source (their homes).

We contest that an intent-to-treat analysis is inappropriate, given the authors' own published intervention adherence rate (46%). Multiple imputation analysis is simply an amplification of the data set and agreement between the original data set is a moot point. The homogeneous Danish population would make it difficult to externally validate this to other much more heterogeneous populations (i.e. New York).

It is questionable if the study is a true RCT as it lacked blinding and utilized a self-reported and self-measured primary outcome which opens it up to a majority of biases. Although the researchers cited their study for the equivalence of self-testing with healthcare professional testing, this may be inappropriate for research purposes and better suited for pandemic infection control [5].

Although the goal of the study was to publish the researchers' heard-earned data, contextualization in these volatile times is paramount. This study received 90,000 tweets by 60,000 users within 4 days of publication [4]. The majority of these tweets championed the study as evidence of the impotence of masks in the control of the COVID-19 pandemic. The authors of the study would agree that this is a gross misinterpretation of the research, which further points to the fact that the wording of the conclusion should have been chosen slightly more judiciously.

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**Disclosures:**

No disclosure to claim.

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Edward Siguel, MD, PhD • Self employed in biomedical research, MD, USA. • 23 November 2020

## Thought experiments and science predict that facemasks reduce viral loads and reduce severity of infection

The study is misleading; it did not consider adequately too many critical variables (factors) that have major impact on measured outcomes. Thought experiments from science predict that facemasks reduce viral loads and severity of infection.

Statistics describe outcomes, but does not explain causes. It is impossible to conduct experiments on all possible observations and outcomes, and it is not necessary. We can use “thought experiments”, which Einstein used to create Relativity. We had data on the movement of planets for over 100 years, but it took “thought” experiments for Newton to predict planetary movement via equations.

We understand enough about viruses to know the body produces and expels them, mostly via mouth and nose. We know an infected person can expel many viruses. A well-designed mask, and substantial obstruction, will reduce the number of virus expelled far into the air. A mask will absorb viruses. This is not “genius” physics. I knew about it since I was about 6 yo. My parents taught me to use a handkerchief, hold it to my nose, to prevent spreading “stuff” when I cough. It worked. There is no doubt that holding a paper towel or similar paper or cloth to the mouth reduces the amount of “stuff” going out when I cough.

To those who doubt it and need more “studies”, I propose they put themselves in front of people coughing without covering their mouth. Although it may not infect them, the fluids they get in the face and m provide evidence of how facemasks work.



Thus, a thought experiment and science provide probative evidence that facemasks can reduce the amount of “stuff” an infected person sends to the air. How much of a reduction depends on the nature of the facemask, how tight it is, how much it absorbs and retains fluid, etc. If everybody used facemasks in public places, viral loads in public places are reduced.

We do not need more studies of the obvious; we do not need a sample size of 1,000 people thrown out of 10$^{th}$ story windows to predict broken bones when they hit the concrete sidewalk. If a study of 10,000 people who took Vitamin EZY434 proved they fly like birds, I would not believe it because my thought experiment says it cannot be true.

Similarly, facemasks reduce particles absorbed from air. Known for years in construction, surgery, labs, etc.

Matthew A. Spinelli, David V. Glidden, Efstathios D. Gennatas, George W. Rutherford, Monica Gandhi • Departments of Medicine and Epidemiology, University of California, San Francisco • 20 November 2020

## Cluster randomization and adherence assessment are needed to test masks' true potential

We read with interest the study evaluating mask mandates in Denmark by Bundgaard and colleagues.[1] We commend the authors for performing a randomized trial of a non-pharmaceutical intervention in the midst of the pandemic. However, the study makes it difficult to draw conclusions about the impact of masks in preventing incident infection or severe COVID-19. Although masks were provided and recommended to participants, masking was not commonplace in Denmark at the time, and 14% of participants reported experiencing social harms due to masking. Only 46% of participants reported wearing a mask as recommended, and overreporting of adherence, as has been seen in previous prevention studies for stigmatizing interventions,[2] likely occurred. Notably, due to the complexity of interpreting self-reported adherence, HIV and sexually-transmitted infection prevention trials are now designed to incorporate objective assessment of adherence.

The study would have benefitted from inclusion of implementation science principles: understanding the desired behavior in its social context, cluster randomization, and assessment of intervention fidelity.[3] Recommending a potentially stigmatizing intervention in a minority of individuals within a community is, we believe, a major flaw in a study designed to evaluate a policy intervention. Cluster randomization would have allowed an entire community to be randomized to the recommendation, minimizing social harms to the individual and likely increasing intervention adherence. Assessment of intervention fidelity and acceptability, such as through direct observation within the community, would allow a more accurate interpretation of self-reported adherence data.

Use of cluster-randomization has other benefits. Masks are likely to be more effective in preventing forward transmission, in the context of high community uptake and adherence. By randomizing isolated members in the community to the mask recommendation, this study design cannot answer if "masks protect you."[4] Second, given the high proportion of asymptomatic COVID-19 infections, we do not know how many individuals were infected within their household bubbles. An optimal design would pursue a cluster-randomized approach, with sufficient power to detect incident (with PCR) rather than prevalent (with serology) infections, and assess disease severity via cataloging clinical outcomes (do masks lead to less severe infections via reduced inoculum?[5]). A mask recommendation for isolated members of a community is unlikely to be effective. We suggest that future studies assess the impact of recommendations to wear masks at the community-level, which will be more informative for public health officials trying to stem transmission and disease while awaiting an effective and widely available vaccine.



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Michael Cook • Vis a vis symposiums • 22 November 2020

### Authors state major limitations of study

The authors state the limitations of the study: Inconclusive results, missing data, variable adherence, patient-reported findings on home tests, no blinding, and no assessment of whether masks could decrease disease transmission from mask wearers to others. Asian countries have very low levels of COVID and for decades people wear mask if they think they have flu or a cold. The authors clearly state they could not assess this.

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Simon Thompson • Independent researcher • 22 November 2020

### This is extremely inadequate research to support forcing the entire world to wear masks

Before making any recomendations to wear masks adequate research would be needed but this hasn't occured. Whilst such measures are often described as a recommendation in the real world people are being forced to wear masks and in some countries quite agressively. This study finds no significant effects in relation to the alleged Sars-cov2 but does not look at the many other possible effects of wearing these. For example there has been a doubling in shootings in NY this year. Could the masks be contributing to this? Wh… effects on overall health? What are the dangers of conditioning people to accept forced medication i… violation of informed consent laws? Without having done any proper research to establish the long … effects it is incredibly reckless to be forcing masks on the entire world and this study shows how little is known about it. It is time to immediately end these impositions and any further experimentation on the public.



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Max Longin • Dipl.Math., Denmark, private • 23 November 2020

### This study design would not even proof that a 100% protection has a protective effect

Imagine a 100% perfect protection against COVID-19 (a hermetic room), what outcome should be expected for this by-definition safe group using this study design?

Here is the math only for estimating

- the false-positive antibody-tests

- positive test due to before-baseline infections

But as the study design grants protection at average only 4.5 hours/day further infections outside the room (in the study false-classified as noneffective protection) should be added to the calculated expectations.

The study reports antibody testing has an estimated 99,2% specificity. For about 2400 tests this leads to an expectation of 2400*0.008=19 false-positive tests in each antibody test group.

IgG-antibodies form very delayed and persist very long. So in non-increasing rate of new infections (as the case in 05/2020 in Denmark) about 80% of all true-positive IgG tests at study-end show infections before study-baseline. So the expectation of positive tests due to before-baseline infections in the control group is 10.4 (80% of 13 (=32-19) „true-positive“ IgG tests)

The mentioned false-detection arises solely by a test-property (specificity) and before-baseline events, so the expectations for the control group for false-positive test (19) and for true-positive tests due to before-baseline infections (10.4) equals the expectations for the safe group, adding up to: expectation(IgG-SafeGroup)=29.4

IgM-tests respond from >2-6 weeks after infection. So about 50% of the IgM true positive tests are likely due to before-baseline infections. Analogue to above 19 false positive and 9 positive IgM tests (50% of 18 (=37-19) „true-positive“ IgM tests) due to before-baseline infections sum up to: expectation(IgM-SafeGroup)=29

PCR-tests hardly suffer from specifity and time lags in the study, so no positive PCR-tests should be expected in the safe group: expectation(PCR-SafeGroup)=0

A temporally evenly distributed health care diagnosis during study will again suffer from the delay from infection to diagnosis (first 9 days (=30% of 30 days) diagnosis will likely show before-baseline infections). So 0,3*10=3 cases are likely due to before-baseline infections and have to be expected for the safe group: expectation(HealthCare-SafeGroup)=3



Even without additional expected infections at home, friends etc. - falsely assigned as inside the hermetic room the expected outcome in the by-definition safe group is already about 75% of the control outcome (or 90% of the face-mask-group).

Altogether this study design expects for a by-definition 100%-protection:

- measure an Odd Ratio of ≥0.75 (≤25% protection),

- include OR=1 (i.e. no-protection-at-all) in the 95%-Confidence Interval and

- exclude OR≤0.4 (≥60% protection) from 95%-CI

Janet Rand, OD • Concerned US citizen • 20 November 2020

## Mis-leading study . Results need to be made more clear.*" Exposure was to persons NOT wearing masks"*

This study does NOT show that mask wearing in ineffective in mitigating the spread of Corona Virus / COVID-19 / SARS-CoV-2. It shows (what we already knew) that wearing a mask does not protect the person wearing the mask as much as we would like. The reason you wear a mask is to keep your viral particles to yourself - don't spread them to others. Unfortunately, anti-maskers are using this study as "prof" that they don't need to wear masks. This is irresponsible and should be made clear in the title of the study. From the discussion: "The findings, however, should not be used to conclude that a recommendation for everyone to wear masks in the community would not be effective in reducing SARS-CoV-2 infections, because the trial did not test the role of masks in source control of SARS-CoV-2 infection. During the study period, authorities did not recommend face mask use outside hospital settings and mask use was rare in community settings (22). This means that study participants' exposure was overwhelmingly to persons not wearing masks."

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Dr Rosamond A K Jones • #UsforThemUK • 18 November 2020

## Will mandatory mask usage be scaled back in light of these results?

Dr Bundgaard and colleagues are to be congratulated on this well-constructed randomised trial, at a time when much policy has been based on weak observational or laboratory-based studies. Their results highlight the dilemma that lack of evidence for benefit is unlikely to alter public policy. The suggestion that mask wearing is for the protection of others, rather than of the wearer, has created a climate of discrimination against those with genuine medical exemptions. This is especially worrying when applied to school children, known to play a very small role in transmission of Sars-Cov-2. In particular, the creeping use of masks in classrrooms in the UK, has resulted in many reports of children feeling alienated and unable to understand their teachers. Parents of primary school children are being instructed to wear masks when collecting their children from the school playground, giving children a potent message that they and their parents are all a danger to one another. The long-term mental health impacts of this are yet to be fully realised.



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Brenda Marfin • Not affiliate. I have a Ph.D. In educational leadership • 18 November 2020

## Mis-representation of research purpose

Members of the general public are referencing this research as a battle cry that communities do not need to wear masks in public. After reading the entire article, I ascertained that telling the general public to stop wearing masks was not the purpose or outcome of this research.
During these tumultuous times it might be a moral imperative to include some type of explanation with this research. Very few individuals outside of the medical profession will take the time to thoroughly read the article and analyze the outcomes.

Sincerely,

Brenda Marfin, Ph.D.
Unassociated at this time while caring for my husband with end stage renal disease and Alzheimer's. I depend on the kindness (and myself) of others to wear a mask.

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Ambuj Kumar, MD, MPH • Professor, Department of Internal Medicine Director, Morsani College of Medicine, University of South Florida, Tampa • 19 November 2020

### In absence of an objective mechanism to track the intervention what are we counting?

The effort by Dr. Bundgaard and colleagues is commendable. However, the trial design and the associated results remind me of the randomized controlled trials assessing the efficacy of a "prayer" intervention. The fundamental issue with mask intervention and social distancing, like prayer, is the lack of objective mechanisms to ensure and track compliance or non-compliance (lack of an accurate method to track who is praying or not praying). As an example, the authors state that only "46% of participants wore the mask as recommended" in the mask group but failed to ask participants in the no mask group about their usage of the mask. Furthermore, a mask is considered an added layer of protection with social distancing and therefore the mask's added effects would be challenging to deduce. Accordingly, given this basic challenge of delivering an intervention without tracking/confirmation mechanism, the results, at best, can be considered anecdotal. The desire for evidence from a randomized controlled trial for an intervention question is understandable. However, logistical challenges associated with the reliable implementation of the intervention (i.e., mask) and tracking of adherence makes the conduct of a randomized trial to assess the efficacy of mask a non-starter. The efficacy of a mask needs to be framed in the context of reducing the risk and not binary choices of works or does not work.

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Eric Thompson • Independent Researcher • 18 November 2020

### Please *clarify* your policy recommendations



In light of your recent research, will you please **clarify** your policy recommendations? Thank-you

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El Rowan • Private • 19 November 2020

### Tested recommendation, not adherence to recommendation

While I commend the researchers and it does demonstrate whether *recommending* masks provides benefit, the experiment does not demonstrate whether mask-wearing *actually* took place. Research in other arenas has shown people are not honest when providing answers to surveys, and these people would have likely had reason to be less than honest about the frequency with which they wore a mask and the coverage of their mouth and nose while wearing one. It may be better to find people with serious concern about NOT wearing

a mask to act as the experimental group, and those who are entirely opposed to mask-wearing as the control group. This would be answer the question of whether wearing a mask provides benefit. I think people are misunderstanding the intent of this study, which was to test the power of recommendation with the hope that those in the experimental group would be honest in their responses. We will never know if they were honest or used the masks properly.

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Hans Gaines • Karolinska Institute, Stockholm, Sweden • 18 November 2020

## Risk for bias?

An important large-scale study investigating the benefit of bearing a mask to reduce the risk of aquiring COVID-19 during an daily average of 4,5 hours stay outside the home during one month.

To be able to do that, one must eliminate the possible bias that the participants are instead infected during the daily 19,5 hours they stay at home.

A total of 52 participants in the mask group and 39 control participants reported COVID-19 in their household. Of these, 2 participants in the face mask group and 1 in the control group developed SARS-CoV-2 infection…'

However, more participants may have been exposed and infected by household members, without participants reporting COVID-19 in their household, if the members experienced asymptomatic infection or only mild disease, not suspected to be due to COVID-19.

The possible inclusion of misdiagnosed subjects - infected trough household contact but estimated as infected during outside the home should influence both groups - with or without masks - equally. And the true difference between the groups, and thus the benefit of wearing a mask, should increase if this bias had been controlled, although with wide confidence intervals, due to the relatively low number of infection.

The reported finding of only 3% (3/95) infected through household contacts during the study appear to be surprisingly low, supporting the proposed risk for bias, due to misdiagnosis.



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Eemil Zhang • Independent Researcher • 18 November 2020

## Perceptual error in viewing COVID-19 spread as linear, not exponential.

In the discussion section the authors state that "Testing at the end of follow-up, however, may not have captured any infections contracted during the last part of the study period, but this would have been true in both the mask and control groups and was not expected to influence the overall findings.". This statement assumes a linear spread of infection among both groups. COVID-19 however has been spread exponentially (Lammers, Crusuis, Gast 2020). As such infections contracted during the last part of the study period would be largely significant to the overall findings.

Brendan Moran • NHS COVID Clinical Assessment Service • 19 November 2020

## Timing is everything

This study pooled participants from two cohorts split two weeks apart in the months following the peak of first wave of infections in Denmark.

Self-reported pre-study baseline seropositive prevalence was 1.7% and these participants were excluded from the study.

Of those with unknown baseline seropositivity, 2% were positive at the end of the study.

Of those with known baseline seropositivity, around 1.7% appear to have seroconverted during the month of the study.

Do these very similar percentages spread across time raise concerns about the false positive rate of the self-reported antibody test used in a low prevalence population?

Even without false positive rate, to achieve 80% sensitivity, this lateral flow antibody test has to be performed at least 15 days after symptom onset. It takes an average of 5-6 days to develop symptoms following exposure, so this creates at least a 3 week lag. Given the study only lasted 1 month in each cohort, any protective effect of mask-wearing will be diluted by late sero-conversions infected prior to the study. This effect will be balanced in the control group, but still increases the OR towards 1 even if masks were having an effect when both groups are pre-loaded equally. Taking this into account and any post-study seroconversions missed in the control group could possibly have led to a significant result. The PCR and clinically diagnosed outcomes will not suffer from this lag so much, and it is noteworthy that mask wearers scored 0 and 5 cases respectively versus 5 and 10 for controls, whilst IgG seropositivity was higher than IgM in mask wearers and vice versa in controls.

The study was also underpowered for detecting a protective-to-wearer effect of somewhere less thar
which could be a more reasonable estimate of efficacy.



PREVIOUS ARTICLE NEXT ARTICLE