Study protocol: The protective effect of face mask wearing against respiratory tract infections: a pragmatic randomized trial

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Abstract

Background: Face masks have been strongly advised or mandated in many countries to curb the transmission of respiratory infections during the COVID-19 pandemic. However, the magnitude in risk reduction by wearing face masks in real life settings is still unclear. Randomized trials are needed to examine the effectiveness of face masks on transmission of respiratory viruses in real life settings.

Objectives: The primary aim of this study is to examine whether wearing face masks has a protective effect on self-reported tract infection compared with not wearing face mask in public settings in Norway.

Methods: This study is a pragmatic, two-armed cluster randomized superiority trial including participants in Norway. Participants will be randomized to one of the following two arms: control group or medical masks in a 1:1 ratio.

The intervention is to ask participants in the intervention groups to wear face masks when close to others outside their home, e.g., in public spaces like shopping centres, and streets and on public transport. The control group will be asked not to wear face masks when close to others outside their home, e.g., in public spaces like shopping centres, and streets and on public transport. Participants will continue to use, or not use, face masks at work independent of which group they are allocated to. The study period is 14 days and participants will be asked to complete a baseline and follow-up questionnaire.

The primary outcome is self-reported respiratory infection. Secondary outcome are self-reported Covid-19 prevalence and Covid-19 incidence based on registry data. We estimate a need for 1346 participants in each study arm to demonstrate a statistically significant difference ($p<0.05$) with 80% power.

Introduction

Governments across the world have resorted to many different public health and social measures to curb the transmission of respiratory infections during the COVID-19 pandemic (Hirt et al., 2022) . Primarily, respiratory infections and SARS-CoV-2 is spread through respiratory droplets and fine respiratory aerosol (Chou et al., 2020; van Doremalen et al., 2020; Wilson et al., 2020). Hence, wearing respiratory protective devices, like face masks, is a simple intervention that will serve as mechanical barriers and prevent the spread of respiratory droplets produced while talking, coughing, or sneezing (Cheng et al., 2021; Rader et al., 2021). The risk reduction of wearing face masks is most likely achieved by avoiding infected individuals infecting others, but also protecting the person wearing it from virus entering through the nose and mouth. However, the magnitude in risk reduction by wearing face masks in real life settings is still unclear.

A systematic review including 39 studies (18 randomized controlled trials (RCT)) examined the effectiveness of face masks in community and health care settings for preventing respiratory infections (Chou et al., 2020). The authors concluded that evidence on mask effectiveness for respiratory infection prevention is stronger in health care than community settings (Chou et al., 2020). A more recent meta-analysis including six studies shows that wearing face masks in public is associated with a relative risk reduction in the incidence of COVID-19 of 53% (RR 0.47 (95% Confidence Interval (CI) 0.29 to 0.75) (Talic et al., 2021). The authors emphasized that their conclusion was based on a limited number of adequately performed studies and only one RCT (Talic et al., 2021).

Specifically, two cluster RCT studies have examined the effectiveness of wearing face masks in public community settings (Abaluck et al., 2022; Bundgaard et al., 2021). One of these concluded that face masks were effective in reducing SARS-CoV-2 transmission (risk ratio (RR): 0.89, 95% CI 0.78 to 1.00) (Abaluck et al., 2022), whereas the other reported no statistically significant risk reduction (odds ratio (OR): 0.82, 95% CI 0.54 to 1.23) (Bundgaard et al., 2021). Limitations like rural study setting (Abaluck et al., 2022) and insufficient statistical power to evaluate effectiveness (Bundgaard et al., 2021) limits the validity of the findings.

There is still need for well-designed and well-conducted RCT's with sufficient statistical power to examine the effectiveness of face masks on transmission of respiratory viruses in real-life community settings.

Objectives

The primary aim of this study is to assess whether wearing face masks has an protective effect on self-reported respiratory tract infections compared with not wearing face masks in public settings in Norway.

Methods

Trial design and study setting

This study is a pragmatic, two-armed cluster randomized superiority trial including participants in Norway. Participants will be randomized to one of the following two arms: control group or medical masks in a 1:1 ratio.

The trial will be fully remote and without any personal interaction between investigators and participants.

Intervention descriptions

This study aims to determine the impact of wearing face masks in real life circumstances. Hence, the intervention is to ask participants in the intervention groups to wear face masks when close to others outside their home, e.g., in public spaces like shopping centres, and streets and on public transport. The control group will be asked not to wear face masks when close to others outside their home, e.g., in public spaces like shopping centres, and streets and on public transport. Participants will continue to use, or not use, face masks at work independent of which group they are allocated to. The study period is 14 days. Figure 1 illustrates the trial timeline.

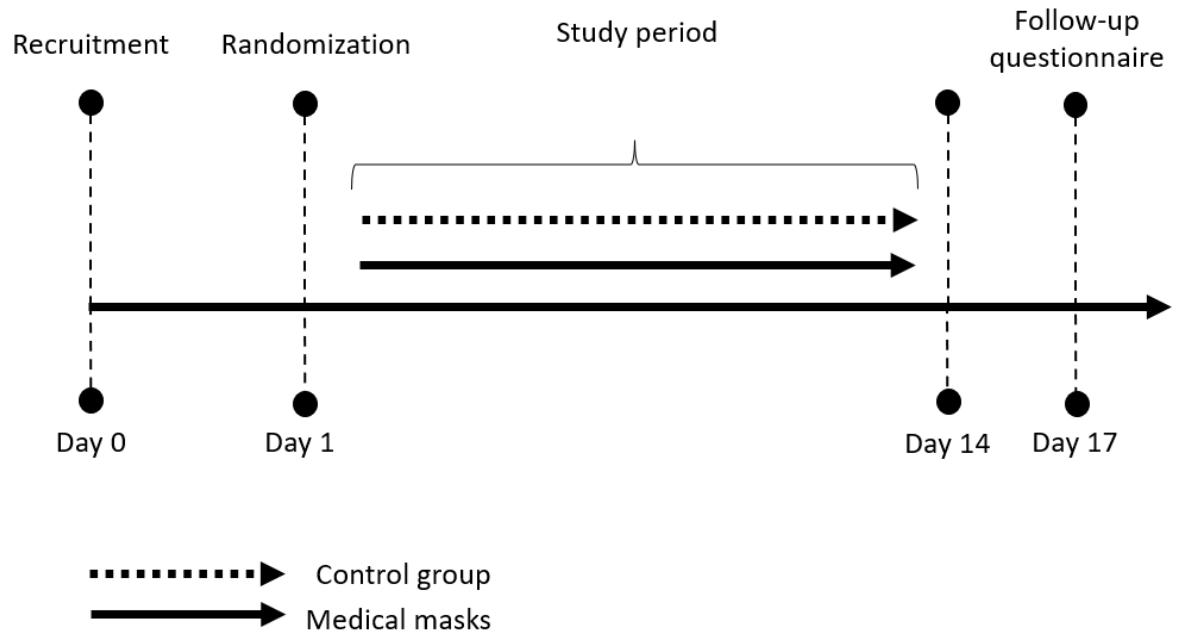

Figure 1 Trial timeline and design

Criteria for discontinuing or modifying allocated interventions

If the health authorities issue a general recommendation to wear facemasks in public during the study period, the trial will be discontinued. An online questionnaire will be distributed at follow-up to map any potential detrimental effects of the face masks for the participants. No other criteria will be applied.

Strategies to improve adherence to interventions

We do not plan to maintain any form of contact with the participants between trial enrolment and data collection.

Relevant concomitant care permitted or prohibited during the trial

We will not give any advice about concomitant care or interventions.

Participants, eligibility criteria and recruitment

Participants will be recruited via an online portal that will be distributed as widely as possible in the Norwegian public. The project group will promote the trial through media, social media outlets and the project webpage hosted by the Norwegian Institute of Public Health. The webpage will include detailed information about the trial and link to the Nettskjema-platform, where those who wish to participate can sign the consent form.

Members of the public can take part as long as they

- Are at least 18 years of age
- Are willing to be randomized to wear, or not to wear, face masks outside their home when close to others for a 14-day period
- Provide informed consent

Who will take informed consent?

Informed, electronically signed consent (minID or BankID) will be collected in the same webpage where people can sign up to participate and consent to being randomized to one of the groups. Participants will also consent to the collection and use of information from the questionnaire and national registers.

Data collection and outcomes

All participants will be asked to complete a baseline questionnaire before randomization. Day 1 of the trial period is the first day the individuals participate in the trial. The intervention group will be asked to wear face masks until day 14. Three days later, on day 17, the participants will be asked to complete an online follow-up questionnaire.

The primary outcome is

Self-reported respiratory infection: The participants will be asked whether they have experienced symptoms of the common cold, influenza or COVID-19 in the previous 14 days. If answering yes to this question the participants will be asked to indicate whether they experienced any of the following symptoms:

- Headache
- Fever
- Blocked or runny nose (airways)
- Reduced sense of smell or taste
- Reduced appetite
- Sore throat (airways)
- Cough (airways)
- Sneezing (airways)
- Body ache or muscle pain
- Exhaustion
- Heavy breathing (airways)
- Stomach pain

We define respiratory infections as experiencing symptoms of common cold, influenza or COVID-19, and having

- 1 respiratory symptom (stuffed or runny nose, sore throat, cough, sneezing or heavy breathing) and fever, or
- 1 respiratory symptom and at least 2 more symptoms (body ache, muscular pain, fatigue, reduced appetite, stomach pain, headache, and/or loss of smell).

Secondary outcomes:

Covid-19 prevalence based on survey data: Positive cases will be those persons who have answered "Yes" to the survey item "Have you tested positive of COVID-19 in the last two weeks?". We will analyse and report this outcome using the same model as for the primary outcome.

Covid-19 incidence based on registry data: Positive cases will be those notified to the Norwegian Surveillance System for Communicable Diseases (MSIS) with a positive PCR-test for covid-19. We will analyse and report this outcome using the same model as for the primary outcome.

Participant enrolment and timeline

Participants will be enrolled continuously during the winter and spring of 2023, or later if the trial is postponed (Table 1).

Table 1: Participation timeline

	Enrolment/ allocation	Post/allocation and follow-up questionnaire	Registry data
	Day 1	Day 17	Day 17
Recruitment and baseline assessment			
Eligibility criteria	X		
Informed consent	X		
Randomization			
Intervention: Advise to wear face masks	X		
Control: Routine life	X		
Outcome measures			
Symptoms of respiratory symptoms		X	X
Positive COVID-19 tests results		X	X
Participant characteristics			
Age, gender, vaccination status, notified tests results (COVID-19)	x		x

Sample size

The prevalence of symptoms of self-reported upper respiratory infections varies over time. National representative numbers from Symptometer show that the proportion of the population who have reported upper respiratory infections in a given week during has varied between from 2% to 8% (week 45, 2020 to week 48, 2021) (Folkehelseinstituttet, 2021).

Given that 10% experience symptoms within the study period of 14-days in the control group and wearing face masks reduces this share with 30% (relative risk reduction), and thereby the share that experience symptoms at least once in the intervention group is 7%, we estimate a need for 1346 participants in each study arm to demonstrate a statistically significant difference ($p<0.05$) with 80% power. Assuming loss to follow-up and that the secondary outcome require a higher sample size to detect effects, we will need around > 4000 participants self-reporting on the primary outcome to demonstrate a statistically significant difference ($p<0.05$) with 80% power.

Assignment of interventions: allocation

Sequence generation

We will use a 1:1 randomization by means of computer-generated random numbers.

Concealment mechanism

The allocation will be concealed as the participant themselves will be directly informed of their allocation as soon as they have agreed to take part in the trial and completed the online consent form.

Implementation

Generation of allocation sequence, enrolment of participants and assignments of participants will be all handled by the Nettskjema-form.

Assignment of interventions: blinding

Who will be blinded?

Only the data analysists will be blinded to allocation.

Data collection and management

Plan for assessment and collection of outcomes

Our outcome data will be collected from an online questionnaire at baseline as well as an end-of-follow up questionnaire that the participants will be asked to complete on Day 17 of the trial period, and from national registries.

The questionnaire includes questions on the following:

- Self-reported respiratory infections
- Regular use of face masks
- Use of face masks outside

From the national registries we will collect the following data:

- COVID-19 (YES/NO) (MSIS-database)
- Results of COVID-19 test (POSTIVE/NEGATIVE) (MSIS-database)
- COVID-19 vaccination status (SYSVAK)

Plans to promote participant retention and complete follow-up

We will send up to two reminders to participants who have not withdrawn and who have not submitted a completed questionnaire.

Data management

We will use the university of Oslo's solutions for electronical signed consent form (MinID/BankID) in the web-based survey platform Nettskjema, and their secure storage of research data (TSD).

We will collect directly identifiable data such as name, person identification number and e-mail address. Along with the code for linking data, the personal identification number will be sent to the registries. Each register will delete the personal identification number before register-data and code for linking are delivered and stored in TSD. The questionnaire-data are processed in the same way.

The codes for linking data to the person identifier will also be kept in TSD. The only researchers that will have access to the data is Annlaug Selstø, Runar Solberg, Ingeborg Hess Elgersma and Petter Elstrøm.

Ethics

Research ethics approval

The study protocol has been approved by the Regional Ethics Committee (REK Sørøst, ID number 536544).

All participants will have to register and consent to participation through an online portal with information about the goal of the trial and eligibility criteria. To register they will need to use the MinID- or BankID identifier. After completing the consent form, the participants will be randomized and will receive information about which study arm they have been allocated to, and they will be advised accordingly to wear or not to wear face masks. After 17 days the participants will receive an e-mail with a link to an online data collection form.

Participation in the trial entails negligible risk and may yield important findings that can inform decisions about infection control measures in the ongoing and future epidemics. Our assessment is that the risk-benefit of the trial is highly favourable.

Statistical analysis

We will estimate adjusted risk ratios (aRR) and adjusted risk differeneces (aRD). We will estimate relative risks using generalized linear models (GLM).

For the primary outcome (respiratory infection) we will adjust for the covariates:

- Sex
- Age (continuous)
- Having children (dummy)

as these variables likely related to the associated with the primary outcome (Administration, 2021; CHMP, 2015).

We will adjust for the covariates sex (male or female), age (continuous; years), having children (dummy-variable), and immune status (measured in two variables: sum of corona vaccines and registered COVID-19 infections, and time since last vaccine/COVID-19 infection) for the secondary outcomes concerning COVID-19 infections.

While we aim to prevent the occurrence of missing data, if complete data are not available for more than 5% of observations, we will evaluate whether the data are plausibly missing completely at random (MCAR) (Jakobsen et al., 2017). If we judge that the data are MCAR, we will perform complete case analysis. Otherwise, will we use multiple imputation by chained equations (MICE), using a sufficiently large number of imputations (e.g., 50).

We will report results as sample prevalence's and the estimated relative risks and corresponding risk differences, along with 95% confidence intervals.

Plan to give access to the full protocol, participant level-data and statistical code

We intend to give full access to the protocol, participant level-data dataset and statistical code to anyone who is interested, after securing that the dataset is fully anonymized.

Oversight

Adverse event reporting and harm

We will ask the participants whether they needed any medical attention during the trial period, and specifically ask for injuries.

Plan for communicating important protocol amendments to relevant parties (trial participants and ethical committees)

We will report important protocol modifications (e.g., changes to eligibility criteria, outcomes, analysis, change in interventions) to the Regional Ethics Committee.

Dissemination plans

We plan to communicate trial results to the public and other relevant groups via publication in peer-reviewed biomedical journals, social media and through the Norwegian Institute of public health website.

Trial status

Conception 21. September 2022.

Declarations

Funding

All running costs are covered by the Norwegian Institute of Public Health

Availability of data and materials

The final anonymized trial dataset without any linked registry data will be freely available to the public

Competing interest

The authors declare that they have no competing interest.

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