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CENTRE FOR EPIDEMIC INTERVENTIONS RESEARCH

Methodological insights and lessons learned from conducting a pragmatic randomised trial on surgical face masks

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16.08.2024

Outline

- Study rationale, design and key findings
- Methodological considerations
- Reactions to the findings
- Constructive critical feedback and lesson learned

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Study rationale, design and key findings

Study rationale

- The effectiveness of face masks as a protective measure against infection is uncertain
- Observational evidence supports a reduction in respiratory infections with face mask use
- However, randomised trials face challenges, especially in achieving sufficient statistical power, contributing to uncertainty in their findings

Study design

- **Design**: Pragmatic randomised trial
- **Object**: To assess the personal protective efficacy of wearing surgical face masks in public settings
- **Intervention:** Wear, or not wear, surgical face masks in public over 14-days
- **Primary outcome**: Self-reported respiratory symptoms consistent with a respiratory infection
- **Participants:** Adults aged 18 and above, with no exclusion criteria applied

Study findings

- Participant groups were well-matched at baseline

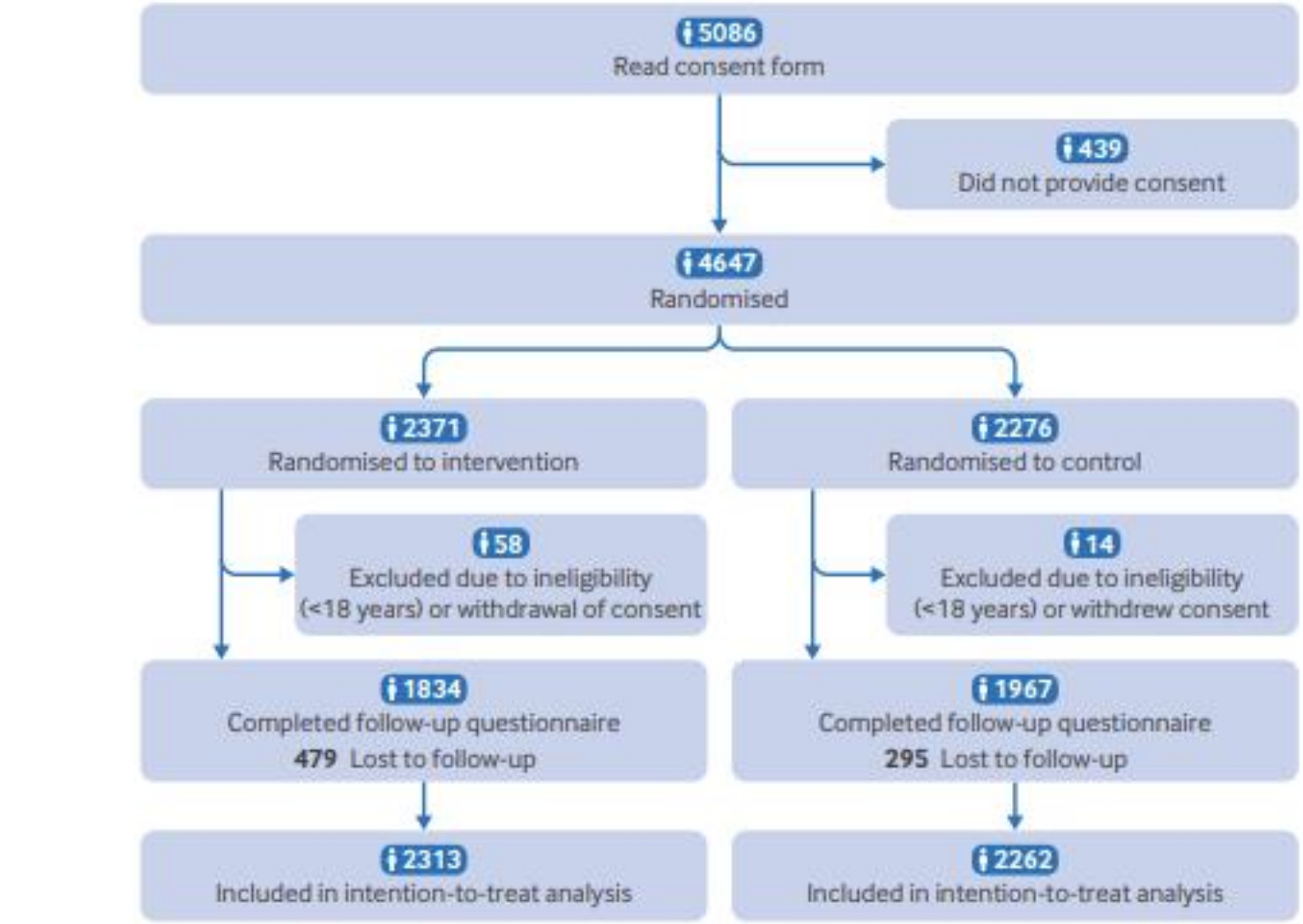

Fig 1 | Flow of participants through trial

Study findings

Table 3 | Effects of wearing a surgical face mask on primary and secondary outcomes. Values are number (percentage) unless stated otherwise

	Participants		Marginal odds ratio* (95% CI)	P value	Absolute risk difference† (% (95% CI)
	Intervention arm (n=2313)	Control arm (n=2262)			
Prespecified primary outcome					
Self-reported respiratory symptoms	163/1834 (8.9)‡	239/1967 (12.2)‡	0.71 (0.58 to 0.87)§	0.001§	−3.2 (−5.2 to −1.3)§
Prespecified secondary outcomes					
Self-reported covid-19 (complete case analysis)	21/1834 (1.1)	21/1967 (1.1)	1.07 (0.58 to 1.98)	0.82	0.1 (−6.0 to 8.0)
Registered covid-19 (complete case analysis)	0/1834¶ (0)	2/1967¶ (<0.1)	NE**	>0.99	NE**
Non-prespecified sensitivity analyses					
Self-reported respiratory symptoms (complete case analysis)	163/1834 (8.9)	239/1967 (12.2)	0.71 (0.57 to 0.87)	0.001	−3.3 (−5.2 to −1.3)

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Adherence

- Among participants in the intervention arm:
  - 450 (25%) reported always wearing a face mask
  - 753 (41%) wearing face masks more than 75% of the time
  - 265 (14%) wearing face masks 75-50% of the time
  - 357 (19%) wearing face masks less than 50% of the time.

- Among participants in the control arm, 1865 (95%) reported not wearing face masks.

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Methodological considerations

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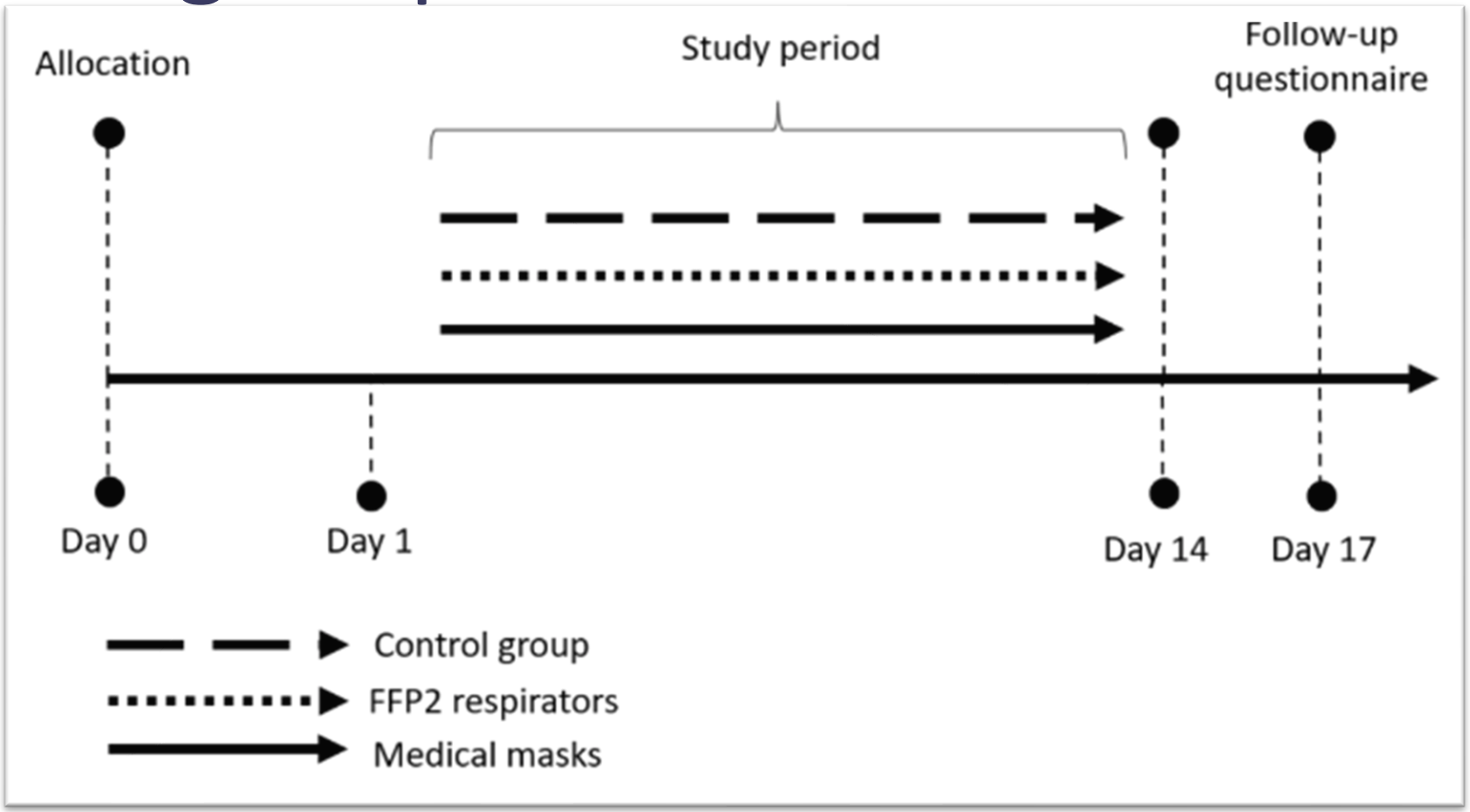
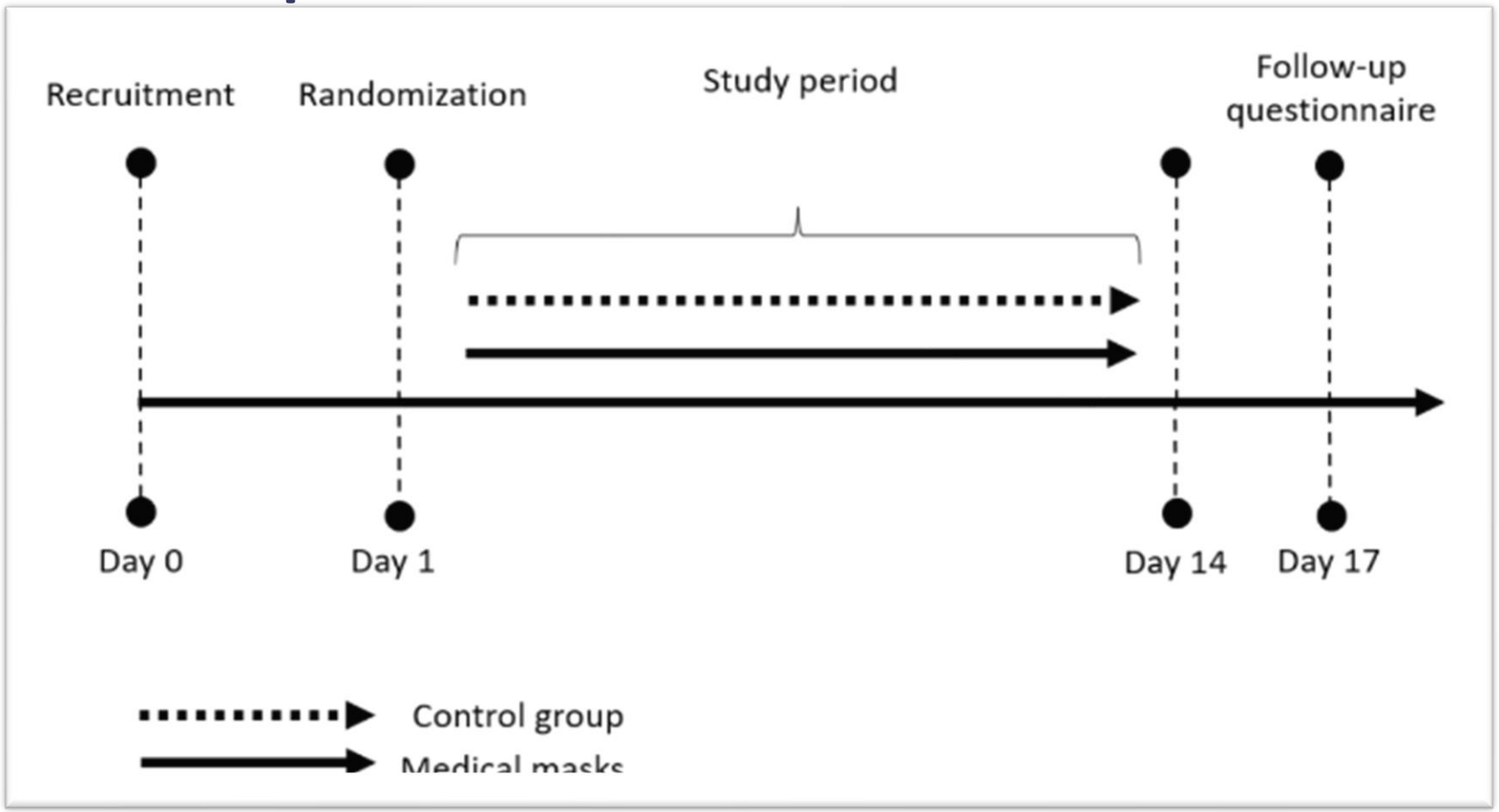
Type of facemasks

The original protocol

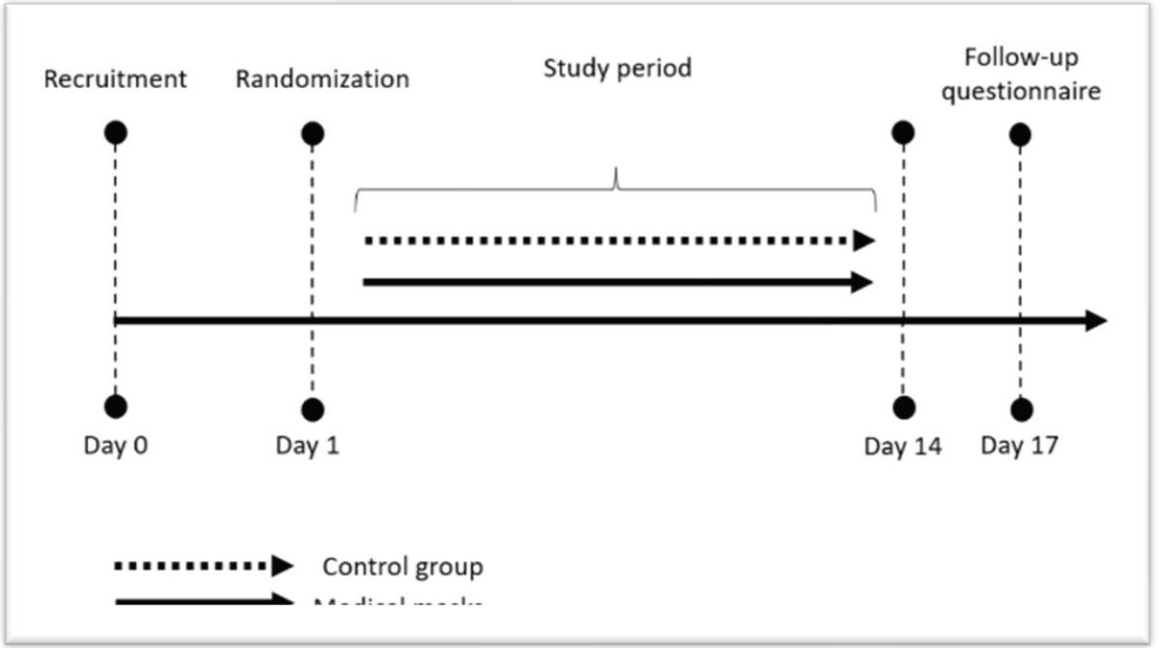


The final protocol



The final protocol

- Sample size consideration
- Simplify for the trial participants and pharmacy staff
- In line with WHO recommendations



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Recruitment

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- Participants were recruited from multiple locations across Norway
  - Publicity through Norwegian TV, radio and various media channels

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  - Paid print advertisement on public transport

Recruitment

"In doubt about how well face masks work? - So are we. Help us find out - join the face mask study.

- Norwegian institute of Public Health“

Recruitment

- Participants were recruited from multiple locations across Norway
  - Publicity through Norwegian TV, radio and various media channels
  - Paid print advertisement on public transport
  - Engaging two data collection firms that invited members of their survey panels to take part in the study

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Outcomes

Outcomes

- Primary outcome:
  - Self-reported respiratory symptoms consistent with a respiratory infection
- Secondary outcomes:
  - Self-reported COVID-19
  - Positive COVID-19 test results registered in Norwegian Surveillance System for Communicable Diseases
  - Adverse effects

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Drop out and missing data

Drop out and missing data

- Intervention group: 20.7% loss to follow-up
- Control group: 13.1% loss to follow up
- Prespecified: Multiple imputation. Complete case = main analysis
- Non-prespecified
  - Manski-type bounds
  - Three different scenarios of missing outcome data

Table 1 Three scenarios of missing outcome data on incidence of infection

	Control arm		Intervention arm	
	Did not drop out	Dropped out	Did not drop out	Dropped out
Scenario 1	Reference	50% lower	No difference	No difference
Scenario 2	No difference	No difference	Reference	50% higher
Scenario 3	Reference	50% lower	Reference	50% higher

H

Drop out and missing data

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Self-reported respiratory symptoms (complete case analysis)	163/1834 (8.9)	239/1967 (12.2)	0.71 (0.57 to 0.87)	0.001	−3.3 (−5.2 to −1.3)
Manski-type bounds††	163/2313 (7.1) to 642/2313 (27.8)	239/2262 (10.6) to 534/2262 (23.6)	0.64 to 1.24 (0.52 to 1.42)	NA	NA
Scenario 1‡‡	206/2313 (8.9)	257/2262 (11.4)	0.76 (0.63 to 0.92)	0.006	NA
Scenario 2§§[j]	227/2313 (9.8)	275/2262 (12.2)	0.79 (0.65 to 0.95)	0.01	NA
Scenario 3¶¶	227/2313 (9.8)	257/2262 (11.4)	0.85 (0.70 to 1.03)	0.08	NA

Drop out and missing data

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Reactions to the findings

Personal protective effect of wearing surgical face masks in public spaces on self-reported respiratory symptoms in adults: pragmatic randomised superiority trial

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Cite this as: *BMJ* 2024;386:e078918

Linked Opinion
The polarised discourse around face masks is hindering constructive debate

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Runar Barstad Solberg [1], scientist [1], Atle Fretheim, professor and research director [1 2], Ingeborg Hess Elgersma, scientist [1], Mette Fagernes, senior adviser [3], Bjørn Gunnar Iversen, senior medical officer [3], Lars G Hemkens, senior scientist [4 5 6], Christopher James Rose, statistician [1 7], Petter Elstrøm, senior scientist [1]

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Accepted 29 May 2024

Abstract

Objective To evaluate the personal protective effects of wearing versus not wearing surgical face masks in public spaces on self-reported respiratory symptoms over a 14 day period.

Design Pragmatic randomised superiority trial.

Setting Norway.

Participants 4647 adults aged ≥18 years: 2371 were assigned to the intervention arm and 2276 to the control arm.

Interventions Participants in the intervention arm were assigned to wear a surgical face mask in public spaces (eg, shopping centres, streets, public transport) over a 14 day period (mask wearing at home or work was not mentioned). Participants in the control arm were assigned to not wear a surgical face mask in public places.

Main outcome measures The primary outcome was self-reported respiratory symptoms consistent with a respiratory infection. Secondary outcomes included self-reported and registered covid-19 infection.

Results Between 10 February 2023 and 27 April 2023, 4647 participants were randomised of whom 4575 (2788 women (60.9%); mean age 51.0 (standard deviation 15.0) years) were included in the intention-to-treat analysis: 2313 (50.6%) in the intervention arm and 2262 (49.4%) in the control arm. 163 events (8.9%) of self-reported symptoms consistent with respiratory infection were reported in the intervention arm and 239 (12.2%) in the control arm. The marginal odds ratio was 0.71 (95% confidence interval (CI) 0.58 to 0.87;

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BMJ 2024 ; 386 doi: https://doi.org/10.1136/bmj.q1661 (Published 25 July 2024)
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Linked Research
Personal protective effect of wearing surgical face masks in public spaces on self-reported respiratory symptoms in adults

Article | Related content | Metrics | Responses

Atle Fretheim, research director [1], Runar Barstad Solberg, scientist [1], Lars G Hemkens, senior scientist [2]

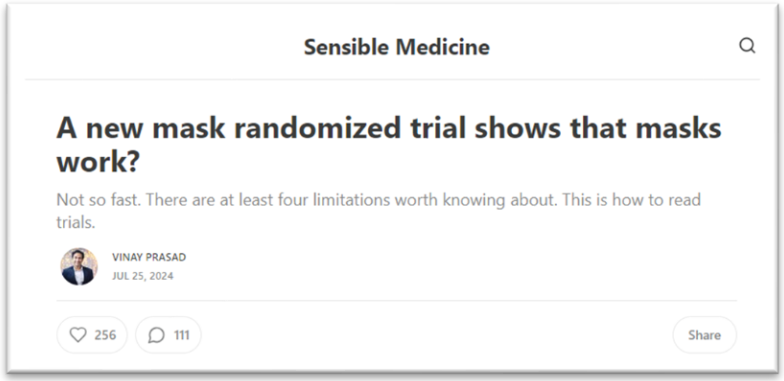
Author affiliations

We need open and nuanced discussions about research findings on public health and social interventions

It has been both fascinating and disheartening to observe heated debates among academics about the use of face masks and various other covid-19 related issues, particularly on social media and mostly from the UK and North America. Large and vocal parts of the academic community seem to be split into two groups holding completely incompatible views, with each side equally convinced that they are right. This area of contention makes a constructive exchange of views and joint reflection almost unachievable, since facts and research findings have limited impact when positions are fixed from the outset.

The lack of nuance from many or most participants, the frequent personal attacks on individuals, and the often harsh wording exchanged makes the discourse on face masks different to what we are typically used to, or aim for, in academia. After receiving several strong responses from researchers and health professionals when they published a study on face masks, the editors of the *Annals of Internal Medicine* stated that the issue has become a "controversial, emotionally laden topic."[1] Certainly, researchers across the globe have supported or opposed the use of face masks since the beginning of the covid-19 pandemic. But after conducting our study in Norway (doi:10.1136/bmj-2023-078918),[2] the general impression was that most researchers there did not hold such a rigid position, and that it is possible to debate the effectiveness of face masks without the risk of rejection. The contrasting and strongly held positions that dominate the discourse in some other countries would qualify as fringe views in our setting. Instead, a Norwegian researcher might say something like "Masks are probably helpful, but I don't know how important they are in reducing the spread of covid-19"—a nuanced position that would be considered mainstream here.

From experience, we have learnt that suggesting uncertainty about the effectiveness of face masks is frowned on


Sensible Medicine
A new mask randomized trial shows that masks work?
Not so fast. There are at least four limitations worth knowing about. This is how to read trials.
VINAY PRASAD
JUL 25, 2024
256
111
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Vinay Prasad is Wrong about Masking
As pertains to the interpretation of this paper
ADAM CIFU, MD
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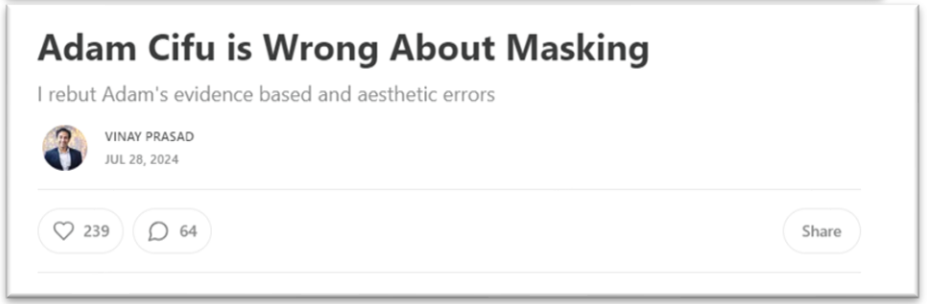
Adam Cifu is Wrong About Masking
I rebut Adam's evidence based and aesthetic errors
VINAY PRASAD
JUL 28, 2024
239
64
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Walz administration threatened voters for not masking up; critics tear apart new mask study
Hotline to report stay-at-home violations, medical license investigation of Walz's challenger and threat to report unmasked voters to authorities. Norwegian mask study finds little reduction in infection but also "zero evidence that anyone ever wore a mask."


Personal protective effect of wearing surgical face masks in public spaces on self-reported respiratory symptoms in adults: pragmatic randomised superiority trial
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Outcomes

- From the reviewers

Second – mainly a strength that can be further strengthened – the primary outcome is clinically meaningful and well-defined, but it is not really "self-reported respiratory infection." The

Sensible Medicine

Commentary

The easy interpretation of this study is: masks work to decrease respiratory infections during cold and flu season in Norway. The endpoint is a good clinical one that we care about: "Do you feel sick?" Sure, it is not hospitalization or death but that would require a giant study.

"The treatment in this study is *not mask wearing*" and the "outcome was *not illness*" but "clicking the right boxes in an online survey," he said, assailing the "absurd" design. "The study staff never had in-person contact with any participants. We have zero evidence that anyone ever wore a mask!" Recht wrote.

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Constructive critical feedback and lesson learned

Constructive critical feedback and lesson learned

- Unblinded self-report of a subjective outcome
  - Risk of bias
  - Unblinded participants might report symptoms differently based on beliefs/expectations
  - One subgroup analysis suggest that beliefs is associated with the intervention effect
  - Potential solutions:
    - Placebo masks (may be difficult in practice)
    - PCR testing from all participants (may decrease willingness to participate, and/or may increase drop out)
  - Lessons learned:
    - If possible, introduce placebo to reduce risk of bias
    - New study of air purifiers

Constructive critical feedback and lesson learned

- Little difference of positive COVID-19 tests
  - Secondary outcome
  - Data too sparse for a meaningful interpretation

  - Lessons learned:
    - Use of registry data (if possible)
    - Tactics to reduce loss to follow-up and missing outcome data

Constructive critical feedback and lesson learned

- Differences in behaviour
  - e.g more social distancing in intervention group may explain the difference in results (rather than the face mask as such)
    - Differences in behaviour can be seen as an intervention effect

  - Lessons learned:
    - If possible, collect data on relevant behaviour

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Thank you for your attention.
Any Questions?

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