The GLasses Against transmission of SARS-CoV-2 in the communitY (GLASSY) trial – Statistical analysis plan

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This document is an addition to the detailed research protocol(1). The RCT has been registered in clinical trials (NCT05217797). This document was posted online before the analysis of the data took place.

Plan for reporting and analysis.

All statistical tests will be performed with a 5% significance level. 95% confidence intervals will be calculated around risk ratios. The analysis will be conducted on the basis of the Intention-to-treat principle (ITT), and in accordance with the CONSORT guideline for randomized controlled trials.

The analysis will be blinded, that is all statistical analyses will be carried out with trial arms described only as 'A' and 'B'.

We plan to split the result sections in four blocks, and analyses pertaining to each block will be discussed further below: (1) Baseline characteristics and recruitment; (2) Main analysis; (3) Subgroup analysis; (4) Harms. The final article may not use this exact structure.

1) Baseline characteristics and recruitment

In text and in float diagram: For each arm, we describe the numbers of participants screened, met the eligibility requirement, consented, were randomly assigned, received intended treatment, and were analysed for the primary outcome, as well as the number of participants who registered twice, or filled out multiple questionnaires (the number of duplicates).

Figure (in appendix): Recruitment over time, including no-response, including important dates. Dates defining the periods of recruitment and follow-up.

Table: baseline demographic and clinical characteristics for each group + number analysed.

We will also report on compliance, e.g. the use of glasses in the two groups.

	A (n =)	B (n =)
Female (N, %)		
Age (SD)		
Used public transport (N, %)		
Facemask use		
-Always (N, %)		
-Almost always (N, %)		
-Often (N, %)		
-Sometimes (N, %)		
-Almost never (N, %)		
-Never (N, %)		
COVID-19 test		
- Had a COVID-19 test taken (N, %)		
-At test station (N, %)		
-Home test (N, %)		
-Did not test (N, %)		

2) Main Analysis

Primary outcome:

<u>COVID-19 prevalence based on registry data:</u>

Positive cases will be those persons who have been notified with COVID-19 in the Norwegian Surveillance System for Communicable Diseases (MSIS). Prevalence will be reported per group and unadjusted risk ratios and risk differences will be calculated where the risk for each group will be assessed as:

- Numerator: The number of positive cases from day 3 to day 21 after inclusion in the trial. Date of sample collection is considered the date of the positive test.
- Denominator: Total number of participants assigned to the group
    - including no-response

Secondary outcomes:

<u>COVID-19 prevalence based on survey data:</u> Positive cases will be those persons who have answered "Yes" to the survey item "Have you taken a COVID-19 test the last 14 days?" AND "Positive" to the survey item "What was the result of the test?".

Prevalence will be reported per group and risk ratios and risk differences will be calculated where the risk for each group will be assessed as:

- Numerator: The number of positive cases from day 1 to day 17 after inclusion in the trial. The test date was recorded in the survey.
- Denominator: Total number of participants assigned to the group
    - including no-response

Episode of respiratory infection

Participants were asked whether they had experienced any of the following symptoms during the last two weeks:

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

On the basis of the list of symptoms we consulted a panel of infectious disease specialists in order to define a case of a respiratory disease. The definition chosen fulfils one of two criteria:

1) Fever + one airway specific symptom (in brackets above)
2) Three symptoms (not including fever), where at least one of them is airway specific.

Prevalence will be reported per group and risk ratios and risk differences will be calculated where the risk for each group will be assessed as:

- Numerator: The number of persons reporting a respiratory disease
- Denominator: Total number of participants assigned to the group
    - including no-response

We will also conduct a t-test to compare the average total number of symptoms in the intervention- and control group (in supplementary appendix or in main text).

Health care use from national registries

1. At least one consultation concerning respiratory symptoms as registered in Norwegian Patient Registry (NPR) or Registry for Primary Health Care (KPR), from day 3 to day 28 of the study period (see table A1 for diagnoses codes).
2. Health care use (at least one consultation) for injuries (from day 1 to day 21 as registered in NPR or KPR (see table A1 for diagnoses codes).
3. Health care use (all causes) as registered in NPR and KPR from day 1 to day 21 of the study period (at least one consultation)

Health care use self-reported:

1. Health care use for respiratory symptoms, self-reported, from day 1 to day 17 of the study period
2. Health care use for injuries, self-reported, from day 1 to day 17 of the study period
3. Health care use (all causes), self-reported, from day 1 to day 17 of the study period

We will also present risk differences.

3) SUBGROUP ANALYSIS

The following subgroups will be analysed for the primary outcome and for the secondary outcome COVID-19 prevalence based on survey data:

1. Contact lenses: “Yes”, “No”,
2. COVID-19 previously (before 5 weeks) – based on registry data from MSIS. “Yes”, “No”
3. Vaccination status: “Unvaccinated”, “Vaccinated 1 dose (3 weeks before inclusion)”, “Vaccinated 2 doses (1 week before inclusion)”, “Vaccinated 3 doses” (1 week before inclusion)
4. Facemask: “Always”, “Almost Always” “Often”, Occasionally”, “A few times, “Never”

If fewer there are fewer than 5 participants in a group, we will not report results for the group.

4) HARMS

In addition to reporting under secondary outcomes, we will report the number that have reported having headaches per group. Use of sunglasses/normal glasses can potentially lead to headache because of increased squinting.

The reporting on health care use for injuries will also be included in the reporting on harms.

The number of persons who reported harms in the open question on negative experiences in participating in the trial will also be reported, categorized by type of comment.

References

1. Fretheim A, Hemkens LG, Helleve A, Elgersma IH, Elstrøm P, Kacelnik O. The GLasses Against transmission of SARS-CoV-2 in the communitY (GLASSY) trial: A pragmatic randomized trial (study protocol) [Internet]. medRxiv; 2022 Feb [cited 2022 Mar 28] p. 2022.02.04.22270120. Available from: https://www.medrxiv.org/content/10.1101/2022.02.04.22270120v1

Appendix A

Table A1: Selected ICD-10 and ICPC-2 codes

Category	Code
Respiratory symptoms (ICD-10)	J00-J06, J09-J18, J20-J22
Respiratory symptoms (ICPC-2)	A03, A77, F70, F72, F73 H71, R01-R23, R29, R71-R83, R99, R991, R992
Injuries (ICD-10)	S00-S99, T00-T79
Injuries (ICPC-2)	A80, A81, A88, F75-F79, L72-L81, N79-N81, S17-S19