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Study Protocol

Effects and Safety of Facemask Use on Healthy Adults During Exercise: A Systematic Review and Meta-analysis Protocol

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Abstract

Background: Facemasks are used to minimize SARS-CoV-2 spread during the COVID-19 pandemic. However, facemask use during exercise is associated with possible adverse effects. **Objectives:** To compare the effects of facemask use vs. non-facemask use on subjective responses, COVID-19 incidence, and physiologic changes in healthy adults during exercise. **Methods:** The systematic review (PROSPERO registration number: CRD42022296247) will follow the PRISMA-P guidelines and use electronic databases Science Direct, PubMed, Google Scholar, Herdin, and EbscoHost. This will cover randomized parallel groups or randomized crossover studies investigating tolerability, physiologic effects, and the impact on SARS-COV2 incidence of commercially-available cloth, surgical, or FFR/N95 facemasks compared to no-facemask conditions during exercise among healthy adults, including studies published from the earliest date to January 31, 2022. Outcomes of interest will be facemask tolerability in 10 domains of comfort and objective cardiopulmonary, gas exchange, and metabolic responses. Mean differences (MD) or standardized mean differences (SMD) with a 95% confidence interval (CI) will be calculated overall and for subgroups using RevMan software (version 5.4.1). Pooled and subgroup estimates will be calculated using random-effects meta-analysis. The chi-squared test, I2 statistics, and visual analysis will assess heterogeneity. The GRADEpro will determine the certainty of the level of evidence. **Expected Results:** An evidence-based recommendation using GRADE on the changes attributed to facemask use during exercise will be available. This will be useful for organizations when developing appropriate guidelines for exercising while mitigating the risk of SARS-CoV-2 transmission. Future researchers may use this study when redesigning comfortable facemasks without compromising filtration capability.

Key Words*: masks, COVID-19, SARS-CoV-2, exercise, incidence*

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious respiratory illness caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2 virus). Implementing lockdowns and social distancing reduces outdoor activities and interpersonal contact, negatively implicating physical and mental health.[1] During exercise, the substrate and oxygen requirements in the working skeletal muscles are elevated, affecting the resting blood flow to the muscles, resulting in increased cardiac output and respiratory rate for oxygen consumption. Oxygen uptake and ventilation also increase linearly due to the increased work rate.[2]

Surgical facemasks reduce infection risk by blocking large-particle droplets containing germs. It is recommended for vulnerable populations and healthcare workers.[3] However, wearing a facemask during exercise would cause rebreathing of carbon dioxide or reduce oxygen consumption, leading to lowered arterial oxygen saturation.[4] Training at greater intensities could

increase moisture retention, resulting in the deformation of less rigid masks affecting breathability and filter efficiency.[5] When wearing a facemask during exercise, the body becomes more efficient at producing work (VO2) by 7%. [6]

Two systematic reviews had contrasting results, the first of which concluded that wearing facemasks while exercising has minor and no effect on physiological response and exercise performance.[7] The use of a non-disposable or disposable mask is safe while exercising vigorously. On the other hand, another review reported that oxygen saturation while using a facemask during strenuous exercise decreased the individual's oxygen saturation. N95 and surgical masks negatively affected lung function and gas exchange capacity but not maximal physical performance.[8] Exhausting high-intensity activities decreased availability and absorption of oxygen resulting in a more significant proportion of anaerobic metabolism. There were no reports on the facemasks' detrimental consequences on maximal performance. However, reports show higher perceived exertion while exercising with facemasks.[8]

No reviews and meta-analyses reported the certainty of the level of evidence, the direction of effect, and the strength of recommendation on facemask use among healthy adults during exercise. This review will determine the level of evidence using the Grading of Recommendations Assessment, Development and Evaluation profiler Guideline Development Tool (GRADE), informing stakeholders on the certainty of the evidence, and avoiding misguided recommendations.[9] The review will only include randomized controlled trials and randomized crossover studies, minimizing the risk of bias in lower study types.[9]

This review will compare the effects of facemask and non-facemask use during exercise in healthy adults. We primarily aim to compare the effects of facemask use on the subjective responses and COVID-19 incidence of healthy individuals during exercise compared to those not wearing facemasks. The secondary objective of the review is to compare the effects of facemask use on the physiologic changes of healthy individuals during exercise compared to those not wearing facemasks.

METHODS

This systematic review and meta-analysis is registered under the International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42022296247) and conducted based on the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols statement.[10] (Supplement A)

Eligibility Criteria. Only randomized studies investigating the effects of commercially-available facemasks vs. non-facemask use on subjective responses, COVID-19 incidence, and physiologic changes in healthy adults during exercise will be included in this review. There will be no restrictions on language. We will exclude studies that are non-randomized, observational, and case. We will exclude studies that compare two different facemask models without control, reporting only preliminary results, protocols, or ongoing. Studies with ill individuals or children as participants and those that used non-commercially available masks, such as industrial masks, will be excluded.

These are the primary outcome measurements of the review:

1. Borg's rate of perceived exertion is a scale that measures the person's physical activity intensity level or how hard the person feels their body is working.[11]
2. Perceived discomfort. This has 10 questions comprising humidity, heat, breathing resistance, itchiness, tightness, saltiness, unfit, odor, fatigue, and overall discomfort.
3. COVID-19 incidence.

These are the secondary outcome measurements of the review:

1. Heart rate (HR). It is the number of times the heart beats per minute.[12]
2. Blood pressure (BP). Diastolic blood pressure measures arterial pressure when the heart is at rest, whereas systolic blood pressure measures arterial pressure when the heart contracts.[12]
3. Respiration rate (RR). It is the number of breaths a person takes per minute.[12]
4. Oxygen saturation (SPO2). It is the ratio of oxygenated hemoglobin to total hemoglobin.[13]

5. Tidal volume (TV). It measures the amount of air one inhales during a normal breath.[14]
6. Maximum rate of oxygen (VO2 max). It is the highest amount of oxygen used during vigorous activity.[15]
7. End Tidal CO2 (ETCO2). It is the amount of carbon dioxide emitted after an exhaled breath, which reflects ventilatory status.[16]
8. Lactate. Blood lactate level is an indirect indicator of metabolic activities within exercising muscle.[17]

Search Strategy and Data Sources. These databases will be searched: Science Direct, PubMed, Google Scholar, Herdin, and EbscoHost, including all dates until January 31, 2022. Keywords will be synonymous with facemasks, exercise, physiologic outcomes, and randomized trials using search strategies appropriate to the database (Supplement B). These Boolean terms and three sets of keywords will be used in the search strategy:

Keywords 1: randomized controlled trial [pt] OR controlled clinical trial [pt] controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab] AND animals [mh] NOT humans [mh]

Keywords 2: mask OR cloth mask OR KN95 OR N95 OR FFP*mask

Keywords 3: aerobic exercise [MeSH Terms] OR breathing exercises [MeSH Terms] OR sport performance OR cardiopulmonary exercise OR walk OR resistance training OR squat

Study Selection and Data Extraction. Two reviewers will independently search the databases using the agreed search strategy, then screen the titles and abstracts using the eligibility criteria. Another two independent reviewers will evaluate the relevance of the initially included studies by reading the full-text articles. The reviewers will reach a consensus by discussion throughout the review process. A third independent reviewer will be available for arbitration.

Methodological Quality Assessment. Two independent reviewers will appraise the studies using Risk of Bias Assessment Tool 1 by Cochrane Collaboration Group,[18] and all conflicts will be settled through dialogue. A third reviewer will be consulted to settle the disagreement.

Data Extraction. Two independent reviewers will extract data from the included studies using data collection forms, comprising authors' characteristics, participants' characteristics, intervention groups, and outcomes. Missing information will be requested through e-mail from the studies' corresponding authors.

Data Analysis and Synthesis. The characteristics of participants, masks used, exercise testing methodologies, outcome measures, COVID-19 incidence, and risk of bias assessment of all included studies will be reported in the narrative synthesis.

A paired t-test will analyze continuous data from a crossover trial with dual interventions collected at two periods if no carry-over and period effects are suspected. Intervention measurement (I) minus control measurement (C) will be compared. The mean difference (MD) and its standard error (SE (MD)) will be extracted, if reported, to estimate the test effects.[18] If not stated, the standard error will be determined using the confidence interval for a mean difference, a paired t-statistic, or the p-value from a paired t-test using the RevMan 5.4 calculator.[18]

The standard difference may be imputed when the standard error and standard deviation of the differences are not known. Some included studies in the meta-analysis may report the standard deviation of differences, which may be borrowed if they use the same measurement scale. The standard deviation can be determined using the number of participants, mean, and upper and lower limits of each group's 95% confidence intervals. The influence of imputed data on the meta-analysis conclusions will be assessed using sensitivity analyses.[18]

For randomized crossover trials that did not report the period and carryover effects, only data from the first period will be used. When only the first intervention phase is included, more than half of the data in the research is lost. These findings will be explained by the identified biases using study-level risk of bias assessments.[18]

For studies that report facemask effects in three trial arms, all relevant facemask groups will be

combined into one group and compared against the no facemask group. Sample sizes and the number of persons with events will be merged across groups for binary outcomes. For continuous outcomes, mean scores and standard deviations will be merged using the RevMan 5.4 calculator.[18]

RevMan 5.4 by the Cochrane Collaboration will be used for meta-analysis, combining and analyzing the results through tables and forest plots.19 Using the Forest Plot, RevMan 5.4 will determine the pooled effect sizes for humidity, heat, breathing resistance, itchiness, tightness, saltiness, unfit, odor, fatigue, overall discomfort, COVID-19 incidence, heart rate, systolic blood pressure, diastolic blood pressure, respiration rate, tidal volume, oxygen saturation, maximum rate of oxygen, end-tidal carbon dioxide, and the blood lactate level. The Generic inverse variance result will be used to enter estimates and standard errors. More comprehensive studies with lesser standard errors are accorded more weight than smaller studies with more significant standard errors. The random-effects model will be used considering the studies utilized different types of facemasks, exercise intensities, and exercise protocols.[18]

For dichotomous outcomes, the risk ratio (also called the relative risk); or the odds ratio (OR) are the effect measures that will report adverse events when wearing and not wearing facemasks during an exercise. These summary statistics can be calculated:

$$Risk\ Ratio = \frac{Risk\ of\ event\ in\ 'with facemask'}{Risk\ of\ event\ in\ 'wiithout facemask'} = \frac{\frac{A}{(A+B)}}{\frac{C}{(C+D)}}$$

$$Odds\ Ratio = \frac{Odds\ of\ event\ in\ 'with facemask'}{Odds\ of\ event\ in\ 'without facemask"} = \frac{\frac{A}{B}}{\frac{C}{D}}$$

The methods for determining heterogeneity will estimate the probability of similar results occurring only through chance.[19] When the forest plot reveals that the trees are widely spaced and at least two lines in the plot do not overlap, visual heterogeneity is evident. Cochran's Q (I^2) will evaluate the studies' heterogeneity. A 60% heterogeneity cut-off score will be used in this meta-analysis, and a chi-square test of <0.10 indicates significant heterogeneity where the disparities between studies cannot be explained solely by chance.[20]

Subgroup Analysis. Subgroup analysis will investigate the cause of heterogeneity. The outcomes will be grouped based on the types of facemasks, exercise tolerance intensity used (i.e., submaximal or maximal), and risk of bias (high-level vs. low-level bias).

We will perform a subgroup analysis of the randomized parallel-trial group trials, crossover trials that did not report period and carryover effects, and the crossover trials that report period and carryover effects. The subgroup analysis will consider the differences in test periods, which are relatively shorter in crossover trials than the randomized parallel-trials. Additionally, it will determine the effects of wide CI on overall effect results when considering only the statistical results of the first trial period in studies that did not report period and carryover effects.

Subgroup analysis will analyze the results' robustness, including the effects of substantial assumptions, imputed data, ambiguous results, and research with a high risk of bias. The publication bias will be determined using the funnel plot.[18]

The GRADE Approach. The GRADE is used in evaluating the level of quality of evidence. GRADEpro GDT, a software for creating evidence summaries and healthcare recommendations, will be used.21 It addresses the shortcomings of previous grading systems, such as explicit, comprehensive criteria for rating the quality of evidence, a transparent process of upgrading evidence to recommendations and interpreting the strength of recommendations.[21] The study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias of the gathered articles will be considered when grading the outcome measures based on the quality of evidence in GRADE.[21]

EXPECTED RESULTS

This study will show that facemask use will clinically and significantly affect Borg's RPE, humidity, thermal sensation, breathing resistance, itchiness, tightness, saltiness, misfit,

odor, fatigue, overall discomfort, HR, BP, RR, TV, SPO2, VO2 max, ETCO2, lactate, and COVID-19 incidence among healthy adults during exercise. Facemask use is associated with discomfort during exercise; however, it must be used to prevent the risk of SARS-CoV-2 transmission. These findings will enable healthcare professionals to give evidence-based recommendations, inform the public about performing physical activity safely amidst the pandemic, and guide manufacturers on redesigning facemasks that promote comfort and ease of breathing without sacrificing their filtration efficiency.

Individual Author's Contributions

V.C.D.III, M.S.J., M.S.: Co-wrote the paper and will analyze data. V.C.D.III.: will appraise the papers. F.S.J., K.M., L.E., L.A., C.A., A.B., J.M., A.P.: Co-wrote the paper and will conduct data extraction.

Disclosure Statement

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Conflicts of interest

V.C.D.III is part of the editorial board of the Philippine Journal of Allied Health Sciences. The remaining authors of this paper declare no conflicting interests.

Supplementary Materials

Supplement A. PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 Checklist

Supplement B. Search Hits

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