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The influence of N95 and FFP2 masks on cardiorespiratory variables in healthy individuals during aerobic exercise: a systematic review and meta-analysis

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Study carried out at the Faculdade de Ciências Médicas e da Saúde de Juiz de Fora – SUPREMA – Juiz de Fora (MG) and at the Universidade Paulista – UNIP – Volta Redonda (RJ) Brasil.

ABSTRACT

Objective: In view of the current COVID-19 pandemic, the objective of this study was to determine, through a systematic review and meta-analysis, whether the use of N95/FFP2 masks during aerobic exercise has a significant impact on HR, RR, SpO_2, and blood pressure (BP) in healthy individuals. **Methods:** We searched the MEDLINE database for studies published in English between 2005 and 2021. To reduce bias and increase reliability, only randomized controlled trials and randomized crossover clinical trials were considered for inclusion. The selected outcomes included HR, RR, SpO_2, and BP, with perceived exertion being evaluated by means of the Borg scale. **Results:** Eight controlled trials were included in the meta-analysis. Seven evaluated HR ($p > 0.05$), five evaluated RR ($p > 0.05$), five evaluated SpO_2 and BP ($p > 0.05$ for both), and six evaluated perceived exertion, presenting controversial results such as risk ratios that were grouped for each variable. **Conclusions:** This study suggests that N95 and FFP2 masks do not have significant effects on HR, RR, SpO_2, and BP during aerobic exercise in healthy individuals.

Keywords: N95 respirators; Heart rate; Respiratory rate; Oxygen saturation; Blood.

INTRODUCTION

Protective masks are essential pieces of personal protective equipment for health professionals, especially those who deal directly with airway infections, as in the case of the current COVID-19 pandemic.[1-3] In a study that was conducted in Singapore in 2020 and in which 30 health professionals wore N95 masks when providing care to patients who tested positive for SARS-CoV-2 infection, there was no patient-to-professional disease transmission.[4]

In a study that was conducted in South Korea in 2015 and in which 97 COPD patients wearing N95 masks were investigated, there were considerable changes in RR, SpO_2, and end-tidal carbon dioxide levels before and after mask use.[5] In another study conducted in 2020, young people who had no comorbidities and who were nonsmokers performed aerobic physical exercise wearing N95 masks for an average of 75-150 min per week and showed no considerable changes in gas concentrations.[6] Kim et al. evaluated 20 healthy young people participating in low- to moderate-intensity physical activity for 1 h while wearing four different models of N95 masks and found no significant gas exchange abnormalities.[7]

According to Chandrasekaran et al.,[8] the use of N95 masks for long periods of time could lead to changes in muscle metabolism; cardiorespiratory stress; changes in the excretory and immune systems; and changes in the brain and central nervous system. This is due to the fact that N95 masks create a closed rebreathing circuit, leading to hypercapnic hypoxia.[8-11]

In a study by Fikenzer et al.,[12] 12 healthy men underwent ergospirometry and impedance cardiography before and after the use of N95 masks, which significantly reduced pulmonary function parameters and peak blood lactate response. However, there is a lack of studies analyzing the correlation between the use of N95/FFP2 masks and possible changes in SpO_2, RR, HR, respiratory resistance, and blood pressure (BP) in the context of the current COVID-19 pandemic.[13-16]

The objective of this study was to determine, through a systematic review and meta-analysis, the effects of N95/FFP2 masks on BP, HR, RR, SpO_2, and perceived effort during aerobic physical activity in healthy individuals.

METHODS

Search strategy

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The study protocol was registered with the International Prospective Register of Systematic Reviews (Registration no. CRD42021282318).

We searched the MEDLINE database for articles originally published in English in the last 15 years. Only randomized controlled trials or randomized crossover clinical trials were selected for the review; therefore, the sample of

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studies tended to be homogeneous and avoided biases commonly found in cross-sectional and observational studies. Two independent evaluators searched the MEDLINE database, and, in case of divergence between the two, a third evaluator was consulted. Disagreements were resolved by consensus.

The search terms "N95," "FFRs," "FFP2," "Effects," "Physiological," "Gas," and "Blood" were used in order to identify relevant studies. The MeSH list of descriptors was used in order to identify variations of the aforementioned search terms.

Inclusion and exclusion criteria

The inclusion and exclusion criteria are shown in Chart 1.

Data extraction

Our research group previously selected the information for data collection by separately searching the included studies for the following: title, name of the first author, year in which the study was conducted, year in which the study was published, country of origin, number of participants, mean/median and standard deviation of each variable with and without masks, aerobic interventions used, and outcomes (i.e., HR, RR, SpO_2, and BP as primary outcomes; and respiratory resistance and perceived exertion—as assessed by the Borg scale—as secondary outcomes). All of the authors independently collected the data. To evaluate the articles, two evaluators who were not part of our research group established search strategies and performed critical analyses. After the reading of the articles in their entirety, studies were excluded from the review if there were methodological biases, a lack of direct correlation with the topic of interest, or failure to provide raw data.

Statistical analysis

For the meta-analysis and risk of bias calculation, we used the following programs: Review Manager, version 5.4 (RevMan 5; Cochrane Collaboration, Oxford, UK); Microsoft Excel; and MedCalc (MedCalc Software Ltd, Ostend, Belgium). Fixed and random statistical analyses were performed, with the studies being considered homogeneous. The 95% CI was calculated for each study individually and then for all of the selected studies. The mean and standard deviation of each study were identified, and the level of significance was set at $p \leq 0.05$. The I^2 statistic was calculated in order to evaluate heterogeneity among the included studies. If I^2 was greater than 50%, we chose to use a random-effects model to match the results, and if I^2 was less than 50%, we created a fixed-effects model. The risk of publication bias was evaluated by examining a funnel plot for asymmetry.

RESULTS

Study selection

We identified 879 studies involving the use of face masks; however, after the application of the inclusion and exclusion criteria (Chart 1), only 20 studies remained. Another 10 studies were excluded after they were read in their entirety, because of methodological biases, a lack of direct correlation with the topic of interest, or failure to provide raw data. Of the remaining 10 studies, only 8 had the raw data available before and after the intervention for statistical analysis and were therefore eligible for inclusion in the meta-analysis. The analyzed studies involved 306 volunteers in the 7- to 64-year age bracket, 68.95% of whom were male. Figure 1 shows a flow chart of the study selection process.

Interventions and findings

Of the 10 studies that were included in the systematic review, 8 assessed BP, 9 assessed HR, 5 assessed RR, and 5 assessed SpO_2. Most of the clinical trials showed no significant changes in the study variables after the use of N95/FFP2 masks during low- or high-intensity aerobic exercise in healthy individuals, and 2 studies that were aimed at assessing all or most of the clinical variables analyzed in this review corroborated this finding.

Chart 1. Inclusion and exclusion criteria.

Inclusion criteria
Design: randomized controlled trials or randomized crossover clinical trials
Language: English
Involving humans only
Intervention: use of N95/FFP2 masks
Exclusion criteria
Intervention: unclear, poorly described, or inadequate
Publishing form: abstract only
Main variables analyzed
HR
RR
Blood pressure
Oxygen saturation (SpO_2)
Perceived exertion (as assessed by the Borg scale)

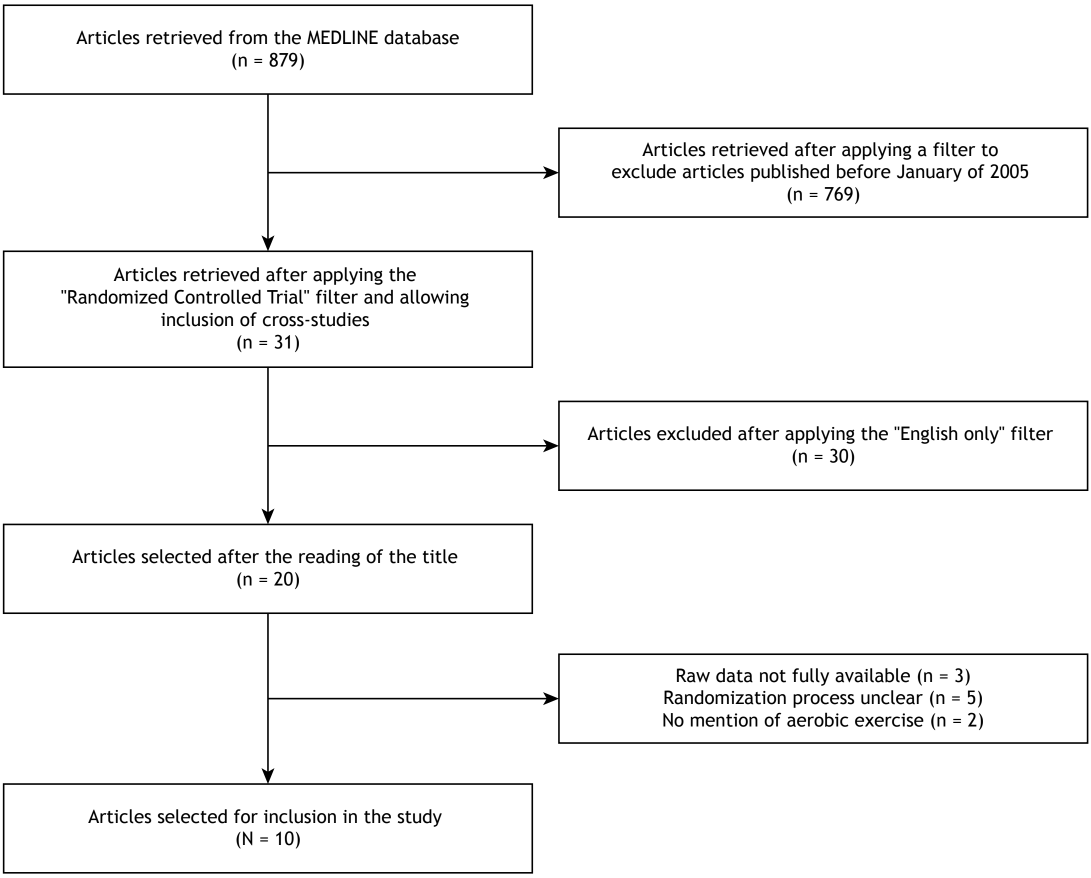


Figure 1. Flowchart of the study selection process.

In general, the interventions were of short duration, ranging from 3 min to 12 h on the same day, and participants were instructed to refrain from caffeine consumption in all studies, with the control and experimental groups being evaluated on different days.[(6,16-19)] Interventions varied greatly among the studies, and some used different devices and methods to measure the study variables. Interventions included walking,[(5,20)] treadmill walking,[(18,19)] medium- to high-intensity interval exercise on a cycle ergometer,[(6,12,16,21)] and going up and down stairs.[(22)]

Meta-analysis

Only 8 of the 10 studies included in this review provided sufficient data to analyze BP, HR, RR, and SpO_2 in the face of aerobic interventions with and without N95/FFP2 masks.[(6,12,16,18,19,21-23)] Therefore, only the aforementioned 8 were included in our meta-analysis, totaling a sample of 166 volunteers. The standardized mean difference ranged from −0.32 to 0.17 for BP, −0.27 to 0.13 for SpO_2, −0.10 to 0.27 for HR, and −0.16 to 0.28 for RR with the use of a fixed-effects model and with no statistically significant changes for any of the variables. Figures 2-5 show the analysis of the data for each of the included studies.

Figure 6 presents a synthesis of the results, a general test of heterogeneity, and differences between the subgroups. The results on the left indicate favorable values for the influence of N95/FFP2 masks on the study variables when compared with no mask use. The heterogeneity test applied in the analysis showed no significant heterogeneity among the studies; therefore, fixed-effects models were used. All of the studies investigated the effects of the use of N95/FFP2 masks on some of the variables analyzed by comparing values obtained with and without mask use.

BP

As can be seen in Figure 2, the use of N95/FFP2 masks during aerobic exercise had no significant effect on BP in any of the analyzed studies, as evidenced by the diamond crossing the vertical line of null effect, with the diamond representing the synthesis of CIs and relative risks.

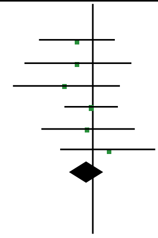
SpO_2

As can be seen in Figure 3, the use of N95/FFP2 masks during aerobic exercise had no significant effect on SpO_2, as evidenced by the diamond crossing the vertical line of null effect. Although Mapelli et al.[(21)] showed that the use of N95/FFP2 masks had a significant

Study or Subgroup	Use Mean	Use SD	Use Total	Non-use Mean	Non-use SD	Non-use Total	Weight	Std. Mean Difference IV, fixed, 95% CI	A	B	C	D	E	F	G
2.1.4 Blood pressure															
Egger 2021[16]	107.3	8	24	109	7.4	24	3.4%	-0.22 [-0.78, 0.35]	?	?	?	?	+	+	−
Epstein 2021[6]	210	18.8	12	214	18.2	12	1.7%	-0.21 [-1.01, 0.59]	?	?	?	?	+	+	−
Fikenzer 2020[12]	154.6	18.8	12	164	27	12	1.7%	-0.39 [-1.20, 0.42]	?	+	+	?	+	+	−
Kienbacher 2021[22]	139	12	48	139	14	48	6.9%	0.00 [-0.40, 0.40]	?	?	?	?	+	+	−
Mapelli 2021[21]	226	16	16	227	15	16	2.3%	-0.06 [-0.76, 0.63]	?	?	+	+	+	+	−
Shi 2016[23]	147	16	16	143	14	16	2.3%	0.26 [-0.44, 0.96]	?	?	?	?	+	+	−
subtotal (95% CI)			128			128	18.3%	-0.07 [-0.32, 0.17]							

Heterogeneity Chi² = 1.95, df = 5 (P = 0.86); I² = 0%
Test for overall effect: z = 0.57 (P = 0.57)

Std. Mean Difference IV, fixed, 95% CI



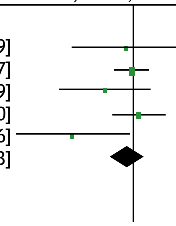
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of parcipants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Figure 2. Forest plot of the included studies evaluating blood pressure in fixed- and random-effects models, with a standardized mean difference and a 95% confidence interval.

Study or Subgroup	Use Mean	Use SD	Use Total	Non-use Mean	Non-use SD	Non-use Total	Weight	Std. Mean Difference IV, fixed, 95% CI	A	B	C	D	E	F	G
2.1.3 O_2 saturation															
Epstein 2021[6]	97.8	0.6	12	97.9	1.1	12	1.7%	-0.11 [-0.91, 0.69]	?	?	?	?	+	+	−
Goh 2019[18]	99.2	065	106	99.2	0.81	106	15.2%	0.00 [-0.27, 0.27]	?	?	+	−	+	+	−
Kienbacher 2021[22]	97.63	1.26	16	98.13	1.09	16	2.2%	-0.41 [-1.12, 0.29]	?	?	?	?	+	+	−
Kim 2016[19]	97.1	1	48	97	1	48	6.9%	0.10 [-0.30, 0.50]	?	?	?	?	+	+	−
Mapelli 2021[21]	95.1	3.1	12	97.3	1.2	12	1.5%	-0.90 [-1.75, -0.06]	?	?	+	+	+	+	−
subtotal (95% CI)			194			194	27.6%	-0.07 [-0.27, 0.13]							

Heterogeneity Chi² = 5.59, df = 4 (P = 0.23); I² = 28%
Test for overall effect: Z = 0.65 (P = 0.52)

Std. Mean Difference IV, fixed, 95% CI



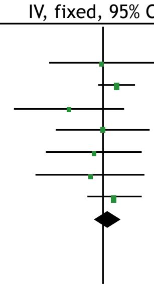
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of parcipants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Figure 3. Forest plot of the included studies evaluating oxygen saturation in fixed- and random-effects models, with a standardized mean difference and a 95% confidence interval.

Study or Subgroup	Use Mean	Use SD	Use Total	Non-use Mean	Non-use SD	Non-use Total	Weight	Std. Mean Difference IV, fixed, 95% CI	A	B	C	D	E	F	G
2.1.1 Heart Rate															
Egger 2021[16]	105.9	11.9	12	106.2	14.8	12	1.7%	-0.02 [-0.82, 0.78]	?	?	?	?	+	+	−
Epstein 2021[6]	110.2	7.73	106	108.4	9.84	106	15.1%	0.20 [-0.07, 0.47]	?	?	?	?	+	+	−
Fikenzer 2020[12]	182	11.2	12	187	8.3	12	1.7%	-0.49 [-1.30, 0.32]	?	+	+	?	+	+	−
Goh 2019[18]	191	7	16	191	9	16	2.3%	0.00 [-0.69, 0.69]	?	?	+	−	+	+	−
Kienbacher 2021[22]	168.81	12.84	16	170.5	11.71	16	2.3%	-0.13 [-0.83, 0.56]	?	?	?	?	+	+	−
Kim 2016[19]	167.2	16.1	12	170	14	12	1.7%	-0.18 [-0.98, 0.62]	?	?	?	?	+	+	−
Mapelli 2021[21]	108	19	48	105	19	48	6.9%	0.16 [-0.24, 0.56]	?	?	+	+	+	+	−
subtotal (95% CI)			222			222	31.7%	0.08 [-0.10, 0.27]							

Heterogeneity Chi² = 3.69, df = 6 (P = 0.72); I² = 0%
Test for overall effect: z = 0.89 (P = 0.37)

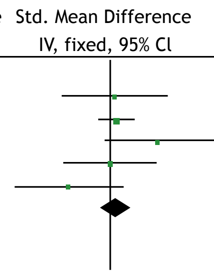
Std. Mean Difference IV, fixed, 95% CI



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of parcipants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Figure 4. Forest plot of the included studies evaluating heart rate in fixed- and random-effects models, with a standardized mean difference and a 95% confidence interval.

Study or Subgroup	Use Mean	Use SD	Use Total	Non-use Mean	Non-use SD	Non-use Total	Weight	Std. Mean Difference IV, fixed, 95% CI	Risk of Bias A B C D E F G
2.1.2 Heart Rate									
Epstein 2021[6]	28.4	3.2	12	28.1	7.1	12	1.7%	0.05 [-0.75, 0.85]	? ? ? ? + + −
Fikenzer 2020[12]	23.5	3.53	106	23.2	3.73	106	15.2%	0.08 [-0.19, 0.47]	? + + ? + + −
Goh 2019[18]	40.9	5.1	12	36.8	5.9	12	1.6%	0.72 [-0.11, 1.55]	? ? + − + + −
Kim 2016[19]	36.63	5.4	16	36.69	7.45	16	2.3%	-0.01 [-0.70, 0.68]	? ? ? ? + + −
Mapelli 2021[21]	37.1	4.5	12	41.5	8	12	1.6%	-0.65 [-1.48, 0.17]	? ? + + + + −
subtotal (95% Cl)			158			158	22.4%	0.06 [-0.16, 0.28]	



Heterogeneity: Chi² = 5.35, df = 4 (P = 0.25); I² = 25%
Test for overall effect: z = 0.56 (P = 0.58)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of parcipants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Study or Subgroup	Use Mean	Use SD	Use Total	Non-use Mean	Non-use SD	Non-use Total	Weight	Std. Mean Difference IV, fixed, 95% Cl
subtotal (95% Cl)			702			702	100.0%	0.01 [-0.10, 0.11]

Heterogeneity: Chi² = 18.40, df = 22 (P = 0.68); I² = 0%
Test for overall effect: z = 0.18 (P = 0.86)
Test for subgroup differences: Chi² = 1.81, df = 3 (P = 0.61), I² = 0%

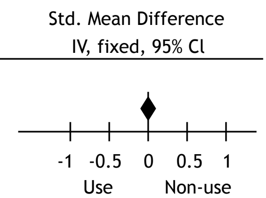


Figure 5. Forest plot of the included studies evaluating respiratory rate in fixed- and random-effects models, with a standardized mean difference and a 95% confidence interval.

effect on SpO_2, their findings did not affect the overall result, because the study sample was small.

HR

As can be seen in Figure 4, the use of N95 masks during aerobic exercise had no significant effect on HR in any of the analyzed studies, as evidenced by the diamond crossing the vertical line of null effect.

RR

As can be seen in Figure 5, the use of N95/FFP2 masks during aerobic exercise had no significant effect on RR in any of the analyzed studies, as evidenced by the diamond crossing the vertical line of null effect.

As can be seen in Figure 6, a synthesis of the values collected before and after the interventions for all of the variables in the studies selected for the present meta-analysis showed that the use of N95/FFP2 masks during aerobic exercise had no significant effect on the study variables, as evidenced by the association of CIs and relative risks with the diamond crossing the vertical line of null effect in the forest plots.

Chart 2 presents a summary of the studies selected for this systematic review, including sample size, patient age, type of analysis, interventions performed, systolic BP, HR, RR, SpO_2, and perceived effort. Values of $p < 0.05$ were considered to denote a significant change in the variables analyzed.

Publication bias

A funnel plot was used in order to assess the risk of publication bias (Figure 6). A symmetrical distribution is evident for HR, RR, and BP, whereas, in the studies that analyzed SpO_2, asymmetry is evident.

DISCUSSION

This study showed that the use of N95/FFP2 masks in healthy individuals performing aerobic exercise is safe and did not significantly change any of the variables studied. Interventions varied across studies, including aerobic exercise of different intensities, helping us assess the behavior of cardiorespiratory variables during walking and high-intensity interval training. The findings of the present study show that people can train while wearing masks and protect themselves from airway infections, without negative effects on physiological and perceptual responses to exercise.

We found that the effects of the use of N95/FFP2 masks during mild to moderate aerobic exercise presented categorical results regarding changes in BP, HR, and SpO_2 in maximum and submaximal parameters; it is possible to affirm that these variables were not significantly affected by the respective interventions.[6,12,17-22] We can affirm that BP, HR, and SpO_2 do not undergo clinically significant changes with the use of N95/FFP2 masks.

According to Harber et al.,[14] increased cardiopulmonary work is seen in individuals with COPD or asthma. This can be due to decreased circulating oxygen levels and/or blood acidosis caused by insufficient inspiration or respiratory disease. The study in question was carried out on three different days, and the groups of individuals with respiratory disease performed light- to moderate-intensity physical activities lasting an average of 8-10 min each. The study variables were tidal volume, minute ventilation, inspiratory flow rate, expiratory flow rate, inspiratory time, expiratory time, RR, mean total respiratory cycle time, and the duty cycle, which represented the proportion of the

Chart 2. Summary of the included studies and main results for systolic blood pressure, heart rate, respiratory rate, oxygen saturation (SpO_2), and perceived exertion (as assessed by the Borg scale).

Study, year	Sample	Intervention	Variables analyzed				
			BP	HR	RR	SpO_2	PE
Epstein et al., 2021[6]	16 volunteers (men only) mean age: 34 ± 4 years cross analysis	no mask use vs. surgical mask use vs. N95 mask use Participants underwent exercise testing on a cycle ergometer with a ramp protocol. initial load of 25 W at a constant speed of 55-65 rpm The initial load was increased by 25 W every 3 min until exhaustion. six tests, with a minimum rest period of 24 h between tests A 12-lead ECG was used in order to assess HR, SaO_2, and BP. RR was noninvasively assessed by means of nasal prongs.	= BP $p > 0.05$	= HR $p > 0.05$	= RR $p > 0.05$	= SpO_2 $p > 0.05$	= PE $p > 0.05$
Fikenzer et al., 2020[12]	12 volunteers (men only) mean age: 38.1 ± 6.2 years cross analysis	no mask use vs. surgical mask use vs. N95/FFP2 mask use Cycle ergometer with a ramp protocol at a speed of 60-70 rpm and a workload of 50 W, which was increased by 50 W every 3 min until voluntary exhaustion. An ECG and a digital spirometer were used in order to assess cardiac and pulmonary parameters, respectively.	= BP $p > 0.01$	= HR $p > 0.01$	↓ RR $p < 0.05$	N/A	N/A
Morishita et al., 2019[17]	50 volunteers (32 men and 18 women) mean age: 36 ± 14 years cross analysis	use of N95 masks vs. no use of N95 masks in a clinical environment and near a highway An ECG and an HR monitor were used in order to assess variations in HR. A BP monitor was used in order to analyze variations in BP every 10 min. 2 hours of observation, 5 days a week, in two different weeks	= BP $p > 0.01$	= HR $p > 0.01$	N/A	N/A	N/A
Shi et al., 2016[23]	24 volunteers (13 men and 11 women). The initial sample consisted of 30 volunteers. Six volunteers withdrew from the study. mean age: 23 years cross analysis	use of N95 masks vs. no mask use 1-h walks Variations in HR were assessed by Holter monitoring during the test. Variations in BP were analyzed with an automated BP monitor. BP was measured every 15 min during the day and every 30 min at night.	= BP $p > 0.05$	N/A	N/A	N/A	N/A

Continue...

Chart 2. Summary of the included studies and main results for systolic blood pressure, heart rate, respiratory rate, oxygen saturation (SpO_2), and perceived exertion (as assessed by the Borg scale). (Continued...)

Study, year	Sample	Intervention	Variables analyzed				
			BP	HR	RR	SpO_2	PE
Egger et al., 2021[16]	16 well-trained volunteer athletes (men only) age range: 20-34 years cross analysis	use of FFP2 masks vs. no use of FFP2 masks the Borg scale, a metabolic test system, a 12-lead ECG, and manual BP assessment initial workload of 100-150 W, increased by 50 W every 3 min on an electromagnetic cycle ergometer The test was interrupted when volunteers were unable to cycle at a minimum speed of 50 rpm for more than 10 s. an interval of at least 48 h between evaluations with and without FFP2 masks	= BP $p > 0.01$	= HR $p > 0.01$	N/A	N/A	= PE $p > 0.05$
Kienbacher et al., 2021[22]	48 volunteers (44 men and 4 women) mean age: 28 ± 8 years triple-test cross analysis	use of personal protective equipment (overalls, glasses, and gloves) and FFP2 masks without an exhalation valve vs. no use of FFP2 masks climb and descend stairs at a fast pace with a backpack and oxygen cylinder, followed by 12 min of chest compressions and bag-valve-mask ventilation a rest period of 30 min between tests BP, HR, and SpO_2 were assessed with a portable monitor/defibrillator.	= BP $p > 0.05$	= HR $p > 0.05$	N/A	= SpO_2 $p > 0.05$	↑ PE $p < 0.05$
Rebmann et al., 2013[20]	10 volunteer nurses (9 women and 1 man); 9 completed the study. age range: 24-48 years (mean age, 35 years)	use of N95 masks vs. use of N95 masks with a surgical mask overlay use of N95 masks for 12 h daily for 2 days Variables were analyzed every 30 min with a saturation sensor. an interval of 1 or more days between analyses	= BP $p > 0.05$	= HR $p > 0.05$	N/A	N/A	↑ PE $p < 0.05$
Goh et al., 2019[18]	106 volunteer children (59 boys and 47 girls) age range: 7-14 years cross analysis	no use of masks vs. use of N95 masks without a valve vs. use of N95 mask with a valve Reading in 3 5-min intervals: 1st—no mask (control); 2nd—wearing a valveless mask; and 3rd—wearing a valved mask Nasal cannulas with a multiparameter ECG monitor and a continuous monitoring system were used in order to evaluate SpO_2, HR, and RR.	N/A	= HR $p > 0.05$	= RR $p > 0.05$	= SpO_2 $p > 0.05$	↑ PE $p < 0.05$
Kim et al., 2016[19]	12 volunteers (men only) mean age: 23.5 ± 1.6 years cross analysis	use of N95 FFRs or similar vs. no mask use Individuals walked for 1 h at 5.6 km/h on a treadmill at a 0% slope. temperature, 35°C; relative humidity, 50% tests performed on two different days (first without an FFR, then with an FFR) A pulse oximeter with a transcutaneous carbon dioxide sensor connected to the ear, a monitoring chest strap, and an HR monitor were used in order to evaluate SaO_2, RR, and HR, respectively.	N/A	= HR $p > 0.05$	= RR $p > 0.05$	= SpO_2 $p > 0.05$	= PE $p > 0.05$

Continue...▶

Chart 2. Summary of the included studies and main results for systolic blood pressure, heart rate, respiratory rate, oxygen saturation (SpO_2), and perceived exertion (as assessed by the Borg scale). (Continued...)

Study, year	Sample	Intervention	Variables analyzed				
			BP	HR	RR	SpO_2	PE
Mapelli M et al., 2021[21]	12 volunteers (6 men and 6 women) mean age: 41 ± 12.4 years cross analysis	no use of FFP2 masks vs. FFP2 mask use maximal progressive exercise testing on a cycle ergometer Spirometry and a BP monitor were used in order to analyze variables.	= BP $p > 0.05$	= HR $p > 0.05$	= RR $p > 0.05$	↓ SpO_2 $p < 0.05$	

BP: blood pressure; PE: perceived exertion (as assessed by the Borg scale); ECG: electrocardiogram; FFP2: filtering facepiece 2; FFR: filtering facepiece respirator; ↑: significant increase in the variable; ↓: significant decrease in the variable; and =: no significant change in the variable. $p > 0.05$ or $p > 0.01$ indicates no significant difference between the control and intervention groups.

total respiratory cycle during which inspiratory effort was made.

A decrease in the amount of oxygen is mainly detected by the central chemoreceptors in the carotid body. These chemoreceptors induce respiratory upregulation by the effect of the vagus and glossopharyngeal nerves on the ventral respiratory group. Although this is true, it occurs in situations that significantly affect the amount of oxygen available.

Changes in the variables discussed in this review may be more commonly observed in individuals with preexisting heart and lung disease.[5,13-15] Therefore, on the basis of the studies that were aimed at investigating BP, it cannot be affirmed that N95/FFP2 masks cause significant changes.[6,12,16,17,20-,23] This is also true for the studies that evaluated SpO_2 and HR.[6,12,16-22]

Of the 5 studies that evaluated changes in RR,[6,12,18,19,21] only 1 found a significant decrease in RR.[12] Respiratory resistance was analyzed as a secondary variable, and the 2 studies that analyzed it presented conflicting results; 1 found significant changes, and the other did not.[6,16] These results can be explained by reduced VO_2max, decreased inspiratory ventilation, and the formation of a negative pressure rebreathing nucleus in some cases.[8,12,24,25] Despite not being included in this review (because they did not meet the inclusion criteria), several clinical studies analyzing respiratory resistance showed significant changes.[1,23,24] However, well-structured clinical trials involving larger samples and a variety of interventions are required in order to confirm this.

Although some of the studies evaluating RR and respiratory resistance showed significant changes in both, these findings are not enough to confirm that the use of N95/FFP2 masks causes significant changes in these variables. Respiratory resistance, which was measured noninvasively by means of nasal prongs and metabolic tests, was increased in one of the two studies evaluating it.[12,16] With different interventions and small samples, respiratory resistance is a variable for which there is no consensus regarding changes caused by N95/FFP2 mask use.

Some studies have shown that respiratory resistance increases with the use of N95 masks during mild- to moderate-intensity aerobic exercise.[1,12,24] Despite an increase in the number of studies, there is a lack of well-designed experimental and longitudinal studies evaluating the physiological changes caused by mask use. The studies evaluating respiratory resistance included in this review confirm that the use of N95/FFP2 masks during mild to intense aerobic exercise significantly influences this variable.[6,16] Respiratory resistance has been the target of large studies, especially because of the COVID-19 pandemic; therefore, reduced VO_2max, decreased inspiratory ventilation, and the formation of a negative pressure rebreathing nucleus remain under investigation.[8,12,24-26]

Conflicting results were also found in the six studies that evaluated ratings of perceived exertion on the

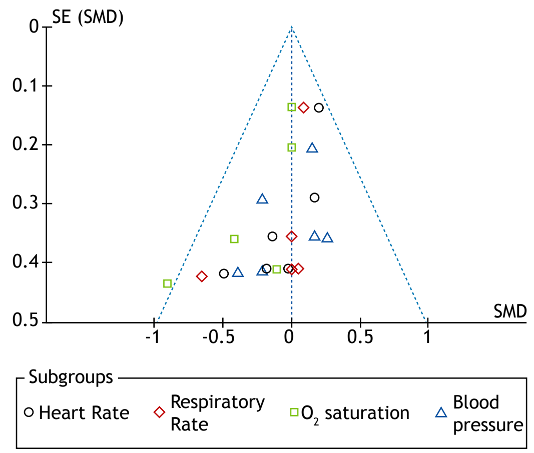


Figure 6. Funnel plot of the included studies with all of the study variables, showing asymmetry in the distribution of studies examining oxygen saturation. SE: standard error; and SMD: standardized mean difference.

Borg scale.[6,16,19-22] Three studies showed increasingly significant changes,[21-23] whereas the remaining three showed no significant changes.[6,16,19] Further clinical studies are needed in order to fill this gap because it was impossible to analyze the correlation between changes in ratings of perceived exertion and the study samples given the differing interventions, patient characteristics, and exercise intensities across studies.

The evidence developed in the 1990s suggests that the restrictive gas stimulus to oxygen chemoreceptors caused by the respiratory nucleus of face masks results in a decrease in available oxygen, triggering sympathetic stimulus and increasing HR and RR by activation of the ventral respiratory group through the activity of the vagus and glossopharyngeal nerves in the upregulation of these chemoreceptors.[27,28] However, the hypothesis that face masks are capable of causing changes in the cardiorespiratory system has been questioned, especially because of their widespread use during the current COVID-19 pandemic, which has demonstrated that this hypothesis is inconsistent with the results of related studies.

Of the 5 studies evaluating RR, only 1 found a significant change contributing to a decrease in RR, a finding that can be attributed to the small sample size (N = 12). The variation between intensity of cardiorespiratory stimulus and burst cannot be confirmed, and nor can the changes related to the use of masks. Clinical trials involving different interventions and larger samples are needed in order to reach a definitive conclusion.[1,2,6,12-14,16,17,26-28] Rebmann et al.[20] also evaluated these variables; however, the evaluations were performed with participants wearing either an N95 mask alone or an N95 mask and a surgical mask, showing no considerable changes. In contrast, Fikenzer et al.[12] observed a decrease in RR. In that study,[12] which is one of the five studies analyzing the variability of RR, the intervention consisted of incremental exercise performed on a cycle ergometer at a speed of 60-70 rpm, the workload being increased by 50 W (as a ramp) every 3 min until voluntary exhaustion. This reinforces the assumption that the variability and intensity of aerobic exercise play a highly relevant role in clinical changes. In recent studies,[5,13,14] individuals presenting with COPD of varying severity and wearing face masks were investigated; mask use was found to cause significant changes in some of the aforementioned physiological parameters, especially respiratory parameters, with a higher degree of disease severity translating to more significant changes. Therefore, clinical conditions and aerobic exercise intensity have strong clinical relevance.

There were no significant changes in HR, BP, and SpO_2 in individuals in the 7- to 64-year age bracket wearing N95/FFP2 masks in comparison with those not wearing them.[6,7,12,16-18,21,22] Of the 10 studies included in this review, 8 had BP as one of the study variables, and none of the interventions resulted in significant changes in BP.[6,12,17,18-23] Thus, it cannot be inferred that BP changes significantly during and after mask use because the interventions ranged from mild to moderate aerobic exercise in samples of 12-50 participants in the studies showing no significant changes in BP; although these studies together analyzed a total of 188 individuals (i.e., a considerable sample size), studies examining larger samples are needed.

In the 5 studies analyzing SpO_2, no significant changes were observed during submaximal exercise (mild- to moderate-intensity aerobic exercise); one study found a significant change in SpO_2 during maximal exercise.[6,18,19,21,22] The sample size (a total of 198 volunteers) and the differing interventions across studies suggest that N95 and FFP2 masks can cause no changes in SpO_2 during mild- to moderate-intensity aerobic exercise. These results may be conflicting because of the differing exercise intensities across studies.

Nine studies evaluated HR with and without mask use during the interventions, which ranged from mild- to moderate-intensity aerobic exercise,[6,12,15-19,21,24] showing no significant changes in HR. A total of 282 individuals underwent HR analysis. Given that the findings regarding HR were the same in all 9 studies, the changes observed in the individuals who wore N95/FFP2 masks during aerobic exercise appear to be nonsignificant. However, it is of note that some of the studies that did not meet the criteria for inclusion in this review showed significant changes in HR. These changes may be due to the sample size, a lack of randomization and control (leading to heterogeneity and increased bias), the type of mask used, and the rest period between peak activities, which was considered high.

One of the limitations of the present study is the use of only one database for article retrieval. Another limitation is the fact that we did not assess the quality of the evidence using the Grading of Recommendations Assessment, Development and Evaluation method, which is based on analysis of the risk of bias of the selected studies. It is also important to point out the limitations of the studies included in this review: (1) limitations related to the study design (i.e., the difficulty in evaluating physiological parameters in individuals wearing N95/FFP2 masks); (2) differing methods across studies, including differences in exposure time, type of aerobic exercise, and exercise intensity; (3) small sample sizes; (4) differing mask brands and seals across studies; (5) use or lack of use of an exhalation valve; (6) unblinded analyses or inadequate randomization; and (7) inadequate rest period and use of the same sample subjected to different interventions, introducing systematic bias.

FINAL CONSIDERATIONS

This study suggests that wearing N95/FFP2 masks during aerobic exercise does not have significant effects on the variables analyzed, their use therefore being safe for human health. Respiratory resistance and perceived exertion (as assessed by the Borg scale) during aerobic exercise showed results that are conflicting and inconclusive. Therefore, further clinical trials are required, involving larger samples and different interventions. Finally, we can affirm that, in cases of preexisting diseases of the cardiorespiratory system, changes in HR, RR, and SpO_2 tend to be more significant.

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AUTHOR CONTRIBUTIONS

GLSL, TCR, GPLSJ, and MTM: study conception and design; statistical analysis; and writing of the manuscript. GLSL, TCR, and GPLSJ: data analysis and interpretation. MTM: critical revision of the manuscript for important intellectual content.

CONFLICTS OF INTEREST

None declared.

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