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BRIEF COMMUNICATION

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Well-Designed Studies are Needed to Assess Adverse Effects on Healthy Lung Function after Long-Term Face Masks Usage

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Abstract

Face coverings, especially cloth masks, were the critical personal protective equipment during the COVID-19 pandemic. The advantages of such masks were well understood and widely used across the world. With this idea in mind, we have reviewed the available data and literature to identify whether masks exert an untoward effect on lung function in otherwise healthy persons. Interestingly enough, we have found no well-designed studies to assess whether masks have an unintended negative consequence on healthy lung function. Moreover, we are also aware that there could exist a differential impact of facial coverings depending on the type of masks exposed to. In addition, there could also be some ethical challenges in order to implement these cohort studies. We are recommending the need for thorough evaluations of long term mask utilization.

Key word: design of experiments, longitudinal study, clinical impact of face masks.

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Facial coverings are an important tool for preventing the transmission of many airborne infectious disease, and more recently SARS-CoV-2 especially before the introduction of vaccines for this pandemic in December 2020 (1-2). The usage of facemasks in public places decreased by April 2021 due to the rapid increase in vaccinated individuals. However, the percentage of non-vaccinated individuals in several states in the U.S. has remained high throughout the summer of 2021. The emergence of the "delta variant" among non-vaccinated individuals (3) and the increase in new COVID-19 cases beginning in July 2021 (3) has led many policymakers to consider reinstituting universal facemask usage indoors and in public places. These mandates have been instituted in the U.S. and across numerous countries world-wide.

Cloth masks and non-surgical face masks have been frequently worn by the general public during the COVID-19 pandemic as has been recommended by the World Health Organization (WHO) and country-level health advisors (the CDC, etc.) (1-5). Similarly, healthcare workers frequently wear surgical face masks and other hospital-based face masks (6). When used appropriately, cloth or surgical face masks prevent the spread of SARS-CoV-2 particles from mask-wearing individuals (7-10).

Certainly facial coverings along with other preventive measures such as the 6 feet social distancing, handwashing, not touching the face, etc., have played a significant role in controlling the transmission of the COVID-19 (11). However, several studies recently conducted demonstrate that improper usage of facial coverings and not using appropriate masks might not prevent viral transmission effectively (12).

Few studies have evaluated the potential adverse effects of prolonged facial covering utilization and oxygen consumption or inhalation of toxic materials in otherwise healthy individuals (13-17). There is a need for large-scale prospective cohort studies among healthy individuals to determine whether prolonged use in healthy mask wearers experience adverse effects due to long term mask exposure. Prospective cohort studies in epidemiology have several advantages including smaller sample size and relative ease in identifying effect size and relationships: for example, (18-21). Critical questions including whether temporal relationships between mask usage and adverse outcomes remain unanswered due to the lack of well-designed prospective studies.

A pilot study of twelve healthy males indicated that they experienced considerable discomfort and reduced cardiopulmonary exercise capacity while wearing masks (13). However, there was no significant difference in terms of cardiac response with and without mask usage. A separate study of healthcare workers wearing masks on an average of 4 hours/day for one week concluded that participants experienced frequent subjective discomfort and difficulty breathing (14). Unfortunately, baseline lung function were not assessed in any of these healthcare workers. To date, the only study inclusive of baseline lung function (eg Spirometry) included only six healthy individuals, and determined that neither oxygen saturation nor comfort were affected by mask usage (15-16). While this small data set suggests mask usage is safe for healthy individuals, a recent study demonstrated that persons wearing masks had a significant increase in intraocular pressure when compared with participants who did not wear a mask (17). Most of these studies use subjective reports of discomfort during exercise or do not report on discomfort while wearing masks. Further, variables used to assess the level of discomfort in previous studies were inconsistent, which makes conclusive relationships difficult to establish. In fact, several studies reported inconsistencies in the data among individuals wearing masks (22).

Prospective cohort study:

Through this perspective, we wish to conduct a population-based prospective study among healthy individuals across the populations to identify whether face mask usage is associated with adverse events on the upper and lower respiratory tracts and natural functioning of lungs. Although a prospective cohort study design is provided in the Appendix for interested readers, in the below paragraphs we summarize the design for general readers.

This kind of impact evaluation requires information from a large population-based sample followed by a thorough investigation of the data collected. Such an exercise will be useful to determine any adverse effects of long-term facemask usage. In the following paragraphs, we will briefly summarize our ideas outlined in the technical Appendix provided here in a non-technical way.

The healthy population will be sampled from all age groups and across several geographical regions to take into account demographic and environmental effects. Each individual selected for the study will be randomly assigned to wear or not wear a facemask using a stratified systematic sampling. Those two populations will be used for the prospective cohort study. During the follow-up period, we anticipate some migration of study participants. For each study participant, we would consider the origin of enrollment. Under a clinical set-up, the required measurements of all the recruited individuals at both time points (i.e. base line and study conclusion) will be collected. Summarized information from all the participants will be tabulated in a 2x2 table to express the number of individuals who developed adverse lung function during the study period.

We have reviewed impact-of-mask studies that were conducted and published during 2020-2021. We have proposed to use a prospective cohort study design for the data collection that can assist in deriving meaningful conclusions.

We conclude that there is no clear evidence that continuous long-term usage of facial coverings does not harm the otherwise naturally functioning respiratory tract. The proposed study will provide the incidence of lung dysfunction associated with facemask usage with probabilistic confidence intervals within the predicted value. It is important to note that IRB (Institutional Review Boards) approval for the experimental design provided will be necessary.

Limitations:

We are aware that there could exist various risk factors based on the type of masks used (for example, N95, surgical masks, standard cloth masks, etc.,). Practical challenges like recruiting populations for each arm of the study cohorts with similar covariates might be an issue for implementations. The IRBs also need to handle ethical issues like who is part of the mask-wearing group and who is not. What we are proposing is a need for a thorough prospective cohort study that can take care of differential impacts due to the type of masks used along with other differential mentioned in this piece.

The recommended prospective cohort study has also limitations that can be overcome with careful data collection. One of the limitations of such studies is that the time consumed in the data collection could be prolonged.

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ASRSR and SGK designed the study, and ASRSR wrote the first draft, conceptualized the study and developed the methods. SGK have contributed in writing, editing and discussions. All authors approved the manuscript.

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APPENDIX: Prospective Cohort Study Design for Determining if There is Any Adverse Effects on Healthy Lungs Due to Long-Term Use of Masks

Suppose there is a large population of size $P(t_o)$ at a time t_o in a geographical region S that is pre-determined to have healthy functional lungs. Here,

$$P(t_0) = \int_0^\infty P(t_0, a)da, \qquad (1)$$

Where $P(t_o, a)$ is the population of age a at t_o. The region S can be further divided into k geographical regions to include in the study, such that

$$S = \bigcup_{m=1}^{k} S_m \qquad (2)$$

Equation (2) indicates that these *k*-subregions are all independent, and the study can be restricted to the usual residence of stay by the individuals at the beginning of the study by ignoring the migration of an individual if any within the study period. A random sample of size $Q(t_o,a)$ proportionate to the population at various ages are selected with a sufficient statistical power calculation α, say α=90%. Here

$$Q(t_0,a) = M(t_0,a) + N(t_0,a), \qquad (3)$$

Where $M(t_o,a)$ and $N(t_o,a)$ are the populations of age *a* at t_o who are using masks and not using masks, respectively. Suppose that $M(t_o,a)$ for all *a* have agreed to use face masks according to the COVID-19 norms and have agreed to use them for a minimum prescribed hours/day for a sufficiently long period of time, say until t_1 for $t_1>t_o$. The quantity $N(t_o,a)$ is the individuals at age *a* and at time t_o who agreed not to use face masks at least until t_1 for $t_1>t_o$. Therefore the total population recruited for the prospective cohort study is

$$Q(t_0) = \int_0^\infty Q(t_0,a)da$$

$$= \int_0^\infty M(t_0,a)da + \int_0^\infty N(t_0,a)da \qquad (4)$$

Let $Q(t1)$ be the population in the study design at the time t_1 who were recruited at t_o described above. This is expressed as

$$Q(t_1) = \int_0^\infty M(t_1,a)da + \int_0^\infty N(t_1,a)da\,, \qquad (5)$$

Where $M(t_1,a)$ and $N(t_1,a)$ are the populations of age *a* at t_o who are using masks or are not using masks, respectively. The number of individuals whose lungs are damaged during (t_o,t_1) are

$$E(t_1) = \int_0^\infty M_e(t_1,a)da + \int_0^\infty N_e(t_1,a)da, \qquad (6)$$

Where $M_e(t_1,a)<M(t_1,a)$ and $N_e(t_1,a)<N(t_1,a)$ for each *a*. (Note that the subscripted terms are defined in the following table.) Using the data collected through equations (1) to (6) above, we can create a 2×2 table as in Figure A1 for each age *a* at t_1. The number of individuals at age *a* and at t_1 whose lungs become damaged are

$$E(t_1,a) = M_e(t_1,a) + N_e(t_1,a).$$

Figure A1

The 2x2 table of masks usage information and lungs damaged data

	Lungs Damaged	Lungs Not Damaged	Totals
Population Used Masks	$M_e(t_1,a)$	$M(t_1,a) - M_e(t_1,a)$	$M(t_1,a)$
Population Not Used Masks	$N_e(t_1,a)$	$N(t_1,a) - N_e(t_1,a)$	$N(t_1,a)$
Totals	$E(t_1,a)$	$Q(t_1,a) - E(t_1,a)$	$Q(t_1,a)$

Using the data in Figure A1, one can test the hypothesis that "no significant difference between incidence of lung damage is due to mask usage."

The incidence of lungs damage due to mask wearing is

$$\frac{M_e(t_1,a)}{M(t_1,a)} \qquad (7)$$

The incidence of lungs damage due to not wearing of masks usage is

$$\frac{N_e(t_1,a)}{N(t_1,a)} \qquad (8)$$

The entire procedure described up to computation of incidences can be repeated for each S_m in (2) so that any geographical variations of lungs damage observed can be studied. The population at t_o, the cohort of survivors at t_1, and the population whose lungs damaged at t_1 in S_m regions also adds to $P(t_o)$, $Q(t_1)$, and, $E(t_1)$, respectively. This gives us

$$\sum_{m=1}^{k}\int_0^\infty P(t_0{:}\,S_m,a)da = P(t_0) \qquad (9)$$

$$\sum_{m=1}^{k}\int_0^\infty Q(t_1{:}\,S_m,a)da = Q(t_1) \qquad (10)$$

$$\sum_{m=1}^{k}\int_0^\infty E(t_1{:}\,S_m,a)da = E(t_1)\,, \qquad (11)$$

where $P(t_o{:}\,S_m,a)$ is the size of the population who are at age *a* at t_o in the region S_m, $Q(t_1{:}\,S_m,a)$ is survivors of the population who are at age *a* at t_1 in the region S_m, and, $E(t_1{:}\,S_m,a)$ is the size of the population with lungs damaged who are at age *a* at t_1 in the region S_m for $m=1,2,\ldots,k$.

Please note that what we propose is a theoretical design and actual implementation on human subjects may need IRB approvals at respective institutions.