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1. Background Summary:

The virus, “Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2), commonly known as COVID-19, primarily targets epithelial cells in the lungs, causing viral pneumonia and acute respiratory distress syndrome (ARDS) (Chilosi et al.). Ever since this virus broke out, it has affected millions of people globally, directly impacting their immune systems and causing severe respiratory failures, pneumonia being the most prevalent (Yazdanpanah et al.), leading some to death. Although the transmission is identified to be through the respiratory droplets that are expelled/absorbed by our mucosal membranes (Yazdanpanah et al.), it is imperative to know what behaviors/habits aid the virus in suppressing the immune system. Understanding such activities and their correlation with COVID-19 symptoms can equip us to avoid them better and prepare to minimize their effects.

Similarly, contents present in cigarettes genetically alter the alveolar epithelial cells and cause severe respiratory diseases (Spira et al.). Smoking causes permanent lung damage and increases the risk of asthma (Pietinalho et al.). As both diseases target the epithelial cells in the lungs, toxic substances in a cigarette may leave an individual vulnerable to COVID-19 infection and facilitate the pathogens, putting the patient in grave danger. Therefore, this paper intends to design a research that checks whether COVID-19 patients with a smoking history are at a greater risk of hospitalization or Intensive Care Unit (ICU) than non-smokers. For the scope of this paper, we assume that the patient is hospitalized as soon as they develop severe symptoms.

2. Hypothesis:

Patients with a smoking history (current or former), if tested positive for COVID-19, are more likely to develop severe COVID-19 symptoms such as interstitial pneumonia or asthma (Chilosi et al.) and get hospitalized sooner than patients without any smoking history because both smoking and COVID-19 damage the epithelial cells in the lungs responsible for safe respiration.

3. Outline of Research Design:

Type of research design:

Retrospective Cohort Observational Study.

Sampling strategy:

We will use stratified probability sampling with the population being all the COVID-19-positive people who were hospitalized within 14 days due to severe COVID symptoms (in our targeted area). The patients will be categorized into strata of never smoked, current smokers, and former smokers based on their smoking habits.

Variables:

Independent variable:

Category of admitted COVID-19-positive people (non-smoker, former smoker, current-smoker), which will be a qualitative nominal variable.

Dependent variable:

The time (t) taken in days to develop severe COVID-19 symptoms after a patient has tested positive for the virus. Although time is continuous as we count the days until the patient gets hospitalized, we will consider this variable quantitative discrete.

Potential confounding variables:

Pre-existing chronic illnesses like lung cancer, asthma, and COPD in patients of all categories may expedite the time taken to get hospitalized. Secondly, the a time delay between the patient's exposure to COVID-19 and their getting tested. Additionally, as a result of interaction with smokers, patients might have been passively smoking, which cannot be quantified or evaluated.

4. Narrative description

In order to test our hypothesis, we will perform a retrospective cohort observational study. We aim to conduct our study in one hospital in a big urban city that has enough resources to accommodate a lot of patients (larger sample size). This data can be prone to information bias resulting from a lack of up-to-date patient information or mishandling of data. To mitigate this, we would collect data from an urban hospital, assuming it maintained reliable and easily accessible health records of its patients. However, except for these conditions, the hospital would be selected randomly.

Considering the data from the population of all the COVID-19-positive cases in the selected hospital. Evaluating future cases, prospective data collection could be biased, as we could unintentionally focus on specific cases of smokers. This confirmation bias will thus mislead our analysis, making our data not entirely reliable. Evaluating past cases (retrospective) can help mitigate this as we would consider all the cases from a selected hospital without looking at patient information first during data collection. Thus, from a dataset of COVID positive cases from February 2020 till February 2021 (retrospective), we will filter the people as follows:

1. Admitted 14 days after being tested positive -since, after a significant time interval of 14 days, there might be ambiguities to the reason for hospitalization.
2. Prisoners -since prisoners have poorer health and immune conditions as compared to non-prisoners, due to worse diet and un-hygienic prison surroundings.
3. Patients younger than 18 years -since younger people have higher immunity than elderly people, these might be outliers in our dataset.
4. Patients with incomplete smoking records from our sample -since inaccurate records will make our data prone to errors.

From the filtered population, using stratified sampling, we will divide them into 3 strata. The data will be collected from the hospital we choose to observe in our study. Our independent qualitative nominal variable will be the category in which we will classify the patients based on self-reports, making our three comparison groups:

- Non-smokers: Patients who self-reported to have never smoked or have smoked less than 100 cigarettes in their lifetime.
- Current smokers: Patients who self-reported to have smoked more than or equal to 100 cigarettes in their lifetime and still smoke on a daily basis.

- Former-smokers: Patients who self-reported to have smoked more than or equal to 100 cigarettes in their lifetime but don't smoke on a daily basis. If the patient quit smoking 2 years before exposure to COVID-19, the patient will be considered a non-smoker.

This categorical classification is also prone to errors due to information bias, arising from memory bias in recalling whether the person smoked more than 100 cigarettes or not. Also, people might intuitively not report smoking as a habit, due to social norms considering smoking as a bad habit, making our analysis prone to errors. We try to mitigate this by comparing the self-reported smoking habits of patients to their hospital-recorded nicotine levels and discarding mismatching patient information.

Our dependent variable will be treated as quantitative discrete because the time (t) taken to develop severe symptoms and get hospitalized is counted in days (whole numbers) and cannot take a value in a range.

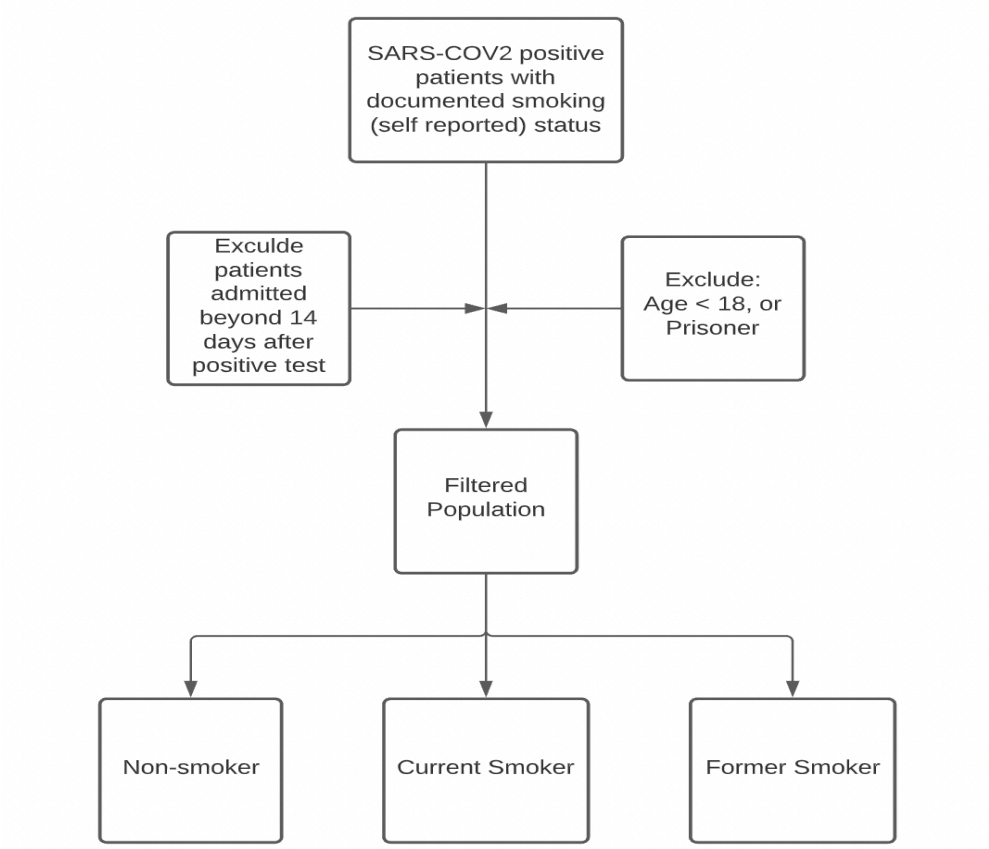

Fig.1 shows the sampling method in our retrospective cohort study and the filtration process that would foster a reliable result from our study. The comparison groups are further derived from the filtered population for effective evaluation.

In our cohort study, we would then note the time period for each of our patients from the day they tested positive to the day they were admitted to the hospital as a result of severe COVID-19 symptoms. We assume that patients get hospitalized when they develop severe symptoms. Then, we separately calculate the average days that patients from our comparison groups (non-smokers, current smokers, former smokers) took to get admitted. Firstly we calculate the cumulative days for all patients in a comparison group (e.g. 500 days for

non-smokers) and divide it by the total number of patients in the group (e.g. 42 patients, 500/42 = 12 days).

Designing three comparison groups and calculating the difference between the average days it takes for the respective patients to get hospitalized gives us an insight into whether smoking has an effect on the timely development of severe COVID symptoms due to damage to epithelial cells in the lungs.

Potential confounding variables at play are pre-existing chronic illnesses like lung cancer, asthma, and COPD in patients of all categories, since these may expedite the time taken to get hospitalized due to weakened immunity of the patients by these diseases.

Secondly, there can be a time delay between the patient's exposure to COVID-19 and their getting tested due to delayed testing at centers, or delayed symptom development in a person. To potentially mitigate this, we evaluate cases from an urban hospital, under the assumption that urban cities will have better and more accessible covid testing facilities. However, we recognize that such ambiguities won't be completely resolved.

Additionally, upon interaction with other smokers, some patients might have been exposed to second-hand smoke. Since this cannot be completely evaluated or quantified accurately, we will ignore this, assuming its effect to be minimal

5. Conclusion

"Smoking tobacco is the leading cause of preventable illness in the United States and around the world"(Goldenberg et al.). With the outbreak of this highly contagious virus, it is more important than ever to raise awareness about smoking's association with COVID-19 severity. This study lays the basis of the correlation between these two diseases (random selection of hospital removing biases and making it reliable) as causation might only be drawn from an intervention that might put the patient at risk (unethical). The proposed study tests our hypothesis by providing the procedure for evaluating predictions regarding the association of smoking habits with the timely development of severe COVID symptoms in patients. The hypothesis may be falsified if no significant difference is found between the average of time taken (days) for COVID symptom development in our comparison groups (non-smokers, current smokers, former smokers).

If the results of this study are in line with the hypothesis (highly likely), smokers are at greater risk in this pandemic. Further research and multivariable analysis that accounts for more extraneous variables such as race, gender, weight, age, and comorbidities will strengthen the claim of this paper. The findings might encourage individuals to quit smoking now more than ever and minimize the risk of developing severe complications.

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[1] **#sourcequality:** PAARC criteria is followed by the source cited. The source has credible authority as it is a peer-reviewed research article. The source has specific purpose of evaluating impact of smoking on clinical COVID symptom severity. Good currency as study was conducted in 2020. This source was relevant too as it helped provide the basis for my hypothesis to evaluate the time taken for COVID symptom severity in smokers and non-smokers.

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