Review of: "Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19"

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Review of Miyara et al. Low incidence of daily active tobacco smoking in patients with symptomatic COVID-19.

https://www.qeios.com/read/article/569

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The authors report having observed lower prevalence of current daily smoking among SARS-CoV-2 positive (RT-PCR) COVID-19 in- (N=343, smoking prevalence 4.4%)) and outpatients (N=139, smoking prevalence 5.3%) compared to the age and sex adjusted general population of smokers recorded in 2018 in France. The main question is whether this comparison is devoid of selection bias and what is the level of evidence.

A matched case-control study would have provided more insight, however, even this would also have a level 4 (weak) evidence (see: Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence https://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf)

Specific comments:

The report is about prevalence and not incidence of smoking.

The wording (Abstract/Conclusions and relevance) and Discussion first sentence: "daily smokers have a very much lower probability of developing symptomatic or severe..." is inadequate. Only sufficiently powered cohort studies can provide data about probability of developing a health disorder.

Introduction. A recent meta-analysis including more studies that Lippi & Henry (ref. 2 of the paper) concluded that among individuals history of smoking is associated with COVID-19 progression (12 papers, 9,025 patients, OR: 2.25, 95% CI 1.49-3.39) (1).

Material and methods Patients and design, 2nd paragraph "but not in ICUs (inpatients). However, Table 3 shows that IN3 inpatient has been transferred to ICU.

Definitions and data collected: 1. "group of ex-smokers" Data about duration of abstinence (time since quitting) is not provided, according to this sentence an ex-

smoker/former smoker could be anyone who quit smoking e.g. 24 hours prior to the assessment. 2. Former smokers' prevalence seem to be high and no sex and age adjusted data are shown. This is important because ex-smokers may have residual excess risk depending on; first: the duration of abstinence and eventually: duration x intensity of smoking e.g. pack-years. 3. Biochemical verification of smoking status is not provided.

Discussion: 1. As mentioned above, to speak about probability of developing a health disorder necessitates sufficiently powered cohort studies. 2. The fact that the prevalence rate of smoking in this hospital sample is lower than that of the general population does not equal a protective effect. Again, only sufficiently large cohort studies can answer this question. 3. Further in the Discussion it is said that most of the outpatients were health care professionals. This group may have, by itself, a lower smoking prevalence than the general population (2). 4. It would have been more adequate to compare data of the same catchment area i.e. the Paris region that has the lowest smoking prevalence (21.3 %) in France (3) 5. "smoking protection is likely to be mediated by nicotine" and "reference 17". Recent studies report that smoking is associated with increased ACE2 expression (4-7) and it is hypothesized that nicotine exposure can increase risk for COVID-19 not only in the lung but also in the brain (8).

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7. Olds & Kabbani: Is nicotine exposure linked to cardiopulmonary vulnerability to COVID-19 in the general population? The FEBS Journal. doi:10.1111/febs.15303

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