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Authors' Response

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Dear Editor,

We read the comments by Rossato and Di Vincenzo with enthusiasm and appreciate their interest in our study, which helps deepen the discussion on smoking and COVID-19 [1]. Indeed, smoking is a major health issue worldwide, as it is associated with a variety of poor outcomes, including COVID-19. Because of widespread tobacco use in Serbia (36.6%) [2], it is estimated that male smokers live 15 years shorter and women smokers live 17 years shorter than their non-smoking age-matched counterparts [3]. Furthermore, research on household budget suggests that smokers in Serbia would rather spend money on cigarettes than on food, clothes and education [4].

That being said, the prevalence of smokers among hospitalized patients with COVID-19 in the Beronja et al. study (40.7% ever smokers vs. 59.3% non-smokers) is even slightly higher than the prevalence of smoking in the general population in Serbia [2,5]. Nevertheless, it would be unrealistic to expect that smokers make up the majority of hospitalized patients with COVID-19, because there are almost twice as many non-smokers in the Serbian general population and smokers may be less susceptible to catch COVID-19 [6]. While data from one center, such as that from the Beronja et al. study [5], cannot be generalized to the entire country, they are suggestive of the distribution of smokers and non-smokers in the Serbian population. This high prevalence of tobacco consumption requires more intense and systematic structural measures of smoking prevention and cessation, but these aspects fall outside of the scope of the Beronja et al. study [5].

In the study of Beronja et al. [5], women accounted for 68.7% of patients treated for severe COVID-19 in the hospital setting. This result was certainly unexpected, given that the body of literature suggests that men are at risk of poorer COVID-19 outcomes [7]. It should be kept in mind that women in Serbia make up the majority of informal (i.e. unpaid) caregivers of family members, particularly in multi-generational households, and were therefore, more exposed to COVID-19 [8]. This burden associated with care giving can lead to general health deterioration, which may be associated with greater needs for hospital attention when infected with COVID-19 [9]. An analysis of more than one million people in Canada suggests that women are especially susceptible to COVID-19 during peaks of epidemic waves over the first two pandemic years and at those times the

proportion of women with COVID-19 exceeded that of men [10]. This is, no doubt, intriguing and merits further exploration especially through the lens of gender inequity.

Pre-existing chronic illnesses of hospitalized COVID-19 patients were proven critical for understanding of COVID-19 prognosis and outcomes in different studies [1,11], including a study conducted in the Serbian population, where diabetes, neurological disorders, and recent injuries/fractures were associated with a higher risk of respiratory failure due to COVID-19 [12]. For this reason, in the study of Beronja et al. [5], major chronic illnesses were accounted for. Out of those, presence of respiratory illnesses and obesity were associated with poorer COVID-19 outcomes among smokers. However, none of the pre-existing chronic illnesses were predictive of poorer survival in non-smokers hospitalized with COVID-19 [5]. Thus, studies focusing on interactions between nicotine and components of the immune system among people with and without chronic illnesses who smoke are necessary to identify the underlying mechanisms of how tobacco prevents the onset of the infection, but conversely, contributes to deterioration once a smoker becomes infected.

Effects of smoking on different aspects of health must not be underestimated. Smoking behaviors should be continuously scrutinized and recorded. Continuous education campaigns about detrimental effects of tobacco are needed not only in prevention of chronic non-communicable diseases, but also in relation to outcomes of acute infectious diseases.

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