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LETTER TO THE EDITOR

# Don't worry! The next generation would be more resistant to SARS-CoV-2

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This letter addresses our concerns regarding the paper "SARS-CoV-2 will continue to circulate in the human population: an opinion from the point of view of the virus-host relationship" published recently in the Inflammation Research [1]. Oberemok et al., the authors of this flawed paper, have used speculation to forecast upcoming events about COVID-19 pandemic. Besides some major shortcomings, the basis for these predictions is not clear. In our previous papers we noted the advantages of low dose radiation therapy (LDRT) and discussed that some drug-based therapies such as using antivirals can drive the virus into evolution through new mutations [2–6]. While nobody really knows what will happen in the future with current and future SARS-CoV-2 strains and how they will evolve under different levels of selective pressure, Oberemok et al. state that "Deaths among people of reproductive age will gradually lead to a human population in which the next generations will be more resistant to this virus". They also state that "Taking into consideration the natural genetic mechanisms of mutations and recombination, it is impossible to imagine how to deprive a virus of the opportunity to generate new strains and time to time threaten our world with new pandemics". Oberemok et al. only focus on the natural selection of humans and ignore the key point that, at least in the case of widespread use of vaccines and antiviral drugs, natural selection of the SARS-CoV-2 will also drive the virus to more mutations through an evolutionary process [7]. As they infect people, all viruses mutate and SARS-CoV-2 is not likely an exception [8]. This is exactly the reason why modulation of the host immune response, in contrast with using antiviral agents, reveals the advantage of exerting less-selective pressure on the virus [7]. The immune response of the host, viral replication, and viral mutation rate are among the major factors that affect human-to-human transmission of SARS-CoV-2 [9]. Using an antiviral therapeutic agent has always been a significant concern because it has the potential to produce drug resistance due to rapid viral mutations [10]. Our experience about other life-threatening viral infections such as HIV lead us to this conclusion that in many individuals, in the presence of the selective pressure of antiviral drugs, residual replication of the virus results in the emergence of drug-resistant strains, finally causing a therapeutic failure [11–13]. A report published recently in Science warns about the dangers of the selective pressures caused by the advent of vaccines or new therapies and states "Perhaps there's just little selection pressure on the virus as it races through millions of immunologically naïve people, scientists say. That could change with the advent of vaccines or new therapies, forcing the virus to evolve" [14]. Given this consideration, next generations will not necessarily be more resistant to new variants of the virus. In Fig. 1 we provide a more realistic picture about the future of COVID-19 compared to the original figure of the Oberemok et al. This representation is one of many possible outcomes, but it is more consistent with viral behavior and current research that the forecast of Oberemok et al.

In addition, to answer the key question why we are now more frequently seeing young patients dying from COVID-19, this paper blames the mutations and states "Since SARS-CoV-2 mutates constantly and more frequently than other RNA viruses (coronaviruses possess the longest genomes of all known RNA viruses, so more errors are made when they are copied; …, for instance, by reducing the average age of patients with a severe course of the disease. As global infection has progressed, we are now more frequently seeing young patients dying from COVID-19". Oberemok et al. have not considered the fact that there are a wide variety of

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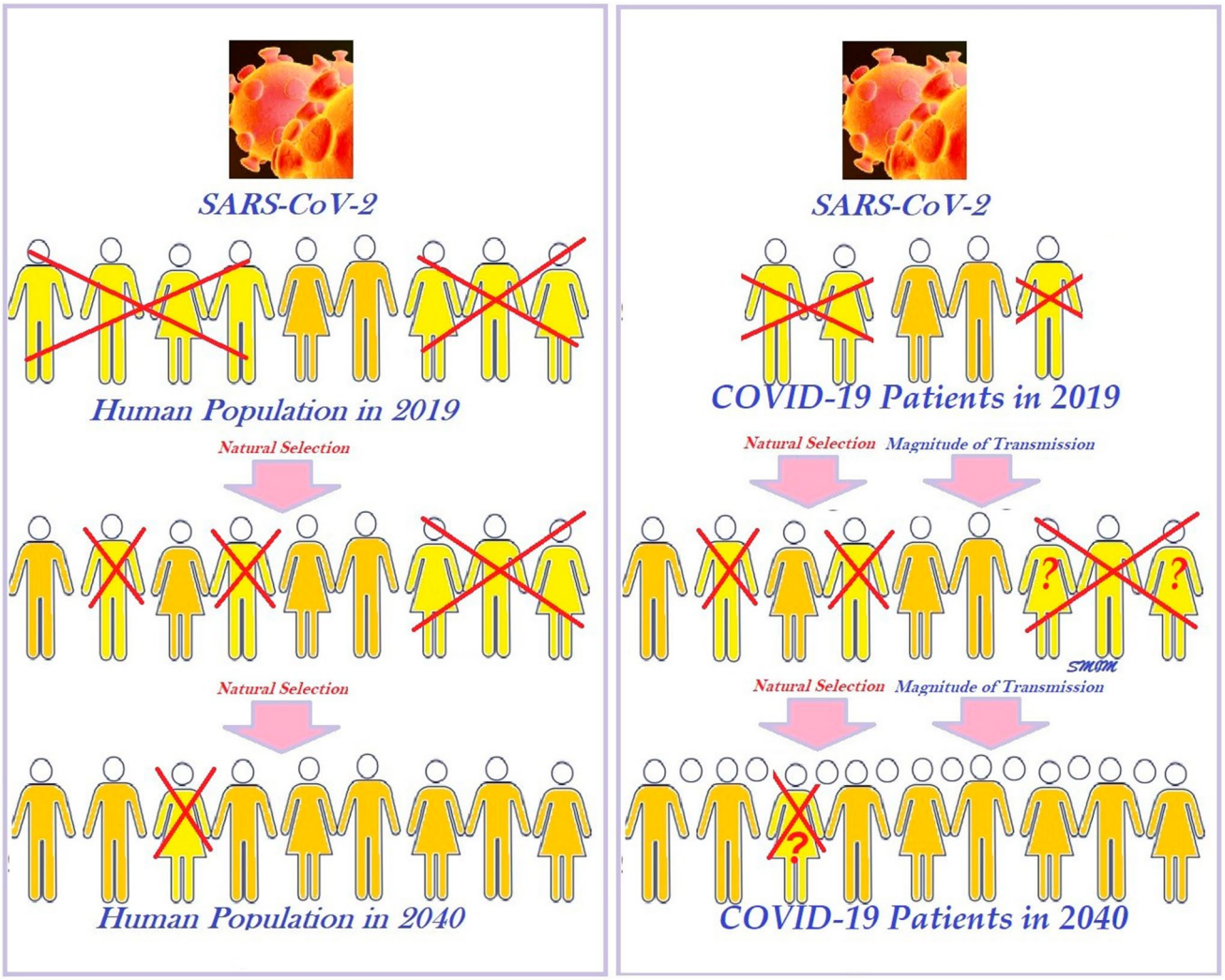


**Fig. 1** A more realistic picture about the future of COVID-19 compared to the original figure of the Oberemok et al. Left: adopted from Oberemok et al. Right: some mutations increase the magnitude of transmission of SARS-CoV-2. Taking this factor and current uncertainties in to account, prediction of the future will me much more complicated that what is pictured by Oberemok et al.

factors behind frequently observing young patients dying from COVID-19. For example, in Mexico City, where two-third of the confirmed cases of COVID-19 were never intubated before they died, daughters traditionally take care of their parents as stated by the Mexico's President Lopez Obrador "We have millions of [amateur] nurses because in this crisis, this pandemic, we're not going to solve it in hospitals, we have to solve it at home". Moreover, the 35–55 years old patients who died of COVID-19 in Mexico City were concentrated in working class neighborhoods [15].

Given these considerations, Oberemok et al. predict that "… this new coronavirus … will take its place next to the seasonal flu viruses, where the infection rate is high and the mortality rate is very low. In the near future, your doctor will routinely prescribe you something like 'covidol' and say that in the coming days you are likely to recover". However, Oberemok et al. entirely ignored the negative role of antiviral drugs in exerting strong selective pressure on the virus and in a misleading manner state "Therefore, it is necessary to control viruses constantly with new drugs developed for use against both new strains of viruses and new species of viruses to save the lives of virus-sensitive people".

This letter cautions readers to carefully evaluate current viral research in predicting the progress of the SARS-CoV-2 outbreak. These projections should include both natural selection as well as the magnitude of transmission. The hazards of antiviral agents and mutation generation present significant concerns to control of the SARS-CoV-2 pandemic. Other approaches including low dose radiation therapy offer significant advantages over antiviral agents, and should receive careful consideration as a treatment option.

## Compliance with ethical standards

**Conflict of interest** None declared by the authors.

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