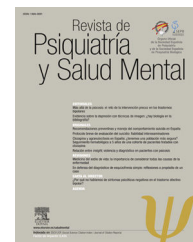




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LETTERS TO THE EDITOR

COVID-19 natural herd immunity and risk of neuropsychiatric disorders



Inmunidad natural de grupo y riesgo de trastornos neuropsiquiátricos de la COVID-19

Dear Editor:

The current global COVID-19 pandemic, caused by the SARS-CoV-2 virus, has affected over 200 countries with more than seven million confirmed cases and about 415,000 deaths worldwide as of June 12, 2020.¹ Its rapid expansion has collapsed the healthcare systems in most countries and quarantine measures taken by governments to flatten the curve of the disease are causing a socio-economic impact without precedent. These circumstances have led to many negative psychological consequences for the population, causing an increase in the incidence of psychiatric disorders.^{2,3} After several months struggling, many countries are finally coming out of the so-called “first wave” of the COVID-19 pandemic, and population-level seroepidemiological studies are beginning to be published showing a low prevalence of community infection.⁴ The lack of a vaccine until at least the first half of 2021, the socio-economic costs of lockdown and strengthening preparation of healthcare systems for facing the pandemic have made the concept of natural herd immunity reemerge as a possible strategy for coping with a more than probable “second wave” as social distancing measures are relaxed.⁵

Herd immunity is an epidemiological phenomenon observed when a large enough number of individuals in a population, by having acquired immunity to an infection, provide indirect protection to the rest of the population that is not immune.⁶ The protection becomes effective when a certain immunity threshold is reached. This threshold varies depending on the basic reproduction number (R_0) of the pathogen, the rate at which the pathogen can spread among the population.⁶ Since the R_0 of SARS-CoV-2 is from 2 to 6, the herd immunity threshold of the disease would be approximately 67%.⁶ Assuming that this threshold was uniform, and in the absence of a vaccine for COVID-19, up to two thirds of the world's population would have to recover from the infection for natural herd immunity to be reached. This would imply that expected deaths from COVID-19 throughout the world would exceed 30 million and lead to saturation of the healthcare systems, which would cause, not only high mortality from COVID-19, but also a higher mortality from all causes.⁶ Such figures would be inadmissible, especially when the immune response to COVID-19 is still not com-

pletely understood, and it is unknown whether recovery from the disease confers effective permanent post-infection immunity.⁷

Another major concern is the potential neuroinvasiveness of SARS-CoV-2 and the relatively little information on possible neuropsychiatric effects the infection could cause. Direct viral infection, through the neuronal pathway by retrograde axonal transport from peripheral nerves or by a hematogenous pathway via the blood-brain barrier, is thought to be the main neuropathogenic mechanism of the virus.⁸ Indirect mechanisms may include angiotensin-converting enzyme 2 down-regulation, myeloid cell trafficking, hypoxia-induced apoptosis, cytokine release syndrome, and gut microbial translocation.⁸ Among the acute neuropsychiatric complications of COVID-19 are mild, such as headache, dizziness, anosmia and dysgeusia or severe manifestations such as delirium, seizures, encephalitis, encephalopathy and cerebrovascular accident.⁹ These acute neuropsychiatric symptoms in COVID-19 cases are similar to those commonly observed in patients with severe infection requiring intensive care management.¹⁰ However, little is known regarding post-infectious neuropsychiatric complications of COVID-19, and it will take years before they can be properly appreciated. In this vein, delayed or chronic neuropsychiatric sequelae have been reported in past coronavirus outbreaks such as the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV).⁹ Neuromuscular complications and demyelinating diseases such as myopathy, peripheral neuropathy, Guillain-Barre syndrome or Bickerstaff brainstem encephalitis, and neurodegenerative processes have been observed.⁹ In addition, psychotic disorders, major affective disorders, anxiety and trauma-related disorders, obsessive compulsive disorders and neurocognitive disorders have been associated with coronavirus infections.^{9,11} Notwithstanding, the magnitude of the current pandemic is much greater than that of the SARS-CoV or the MERS-CoV, and this could lead, apart from a greater mental health burden on society, to seeing in the coming years a dramatic increase in neuropsychiatric sequelae of COVID-19 infection similar to that observed after the 1918 influenza pandemic.^{2,9,11} In the decades following that pandemic, there was an overall increase in the incidence of severe mental disorders such as schizophrenia, especially in the offspring of pregnant women infected by the virus, suggesting a complex interrelationship between infection, immunity, inflammation and the risk of development of neuropsychiatric disorders.^{9,12}

Faced with such an uncertain scenario and in absence of an effective vaccine in the short-to-mid term, it does

not seem recommendable to promote natural herd immunity as a measure for preventing the spread of COVID-19. In addition, it would be important to carry out follow-up studies on everyone who has had COVID-19, including those who were asymptomatic, to examine in detail the appearance of neuropsychiatric disorders in this population. Likewise, post-mortem brain samples should be taken from COVID-19 patients to see the neuroinvasive and neuropathogenic extent of the virus, as well as in vitro studies to understand its neurotropic properties better.

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Conflict of interest

None.

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Suicide. The post-COVID era: A time for action



Suicidio. La era post-COVID: Tiempo para la acción

Dear Editor,

The suicide is a worldwide public health problem included among WHO's priorities. An average of 800,000 persons committed suicide every year in the world¹ and 3600 in Spain; moreover, suicide is the second cause of death in those aged 15 to 29 years old.^{1,2} In Spain, the evolution of the main causes of death, in younger people, over the last decades; shows a clear decrease trend in traffic accidents and HIV, while death by suicide did not suffer a significant decrease for the whole period³ (Figs. 1 and 2).

The satisfactory evolution of deaths due to HIV and traffic accidents is linked mostly to a strong political commitment and appropriate policies (both causes), to the improvement of the clinical management (HIV), and to the active national and international research investment. Although these, mostly multi sectoral, public health measures do not have been successfully applied to improve national suicide rates. This fact is even more appalling if we take into consideration that suicide is also preventable and there is a huge margin for improvement. This is evident if we take into account that the disparities in suicide mortality among the Spanish regions in the year 2017 are of a much more important magnitude than the temporal variations collected over the last decades for the whole country (between 1999 and 2017 the adjusted rates of suicide ranged from 14.1 to 11.8 for males and 4.1 to 3.8 for females but the variations among the Spanish regions in 2017 had a range from 6.3 to