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► **To cite this version:**

Haidar Djemai, Rami Hammad, Ibrahim Dabayebbeh, Saleh Hammad, Abdellah Merzouk, et al..  
COVID-19 and aerobic exercise: possible role of angiotensin converting enzyme 2. Archives of Public  
Health, 2022, 80 (1), pp.231. 10.1186/s13690-022-00983-3 . hal-03859293

**HAL Id: hal-03859293**

**<https://u-picardie.hal.science/hal-03859293v1>**

Submitted on 30 Apr 2024

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RESEARCH

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# COVID-19 and aerobic exercise: possible role of angiotensin converting enzyme 2

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## Abstract

The emergence and circulation of a novel coronavirus (2019-nCoV)—Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—set off a global health crisis. SARS-CoV-2 spreads faster than its two ancestors, SARS-CoV and MERS-CoV. Several modes of transmission have been identified: via respiratory droplets, contact with infected people or contaminated surfaces, and potentially, bioaerosols. Various countries have taken preventive measures that may include partial or total lockdowns lasting weeks. The physical inactivity associated with lockdowns may promote cardiometabolic or other diseases, while physical activity may play a critical role in preventing them. Here we develop the hypothesis of the involvement of aerosols in the contamination process, the role of angiotensin converting enzyme 2 (ACE2), the potential benefits and harm of physical activity during lockdowns, and we suggest directions for future research.

## Highlights

- Physical inactivity during COVID-19 lockdowns may damage health.
- Risk of contamination by aerosols is higher during high-intensity urban outdoor exercise.
- Angiotensin converting enzyme 2 (ACE2) could play key role in SARS-CoV-2 transmission during exercise.
- How ACE2 serum concentration changes as function of exercise intensity and duration must be studied to elucidate role of this enzyme.

**Keywords:** COVID-19, SARS-CoV-2, Physical activity, Outdoor exercise

## Background

The global COVID-19 (previously 2019-nCoV) pandemic has not relented since it began in Wuhan, Hubei, China, in December 2019 [1]. The WHO has declared the new disease caused by SARS-CoV-2 a global public health emergency [1]. In 2021, even with the availability

of treatment and vaccines [2], various countries continue to apply preventive measures that include school closings, restriction of non-food-related economic activity, and prohibition of unnecessary travel [3]. Such measures placed over a third of the world's population under partial or total lockdown for several weeks during each wave of the pandemic [4, 5]. Lockdowns are characterized by more sedentary behavior [6], and considerable loss of muscle mass occurs after weeks without physical activity [3]. So et al. showed that during the 2003 SARS lockdown in China, lasting 7 weeks, levels of physical activity levels fell between 32% and 40% on average [7]. The WHO considers physical inactivity to be the fourth leading cause

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of mortality worldwide. It reports that 60–85% of people around the globe have sedentary lifestyles [8]. The sedentary behavior and physical inactivity associated with lockdowns might contribute to obesity and type 2 diabetes. Here we summarize the results of recent COVID-19 research and describe the health effects of lockdowns. We also discuss the potential benefits and harms of urban outdoor physical activity during COVID-19 lockdowns and the possible role played by angiotensin converting enzyme 2 (ACE2) in contamination.

### SARS-CoV-2 transmission and associated symptoms

Coronaviruses are primarily spread through close contact with other individuals [9]. Infection with SARS-CoV-2 usually occurs via contact with oral, nasal, or ocular mucous membranes, or by inhalation of droplets generated by coughing or sneezing [10]. Droplets can travel 1 to 2 m from their source [11, 12]. Aerosols are solid or liquid particles suspended and dispersed in the air. Some are atmospheric pollutants such as particulate matter of diameter  $\leq 2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ ) or  $\leq 10 \mu\text{m}$  ( $\text{PM}_{10}$ ).  $\text{PM}_{2.5}$  particles were thought to greatly contribute to COVID-19 infections in England [13]. Moreover, relationships between COVID-19 mortality and infectivity and air pollutant concentrations have recently been observed [13, 14].

After an infected expels the virus from their lungs and into the air, it may join with aerosols to form bioaerosols capable of traveling many meters [11, 12]. These bioaerosols can be easily inhaled, thereby entering the respiratory tract. Evidence suggests that most cases of SARS-CoV-1 and MERS-CoV were partly the result of aerosol inhalation [10, 15]. Epidemiological data show that transmissibility is higher for 2019-nCoV than for SARS-CoV or MERS-CoV [16]. Thus, the SARS-CoV-2 pandemic demands stricter measures to limit infection [17].

In some patients, initial clinical signs of this disease include a dry cough, breathing difficulties (dyspnea), and pneumonia [17–19]. In addition to pneumonia and dyspnea, 78% of patients with COVID-19 have been reported to have a fever ( $> 38 \text{ }^\circ\text{C}$ ), and other symptoms are coughing, muscle pain, headache, stomachache, and diarrhea [20]. Loss of taste and smell has also been observed [21].

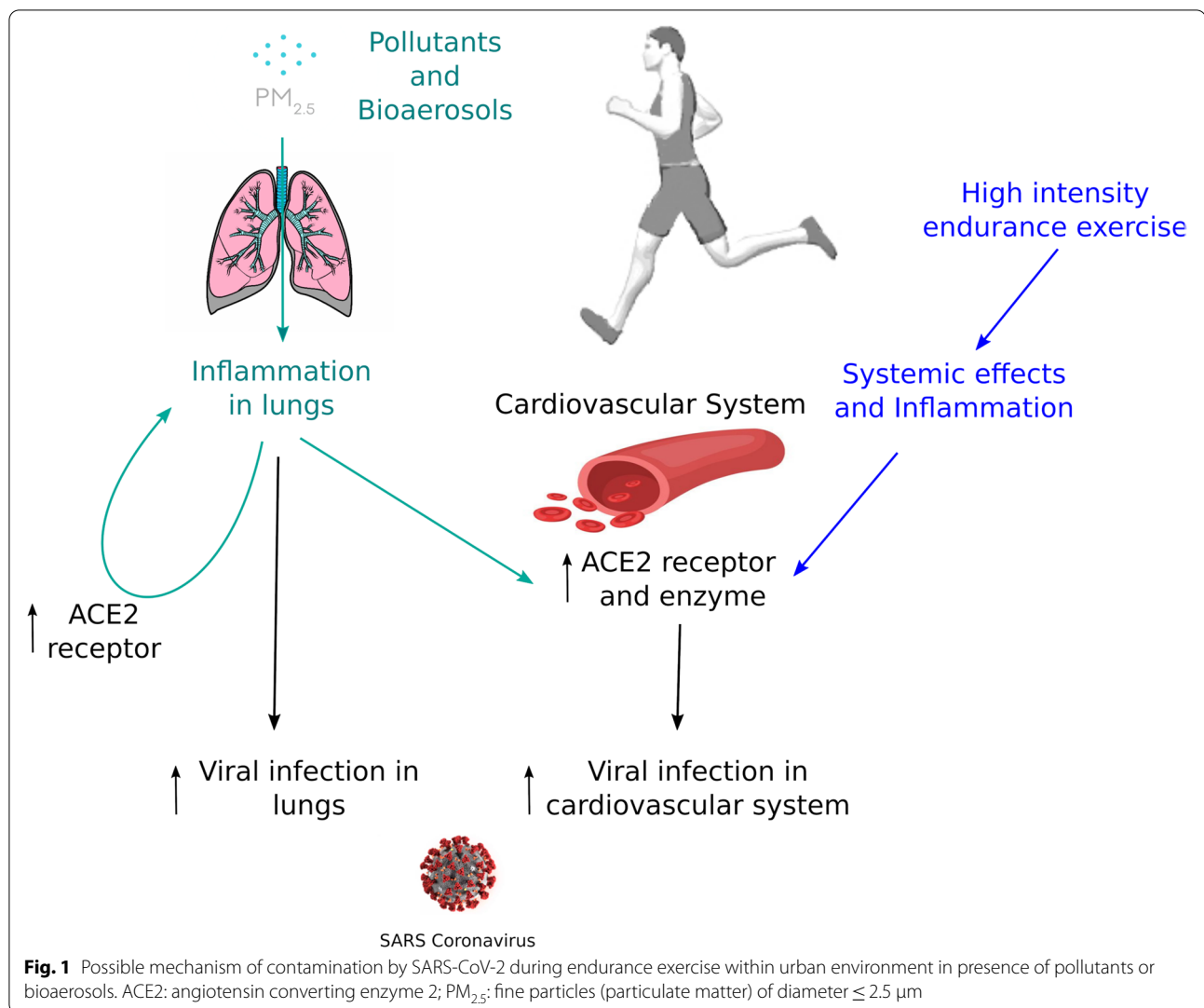
SARS-CoV-2 reportedly infects pulmonary alveolar epithelial cells by endocytosis [19]. It binds to the same ACE2 receptor as SARS-CoV, but with 10 to 20 times higher affinity [22]. Coronaviruses can enter cells expressing ACE2, replicate, spread, and cause disease. ACE2 is expressed on both type I and II alveolar epithelial cells, with expression dominant in the latter type (83%). ACE2 has also been shown to occur in other organs, such as the heart, esophagus, kidneys, bladder, and ileum [2, 23].

### Exercise and COVID-19 during pandemic

According to previous studies, endurance exercise increases ACE2 production through a complex mechanism involving beneficial systemic effects — e.g., increased angiotensin-(1–7) levels and decreased microRNA activity — as well as possible inflammatory responses [24–26]. ACE2 catalyzes the cleavage of angiotensin II into angiotensin-(1–7), a vasodilator that decreases blood pressure. Furthermore, exposure to SARS-CoV-2 apparently increases ACE2 receptor expression in the lungs [19, 27]. Although there is greater secretion of both types of ACE2 (i.e., as enzyme in plasma and as receptor in cardiovascular tissues) in patients with cardiovascular diseases, SARS-CoV-2 might also increase cardiovascular tissue expression of ACE2 in others [27, 28].

Endurance exercise is one of the main drivers of increased oxygen consumption ( $\text{VO}_2$ ) by working muscles: consumption increases linearly with exercise intensity. During endurance exercise, an incremental rise in  $\text{O}_2$  demand and  $\text{CO}_2$  production greatly increases ventilation, bringing athletes toward the ventilatory breakpoint [29]. This respiratory response might facilitate SARS-CoV-2 access to lung tissues. Increased ventilation induces greater recruitment of the pulmonary gas exchange surface to permit the passage of more oxygen into the blood [30, 31]. During aerobic exercise in big cities, greater doses of air pollutants can be inhaled [32]. As  $\text{PM}_{2.5}$  pollutant inhalation not only increases COVID-19 incidence [13] but also inflames lung tissue, it may lead to greater ACE2 receptor expression in alveolar epithelial cells [33]. Because SARS-CoV-2 can attach to fine particles, greater ventilation during exercise could entail rapid and massive transport of virions into the lungs, where they may bind to ACE2 receptors. Specifically, when running outdoors in an environment with a high concentration of fine airborne particles (i.e., pollutants or vapor droplets) and little air flow, large numbers of virions could be inhaled, subsequently affecting the cardiovascular system (Fig. 1) [4]. Further studies are needed to examine this possibility.

As suggested by So et al., it is reasonable to assume that SARS-CoV-2 may be found in sweat, just as it is in other bodily fluids [7]. The rise in body temperature during physical exercise can increase evaporation of sweat, leading to the formation of aerosolized viral particles capable of infecting others [7, 11, 12]. High-intensity endurance exercise in the streets of large cities during a pandemic could promote viral contagion and substantially heighten the risk of COVID-19-related cardiovascular injury. As the means of viral entry during exercise is not fully understood, avoidance of high-intensity outdoor physical activity in populated or polluted areas seems prudent [4].



### Hypothesis

The arguments presented above suggest physical activity during the COVID-19 pandemic promotes health. As lockdowns lasting multiple weeks may increase physical inactivity, sedentary behavior, obesity, and other health risks, regular physical activity may be of critical importance. We hypothesize that physical activity and air pollutants increase ACE2 receptor expression in the cardiovascular system and the lungs, respectively, which may in turn heighten the risk of SARS-CoV-2 infection (Fig. 1).

### Recommendations

During and after the pandemic, several studies have recommended physical exercise. Different protocols have been proposed combining aerobic and anaerobic exercises, indoors and outdoors, at different intensities and

durations [34–36]. In the current situation our hypothesis suggests that high intensity outdoor physical activity requiring a high level of ventilation in urban environment is not recommended. This way, an additional risk of viral infection via bioaerosols can be avoided.

### Conclusion

With the COVID-19 pandemic, among the prevention measures, a large portion of the world's population was subjected to partial or total lockdowns for weeks. If physical activity is known to prevent cardiometabolic or other diseases, physical inactivity associated with lockdowns could play a critical role. Here we develop the hypothesis that the increase of angiotensin converting enzyme 2 (ACE2), caused by both physical activity and polluted urban air, may play a key role in the COVID-19 contamination process.

## Abbreviations

ACE2: Angiotensin converting enzyme 2; PM: Particulate matter.

## Acknowledgements

We thank the Université Paris Cité and the National Institute of Sport, Expertise, and Performance (INSEP) for their full support; Dr. Claude Forest, INSERM, and the Université Paris Cité for assisting in manuscript correction and improvement; and Mr. Jason Miller for English language editing.

## Authors' contributions

HD, RH played a prominent role in writing the manuscript and developing the hypothesis. IMD and PN helped write and review the hypothesis and the manuscript. SH assisted in writing the manuscript. AM and XC both reviewed the manuscript and hypothesis. All authors read and approved the final manuscript.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Availability of data and materials

Not applicable.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no conflict of interest.

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Received: 29 June 2022 Accepted: 13 October 2022

Published online: 10 November 2022

## References

- WHO. Coronavirus. 2020 [Cited 2020 Mar 30]. Available from: <https://www.who.int/westernpacific/health-topics/coronavirus>
- Carethers JM. Rectifying COVID-19 disparities with treatment and vaccination. *JCI Insight*. 2021;6:147800.
- Latella C, Haff GG. Global challenges of being a strength athlete during a pandemic: impacts and sports-specific training considerations and recommendations. *Sports (Basel)*. 2020;8:E100.
- Chen P, Mao L, Nassif GP, Harmer P, Ainsworth BE, Li F. Coronavirus disease (COVID-19): The need to maintain regular physical activity while taking precautions. *J Sport Health Sci*. 2020;9:103–4.
- FITBIT. The Impact Of Coronavirus On Global Activity. Fitbit Blog. 2020 [Cited 2020 Mar 30]. Available from: <https://blog.fitbit.com/covid-19-global-activity/>
- Bentlage E, Ammar A, How D, Ahmed M, Trabelsi K, Chtourou H, et al. Practical recommendations for maintaining active lifestyle during the COVID-19 pandemic: a systematic literature review. *Int J Environ Res Public Health*. 2020;17:E6265.
- So RCH, Ko J, Yuan YWY, Lam JJ, Louie L. Severe Acute Respiratory Syndrome and sport: facts and fallacies. *Sports Med*. 2004;34:1023–33.
- WHO. WHO | Physical inactivity a leading cause of disease and disability, warns WHO. WHO. World Health Organization; 2020 [Cited 2020 Apr 4]. Available from: <https://www.who.int/mediacentre/news/releases/relea-se23/en/>
- Zhu W. Should, and how can, exercise be done during a coronavirus outbreak? An interview with Dr. Jeffrey A. Woods. *Journal of Sport and Health Science*. 2020;9:105–7.
- Lu C-W, Liu X-F, Jia Z-F. 2019-nCoV transmission through the ocular surface must not be ignored. *Lancet*. 2020;395:e39.
- Wang J, Du G. COVID-19 may transmit through aerosol. *Ir J Med Sci*. 2020;189:1143–4.
- WHO. Transmission of SARS-CoV-2: implications for infection prevention precautions. WHO. 2020 [Cited 2020 Jul 14]. Available from: <https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions>
- Travaglio M, Yu Y, Popovic R, Selley L, Leal NS, Martins LM. Links between air pollution and COVID-19 in England. *Environ Pollut*. 2020;268:115859.
- Accarino G, Lorenzetti S, Aloisio G. Assessing correlations between short-term exposure to atmospheric pollutants and COVID-19 spread in all Italian territorial areas. *Environ Pollut*. 2020;268.
- Chowell G, Abdirizak F, Lee S, Lee J, Jung E, Nishiura H, et al. Transmission characteristics of MERS and SARS in the healthcare setting: a comparative study. *BMC Med*. 2015;13:210.
- Chen J. Pathogenicity and transmissibility of 2019-nCoV-A quick overview and comparison with other emerging viruses. *Microbes Infect*. 2020;22:69–71.
- Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–20.
- Verity R, Okell LC, Dorigatti I, Winskill P, Whittaker C, Imai N, et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. *Lancet Infect Dis*. 2020;20:669–77.
- Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579:270–3.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan China. *Lancet*. 2020;395:497–506.
- Gautier J-F, Ravussin Y. A new symptom of COVID-19: loss of taste and smell. *Obesity (Silver Spring)*. 2020;28:848.
- Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh C-L, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science*. 2020;367:1260–3.
- Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Front Med*. 2020;14:185–92.
- Klötting N, Ristow M, Blüher M. Effects of Exercise on ACE2. *Obesity*. 2020;28:2266–7.
- Motta-Santos D, Dos Santos RAS, Oliveira M, Qadri F, Poglitsch M, Mosenko V, et al. Effects of ACE2 deficiency on physical performance and physiological adaptations of cardiac and skeletal muscle to exercise. *Hypertens Res*. 2016;39:506–12.
- Nunes-Silva A, Rocha GC, Magalhaes DM, Vaz LN, Salviano de Faria MH, Simoes E Silva AC. Physical exercise and ACE2-angiotensin-(1-7)-mas receptor axis of the renin angiotensin system. *Protein Pept Lett*. 2017;24:809–16.
- Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol*. 2020;17:259–60.
- Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A, et al. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141:1648–55.

29. Racinais S, Buchheit M, Girard O. Breakpoints in ventilation, cerebral and muscle oxygenation, and muscle activity during an incremental cycling exercise. *Front Physiol.* 2014;5:142.
30. Berry MJ, Dunn CJ, Pittman CL, Kerr WC, Adair NE. Increased ventilation in runners during running as compared to walking at similar metabolic rates. *Eur J Appl Physiol Occup Physiol.* 1996;73:245–50.
31. Dempsey JA, Johnson BD, Saupe KW. Adaptations and Limitations in the Pulmonary System during Exercise. *Chest.* 1990;97:81S-87S.
32. Pasqua L, Damasceno M, Cruz R, Matsuda M, Garcia Martins M, Lima-Silva A, et al. Exercising in Air Pollution: The Cleanest versus Dirtiest Cities Challenge. *Int J Environ Res Public Health.* 2018;15:1502.
33. Lin C-I, Tsai C-H, Sun Y-L, Hsieh W-Y, Lin Y-C, Chen C-Y, et al. Instillation of particulate matter 2.5 induced acute lung injury and attenuated the injury recovery in ACE2 knockout mice. *Int J Biol Sci.* 2018;14:253–65.
34. Dwyer MJ, Pasini M, De Dominicis S, Righi E. Physical activity: Benefits and challenges during the COVID-19 pandemic. *Scand J Med Sci Sports.* 2020;30:1291–4.
35. Rodríguez MÁ, Crespo I, Olmedillas H. Exercising in times of COVID-19: what do experts recommend doing within four walls? *Rev Esp Cardiol (Engl Ed).* 2020;73:527–9.
36. Jáuregui A, Lambert EV, Panter J, Moore C, Salvo D. Scaling up urban infrastructure for physical activity in the COVID-19 pandemic and beyond. *Lancet.* 2021;398:370–2.

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