Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

6. Coronavirus COVID-19 global cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at: https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6. Accessed April 30, 2020.
7. Italian Ministry of Health-COVID-19 pandemic update. Available at: http://www.salute.gov.it/imgs/C_17_notizie_4632_0_file.pdf. Accessed April 30, 2020.

Available online June 22, 2020.
https://doi.org/10.1016/j.jaci.2020.05.049

Reply

To the Editor:

The article by Marco et al[1] titled "Asthmatic patients in COVID-19 outbreak: few cases despite many cases" discusses the prevalence of asthma in patients with coronavirus disease 2019 (COVID-19) in the Northeast of Italy. The low prevalence of asthma in patients with COVID-19 in Italy[1] was consistent with what we observed in our study,[2] but was much lower than those from the United States[3] and Dublin.[4] The reasons behind the regional difference in the prevalance of asthma with COVID-19 are worth discussion.

We searched PubMed and Medline database for articles published up to May 20, 2020, using the keywords "SARS-COV-2," "COVID-19," and "asthma." As shown in Table I,[1-7] the prevalence of asthma with COVID-19 in each country was listed as well as the prevalence of asthma in the general population of the corresponding region.

The studies from China, Italy, and Mexico confirmed the lower rates of asthma patients with COVID-19 when compared with the prevalence of asthma in the corresponding general population (0.9%, 1.92%, and 3.6%, compared with 6.4%, 6.1%, and 5.0%, respectively).[1,2,5] However, recent data released from New York and Dublin indicated the high rates of asthma in COVID-19, which were similar or a little higher than the prevalence of asthma in the general population (9.0% and 8.8%, compared with 10.1% and 7%, respectively).[3,4] The other 2 small cohorts from France and Australia also manifested the high rates of comorbidity of asthma in pediatric patients with COVID-19.[6,7]

The reasons for the regional differences may partially be attributed to the variety in the strictness of prevention and control measures, the public awareness of self-protection, and the detection strategy of SARS-COV-2. However, we also notice that the risk of patients with asthma to COVID-19 in the regions with a low prevalence of asthma seems lower than that in regions with a high prevalence of asthma. The recent study suggested that T_H2 cytokine may decrease the expression of angiotensin-converting enzyme 2 (ACE2) in epithelial cells, but increase another SARS-COV-2 entry protein transmembrane protease serine 2 (TMPRSS2) gene expression. The regulation on the expressions of ACE2 and TMPRSS2 in T_H2-high patients with asthma differed from that in T_H2-low patients with asthma. Therefore, we may speculate that the difference in phenotype and genotype of asthma may contribute to the differential regulation of ACE2 and TMPRSS2 and be partially responsible for the variety in susceptibility of patients with asthma to COVID-19 among different regions.

The other concern is the various clinical characteristics of patients with asthma in the different regions; for example, high body mass index in patients with asthma is more common in the United States than in China and Italy. Obesity is related to an increased risk of COVID-19. Obese patients are also prone to have hypertension, which is a predisposing factor for COVID-19.

TABLE I. Regional differences in the prevalence of asthma in patients with COVID-19

Country	Percentage of asthma with COVID-19 (n/n)	Prevalence of asthma in the general population	References
China	0.9% (5/548)	6.4%	Li et al[2]
Italy	1.92% (20/1043)	6.1%	Caminati et al[1]
Mexico	3.6% (270/7497)	5.0%	Solís et al[5]
USA	9.0% (479/5700)	10.1%	Richardson et al[3]
Ireland	8.8% (17/193)	7.0%	Butler et al[4]
France	8.5% (3/35)	11%	Belhadjer et al[6]
Australia	25% (1/4)	13.9%	Ibrahim et al[7]

The different comorbidities with patients with asthma may also be one of the reasons for the regional differences in the prevalence of asthma in COVID-19.

Asthma is a disease with marked heterogeneity. It would be intriguing to investigate and understand how the heterogeneity of asthma is attributable to the variability in susceptibility and clinical course of asthma with COVID-19.

Junqing Yue, MD[a,b]
Lu Qin, PhD[a,b]
Cong Zhang, MD[a,b]
Min Xie, MD[a,b]

From [a]the Department of Respiratory and Critical Care Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, and [b]the Key Laboratory of Respiratory Diseases, National Ministry of Health of the People's Republic of China and National Clinical Research Center for Respiratory Disease, Wuhan, China. E-mail: xie_m@126.com.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Caminati M, Lombardi C, Micheletto C, Roca E, Bigni B, Furci F, et al. Asthmatic patients in COVID-19 outbreak: few cases despite many cases. J Allergy Clin Immunol 2020;146:541-2.
2. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan [published online ahead of print April 12, 2020]. J Allergy Clin Immunol https://doi.org/10.1016/j.jaci.2020.04.006.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020;323:2052-9.
4. Butler MW, O'Reilly A, Dunican EM, Mallon P, Feeney ER, Keane MP, et al. Prevalence of comorbid asthma in COVID-19 patients [published online ahead of print June 10, 2020]. J Allergy Clin Immunol https://doi.org/10.1016/j.jaci.2020.04.061.
5. Solís P, Carreño H. COVID-19 fatality and comorbidity risk factors among confirmed patients in Mexico [published online ahead of print April 25, 2020]. medRxiv https://doi.org/10.1101/2020.04.21.20074591.
6. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute heart failure in multisystem inflammatory syndrome in children (MIS-C) in the context of global SARS-CoV-2 pandemic [published online ahead of print May 17, 2020]. Circulation https://doi.org/10.1161/CIRCULATIONAHA.120.048360.
7. Ibrahim LF, Tosif S, McNab S, Hall S, Lee HJ, Lewena S, et al. SARS-CoV-2 testing and outcomes in the first 30 days after the first case of COVID-19 at an Australian children's hospital [published online ahead of print May 10, 2020]. Emerg Med Australas https://doi.org/10.1111/1742-6723.13550.

Available online June 22, 2020.
https://doi.org/10.1016/j.jaci.2020.06.002

Global lockdown, pollution, and respiratory allergic diseases: Are we in or are we out?

To the Editor:

We have read with great interest the work by Navel et al[1] about the impact of the current coronavirus disease 2019

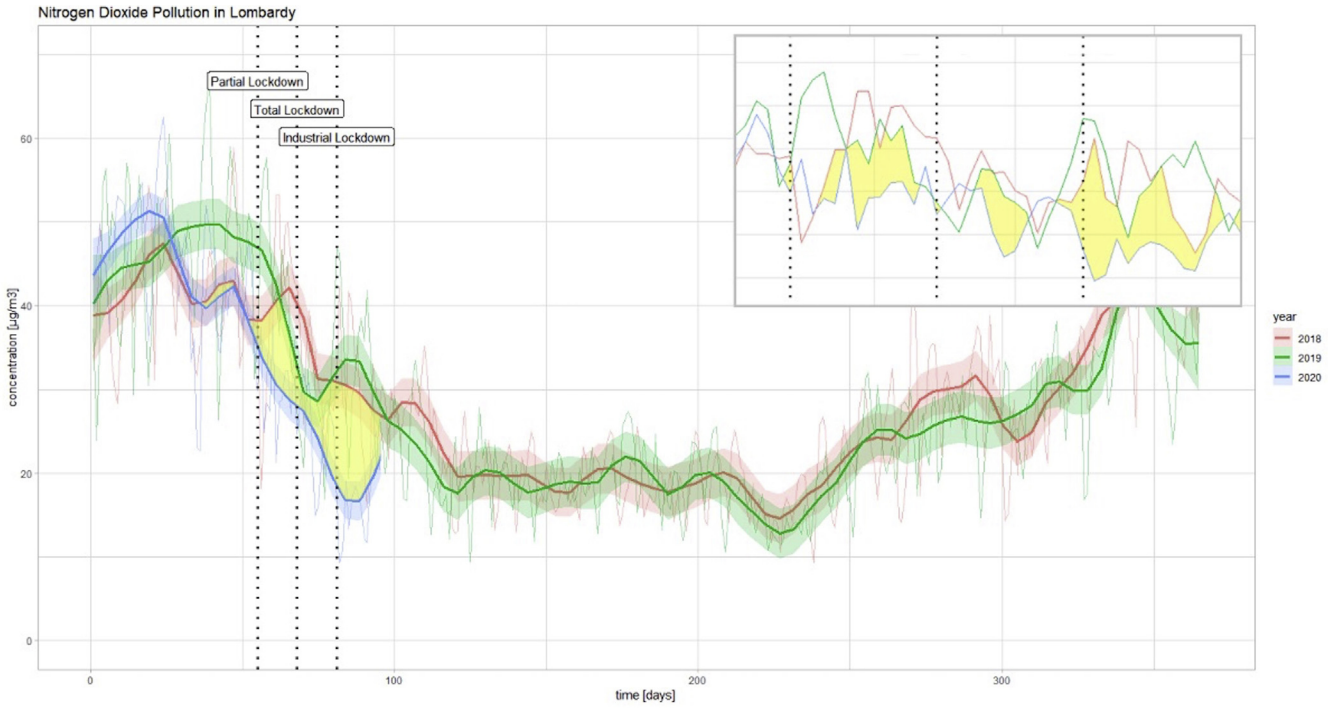

FIG 1. Data on the 2020 concentration of atmospheric NO_2 and the annual trend in the Lombardy region, Italy.[3]

pandemic on the burden of allergic diseases. The authors suggest that, thanks to the global lockdown of the majority of human industrial activities, the substantial reduction in air pollution in the urban areas, a well-known inducer of nonspecific airway inflammation, may have a positive effect on seasonal allergic diseases.[1] Indeed, we are now facing a unique chance to decipher some of the complex interplays between the outdoor allergens, the air quality, and respiratory allergic diseases but, in order to have a full picture, we believe more (f)actors are needed on the stage.[2]

It is true that, especially in the most industrialized areas, the atmospheric concentration of some greenhouse gases, mostly nitrogen dioxide (NO_2), has substantially decreased when compared with the previous years (Fig 1).[3] In the same period, we are facing the usual raise in the concentrations of outdoor aeroallergens such as seasonal pollens: clinical and experimental research has shown that such molecules can interact by several mechanisms with particulate matters and other chemicals, so as to ultimately exacerbate allergic symptoms.[4,5] For instance, pollutants can act as adjuvants by binding to allergens and they can increase the IgE production.[5] However, the expected benefits of improved outdoor air quality on the exacerbation of allergic disorders may also be linked to other phenomena that should be separately analyzed. First, a near-universal face masking policy has been implemented in the vast majority of the countries since the beginning of the pandemic. Although primarily worn to protect themselves and others from severe acute respiratory syndrome coronavirus 2 transmission, masks are also able to reduce the airway exposure to inhaled aeroallergens depending on the presence and on the type of a filter.[6]

Second, the urgent need for social distancing has prompted most of the world's population to be confined at home. We must not forget that indoor air can also be full of several biological aeroallergens (such as those derived from molds or domestic pets) and chemical toxicants (tobacco, cooking smoke, or cleaning products, which, ironically, are being used more often to achieve environmental sanitization).[2,7] When inhaled, such molecules have also been shown to favor oxidative stress of the respiratory mucosa and, thus, to exacerbate inflammatory conditions such as asthma or allergic rhinitis.[2,7] Therefore, the important changes not only in outdoor air quality and pollution but also in our current forcefully indoor lifestyle may yield paradoxical effects on the allergic population. When, in the next years, we will retrospectively analyze the overall effect of this unprecedented situation on the global burden of allergic and respiratory diseases, it is necessary also to include real-world experimental data on the aforementioned factors. We believe that only in this way we can gather robust evidence and finally appreciate the real consequences of the pandemic in this field.

Oreste Gallo, MD
Chiara Bruno, MD
Luca Giovanni Locatello, MD
From the Department of Otorhinolaryngology, Careggi University Hospital, Largo Brambilla, Florence, Italy. E-mail: oreste.gallo@unifi.it.
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Navel V, Chiambaretta F, Dutheil F. Will environmental impacts of social distancing due to the SARS-CoV-2 pandemic decrease allergic disease? J Allergy Clin Immunol 2020;146:70-1.
2. Naclerio R, Ansotegui IJ, Bousquet J, Canonica GW, D'Amato G, Rosario N, et al. International expert consensus on the management of allergic rhinitis (AR) aggravated by air pollutants: impact of air pollution on patients with

AR: current knowledge and future strategies. World Allergy Organ J 2020;13:100106.
3. Buganza E, Donzelli M, Gurrieri GL, Lazzarini M, Scotto di Marco E, Bravetti E, et al. Preliminary analysis on air quality in Lombardy during the COVID-19 emergency [in Italian]. Milan, Italy: Lombardy Regional Agency for Environmental Protection. April 03, 2020. Available at: https://www.arpalombardia.it/Pages/Qualit%C3%A0-dell%E2%80%99aria-durante-l%E2%80%99emergenza-Covid-19%2C-l%E2%80%99analisi-di-Arpa-Lombardia-.aspx. Accessed April 30, 2020.
4. Wooding DJ, Ryu MH, Hüls A, Lee AD, Lin DTS, Rider CF, et al. Particle depletion does not remediate acute effects of traffic-related air pollution and allergen: a randomized, double-blind crossover study. Am J Respir Crit Care Med 2019;200:565-74.
5. Sedghy F, Varasteh AR, Sankian M, Moghadam M. Interaction between air pollutants and pollen grains: the role on the rising trend in allergy. Rep Biochem Mol Biol 2018;6:219-24.
6. Tovey E, Marks G. Methods and effectiveness of environmental control. J Allergy Clin Immunol 1999;103:179-91.
7. Poole JA, Barnes CS, Demain JG, Bernstein JA, Padukudru MA, Sheehan WJ, et al. Impact of weather and climate change with indoor and outdoor air quality in asthma: a Work Group Report of the AAAAI Environmental Exposure and Respiratory Health Committee. J Allergy Clin Immunol 2019;143:1702-10.

Available online June 22, 2020.
https://doi.org/10.1016/j.jaci.2020.05.047

Reply

To the Editor:

We read with interest the relevant comment of Gallo et al[1] concerning our recent Editorial.[2] Globally, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak has upset the lifestyle of humans, increasing sedentary behaviors with quarantine (ie, staying at home, tele-working, screen activities), the fear of contagion (ie, social connections, mass transit, and compulsive disinfecting), and probably a city dweller migration to the periphery of crowed cities and surrounding countryside. As explained by the authors, this exceptional period seems to be salient to explore the complex interplay of interactions between exposome (ie, indoor and outdoor expositions), genetic heritage, lifestyle, and allergic diseases expression. Interestingly, more than half the people stayed at home to prevent the spreading of SARS-CoV-2 during the several months of quarantine, involving a massive decrease in greenhouse gas emissions related to human activities. Considering the irritative factor of air pollution for the respiratory tract, the eyes, and the skin, we could attempt a reduction in allergic exacerbations mediated by nonspecific inflammation. Considering that filtering face piece respirators (FFPs) reduced the penetration of fine particulates ranging from 80% (FFP1) to 99% (FFP3), their global use during the coronavirus disease 2019 pandemic could protect people against outdoor and indoor allergenic components.[3] However, the authors rightly highlighted that people were particularly exposed to biological aeroallergens (ie, dust mites, domestic animals, or molds) and chemical components (ie, ammonia, solvent, tobacco, and cooking smokes) of home indoor environment during quarantine. Similar to the concentration of diesel exhaust particles in a vehicle cabin exposed to heavy traffic, nonventilated houses could condense the toxicity of outdoor air pollution during several days. During the past decades, some countries have developed models of energy other than petroleum to promote more renewable energy sources, that is, wave power, offshore wind power, photovoltaic, or wood. However, it is widely accepted that home exposure to wood smoke causes inflammation in the respiratory system.[4] Promoting warm and humid environment, indoor activities (ie, tele-working, cooking, and indoor sports) could improve the exposition of airborne fungal spores in damp houses, increasing the incidence of asthma and allergic diseases.[5] Outdoor sports practice being prohibited, some people could run or cycle in their home. Moreover, evidence data showed that air pollutant exposure during exercise could decrease the pulmonary and vascular function in healthy individuals, increasing systemic and airways inflammation and amplifying the dose of pollutants during endurance physical activity.[6] Thus, the benefit of the decrease in air pollution could be attenuated by the massive exposure to indoor pollutants, aggravated by the toxicity of disinfectants such as bleach, rubbing alcohol, or quaternary ammonium—massively used to limit the spreading of SARS-CoV-2. Considering that the Hygienic Hypothesis highlighted the major role of microbiome to regulate the immune response to allergens, it would be very interesting to evaluate the impact of the extensive use of hygienic measures on the incidence of allergic diseases.[7] Because of the fear of contagion, people may avoid mass transit and increase their commuting by individual car, which may in turn promote air pollution—and the release of the highly allergenic fine particulate matter. We may therefore see a bimodal response: a decrease in air pollution during the confined period, followed by an increase in air pollution—concomitantly with the effort of worldwide governments to kickstart economic growth (despite ecological engagements). To conclude, it will be salient to analyze the aforementioned factors related to allergic diseases in forthcoming months, to better understand the complex relation between allergens, air pollution, immune response, and exacerbation of allergic diseases.

Valentin Navel, MD[a]
Frédéric Chiambaretta, MD, PhD[a]
Frédéric Dutheil, MD, PhD[b]

From [a]Université Clermont Auvergne, CNRS, INSERM, GReD, Translational Approach to Epithelial Injury and Repair, CHU Clermont-Ferrand, University Hospital of Clermont-Ferrand, Ophthalmology, and [b]Université Clermont Auvergne, CNRS, LaPSCo, Physiological and Psychosocial Stress, CHU Clermont-Ferrand, University Hospital of Clermont-Ferrand, Preventive and Occupational Medicine, Witty Fit, Clermont-Ferrand, France. E-mail: valentin.navel@hotmail.fr.

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

REFERENCES

1. Gallo O, Bruno C, Locatello LG. Global lockdown, pollution, and respiratory allergic disease: are we in or are we out? J Allergy Clin Immunol 2020;146:542-4.
2. Navel V, Chiambaretta F, Dutheil F. Will environmental impacts of social distancing due to the SARS-CoV-2 pandemic decrease allergic disease? J Allergy Clin Immunol 2020;146:70-1.
3. Jung H, Kim JK, Lee S, Lee J, Kim J, Tsai P, et al. Comparison of filtration efficiency and pressure drop in anti-yellow sand masks, quarantine masks, medical masks, general masks, and handkerchiefs. Aerosol Air Qual Res 2014;14:991-1002.
4. Rokoff LB, Koutrakis P, Garshick E, Karagas MR, Oken E, Gold DR, et al. Wood stove pollution in the developed world: a case to raise awareness among pediatricians. Curr Problems Pediatr Adolesc Health Care 2017;47:123-41.
5. Garrett MH, Rayment PR, Hooper MA, Abramson MJ, Hooper BM. Indoor airborne fungal spores, house dampness and associations with environmental factors and respiratory health in children. Clin Exp Allergy 1998;28:459-67.
6. Zhang J, Zhu T, Kipen H, Wang G, Huang W, Rich D, et al. Cardiorespiratory biomarker responses in healthy young adults to drastic air quality changes surrounding the 2008 Beijing Olympics. Res Rep Health Eff Inst 2013;5-174.
7. Weber J, Illi S, Nowak D, Schierl R, Holst O, von Mutius E, et al. Asthma and the hygiene hypothesis: does cleanliness matter? Am J Respir Crit Care Med 2015;191:522-9.

Available online June 22, 2020.
https://doi.org/10.1016/j.jaci.2020.06.003