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race that can explain racial disparities in lung function; however, body proportions, socioeconomic status, and occupational hazards clearly influence capacity.¹⁰ These factors should be measured directly, rather than using race as a rough proxy. Race-based corrections are likely biasing clinical reports of COVID-19 recovery, severity of lung damage, and subsequent recovery treatment plans. Further, race corrections reinforce assumptions about innate biological differences between races, which is a pervasive problem across medical practice.² Overall, we encourage further research into the specific factors that influence lung capacity and raise concerns over the routine use of race-based corrections in spirometry, especially in assessing COVID-19 recovery.

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Are women with asthma at increased risk for severe COVID-19?



Although adults with asthma appear to have a reduced risk of severe COVID-19 compared with younger populations,¹ women with asthma might represent a somewhat susceptible subgroup for severe COVID-19 requiring hospitalisation.² A study by Atkins and colleagues established female sex as an independent risk factor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) hospitalisation among patients with asthma in the UK.² This study and three additional studies from Paris, France, Illinois, USA, and New York, NY, USA, report that 37–53% of all individuals hospitalised with SARS-CoV-2 were women.^{3–5} However, 56–71% of patients with asthma hospitalised for COVID-19 were women in these studies.^{3–5} This increased proportion might be partially explained by the higher baseline prevalence of asthma in women than in men, because data from similar geographical areas suggest 51–65% of individuals with asthma are women.^{6–9} Several mechanisms might

increase the risk of COVID-19-related hospitalisation in women with asthma. The recognition of these mechanisms might guide targeted management strategies.

First, women have a higher disease burden of asthma compared with men overall, with a significantly higher prevalence, rate of hospitalisation, health-care cost, mortality, and severity of disease.¹⁰ Additionally, structural differences such as a reduced airway calibre and increased tendency for bronchial hyper-responsiveness in women might contribute to the risk of hospitalisation with COVID-19.¹¹

Second, asthma severity in men and women is modified by hormonal changes across the lifespan. Greater lifetime exposure to endogenous and exogenous oestrogen is associated with more severe asthma.¹⁰

Third, sex affects the prevalence of the two fundamental immunological asthma endotypes,



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atopic and non-atopic asthma. Non-atopic asthma is more frequent in women than in men, particularly those older than 35 years of age.¹¹ Non-atopic asthma involves lower Th2 activity and greater Th1 activity than atopic asthma does, when bronchial epithelial cells release IL-33, IL-6, IL-23, IFN γ , and tumour necrosis factor- α in response to various irritants, resulting in neutrophilic airway inflammation.¹² The increased prevalence of non-atopic asthma in women might be related to distinct underlying causes of asthma in women, including obesity. Obese women have a disproportionate incidence and severity of asthma because of increased leptin concentrations, which promote inflammatory Th1 pathways.^{10,11} We hypothesise that this sex-related immunopathology of asthma might be exacerbated by the systemic inflammatory response of SARS-CoV-2 infection, which is similarly driven by Th1-related cytokines, including IFN γ , IL-6, MCP1, IP10, and IL-1 β .¹³

We propose that individuals with asthma might be at a lower risk of COVID-19 incidence and severity overall.¹ However, women with asthma have a combination of phenotypic heterogeneities, including a Th1 immunological skewness, a predisposition towards more severe asthma,¹⁰ structural lung parenchymal differences, and hormonal differences, which might increase their susceptibility to severe COVID-19 requiring hospitalisation. Corticosteroids might alter this immunological balance between Th1 and Th2 cytokine pathways.¹⁴ Dexamethasone has proven effective in treating patients with SARS-CoV-2 infection and trials investigating inhaled corticosteroids are underway and eagerly awaited.¹⁵ Tocilizumab is a monoclonal antibody against IL-6, which did not display improvement in mortality in a randomised trial of moderately unwell patients with SARS-CoV-2 infection.¹⁶ However, the specific effect of these therapies in women with asthma and SARS-CoV-2 infection remains unclear. Further studies of SARS-CoV-2 infection in patients with asthma are required but should include sex-stratified analyses to clarify the relationship between asthma, sex, and SARS-CoV-2 infection, and thereby guide targeted treatments. At this stage, women with asthma might benefit from strict adherence to usual asthma preventive therapy. Clinicians and the public should be aware of the phenotypic heterogeneity of asthma

to avoid dismissing the risks of SARS-CoV-2 infection in susceptible asthmatic subgroups. As the body of literature grows, medical professionals should consider the evidence for targeted treatments for specific populations, including inhaled corticosteroids and monoclonal antibodies in women with asthma and SARS-CoV-2 infection.

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