

# Asthma and COVID-19: What do we know now

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**ABSTRACT:** The COVID-19 pandemic has presented challenges in symptomology identification, diagnosis, management and follow-up in common respiratory diseases, and in particular asthma. Research is rapidly ongoing to try and understand how the SARS-CoV-2 virus affects individuals with asthma, as well as, how underlying asthma affects Covid-19 risk, symptomology and prognosis. In light of this unique medical challenge, clinicians are faced with case-by-case based decisions to implement or continue current asthma therapy.

This review will discuss the current literature regarding asthma and COVID-19 based on best available evidence at this time (See box 1).

**KEYWORDS:** COVID-19, asthma, respiratory, biologics, treatment, corticosteroids

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## Does asthma increase the risk of COVID-19 infection (See box 2)?

Early evidence from Wuhan, China was inconclusive regarding the association of increased risk of COVID-19 infection in asthma patients. Several early case studies evaluating co-morbidities of inpatient adults with COVID-19 in Wuhan, China omitted asthma as a pre-existing comorbidity among their patient cohorts and thus a relationship was unable to be assessed.<sup>1-3</sup> Further, nationwide analysis of comorbidities and their impact on 1590 patients with COVID-19 in China found that none of the analyzed cases reported physician diagnosed asthma.<sup>4</sup> Following this Li et al. evaluated 584 patients admitted to hospital in Wuhan, China and found that reports of pre-existing asthma were markedly lower (0.9%, n = 5) than the general population (6.4%) and Zhang et al. who found a very low prevalence of 0.3% (n = 1) in their cohort of 290 COVID-positive patients.<sup>5,6</sup> This was reciprocated in a systematic review of n = 12760 individuals by Khan et al., which found 1.4% (n = 355) of their COVID-19 positive cohort had asthma as a comorbidity.<sup>7</sup> Other studies worldwide have demonstrated an increased prevalence of asthma in COVID-positive individuals and have suggested that the lower prevalence of asthma reported within some studies could be attributed to underreporting, underdiagnosis or poor recognition of chronic respiratory disease in patients with COVID-19 infection.<sup>8</sup> Additionally, another explanation for the differing rates of comorbid asthma seen among studies may be due to the overall differences in rates of comorbidities including asthma in different countries.

Recent studies from the United States and United Kingdom have shown that patients with asthma are over-represented among adult patients with COVID-19, who were admitted to hospital.<sup>9-11</sup> A study conducted by Chiba et al evaluated 1526 PCR confirmed Covid positive patients and found that 220 (14%) of patients had comorbid asthma.<sup>12</sup> However, comorbid asthma was not found to increase risk of hospitalization in this study population.<sup>12</sup> Recent data released from the Center for Disease Control and Prevention evaluated COVID-19 positive patients from several hospitals throughout the United States and showed that 27.3% of COVID-positive inpatients aged 18 to 49 years listed asthma as a comorbidity, with an incidence of 8.9% in the general population.<sup>13,14</sup> Although studies have shown higher rates of comorbid asthma in COVID-19 positive patients, it was not specified whether asthma was allergic or non-allergic in origin.<sup>15,16</sup> Zhu et al. found that once subcategorized, patients with allergic asthma had no statistically significant association with severe COVID-19 symptoms.<sup>16</sup>

## How does COVID-19 affect individuals with asthma?

Currently there are conflicting hypotheses surrounding the complex pathophysiology of asthma in positive COVID-19 patients and ongoing research is required. Theoretically, asthmatic patients are thought to have increased susceptibility and severity of COVID-19 due to decreased anti-viral immune response and increased risk of viral induced exacerbation.<sup>17</sup> However, interestingly it was hypothesized that type

### Box 1. Evidence used in this review.

A search of PubMed from 2018 until 2020 was conducted for publications related to COVID-19 and asthma. No restrictions were placed on article type. 146 articles were found. All 146 articles were reviewed by title and abstract for relevance. Reviews were prioritized where available. Majority of articles analyzed were retrospective studies.



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**Box 2.** Recent studies clinically evaluating patient populations with Covid-19 assessing patient demographics and associations between comorbid asthma and Covid-19 infection.

STUDY	STUDY DESCRIPTION	ASTHMA +/- RISK FACTOR
Zhang et al <sup>1</sup>	Investigations of 140 clinical cases of Covid-19, in Wuhan, China, found that no patients reported asthma or other allergic diseases therefore not suspected to be a risk factor for Covid-19.	–
Chen et al <sup>2</sup>	Investigation of 99 cases of Covid-19, in Wuhan, China, found that no patients reported pre-existing asthma as a comorbidity.	–
Wang et al <sup>3</sup>	Investigation of 138 cases of Covid-19, in Wuhan, China, found that no patients reported pre-existing asthma as a comorbidity.	–
Guan et al <sup>4</sup>	Nation-wide analysis of 1590 cases of Covid-19, in China, found that no patients reported physician diagnosed asthma.	–
Li et al <sup>5</sup>	Evaluated 584 cases of Covid-19, in Wuhan, China, found that reports of pre-existing asthma were markedly lower (0.9%) than the general population (6.4%).	–
Zhu et al <sup>16</sup>	Evaluated 492768 participates in UK Biobank and found that participants with asthma has a higher risk of severe Covid-19 infection, however, once subcategorized to allergic asthma, there was no significant association with severe Covid-19 infection.	?/–
Chhiba et al <sup>12</sup>	Evaluated 1526 patients with PCR confirmed Covid-19, found that 220 (14%) of patients reported comorbid asthma. Asthma was not associated with increased risk of hospitalization.	+
Grandbastien et al <sup>22</sup>	Investigation of 106 cases of hospitalized Covid-19 in Strasbourg, France, found that 23 patients had comorbid asthma.	+
Bhatraju et al. <sup>10</sup>	Case studies were conducted throughout 9 Seattle hospitals, and 24 patients were found with Covid-19 infection, of those patients 3 patients (14%) had pre-existing comorbid asthma.	+
Docherty et al <sup>11</sup>	Evaluation of 16749 hospitalized patients in the UK, it was found that asthma was the fourth highest co-morbidity found to be pre-existing in 14% of cases.	+
Garg et al <sup>14</sup>	Evaluation of underlying conditions and symptoms of hospitalized patients with Covid-19 throughout hospitals in 14 different states found that overall 17% of patients reported comorbid asthma and 27.3% of patients 18 to 49y old reported comorbid asthma.	+

II inflammatory response cytokines (IL-4, -5 and -13) and accumulation of eosinophils seen in asthma may be protective against COVID-19.<sup>17,18</sup>

It is further hypothesized that the type II inflammatory response produced in the respiratory airway of patients with asthma is a protective factor against COVID-19. SARS-Cov-2 uses angiotensin converting enzyme 2 (ACE2) as its cellular receptor, similar to SARS and other seasonal coronaviruses.<sup>15,19</sup> Therefore, increased expression of ACE2 is suspected to increase susceptibility to COVID-19. The respiratory epithelial cells in patients with asthma have decreased gene expression for ACE2 receptors and therefore may be protective against COVID-19 infection.<sup>15,17,19</sup> Non-allergic asthma was not associated with this change.<sup>15</sup> It was also found that type II inflammation is associated with increased TMPRSS2, a protease that allows for effective viral receptor binding, gene expression.<sup>19</sup> However, it is hypothesized that the decrease in ACE2 gene expression overrides the minimal increase in TMPRSS2 gene expression, potentially making asthma associated type II inflammation a protective factor against COVID-19.<sup>16,17,19,20</sup> Additionally, eosinopenia has been observed in patients with COVID-19, and more prominently this was represented in the more severe cases, stabilizing after clinical improvement.<sup>17,21,22</sup> This suggests that eosinophils could

play a protective role against developing more severe clinical outcomes.<sup>21,22</sup>

In contrast, it has also been proposed that asthma associated type II inflammatory response decreases host anti-viral immunity.<sup>23,24</sup> In addition, asthma induced mucus plugging in the lower respiratory tract, limits airflow which could worsen the hypoxaemia from diffuse alveolar damage caused by COVID-19 infection.<sup>25</sup> Poor asthma control is a risk factor for more severe virus-induced exacerbations.<sup>15,24,26</sup> Viral infections, including several coronavirus species, have been shown to trigger asthma exacerbations, contribute to airway inflammation and mucus hypersecretion.<sup>27</sup> However, both SARS and MERS, similar species of coronavirus, were not shown to increase the risk of asthma exacerbation whereas, seasonal coronaviruses do increase this risk.<sup>28</sup> Grandbastien et al found that SARS-Cov-2 infection did not increase severe exacerbations in asthmatic patients.<sup>22</sup> However, similar to other coronaviruses, it is also hypothesized that SARS-Cov-2 will precipitate asthma exacerbation.<sup>27</sup> Therefore, further investigation into the immunopathological mechanism still needs to be elucidated to determine risk of severe exacerbations in asthmatic patients.<sup>27</sup> It is for these reasons among others that it is recommended that asthmatic patients continue their maintenance medications throughout the pandemic.<sup>24,29</sup>

### What do we know about the treatment of asthma during the COVID-19 pandemic? (See box 3,4)

Inhaled corticosteroids (ICS) are a common and effective first line treatment for control of asthma which allows steroids to be applied directly to the respiratory epithelium, allowing for rapid suppression of the airway epithelium inflammation through increasing anti-inflammatory cytokine levels. Several studies hypothesize the type II inflammatory response that occurs in the lungs due to asthma suppresses anti-viral immunity, therefore an inhaled corticosteroid will help to reduce this inflammation and subsequently increase anti-viral immunity.<sup>23,24,27,30</sup> Additionally, early studies have shown that ICS may decrease both ACE2 and TMPRSS2 gene expression on respiratory epithelial cells, decreasing susceptibility of SARS-Cov-2 viral binding to receptors on respiratory epithelium.<sup>20,31,32</sup> Inhaled corticosteroids alone or in combination with bronchodilators have been shown to suppress coronavirus replication and cytokine production.<sup>8,33,34</sup> Interestingly, in an in vivo study, Matsuyama et al. found that ciclesonide, an inhaled corticosteroid selectively suppressed human coronavirus replication in human cultured cells.<sup>33</sup> Additionally, in vitro studies have shown that formoterol, glycopyrronium, and a combination of formoterol, glycopyrronium and budesonide, have inhibitory effects on seasonal coronavirus replication and cytokine production.<sup>35</sup> Further, although corticosteroids are not a mainstay treatment for lung injury caused by COVID-19, it has been suggested they may be beneficial in suppressing the pro-inflammatory cytokine release syndrome associated with the third phase of COVID-19 symptomology.<sup>36</sup> Patients that were given early, low-dose, short-term ICS experienced shorter duration of supplemental oxygen, decreased patient mortality, and improvement of clinical symptoms.<sup>36,37</sup> Finally, systemic corticosteroids, such as prednisone, should be used to treat severe asthma exacerbations regardless of whether evoked by COVID-19 infection or another cause.<sup>29</sup>

Leukotriene receptor antagonists act as an effective add on therapy for asthma control by promoting anti-inflammatory and bronchodilator effects in the respiratory tract. In preclinical models of viral influenza and acute respiratory distress syndrome, Montelukast has been shown to decrease both lung inflammation and cytokine release.<sup>47</sup> Montelukast was also shown to reduce eosinophilic inflammation in upper airway

inflammatory disease by inhibiting epithelial cell cytokine release and promoting eosinophil survival.<sup>47</sup> Bozek et al. found that the rate of Covid-19 infection was significantly lower in a population of elderly patients with severe asthma taking Montelukast, compared to a similar population not taking the drug.<sup>42</sup> Of the hospitalized patients with Covid-19, those taking Montelukast, did not need respiratory therapy or multidrug antiviral treatment.<sup>42</sup> Additionally, Khan et al. found that Covid-19 positive patients that were treated with Montelukast experienced significantly fewer events of clinical deterioration than those not receiving the treatment.<sup>47</sup>

Azithromycin has been shown to be an effective treatment in patients with asthma not adequately controlled by standard inhaler therapy, by decreasing exacerbation frequency and improving quality of life.<sup>45</sup> Additionally, treating asthmatic patients with azithromycin significantly increases IFN production, a cytokine associated with innate antiviral immunity, by respiratory cells and therefore may be effective at reducing risk of severe COVID-19 outcomes.<sup>24</sup> However, this treatment is not recommended as a preventative measure against Covid-19 infection.<sup>48</sup> Allergen immunotherapy (AIT) is a disease modifying therapy for allergic airway diseases, including asthma, whereby immune tolerance towards a specific allergen is developed, through repeated allergen administration.<sup>46,49</sup> AIT treatment in asthmatic patients leads to a desensitization effect and immune tolerance which may be protective against cytokine storms occurring in severe Covid cases.<sup>17</sup> AIT treatment can be continued in asthmatic patients without clinical symptoms of Covid-19 or recent exposure to SARS-Cov-2 virus.<sup>46</sup> However, it is recommended that AIT immunotherapy be temporarily interrupted if patient becomes infected with an acute respiratory tract infection, including Covid-19, until infection is resolved.<sup>46</sup>

Biologics are also used as an add on maintenance treatment for asthma, to reduce the frequency of severe asthma exacerbations. Monoclonal antibodies should be continued in asthmatic patients during the pandemic in order to prevent urgent physician and emergency department visits and hospitalization. If biological therapies are stopped then other medications should be given, such as low dose prednisone, high dose inhaled corticosteroids with long acting beta-2 agonist therapy or long-acting muscarinic therapy, to prevent exacerbations.<sup>30</sup> Many regulatory bodies have recommended that

**Box 3.** Recommended asthma medication administration techniques in Covid negative and positive patients.

ADMINISTRATION APPROACH	ASTHMA TREATMENT IF PATIENT COVID -VE	ASTHMA TREATMENT IF PATIENT COVID +VE	GUIDELINE FOR USE DURING PANDEMIC
Metered-dose inhaler	+	+	Recommended and should be used as first line method under normal circumstances, in hospital and at home. <sup>29</sup>
Dry powdered inhaler	+	+	Recommended and should be used as a substitute for nebulizers during pandemic. <sup>29</sup>
Nebulizer	-	-	Discouraged unless essential. <sup>40</sup>

**Box 4. Asthma maintenance and exacerbation medications, their mechanism of action, current recommendations for use during Covid-19 pandemic and proposed benefits and risks of use.**

ASTHMA TREATMENT	MECHANISM OF ACTION IN ASTHMA PATHOLOGY	SUGGESTED USE DURING COVID-19 PANDEMIC	POSITIVE EFFECTS ON COVID-19	NEGATIVE EFFECTS ON COVID-19
Inhaled Corticosteroids	<ul style="list-style-type: none"> <li>Direct application of steroids to respiratory epithelium</li> <li>Increases anti-inflammatory cytokine levels, allowing for rapid suppression of airway inflammation.<sup>17</sup></li> </ul>	<ul style="list-style-type: none"> <li>Continued or restarted if stopped in patients with asthma.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Reduces asthma associated type II inflammation in the lungs, and subsequently increases host anti-viral immunity.<sup>23,24,27,29</sup></li> <li>Decreases ACE2 and TMPRSS2 gene expression on respiratory epithelial cells, therefore decreasing Sars-Cov2 viral receptor binding.<sup>40</sup></li> <li>Suppress coronavirus replication and cytokine production.<sup>9,31,33</sup></li> <li>Suppresses pro-inflammatory cytokine release syndrome associated with the third phase of Covid-19.<sup>34</sup></li> </ul>	<ul style="list-style-type: none"> <li>May impair antiviral innate immune responses and delayed viral clearance.<sup>31</sup></li> </ul>
Systemic Corticosteroids	<ul style="list-style-type: none"> <li>Used short term for rapid relief of airway inflammation in severe asthma exacerbations.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Should be used as short course of treatment for severe asthma exacerbations regardless of whether evoked by Covid or not.<sup>29</sup></li> <li>Low to moderate dosing (0.5–1mg/kg per day methylprednisolone) and for short duration (&lt;7 d).<sup>38</sup></li> </ul>	<ul style="list-style-type: none"> <li>Acute courses of prednisone should be used to treat acute exacerbations and will not significantly impair the immune response.<sup>29</sup></li> <li>May have a role in treating patients with septic shock.<sup>37,39</sup></li> </ul>	<ul style="list-style-type: none"> <li>Prolonged viral replication was observed in patients with MERS, when treated with systemic corticosteroids.<sup>40</sup></li> <li>Patients with MERS who were given systemic corticosteroids had increased rates of mechanical ventilation, increased mortality rate and delayed viral clearing.<sup>40</sup></li> <li>Concern may prolong viral replication.<sup>29</sup></li> </ul>
Leukotriene Receptor Antagonist	<ul style="list-style-type: none"> <li>Add on maintenance treatment for severe asthma</li> <li>Inhibit the synthesis of leukotrienes thereby decreasing airway inflammation and promoting bronchodilation.<sup>41</sup></li> </ul>	<ul style="list-style-type: none"> <li>Maintenance medications should be continued in asthma patients.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Decreased rate of Covid-19 infection in elderly patients with severe asthma.<sup>42</sup></li> <li>May have a role in decreasing need of respiratory and multidrug antiviral therapy in hospitalized Covid-19 patients.<sup>42</sup></li> </ul>	
Long Acting Beta-2 Agonist	<ul style="list-style-type: none"> <li>Add on maintenance treatment used in combination with inhaled corticosteroids for treatment of asthma</li> <li>Allow for bronchodilation of smooth muscle in the respiratory tract</li> </ul>	<ul style="list-style-type: none"> <li>Maintenance medications should be continued in asthma patients.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>In vitro studies have shown that formoterol has an inhibitory effect on seasonal coronavirus replications and cytokine production.<sup>35</sup></li> <li>Additive inhibitory effects on viral replication and cytokine production were shown when formoterol was used in combination with glycopyrronium and budesonide.<sup>35</sup></li> </ul>	
Anti-muscarinic	<ul style="list-style-type: none"> <li>Maintenance treatment used in asthma patients</li> <li>Block muscarinic receptor binding in the respiratory tract to inhibit bronchoconstriction, inflammation and mucus secretion.<sup>43</sup></li> </ul>	<ul style="list-style-type: none"> <li>Maintenance medications should be continued in asthma patients.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>In vitro studies have shown that glycopyrronium has an inhibitory effect on seasonal coronavirus replications and cytokine production.<sup>35</sup></li> <li>Additive inhibitory effects on viral replication and cytokine production were shown when glycopyrronium was used in combination with formoterol and budesonide.<sup>35</sup></li> </ul>	
Biologics	<ul style="list-style-type: none"> <li>Add on maintenance treatment for asthma, to reduce the frequency and improve control of severe asthma exacerbations.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Continued in asthmatic patients that do not have a subsequent Covid-19 infection</li> <li>If infected with Covid-19, biologics should be discontinued until no longer symptomatic and patient receives negative Covid-19 test swab.<sup>21</sup></li> <li>If biologic therapies are stopped then other medications should be given, such as low dose prednisone, high dose inhaled corticosteroids with long acting beta2 agonist therapy or long-acting muscarinic therapy, to prevent exacerbations.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Omalizumab was shown to possibly be protective against viral induced asthma exacerbations.<sup>29,44</sup></li> <li>Immune response to viral agents not suspected to be affected by the use of biologics for the treatment of asthma.<sup>29</sup></li> </ul>	
Azithromycin	<ul style="list-style-type: none"> <li>Useful when asthma is uncontrolled by standard inhaler therapy.<sup>24</sup></li> <li>Proposed effects on anti-viral immunity, decreasing exacerbation frequency and improving quality of life.<sup>24</sup></li> </ul>	<ul style="list-style-type: none"> <li>If asthma is not controlled by standard therapies, starting azithromycin prophylaxis therapy could be an acceptable treatment approach.<sup>45</sup></li> </ul>	<ul style="list-style-type: none"> <li>Significantly increases IFN production, a cytokine associated with innate antiviral immunity, by respiratory cells and therefore may be effective at reducing risk of severe Covid-19 outcomes.<sup>24</sup></li> </ul>	
Allergen Immunotherapy	<ul style="list-style-type: none"> <li>Causes early desensitization, modulation of B and T cell responses and immune tolerance in patients 1</li> </ul>	<ul style="list-style-type: none"> <li>AIT treatment can be continued in asthmatic patients without clinical symptoms of Covid-19 or recent exposure to SARS-Cov-2 virus.<sup>46</sup></li> <li>It is recommended that AIT immunotherapy be temporarily interrupted if patient becomes infected with an acute respiratory tract infection, including Covid-19, until infection is resolved.<sup>46</sup></li> </ul>	<ul style="list-style-type: none"> <li>The immune tolerance produced by this therapy may be protective against cytokine storms occurring in severe Covid cases.<sup>17</sup></li> </ul>	
Nebulized medications	<ul style="list-style-type: none"> <li>Deliver asthma medications through fine mist using a mask or mouthpiece</li> <li>Ideal for patients who have trouble using inhalers</li> </ul>	<ul style="list-style-type: none"> <li>Avoid during the pandemic</li> <li>Instead a metered-dose inhaler with a valved holding chamber or dry powdered inhaler are preferred.<sup>29</sup></li> </ul>	<ul style="list-style-type: none"> <li>Should only be used in patients who are unable to use other methods of treatment administration to prevent severe asthma exacerbations and avoid preventable hospitalizations</li> </ul>	<ul style="list-style-type: none"> <li>Increased auto-aerosolization and spread or virus into the surrounding environment.<sup>29</sup></li> </ul>



physicians should also encourage self-administered biologic treatment at home if possible, to reduce office visits and help prevent patients from missing their scheduled doses.<sup>20</sup> Appropriate training sessions and in person physician demonstrations are needed to help patients transition from clinic to home administration and prevent unnecessary side effects of biologic injections. Biological therapies should be stopped temporarily if patient develops active COVID-19 and should not be continued again until patient is clinically asymptomatic and receives a negative Covid test swab.<sup>21</sup>

Aerosolized devices are crucial for treatment administration in patients with respiratory illnesses, including asthma.<sup>50</sup> Metered-dose inhalers are ideal devices for treatment administration in many patients as they have a short treatment time, allow for multiple dose administrations and are easy to use.<sup>50</sup> This device has a low risk of viral transmission, however, may not be ideal for patients in acute life-threatening respiratory failure, with cognitive or neuromuscular impairment, or inadequate inspiratory strength.<sup>50</sup> Dry-powdered inhalers are driven into the lungs during inhalation and therefore do not require hand-breathe coordination.<sup>50</sup> However, dry-powdered inhalers can cause irritation to the airway causing cough and subsequently increasing risk of potential viral transmission.<sup>50</sup> Finally, nebulizers are more powerful devices that are associated with longer treatment times and require more maintenance.<sup>50,51</sup> There is conflicting

evidence on the risk of viral aerosolization with the use of nebulizer devices. Wan et al. found that the use of nebulizers in patients with SARS did not increase the risk of transmission of viral particles in a health care setting.<sup>52</sup> However, many hospitals have created strict guidelines surrounding the use of nebulizers in hospital, to decrease the risk of viral aerosolization among patients and health care providers.<sup>51</sup> Recommendations have been made to avoid nebulizer medications during the pandemic. Instead a metered-dose inhaler with a valved holding chamber or dry powdered inhaler are preferred to reduce auto-aerosolization and spread of virus into the surrounding environment.<sup>9,29</sup> Patients currently on nebulized medications should continue on these medications only until their provider can discuss with them the alternative medication options.<sup>29</sup>

### Should treatment guidelines change during the COVID-19 pandemic (See box 5)?

Recommendations have been made from several national and international societies on the management of asthma during the pandemic. These recommendations are consistent and recommend staying on the same maintenance and exacerbation medications during the COVID-19 pandemic.<sup>29,30,40,53</sup> It is also recommended to take additional precautions including avoiding asthma exacerbation triggers, ensuring proper inhaler techniques, maintaining physical distancing and practicing

**Box 5.** Asthma maintenance and exacerbation medications, in Covid negative and positive individuals during the pandemic.

TREATMENT	ASTHMA TREATMENT IF PATIENT COVID -VE	ASTHMA TREATMENT IF PATIENT COVID +VE	GUIDELINE FOR USE DURING PANDEMIC
Inhaled Corticosteroid	+	+	Continued or restarted if stopped in patients with asthma. <sup>29</sup>
Systemic Corticosteroid	+	+	World Health Organization advises against the use systemic corticosteroids for treatment outside of clinical trials. <sup>31</sup> Can be used to treat an asthma exacerbation per national guidelines. <sup>29</sup>
Short-acting Beta Agonist	+	No substantial evidence found regarding efficacy	Treatment for asthma exacerbations should be continued according to current national and international asthma treatment guidelines. <sup>29</sup>
Long-acting Beta Agonist	+	No substantial evidence found regarding efficacy	Treatment for asthma maintenance should be continued according to current national and international asthma treatment guidelines. <sup>29</sup>
Long-acting Muscarinic therapy	+	No substantial evidence found regarding efficacy	Treatment for asthma maintenance should be continued according to current national and international asthma treatment guidelines. <sup>29</sup>
Leukotriene Receptor Antagonist	+	+	Treatment for asthma maintenance should be continued according to current national and international asthma treatment guidelines. <sup>29</sup>
Azithromycin	+	+	If asthma is not controlled by standard therapies, starting azithromycin prophylaxis therapy could be an acceptable treatment approach. <sup>24</sup>
Allergen Immunotherapy	+	-	Asthmatic patients without clinical symptoms of Covid-19 or exposure to SARS-Cov-19 virus can continue therapy. Covid-positive patients should discontinue therapy. <sup>46</sup>
Biologic therapy	+	-	Continue in Covid -ve asthmatic patients for which treatment is indicated and effective. <sup>29</sup>

proper hand hygiene.<sup>53</sup> It is not recommended to step down from any current asthma management plans, unless proven beneficial to a specific patient's situation.<sup>40</sup>

Additionally, the use of telemedicine has rapidly progressed since the onset of the Covid-19 pandemic in an effort to reduce unnecessary in person medical visits.<sup>54,55</sup> Due to this many allergy and immunology clinicians have had to rapidly incorporate telemedicine into their practices.<sup>54,55</sup> A recent meta-analysis found that both tele-case management and tele-consultation were effective telemedicine tools in improving asthma control and quality of life in adult patients.<sup>56</sup> Additionally, telemedicine was shown to be non-inferior to in-person consultations for asthma treatment and management.<sup>54</sup> Clinicians should take into account individualized patient circumstances when choosing between in-person and telemedicine consultations for the diagnosis and treatment of asthma.<sup>55</sup>

### How does COVID-19 impact the future of asthmatic care?

Recommendations have been made by many regulatory bodies to place restrictions on pulmonary function testing for the monitoring and diagnosis of respiratory illnesses.<sup>57,58</sup> Pulmonary function testing should be limited to spirometry, oximetry, and arterial blood gases and testing should only be performed on patients if essential for immediate treatment decisions.<sup>58</sup> These restrictions may lead to delayed diagnosis in non-severe asthmatic patients. Additionally, screening protocols have now become mandatory prior to entry into several workplaces. This may pose a burden to individuals with asthma due to the similarity in symptom profiles, such as shortness of breath and cough. This could potentially restrict these individuals from being present at work during periods of asthma exacerbations and subsequently have potential downstream impacts on vocational success.

Recently there has been a reported shortage of metered-dose inhaler quick relief medications in Canada, the United States and Australia. This is multi-factorial including the recent increase proportion of patients switching to metered-dose treatments from nebulized treatments since the later increases risk of viral aerosolization and viral transmission.<sup>59</sup> In addition, several countries have put restrictions on prescription medication, such as bronchodilators, to reduce unnecessary stockpiling of these medications. In asthmatic patients, this reduced availability of routine medications and fear of visiting crowded emergency facilities could result in an increase of asthmatic morbidity in the general public. Education to reduce exposure to asthma triggers, hand washing, and social distancing is essential to reduce the burden on this population.

To the best of our knowledge there currently is no evidence whether having COVID-19, will increase severity of asthma exacerbations long-term in adult patients. Further studies need to be done investigating the long-term effects of past COVID-19 infection on asthma disease progression.

### Author Contribution

Both listed authors made a substantial contribution to the concept or design of the work; or acquisition, analysis or interpretation of data; Drafted the article or revised it critically for important intellectual content; Approved the version to be published and are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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