

# The short and the long of it

## Asthma control and COVID-19 in children

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Associations between asthma and COVID-19 in adults are well known. However, as children have lower rates of severe COVID-19, this relationship has been less well explored in the paediatric population. Emerging evidence suggests that children with asthma, particularly poorly controlled asthma, may be at higher risk of adverse sequelae from COVID-19.

### Key points

- **Children with well-controlled asthma appear to be no more susceptible to coronavirus disease 2019 (COVID-19) than children without asthma and do not have an increased risk of adverse sequelae from COVID-19.**
- **Prescription of oral corticosteroids or the occurrence of one or more asthma exacerbations in the previous two years is associated with an increased risk of COVID-19 hospitalisation for children with asthma.**
- **Intensive care unit admission, invasive mechanical ventilation and death remain extremely rare in children with asthma and COVID-19.**
- **The association between COVID-19 and long-term asthma control remains unclear, but limited data suggest a worsening of asthma control over a six-month period after COVID-19.**
- **COVID-19 vaccination is recommended for children with severe or poorly controlled asthma, as is close medical surveillance during and after COVID-19.**
- **Good asthma control should be maintained in children during COVID-19 outbreaks, including ensuring good inhaler technique and optimal adherence to therapy, modifying asthma medication if needed and referring to a respiratory specialist if control remains poor.**



**C**hildren experience less severe coronavirus disease 2019 (COVID-19) than adults.<sup>1</sup> Because children have substantially lower rates of severe COVID-19, identification of pre-existing comorbidities that may increase the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been more gradual in children than adults.<sup>2</sup> However, emerging data indicate that children with asthma, particularly those with severe or poorly controlled asthma, are at higher risk of hospitalisation for COVID-19.<sup>3,4</sup>

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## 1. Childhood asthma and susceptibility to SARS-CoV-2

What the evidence suggests so far.

- Children with asthma, including those with severe phenotypes, are no more susceptible to SARS-CoV-2 infection than children without asthma
- Children with poorly controlled or severe asthma may be more likely to be admitted to hospital but do not have increased risk of severe disease

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

The impact of SARS-CoV-2 infection on long-term asthma control remains unclear. Tertiary paediatric health services have seen significant reductions in asthma-related emergency department presentations and hospital admissions during the past two years of the COVID-19 pandemic.<sup>5-7</sup> Although the reasons for reductions in asthma-related illness are difficult to discern, lower exacerbation frequency has been attributed to social distancing, mask wearing, improved hygiene measures and reduced exposure to conventional respiratory viruses.<sup>8,9</sup> As levels of social interaction and environmental exposure return to pre-pandemic norms, it will be essential for medical practitioners who treat children to be aware of the consequences that COVID-19 may have on short- and long-term asthma control, to ensure appropriate management.

### Childhood asthma, SARS-CoV-2 susceptibility and COVID-19 severity

Current evidence suggests that children with asthma are no more susceptible to SARS-CoV-2 infection than children without asthma (Box 1), even though those with severe asthma are more likely to be tested.<sup>4</sup> In Australia, tertiary care centres have seen similar rates of asthma among children testing positive or negative for SARS-CoV-2 on polymerase chain reaction testing.<sup>10</sup> Similar rates of COVID-19 have also been seen in children with and without asthma in the UK.<sup>4,11</sup>

Asthma in paediatric populations is primarily associated with type 2 inflammation.<sup>12</sup> It is hypothesised that downregulation in the

expression of ACE-2 receptors, seen in the type 2 asthma endotype, may act as a defence mechanism against COVID-19.<sup>3</sup> Moreover, recent randomised trial evidence suggests inhaled budesonide treatment may reduce the relative risk of clinical deterioration in adults hospitalised with COVID-19 by 91%, with altered mucosal antiviral inflammation response during the initial phase of SARS-CoV-2 infection hypothesised as a potential causal mechanism for reduced COVID-19 severity.<sup>13,14</sup> Trials with similar methods have yet to be replicated in a paediatric population, but these findings may have important clinical implications, given that inhaled corticosteroids are safe and widely used in children with asthma.<sup>15</sup>

To date, COVID-19-related mortality in children with asthma has been extremely rare. Most studies investigating the risk of adverse sequelae in children with asthma infected with SARS-CoV-2 have used hospital and critical care admission as markers of COVID-19 severity. The largest of these studies was based in the USA, where the overall prevalence of childhood asthma is 5.8%.<sup>16</sup> A cross-sectional study analysed 43,465 children from 800 tertiary care centres who tested positive for COVID-19 and found that asthma was the most common underlying medical condition, affecting 10.2% of patients.<sup>3</sup> Of 18 different pre-existing diseases investigated as potential risk factors for COVID-19 hospital admission, asthma was ranked 12th, with an adjusted risk ratio of 1.23 for hospitalisation. On further analysis, asthma was not found to be associated with severe COVID-19 in those who were hospitalised (defined by intensive care unit admission, need for mechanical invasive ventilation, or death).<sup>3</sup>

These findings have been further supported by data obtained from a similar number of children with asthma and SARS-CoV-2 infection in Scotland, with higher rates of hospital admission seen for children with asthma than those without asthma (106 vs 55/100,000).<sup>4</sup> Nevertheless, the risk of hospitalisation for COVID-19 remained relatively low, with only one in 380 children with poorly controlled asthma being admitted to hospital. Prior hospital admission for asthma or oral corticosteroid prescription in the previous two years was found to substantially increase the risk of COVID-19-related hospital admission, with those who had been prescribed two or more doses of oral corticosteroids being at greatest risk. Another study in children aged 12 to 17 years in England reached similar conclusions, when individual-level data from January 2020 to September 2021 for

## 2. Strategies to support children with asthma during the COVID-19 pandemic

- Ensure asthma medication is optimal, in line with current guidelines, and appropriate for disease severity<sup>23</sup>
- Ensure a written asthma action plan is up-to-date and relevant to the child's specific needs
- Consider increasing the frequency of asthma review for children with severe or poorly controlled asthma
- Encourage optimal adherence to therapy
- Assess inhaler technique to ensure appropriate delivery of medication
- Strongly encourage vaccination against COVID-19, particularly for children with severe or poorly controlled asthma
- Closely monitor children infected with SARS-CoV-2 who have been recently prescribed oral corticosteroids or who have had one or more asthma exacerbations within the past 12 months; consider a lower threshold for presentation to the emergency department for these children
- Be aware that children may become more reliant on short-acting bronchodilators after COVID-19
- If asthma control remains poor, consider specialist referral
- Educate parents and guardians on the importance of maintaining good asthma control and strongly discourage the use of unproven therapies for COVID-19
- Emphasise the importance of avoiding direct and second-hand smoke exposure and vaping

Abbreviations: COVID-19 = coronavirus disease 2019; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

215,873 children with asthma were collated and compared with data for 2,780,630 children without asthma. The risk of hospitalisation was greater for the children with asthma than for those without asthma, and children prescribed one or more oral corticosteroids in the year before the pandemic were more likely to be admitted to hospital with COVID-19.<sup>11</sup>

### Associations between COVID-19 and long-term asthma control

Conventional respiratory viruses, such as rhinoviruses, influenza viruses and respiratory syncytial viruses, can trigger an asthma exacerbation.<sup>17</sup> Although a growing body of evidence suggests that a prior diagnosis of asthma does not increase the risk of severe COVID-19, longer-term associations (i.e. four weeks or more after COVID-19 symptom onset) between COVID-19 and asthma control remain largely unexplored. Substantially higher oral corticosteroid and short-acting beta-agonist prescription fill rates have been found for children over a six-month period after SARS-CoV-2 infection, suggesting that COVID-19 may trigger poor asthma control.<sup>18</sup> Increased inhaler use and worsening asthma control have also been reported among adults who have had COVID-19.<sup>19</sup>

The reasons for these findings are difficult to determine. As expiratory airflow in adults and children with asthma appears to be unaffected by COVID-19, altered pulmonary function is unlikely to be the cause of worsening asthma control.<sup>20,21</sup> An evaluation of the forced expiratory volume in one second (FEV<sub>1</sub>) of 51 children with asthma found they had similar measurements one month after COVID-19 as at baseline.<sup>21</sup> However, all participants were classified as having well-controlled asthma at baseline, with a mean FEV<sub>1</sub> of 97%. Given children with poorly controlled asthma are more likely to develop severe COVID-19, it is plausible that expiratory airflow could be impaired by SARS-CoV-2 infection in this at-risk group. To identify potential exacerbations during the course of acute COVID-19, children with poorly controlled asthma may benefit from using telehealth spirometry.<sup>22</sup>

### Management of children with asthma during COVID-19 outbreaks

As children with well-controlled asthma are not at increased risk of getting COVID-19, nor of having more severe disease, the emphasis should be on maintaining good asthma control in children during COVID-19 outbreaks. Every effort should be made to improve control in children with poorly controlled asthma, such as ensuring good inhaler technique and optimal adherence to therapy, as well as modifying asthma medication if needed. If asthma control does not improve, referral to a respiratory specialist may be needed. COVID-19 vaccination is recommended for children with severe or poorly controlled asthma, as is close medical surveillance during and after COVID-19. Strategies to support children with asthma during the COVID-19 pandemic are summarised in Box 2.

### Conclusion

Although evidence from meta-analyses is lacking, well-designed cross-sectional and cohort studies have shown that children with asthma who have been prescribed oral corticosteroids or have experienced one or more exacerbations in the preceding 12 to 24 months are at increased risk of hospitalisation for COVID-19, whereas children with mild or well-controlled asthma are not. These findings underscore the importance of both optimising adherence to therapy and ensuring up-to-date asthma action plans are in place, as well as highlighting the importance of COVID-19 vaccination in this at-risk group. For children with severe or poorly controlled asthma, close surveillance is needed after SARS-CoV-2 infection to ensure appropriate management. Parents and guardians of children with severe asthma should be strongly discouraged from using unproven therapies for COVID-19. Finally, good asthma control before infection with SARS-CoV-2 is likely to reduce COVID-19 severity, risk of hospital admission and long-term sequelae. **RMT**

### References

A list of references is included in the online version of this article ([www.respiratorymedicinetoday.com.au](http://www.respiratorymedicinetoday.com.au)).

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### References

- Zimmermann P, Curtis N. Why is COVID-19 less severe in children? A review of the proposed mechanisms underlying the age-related difference in severity of SARS-CoV-2 infections. *Arch Dis Child* 2020; Dec 1. Online ahead of print.
- Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020; 109: 1088-1095.
- Kompaniyets L, Agathis NT, Nelson JM, et al. Underlying medical conditions associated with severe COVID-19 illness among children. *JAMA Netw Open* 2021; 4: e2111182.
- Shi T, Pan J, Katikireddi SV, et al. Risk of COVID-19 hospital admission among children aged 5–17 years with asthma in Scotland: a national incident cohort study. *Lancet Respir Med* 2022; 10: 191-198.
- Krivec U, Kofol Seliger A, Tursic J. COVID-19 lockdown dropped the rate of paediatric asthma admissions. *Arch Dis Child* 2020; 105: 809-810.
- Hu N, Nassar N, Shrapnel J, et al. The impact of the COVID-19 pandemic on paediatric health service use within one year after the first pandemic outbreak in New South Wales Australia - a time series analysis. *Lancet Reg Health West Pac* 2022; 19: 100311.
- Pelletier JH, Rakkar J, Au AK, Fuhrman D, Clark RSB, Horvat CM. Trends in US pediatric hospital admissions in 2020 compared with the decade before the COVID-19 pandemic. *JAMA Netw Open* 2021; 4: e2037227.
- Sayed S, Diwadkar AR, Dudley JW, et al. COVID-19 pandemic-related reductions in pediatric asthma exacerbations corresponded with an overall decrease in respiratory viral infections. *J Allergy Clin Immunol Pract* 2022; 10: 91-99 e12.
- Papadopoulos NG, Mathioudakis AG, Custovic A, et al. Childhood asthma outcomes during the COVID-19 pandemic: findings from the PeARL multinational cohort. *Allergy* 2021; 76: 1765-1775.
- Du Berry C, Saunders T, McMinn A, et al. Is cardiorespiratory disease associated with increased susceptibility of SARS-CoV-2 in children? *Pediatr Pulmonol* 2021; 56: 3664-3668.
- Dolby T, Nafilyan V, Morgan A, Kallis C, Sheikh A, Quint JK. Relationship between asthma and severe COVID-19: a national cohort study. *Thorax* 2022; Mar 30. Online ahead of print.
- Fahy JV. Type 2 inflammation in asthma—present in most, absent in many. *Nat Rev Immunol* 2015; 15: 57-65.
- Baker JR, Mahdi M, Nicolau DV, et al. Early Th2 inflammation in the upper respiratory mucosa as a predictor of severe COVID-19 and modulation by early treatment with inhaled corticosteroids: a mechanistic analysis. *Lancet Respir Med* 2022; 10: 545-556.
- Liew F, Openshaw PJM. Inhaled corticosteroids: not just for asthma, but for COVID-19? *Lancet Respir Med* 2022; 10: 526-527.
- Szeffler S, Weiss S, Tonascia J, et al; Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. *N Engl J Med* 2000; 343: 1054-1063.
- Centers for Disease Control and Prevention. Most recent national asthma data. CDC; 2022. Available online at: [https://www.cdc.gov/asthma/most\\_recent\\_national\\_asthma\\_data.htm](https://www.cdc.gov/asthma/most_recent_national_asthma_data.htm) (accessed July 2022).
- Kim WK. Association between respiratory viruses and asthma exacerbations. *Korean J Pediatr* 2014; 57: 26-28.
- Chou CC, Morphew T, Ehwerhemuepha L, Galant SP. COVID-19 infection may trigger poor asthma control in children. *J Allergy Clin Immunol Pract* 2022; 10: 1913-1915.
- Philip KEJ, Buttery S, Williams P, et al. Impact of COVID-19 on people with asthma: a mixed methods analysis from a UK wide survey. *BMJ Open Respir Res* 2022; 9: e001056.
- Lewis KL, Helgeson SA, Tatari MM, Mallea JM, Baig HZ, Patel NM. COVID-19 and the effects on pulmonary function following infection: a retrospective analysis. *EClinicalMedicine* 2021; 39: 101079.
- Amat F, Delaisi B, Labbe JP, Leonardi J, Houdouin V. Asthma may not be a risk factor for severe COVID-19 in children. *J Allergy Clin Immunol Pract* 2021; 9: 2478-2479.
- Richardson CH, Orr NJ, Ollosson SL, Irving SJ, Balfour-Lynn IM, Carr SB. Initiating home spirometry for children during the COVID-19 pandemic – a practical guide. *Paediatr Respir Rev* 2022; 42: 43-48.
- National Asthma Council Australia. Australian Asthma Handbook, Version 2.2. Melbourne: National Asthma Council Australia; 2022. Available online at: <https://www.astmahandbook.org.au> (accessed August 2022).