

Managing asthma in pregnancy

New research and resources for GPs

VANESSA E. MURPHY BMedChem(Hons), PhD

MEGAN E. JENSEN BNutrDiet(Hons), AdvAPD, PhD

Asthma is the most prevalent chronic disease affecting pregnant women. Many women will be managed by their GP at some point during their pregnancy. The GP plays a pivotal role in educating patients and assessing and managing risk factors for asthma exacerbation during pregnancy, which can help optimise asthma management and health outcomes for the mother and child.

Asthma affects more than one in 10 people in Australia, and recent studies show that between 8.4% (South Australia) and 17% (Queensland) of pregnancies are affected, making this an important issue for GPs.^{1,2} This article outlines key new research findings that will assist clinicians in optimising asthma management for their pregnant patients. We describe risk factors for exacerbation of asthma in pregnancy, important aspects of self-management that GPs can help improve, and the potential for a 'treatable traits' approach to asthma management in pregnancy. New resources are also available for health professionals and families affected by asthma in pregnancy on the Asthma in Pregnancy Toolkit website (<https://asthmapregnancytoolkit.org.au>), which covers key aspects of asthma management in pregnancy (Figure).

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Professor Murphy is a Professor, School of Medicine and Public Health at the University of Newcastle; and Deputy Chair, Breathing and Lung Health Research Program at Hunter Medical Research Institute, Newcastle. Dr Jensen is a Senior Lecturer and Research Fellow, School of Medicine and Public Health, at the University of Newcastle and the Breathing and Lung Health Research Program, Hunter Medical Research Institute, Newcastle, NSW.



Key points

- Women with asthma are at increased risk of poor perinatal outcomes, including preterm birth, low birth weight and infant congenital malformations.
- Asthma medications are safe to use throughout pregnancy and women should be encouraged to continue using their prescribed asthma medications throughout pregnancy and postpartum.
- Modifiable risk factors, such as smoking and depression and anxiety, and nonmodifiable risk factors, including multiparity and multiple pregnancy, are associated with worsening asthma symptoms and exacerbations, and should be targeted for management.
- Educating pregnant women about the safety and correct use of their asthma medications and the importance of maintaining good asthma control during pregnancy is essential for improving outcomes for women with asthma during pregnancy.
- Recognising patient characteristics associated with poor adherence, such as lower maternal age, higher parity or being a current or ex-smoker, can help clinicians identify those who may need further education on asthma medication in pregnancy.
- The Asthma in Pregnancy Toolkit provides information and resources, including infographics, webinars and links to relevant guidelines and clinical assessments for health professionals and families.

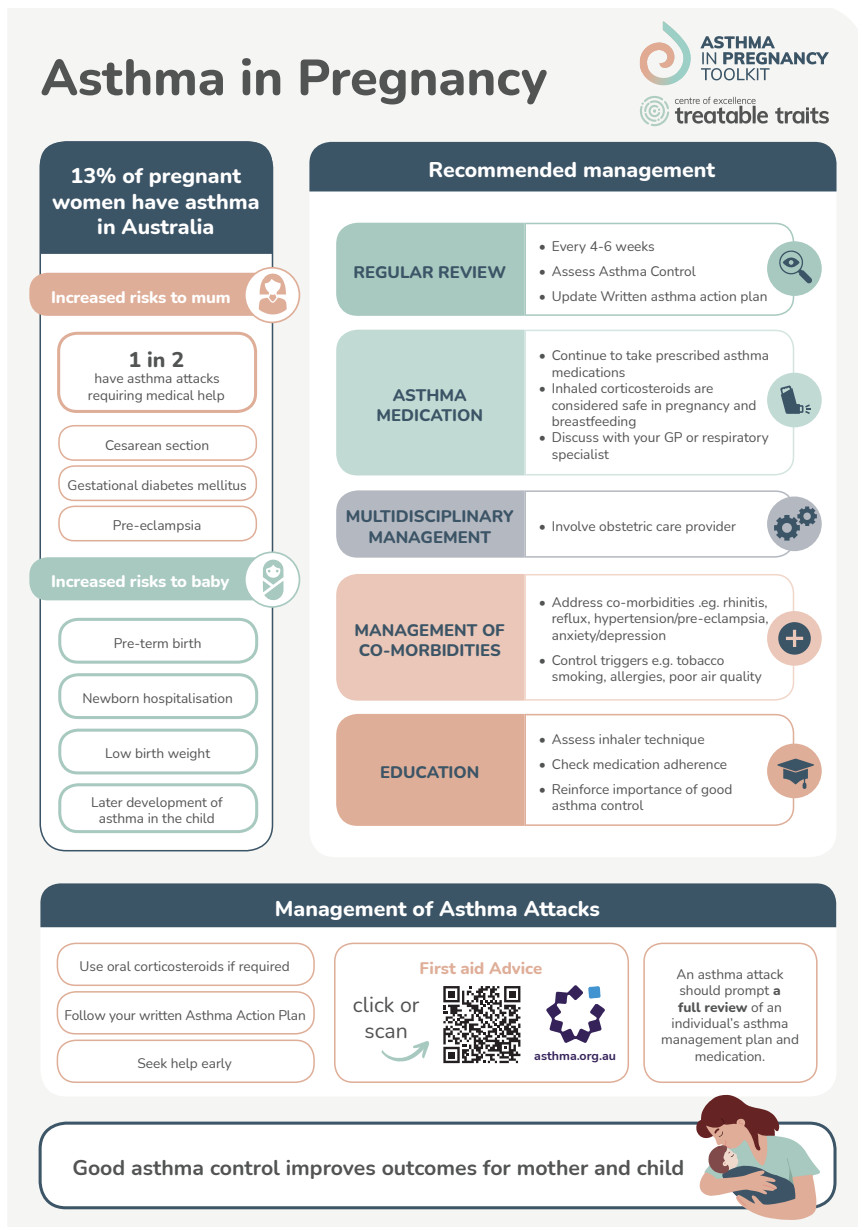


Figure. Infographic summarising asthma in pregnancy.

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Asthma medication use in pregnancy

Asthma medication is generally considered safe to continue during pregnancy. Although randomised controlled trials are limited (as with any medication use in pregnant women), an abundance of data supports the safety of short-acting beta agonists (SABAs), particularly salbutamol, and inhaled corticosteroids (ICS), particularly budesonide.^{3,4} Women whose asthma has been well controlled on a particular ICS are recommended to continue this ICS in pregnancy. The benefit of oral corticosteroids in treating an exacerbation is considered to outweigh any potential fetal risk. Fewer data are available on the safety of biologics; however, registry studies have been established and are currently collecting data. Published data on omalizumab

show a similar rate of poor outcomes (stillbirth, low birth weight, preterm birth and congenital malformations) in pregnant women with asthma who were exposed to omalizumab compared with an unexposed cohort.⁵

A recent study of more than 1000 pregnant women with asthma showed better perinatal outcomes for women with severe asthma who continued using a prescribed biologic during pregnancy, compared with those not using biologics, matched for age, ethnicity, comorbidities, substance use and obesity.⁶

Perinatal and neonatal outcomes

Pregnant women with asthma are at increased risk of poor perinatal outcomes. Consequently, asthma management in pregnancy is important because it has the potential to improve outcomes for both the mother and baby. Our team updated our systematic review and meta-analysis examining the neonatal risks of asthma in pregnancy, including the addition of 18 new studies and more than 15 million pregnancies to the analysis (including >600,000 with asthma), with the following reported outcomes.⁷

- Most risks remained as previously described: infants of women with asthma were more likely to go to the neonatal intensive care unit (NICU) or special care nursery (relative risk [RR], 1.27; 95% confidence interval [CI], 1.25–1.30) and have congenital malformations (RR, 1.36; 95% CI 1.32–1.40).⁸ These results were supported by combining data from studies that adjusted for important confounders.
- The risk for major congenital malformations became statistically significant (RR, 1.18; 95% CI, 1.15–1.21; adjusted odds ratio [aOR], 1.20; 95% CI, 1.15–1.26).

- The risk for respiratory distress syndrome became statistically significant (RR, 1.25; 95% CI, 1.17–1.34).
- Neonatal death was no longer significantly associated with maternal asthma – although perinatal mortality reached significance in the unadjusted analysis, this finding was not supported by the meta-analysis of data adjusted for important confounders.
- No additional data are available on specific congenital malformations.

Women with asthma are at increased risk of preterm birth and having a low birth weight baby. A systematic review and meta-analysis of preterm birth and birth weight outcomes in women with asthma in

pregnancy showed that having an asthma exacerbation in pregnancy increased the odds for having a low birth weight (aOR, 1.15; 95% CI, 1.02–1.29) or small for gestational age (aOR, 1.13; 95% CI, 1.04–1.23) baby, and these data are consistent with previous analyses.^{9,10} No significant association was found between asthma severity, oral corticosteroid use or exacerbations and preterm birth.⁹ However, an earlier meta-analysis showed that women with asthma had a 41% increased risk of preterm birth, which was reduced with active asthma management.¹¹

A recent study from the Hunter New England and Mid North Coast local health districts in New South Wales demonstrated increased risks of several perinatal outcomes in women with asthma during pregnancy, including preterm birth, low birth weight, caesarean section, congenital anomalies and respiratory distress syndrome in the infant.¹²

Outcomes in Indigenous Australian populations

Data from over 25,000 Indigenous mothers and babies in Western Australia showed that having asthma was associated with emergency caesarean section (aOR, 1.27; 95% CI, 1.13–1.44), threatened preterm labour and placental abruption, but not with low birth weight or preterm birth.¹¹ Indigenous women who had exacerbations of asthma (defined as hospitalisation or emergency department visit) were at increased odds of threatened preterm labour (aOR, 1.86; 95% CI 1.37–2.54) and placental abruption (aOR, 2.85; 95% CI 1.24–6.55) compared with Indigenous women without exacerbations. Among Indigenous women living in more remote areas, asthma was also associated with several adverse pregnancy outcomes, including increased risk of emergency and elective caesarean sections, NICU admission and preeclampsia.¹³ In a Queensland study, the prevalence of asthma in pregnancy was higher in Indigenous women (24%) compared with non-Indigenous women (17%).² Compared with non-Indigenous women without asthma, Indigenous women with asthma were more likely to have a neonatal death, preterm birth, low birth weight baby or NICU admission.² More research is needed to understand community needs and codesign culturally safe models of care for Aboriginal and Torres Strait Islander women with asthma during pregnancy.

Worsening symptoms and exacerbations during pregnancy

One of the unique clinical issues for pregnant women with asthma is the possibility of worsening symptoms due to pregnancy, which are unpredictable and vary between individuals.¹⁴ These symptom changes could be related to the immunological changes of pregnancy which favour a T-helper 2 immune environment, mechanical changes related to the growing uterus, or behavioural changes related to medication use and lifestyle factors.¹⁵ The accepted dogma of asthma in pregnancy has been the 'one-third rule', where one-third of patients worsen, one-third improve and one third show no change in symptoms.¹⁶ However, a recent study from the US of more than 300 women with asthma showed a pattern of worsening symptoms in 40%, whereas 60% showed no change during pregnancy.¹⁶ Of interest is the apparent improvement in symptoms seen among all women in the last few

weeks of pregnancy. Understanding the underlying mechanism of this pattern could help in the development of new therapeutic targets or approaches for preventing worsening asthma during pregnancy.

Exacerbations occur in around 20% of women with asthma during pregnancy.^{17–19} A recent population-based study from the United Kingdom showed that exacerbations managed by GPs decreased during pregnancy, compared with prepregnancy, while those involving an emergency department presentation or hospital admission increased, suggesting a potential increase in the severity of asthma exacerbations during pregnancy. The strongest risk factors for exacerbations during pregnancy were a history of exacerbations and reduced ICS use compared with prepregnancy levels.²⁰

A 2022 systematic review and meta-analysis identified moderate or severe asthma (compared with having mild asthma) as the biggest risk factor for exacerbations in pregnancy, with a greater than threefold increased risk (RR, 3.44; 95% CI, 2.03–5.83).²¹ Other key risk factors include having multiple pregnancies (RR, 2.23; 95% CI, 1.10–4.50), depression or anxiety (RR, 1.42; 95% CI, 1.27–1.59), maternal smoking (RR, 1.35; 95% CI, 1.04–1.75), multiparity (RR, 1.31; 95% CI, 1.01–1.68) and maternal obesity (RR, 1.25; 95% CI, 1.15–1.37). An increased awareness of the exacerbation risks associated with nonmodifiable factors, such as multiparity and multiple pregnancy, may lead to proactive management. Targeting modifiable risk factors, such as smoking and depression or anxiety, may also help improve asthma outcomes in women. Smoking and depression or anxiety during pregnancy are associated with the development of asthma or worse asthma control in offspring, making them important targets for management during pregnancy where possible.^{22,23}

Asthma self-management skills in pregnancy

Although the use of ICS reduces the risk of asthma attacks, asthma self-management skills are poor among pregnant women.^{19,24} GPs have an opportunity to assess and improve these skills. Baseline data from 1200 pregnant women with asthma showed that fewer than 15% had a written asthma action plan, fewer than 30% understood what their medications were for, and fewer than 50% had adequate or optimal pressurised metered dose inhaler (pMDI) technique.¹⁹ Only 42% of women used ICS at the first study visit, which is similar to the prevalence of ICS reported globally.²⁵ Of those using ICS for maintenance therapy, 78% were prescribed ICS/long-acting beta agonist (LABA) combination therapy; however, more than one-third were poorly adherent to the prescribed dose and self-reported missing at least 20% of their doses in the past week. Stopping prescribed asthma medications during pregnancy increases the risk of asthma attacks.³ Recent work has demonstrated that a telehealth approach could be used to provide asthma self-management education for pregnant women, with comparable improvements in asthma control to a face-to-face approach and better patient engagement.²⁶

An Australian study of more than 1600 pregnant women with asthma identified risk factors for poor adherence to ICS in early-mid pregnancy (n=610) and persistent poor adherence to ICS during pregnancy (n=612).²⁷ Risk factors for poor adherence included being

a current or ex-smoker, being of non-Caucasian or Indigenous Australian descent, having had an adult diagnosis of asthma and having lower lung function. Risk factors for persistent poor adherence throughout pregnancy were associated with lower maternal age, higher parity and not being prescribed ICS in early pregnancy.²⁷ This study describes important characteristics of patients who might require more education around adherence to ICS in pregnancy.

Another study asked participants why they did not like taking asthma medications in pregnancy.²⁴ The most common reason given was the unpleasant taste or throat or mouth symptoms, which can be alleviated by mouth rinsing after use and using a spacer for pMDIs. The second most common reason, cited by one in five women, was feeling that their medications might be unsafe in pregnancy.²⁸ Educating pregnant women about the correct use of asthma medications, their safety and maintaining good asthma control during pregnancy is a key way that all health professionals, including GPs, can improve outcomes for women with asthma during pregnancy.

Lung function and airway inflammation tests

Spirometry

Spirometry is a test for assessing lung function that can be used in primary care, and is generally safe to perform during most of pregnancy (with the exception of late-term pregnancy), provided the woman has no contraindications related to increased myocardial demand or blood pressure, intracranial or intraocular pressure, sinus or middle ear pressure, intrathoracic or intra-abdominal pressure, or transmissible infections.²⁹ A recent study examined changes in forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) during pregnancy among 770 pregnant women with asthma and 259 pregnant women without asthma.³⁰ Although having asthma decreased overall lung function, women with predominantly mild asthma had minimal changes in FEV₁ and FVC throughout pregnancy. These results indicate that spirometry is still a clinically useful tool in pregnancy and that any changes in lung function of a pregnant patient with asthma are likely to be because of asthma rather than the pregnancy itself.

Fractional exhaled nitric oxide

We have previously summarised the existing knowledge about using fractional exhaled nitric oxide (FeNO) levels to guide ICS treatment in pregnancy.³¹ This approach uses an algorithm to increase the ICS dose when FeNO levels are high, decrease the ICS dose when FeNO levels are low and make no changes to the dose when FeNO levels are mid-range. A LABA is added when symptoms remain uncontrolled. The efficacy study using this approach, published in 2011, showed a 50% reduction in exacerbations during pregnancy.³² However, the more recently published Breathing for Life Trial (BLT) showed no significant differences in primary outcome (a composite of adverse perinatal outcomes: preterm birth, small for gestational age, neonatal hospitalisation or perinatal mortality) or exacerbations of asthma in pregnancy between FeNO-based management and usual care among 1200 pregnant women with asthma (including

smokers and nonsmokers) from six antenatal clinic sites around Eastern Australia.¹⁹ The FeNO-based treatment algorithm will require more optimisation if this approach is to be pursued for use in pregnancy. In addition, FeNO is not currently routinely available to GPs.

Treatable traits for asthma in pregnancy

A treatable traits approach that uses a personalised medicine strategy has been proposed to manage many airway diseases, including asthma in pregnancy.³³ This approach has been used to identify treatable traits in people with severe asthma, with promising results.³⁴ Traits must be clinically relevant to asthma, measurable and treatable, and fall within three domains:

- pulmonary traits (e.g. airway inflammation)
- extrapulmonary traits (e.g. rhinitis, gastroesophageal reflux, depression and anxiety)
- behavioural traits (e.g. smoking, poor inhaler technique, poor diet, physical inactivity).

The BLT study showed a decrease in FeNO levels and an improvement in asthma control in the intervention group, indicating that the intervention was favourably impacting the traits being targeted (eosinophilic airway inflammation and symptoms causing airflow obstruction).¹⁹ A broader treatable traits approach may be useful in the context of pregnancy, and future research should focus on traits with unknown prevalence and clinical relevance in the context of pregnancy. The ideal model of care would target traits that are strongly associated with exacerbations in pregnancy, important for maternal and offspring health, and aligned with the clinical goals of the woman and her managing clinician.

Resources for health professionals, pregnant women with asthma and their family

Most pregnant women with asthma have mild disease and do not require referral to a specialist; therefore, a large proportion of pregnant women will have their asthma solely managed by their GP. In addition, many Australian women have shared obstetric care for their pregnancies. A recent survey showed that midwives and obstetricians lacked the knowledge and confidence to manage asthma in pregnancy, and many did not access guidelines specific to asthma in pregnancy.³⁵ However, these health professionals have regular interactions with pregnant women, giving them the opportunity to contribute to optimising asthma management in pregnancy, and have indicated that they would like to do so.³⁶ Involving obstetricians and midwives in the care of pregnant women requires improved communication between health providers. Antenatal clinicians should reinforce safety messages about asthma medication use in pregnancy and encourage patients to have and follow a written asthma action plan. Women with asthma in pregnancy are at increased risk of infection with respiratory viruses and poor outcomes as a result of infection.³⁷⁻³⁹ Therefore, clinicians also have an important role in educating pregnant patients on the importance and safety of vaccination during pregnancy and encouraging immunisation, particularly against influenza, respiratory syncytial virus and SARS-CoV-2 infections.

1. Resources for asthma management in pregnancy

Asthma Australia (<https://asthma.org.au>)

- Asthma and pregnancy: <https://asthma.org.au/manage-asthma/pregnancy-and-asthma/>
- Inhaler technique: <https://asthma.org.au/devices-techniques/>
- Action plan: <https://asthma.org.au/manage-asthma/asthma-action-plan/>

National Asthma Council Australia (<https://www.nationalasthma.org.au>)

- Action plan library: <https://www.nationalasthma.org.au/health-professionals/asthma-action-plans/asthma-action-plan-library>
- Pregnancy and asthma: <https://www.nationalasthma.org.au/living-with-asthma/resources/patients-carers/factsheets/pregnancy-and-asthma>
- Inhaler technique: <https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/charts/inhaler-technique-checklists>

Asthma in Pregnancy Toolkit (<https://asthmapregnancytoolkit.org.au>)

This toolkit provides information and resources, including infographics, webinars and links to relevant guidelines and clinical assessments for health professionals and families. Examples include:

- Asthma in Pregnancy Toolkit Medications module includes a table summarising the Australian pregnancy safety categories and the descriptions provided in the European Respiratory Society/Thoracic Society of Australia and New Zealand joint taskforce statement on the management of airways diseases during pregnancy:⁴ <https://asthmapregnancytoolkit.org.au/medications/>
- Asthma in Pregnancy Toolkit frequently asked questions, including 'Is my asthma medication safe to take during pregnancy and breastfeeding?', 'When should I see my doctor about my asthma during pregnancy?' and 'If my asthma gets worse while I am pregnant, what should I do?': <https://asthmapregnancytoolkit.org.au/for-families/frequently-asked-questions/>
- Asthma in Pregnancy Toolkit Aboriginal and Torres Strait Islander resources: <https://asthmapregnancytoolkit.org.au/aboriginal-and-torres-strait-islander-resources/>
- Asthma in Pregnancy Toolkit translated summaries of information for families in a range of languages: <https://asthmapregnancytoolkit.org.au/translated-resources/>

Our team developed the Asthma in Pregnancy Toolkit, a world-first online resource for health professionals and families (<https://asthmapregnancytoolkit.org.au>). The Toolkit website contains six information modules for health professionals (Asthma in pregnancy overview, Medications, Treatable traits, Maternity care, Air quality and COVID-19), as well as information for families. The Toolkit and other useful resources for asthma management in pregnancy are summarised in Box 1.

Postpartum care

Regardless of shared care arrangements in pregnancy, it is crucial that a woman with asthma returns to her GP for asthma care after birth. For some women, the first postpartum year is another time of change

2. Practice points for GPs on supporting pregnant women with asthma

- Reinforce the safety and importance of continuing prescribed medications for asthma
- Provide a written asthma action plan
- Encourage the use of a spacer with pressurised metered-dose inhalers (pMDIs)
- Check inhaler technique for patients using pMDIs, breath-activated devices and dry powder inhalers
- Ask about changes in asthma symptoms at each consultation (every four to six weeks) throughout pregnancy
- Refer patients to resources, such as the Asthma in Pregnancy Toolkit, for further information
- Encourage breastfeeding and an asthma check-up postpartum

in asthma symptoms and increased exacerbation risk, possibly because of hormonal changes. Although research in this area is limited, an older study showed that symptoms can worsen in the first three months postpartum in over 50% of women, particularly in those who had an improvement during pregnancy.¹⁶ Self-reported ICS nonadherence was higher at six months postpartum than at any time in pregnancy.²⁴ Most asthma medications are safe to use while breastfeeding, and breastfeeding should be encouraged among women with asthma for many reasons, including the potential for reduced wheeze and bronchiolitis in infants.^{40,41} Despite these potential health benefits for offspring, women with asthma are less likely to initiate breastfeeding (88% vs 98% in the general population) or to be breastfeeding at six months (38% vs 68% in the general population).^{40,42} New strategies are needed to improve breastfeeding among women with asthma.

Conclusion

Asthma is common and exacerbations during pregnancy can have adverse outcomes for mother and baby. Most SABAs, ICS, ICS/LABA and oral corticosteroids are safe to continue in pregnancy and lactation, where indicated for asthma. Women with asthma should be educated on the importance of continued use of their prescribed asthma medication if they become pregnant. Self-management skills, such as proper inhaler technique and medication adherence, should be optimised, and a written asthma action plan provided to every woman with asthma. Targeting management of modifiable risk factors and an awareness of nonmodifiable risk factors that contribute to exacerbations can help improve asthma outcomes in pregnancy. Practice points for GPs on managing asthma in pregnancy are listed in Box 2. **RMT**

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A list of references is included in the online version of this article (www.respiratorymedicinetoday.com.au).

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Managing asthma in pregnancy

What's new in research and resources for GPs?

VANESSA E. MURPHY BMedChem(Hons), PhD; **MEGAN E. JENSEN** BNutrDiet(Hons), AdvAPD, PhD

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