



Asthma in pregnancy: management strategies

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Purpose of review

Asthma is one of the most prevalent chronic medical conditions to complicate pregnancy. With approximately one-third of women experiencing a worsening of control during the course of their pregnancy, identifying those at greatest risk has the potential to improve maternal and fetal outcomes for a large number of pregnancies. Similarly, active management strategies that prioritize asthma control in this vulnerable population can have a far-reaching impact.

Recent findings

Demographic characteristics and patient noncompliance place certain populations of pregnant women at increased risk of poor asthma control during pregnancy. In addition, undertreatment and disparities in care of acute exacerbations during pregnancy likely contribute. Targeted educational interventions and treatment algorithms using objective markers of disease activity have shown improved outcomes in asthma control.

Summary

Active management strategies which focus on identifying patient-specific risk factors, patient and provider education, and targeted treatment interventions can improve asthma care for women during pregnancy.

Keywords

asthma, management strategies, pregnancy, risk factors

INTRODUCTION

Asthma is one of the most common medical conditions encountered during pregnancy, with an estimated 4–8% of pregnancies affected [1,2]. Current guidelines recommend an active approach to the care of the pregnant patient that minimizes exacerbations and maximizes control to optimize the health of both the mother and unborn child [1,3,4]. Although predicting those women most at risk for exacerbations may be challenging, strategies that focus on modifiable risk factors and patient and provider education seem best positioned to succeed.

unchanged [5–11]. Prepregnancy asthma severity seems most predictive of subsequent risk, with women with the most severe disease most likely to worsen during pregnancy [7,12]. The course of asthma control during prior pregnancies may be useful in predicting difficulties in subsequent pregnancies for individual women, with concordance rates of 58–63% reported [8,9,13]. Finally, the stage of pregnancy can have a significant impact on asthma symptoms, with most women noting a peak in the late second or early third trimester, and nearly all returning to their prepregnancy baseline within 3 months postpartum [11,14].

IDENTIFYING RISK FACTORS FOR POOR CONTROL

Patient-specific and general risk factors for poor asthma control and exacerbations during pregnancy should be considered.

EFFECT OF ASTHMA ON PREGNANCY

Prospective studies of the effects of pregnancy on asthma have shown that, on average, about one-third of women will experience a worsening of asthma control during pregnancy, one-third will improve, and the remaining one-third will remain

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Curr Opin Pulm Med 2013, 19:13–17

DOI:10.1097/MCP.0b013e32835a5bf3

KEY POINTS

- Management of asthma during pregnancy requires attention to patient-specific risk factors that may place a woman at increased risk for worsening of asthma control during gestation.
- Disparities in asthma care and medication nonadherence should be addressed frequently to minimize impact on asthma control during pregnancy.
- The use of tools such as spirometry, F_{ENO} , and standardized questionnaires to objectively assess asthma control during pregnancy should be routinely applied to assist in the management of these patients.

DEMOGRAPHIC CHARACTERISTICS

Characteristics such as age, socioeconomic class, and ethnicity may contribute to disparities in asthma care or underlying severity. Unplanned asthma-related visits to the emergency department (ED) have been shown to be increased in pregnant women who are younger, unmarried, of lower socioeconomic status, and of Hispanic, Latino [15], or African-American descent [16]. In a population of 4315 pregnant women enrolled in Tennessee's Medicaid program, black women were significantly more likely to require ED evaluation or hospital admission despite more frequent prescription of inhaled corticosteroids (ICS) than their white counterparts [16]. It is unclear whether these differences represent limitations in access to care, variations in social support, individual patterns in healthcare utilization, or underlying differences in disease morbidity.

Obesity has also been associated with poor asthma control during pregnancy. In a population of 1699 gravidas with asthma, obesity increased the risk of an acute exacerbation, with an odds ratio (OR) of 1.3 [confidence interval (CI) 1.1–1.7] compared with nonobese pregnant controls, even after adjusting for the effects of race and asthma severity [17].

Current literature shows that pregnant women with asthma are more likely to smoke than pregnant women without asthma [18–23], possibly contributing to increased risks of exacerbations [24]. Murphy *et al.* [24] evaluated 80 pregnant women with asthma and found that exacerbations were more common and severe in current smokers (34%) than never smokers (15%), although the results did not achieve statistical significance ($P=0.056$) possibly due to the small sample size.

CONCOMITANT CONDITIONS

As many as 35% of pregnant women will complain of significant nasal symptoms during pregnancy

[25]. The close relationship between allergic rhinitis and asthma in nonpregnant patients has been well documented [26–29], supporting the need to aggressively manage rhinitis in pregnant women as a potential tool for improving asthma control. Kircher *et al.* [30] found that asthma course during pregnancy was directly related to the course of gestational rhinitis, although no objective markers of asthma severity were included for comparison in this study. Although further studies will be needed to test this relationship more carefully, the possible link between gestational rhinitis and asthma control has compelling clinical and mechanistic implications, and may help to identify another subgroup of women at increased risk for poor control during pregnancy.

Concomitant viral upper respiratory tract infections also seem to play a role in worsening asthma control during pregnancy. Women with asthma have been shown to be more likely to have upper respiratory or urinary tract infections during pregnancy than pregnant women without asthma (35 vs. 5%, $P<0.001$), with rates of infection directly related to severity of underlying asthma ($P=0.01$) [21]. The connection between asthma, pregnancy, and vulnerability to viral respiratory infections was especially notable during the 2009 H1N1 influenza epidemic wherein patients with asthma and pregnancy were the two groups found to be at the greatest risk for adverse respiratory outcomes [31–34]. Research by Forbes *et al.* [35] provides a possible mechanism for this increased susceptibility, with reduced innate interferon responses to rhinovirus in peripheral blood mononuclear cells noted in pregnant asthmatics compared with healthy nonpregnant women.

MEDICATION NONADHERENCE AND UNDERTREATMENT

Adherence to national asthma care guidelines can reduce morbidity during pregnancy, with those women with the mildest disease likely to gain the most benefit [12]. Additionally, the use of ICS has been shown to reduce recurrent exacerbations during pregnancy [22,36] and decrease readmission rates following a hospitalization for asthma [36]. However, asthma may be undertreated in pregnant women. In a survey of 502 women with self-reported, physician-diagnosed asthma evaluated within 6 months of delivery, less than 40% with poorly controlled asthma noted the use of a controller medication [20]. Disparities in care exist in the acute care setting which contribute to undertreatment, wherein pregnant women presenting to EDs with acute exacerbations are less likely to

receive appropriate therapy with systemic corticosteroids than nonpregnant women [37,38[■]]. Cydulka *et al.* [37] reported that only 44% of pregnant women ($n=51$) received corticosteroids in the ED compared with 66% of nonpregnant women ($n=500$; $P=0.0002$), and they were 2.9 times more likely to have persistent symptoms at 2 weeks. Similarly, a retrospective comparison found that pregnant women presenting with acute exacerbations ($n=123$) were significantly less likely to be treated with systemic corticosteroids in the ED compared with nonpregnant controls ($n=123$; 51 vs. 72%, $P=0.001$) even after adjusting for severity of exacerbations [38[■]].

Lack of physician comfort with managing pregnant patients or concerns related to possible adverse effects from therapy may also contribute to disparities noted in the care of these women. In a recent survey of general practitioners, respondents had a good understanding of the safety of most asthma medications, but 25% noted that they would either stop or decrease therapy in a patient with well controlled asthma upon learning that she had become pregnant [39[■]]. In addition, only 63% suggested that they would increase her therapy in the setting of increased symptoms.

Patient preferences and noncompliance can significantly alter one's ability to successfully manage asthma according to currently accepted standards, and may negatively impact asthma control. Retrospective reviews of managed care databases have shown that claims for ICS in women with asthma decrease by 22–35% after the diagnosis of pregnancy [40,41]. Although these population-based studies do not allow a direct assessment of the reasons for the reduction of controller medications in pregnancy, nonadherence to prescribed regimens during pregnancy is common, with 40% of women reporting noncompliance with ICS in one series ($n=211$) [42].

The perception of teratogenic risks of asthma medications may influence a patient's decision to continue therapy. In a survey ($n=166$) of pregnant or recently pregnant women with asthma, 44% expressed concern about the possible effects of asthma medications on the fetus [43], while respondents to another survey tended to overestimate the potential risk for all commonly prescribed asthma therapies [44[■]]. In a survey of 501 women with asthma, 39% reported that they had either stopped or reduced the use of their asthma medications during pregnancy, and one-third had done so without discussing their decision with a physician [45]. In addition, 36% of women taking an ICS noted that they would discontinue it if they became pregnant. Careful attention should be directed

toward medication noncompliance as a potential trigger for poor control and associated exacerbations in routine asthma care. In two prospective series of asthma in pregnancy [46,47], reported noncompliance or discontinuation of controller medications contributed to 27–29% of exacerbations.

MANAGEMENT AND MONITORING STRATEGIES

Asthma management during pregnancy is similar to that in the nonpregnant patient, with a stepwise approach to therapy recommended based on asthma severity (initial assessment) and level of control (subsequent evaluations) [1,3,4]. Selection of therapies should consider the risk–benefit ratios of individual therapies during pregnancy, but available data are generally reassuring and support recommendations that the benefits of well controlled maternal asthma currently outweigh any potential risks [1,4].

Spirometry and peak expiratory flow rates (PEFR) are useful objective tools for monitoring pulmonary function during pregnancy as they are essentially unaffected by gestation, and routine measurement is recommended [1,4,48–52]. Asthma control assessments should be performed at each visit using validated screening tools, and may serve as a useful point to initiate discussion with patients who may not perceive the same degree of impairment noted on objective tools such as spirometry or PEFR monitoring [3]. In addition, the combination of tools such as these may help to identify those women experiencing dyspnea from nonasthma-related reasons, prompting additional work-up or education.

The fraction of exhaled nitric oxide ($F_{E}NO$) has been evaluated as a tool for assessing eosinophilic airway inflammation in asthma, and a recently published evidence-based guideline provides strategies for its clinical use in nonpregnant patients [53[■]]. Unaffected by gestational age in healthy pregnancy [54,55], it has been shown to correlate with asthma control in a small cohort of pregnant women with asthma [55]. In a larger randomized, placebo-controlled trial of 220 pregnant women, Powell *et al.* [56[■]] demonstrated that asthma outcomes in pregnancy could be improved through the use of a $F_{E}NO$ directed algorithm in combination with use of the Asthma Control Questionnaire (ACQ) when compared with usual care. In this study population, the combination of $F_{E}NO$ and ACQ monitoring with targeted medication titration in pregnancy resulted in fewer asthma exacerbations (25 vs. 41%, $P=0.011$), reduced unplanned healthcare visits, and improved quality of life (QOL). In addition,

at the end of the study, more women in the $F_{E}NO$ arm were using ICS (68 vs. 42%), and interestingly the mean daily dose of these medications across the study period was lower in the $F_{E}NO$ group than in the control. Of note, the study protocol allowed down-titration in therapies in those patients who were well controlled at 1-month intervals – an approach that some have argued [57] is too aggressive for this vulnerable patient population, and not in keeping with current guidelines which recommend continuing therapies for 3 months once control is achieved before considering a deescalation in dose [3] even in nonpregnant patients.

The development of individualized self-management plans in asthma that focus on patient education and the use of asthma-action plans has been shown to improve medication adherence, QOL, and asthma control in nonpregnant patients [58–61], and appears to have similar effectiveness in pregnant women. In a study of 149 pregnant women, targeted intervention with an asthma educator resulted in overall improvement in self-management skills with decreased nonadherence with ICS (40–21%, $P=0.006$), increased adequacy of inhaler technique (84–96%, $P=0.005$), improved medication knowledge (58–95%, $P<0.0001$), increased use of PEFr monitoring (3–35%, $P<0.0001$), and increased use of an asthma action plan (15–75%, $P<0.0001$) [42]. In addition, in those women with severe asthma, there was a significant reduction in nighttime symptoms ($P<0.0001$) and rescue inhaler use ($P<0.0001$). This is particularly important in light of the survey by Chambers [45], who found that 40% of women would be more likely to continue their medications during pregnancy simply if advised to do so by their obstetrician.

Recent studies examining the role of asthma-related QOL in pregnancy have generated some interesting hypotheses regarding the importance of this subjective measure of the impact of asthma during pregnancy and should begin to guide clinicians and researchers moving forward [44[■],62]. Schatz *et al.* [62] used the Juniper Asthma QOL Questionnaire to examine responses of 310 pregnant women enrolled in a previously published trial [63] of beclomethasone vs. theophylline in mild–moderate asthma and found that the initial overall QOL was significantly lower ($P=0.047$) in those women who later experienced exacerbations compared with those who did not. Interestingly, this was not related to baseline symptom frequency or spirometry. In a more recent cross-sectional study, Powell *et al.* [44[■]] demonstrated a similar relationship between the psychological aspects of asthma and disease control. In a population of pregnant women comprising primarily mild, well controlled

asthmatics, the majority of women described good QOL and overall positive beliefs about their asthma, including perceived asthma control. However, the need for maintenance ICS negatively impacted psychosocial outcomes, and those women with uncontrolled asthma (19%) had more negative illness perceptions. These areas could benefit from future, prospective study, and targeted intervention when designing content areas for asthma management programs for women with asthma in pregnancy.

CONCLUSION

The care of the pregnant patient with asthma requires a multifaceted approach focused on identifying patient-specific risk factors which may increase her risk for worsening asthma control during pregnancy while addressing disparities in care which may not be obvious to all care providers. Careful attention to medication nonadherence and undertreatment can improve compliance in combination with the development of self-management programs that can empower women and their providers to make better informed decisions about this common chronic medical condition in pregnancy. The application of targeted algorithms using objective assessments of disease activity such as $F_{E}NO$ and the ACQ deserves further attention and consideration for wider clinical use as more prospective clinical trials are performed.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 84–85).

1. National Asthma Education and Prevention Program Expert Panel Report. Managing asthma during pregnancy: recommendations for pharmacologic treatment: 2004 update. *J Allergy Clin Immunol* 2005; 115:34–46.
2. Kwon HL, Belanger K, Bracken MB. Asthma prevalence among pregnant and childbearing-aged women in the United States: estimates from national health surveys. *Ann Epidemiol* 2003; 13:317–324.
3. National Asthma Education and Prevention Program Expert Panel Report 3 (EPR-3): guidelines for the diagnosis and management of asthma—summary report 2007. *J Allergy Clin Immunol* 2007; 120 (5 Suppl):S94–S138.
4. Dombrowski MP, Schatz M. ACOG practice bulletin: clinical management guidelines for obstetrician-gynecologists number 90, February 2008: asthma in pregnancy. *Obstet Gynecol* 2008; 111 (2 Pt 1):457–464.
5. Gluck JC, Gluck P. The effects of pregnancy on asthma: a prospective study. *Ann Allergy* 1976; 37:164–168.
6. Juniper EF, Daniel EE, Roberts RS, *et al.* Improvement in airway responsiveness and asthma severity during pregnancy. A prospective study. *Am Rev Respir Dis* 1989; 140:924–931.

7. Schatz M, Dombrowski MP, Wise R, *et al.* Asthma morbidity during pregnancy can be predicted by severity classification. *J Allergy Clin Immunol* 2003; 112:283–288.
8. Schatz M, Harden K, Forsythe A, *et al.* The course of asthma during pregnancy, post partum, and with successive pregnancies: a prospective analysis. *J Allergy Clin Immunol* 1988; 81:509–517.
9. Stenius-Aarniala B, Piirila P, Teramo K. Asthma and pregnancy: a prospective study of 198 pregnancies. *Thorax* 1988; 43:12–18.
10. White RJ, Coutts II, Gibbs CJ, MacIntyre C. A prospective study of asthma during pregnancy and the puerperium. *Respir Med* 1989; 83:103–106.
11. Gluck JC, Gluck PA. The effect of pregnancy on the course of asthma. *Immunol Allergy Clin North Am* 2006; 26:63–80.
12. Belanger K, Hellenbrand ME, Holford TR, Bracken M. Effect of pregnancy on maternal asthma symptoms and medication use. *Obstet Gynecol* 2010; 115:559–567.
13. Williams DA. Asthma and pregnancy. *Acta Allergol* 1967; 22:311–323.
14. Mabie WC, Barton JC, Wasserstrum N, Sibai BM. Clinical observations on asthma in pregnancy. *J Matern Fetal Med* 1992; 1:45–50.
15. Kwon HL, Triche EW, Belanger K, Bracken MB. The epidemiology of asthma during pregnancy: prevalence, diagnosis, and symptoms. *Immunol Allergy Clin North Am* 2006; 26:29–62.
16. Carroll KN, Griffin MR, Gebretsadik T, *et al.* Racial differences in asthma morbidity during pregnancy. *Obstet Gynecol* 2005; 106:66–72.
17. Henderl I, Schatz M, Momirova V, *et al.* Association of obesity with pulmonary and nonpulmonary complications of pregnancy in asthmatic women. *Obstet Gynecol* 2006; 108:77–82.
18. Einarson A, Riondan VL, Gibson PG. Smoking in pregnancy and lactation: a review of risks and cessation strategies. *Eur J Clin Pharmacol* 2009; 65:325–330.
19. Enriquez R, Griffin MR, Carroll KN, *et al.* Effect of maternal asthma and asthma control on pregnancy and perinatal outcomes. *J Allergy Clin Immunol* 2007; 120:625–630.
20. Louik C, Schatz M, Hernandez-Diaz S, *et al.* Asthma in pregnancy and its pharmacologic treatment. *Ann Allergy Asthma Immunol* 2010; 105:110–117.
21. Minerbi-Codish I, Fraser D, Avnun L, *et al.* Influence of asthma in pregnancy on labor and the newborn. *Respiration* 1998; 65:130–135.
22. Stenius-Aarniala BS, Hedman J, Teramo KA. Acute asthma during pregnancy. *Thorax* 1996; 51:411–414.
23. Tata LJ, Lewis SA, McKeever TM, *et al.* A comprehensive analysis of adverse obstetric and pediatric complications in women with asthma. *Am J Respir Crit Care Med* 2007; 175:991–997.
24. Murphy VE, Clifton VL, Gibson PG. The effect of cigarette smoking on asthma control during exacerbations in pregnant women. *Thorax* 2010; 65:739–744.
25. Gani F, Braida A, Lombardi C, *et al.* Rhinitis in pregnancy. *Eur Ann Allergy Clin Immunol* 2003; 35:306–313.
26. Corren J. The relationship between allergic rhinitis and bronchial asthma. *Curr Opin Pulm Med* 1999; 5:35–37.
27. Lombardi C, Passalacqua G, Gargioni S, *et al.* The natural history of respiratory allergy: a follow-up study of 99 patients up to 10 years. *Respir Med* 2001; 95:9–12.
28. Bousquet J, Van Cauwenberge P, Khaltaev N. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001; 108 (5 Suppl):S147–S334.
29. Greisner WA 3rd, Settignano RJ, Settignano GA. The course of asthma parallels that of allergic rhinitis: a 23-year follow-up study of college students. *Allergy Asthma Proc* 2000; 21:371–375.
30. Kircher S, Schatz M, Long L. Variables affecting asthma course during pregnancy. *Ann Allergy Asthma Immunol* 2002; 89:463–466.
31. Jain S, Kamimoto L, Bramley AM, *et al.* Hospitalized patients with 2009 H1N1 influenza in the United States, April–June 2009. *N Engl J Med* 2009; 361:1935–1944.
32. Jamieson DJ, Honein MA, Rasmussen SA, *et al.* H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet* 2009; 374:451–458.
33. CDC Estimates of 2009 H1N1 Influenza cases, hospitalizations and deaths in the United States, April 2009–March 13, 2010. Atlanta: Centers for Disease Control and Prevention; 2010.
34. 2009 H1N1 Flu: Underlying health conditions among hospitalized adults and children. Centers for Disease Control and Prevention, 2010. http://www.cdc.gov/H1N1flu/epi_underlying_conditions.htm. [Accessed 1 August 2012]
35. Forbes RL, Gibson PG, Murphy VE, Wark PA. Impaired type I and III interferon response to rhinovirus infection during pregnancy and asthma. *Thorax* 2012; 67:209–214.
- In-vitro study of pregnant women showing reduced antiviral interferons in response to rhinovirus in asthma, providing an important link between the observed increased susceptibility and morbidity to respiratory viral infections in these patient populations.
36. Wendel PJ, Ramin SM, Barnett-Hamm C, *et al.* Asthma treatment in pregnancy: a randomized controlled study. *Am J Obstet Gynecol* 1996; 175:150–154.
37. Cydulka RK, Emerman CL, Schreiber D, *et al.* Acute asthma among pregnant women presenting to the emergency department. *Am J Respir Crit Care Med* 1999; 160:887–892.
38. McCallister JW, Benninger CG, Frey HA, *et al.* Pregnancy related treatment disparities of acute asthma exacerbations in the emergency department. *Respir Med* 2011; 105:1434–1440.
- Retrospective review of treatment of asthma exacerbations in pregnancy which revealed that pregnant women were significantly less likely to receive appropriate therapy with systemic corticosteroids than nonpregnant controls with exacerbations of similar severity.
39. Lim AS, Stewart K, Abramson MJ, George J. Management of asthma in pregnant women by general practitioners: a cross sectional survey. *BMC Fam Pract* 2011; 12:121.
- Case-based survey of general practitioners which demonstrated that some providers would not correctly advise or treat women with asthma during pregnancy.
40. Enriquez R, Wu P, Griffin MR, *et al.* Cessation of asthma medication in early pregnancy. *Am J Obstet Gynecol* 2006; 195:149–153.
41. Schatz M, Leibman C. Inhaled corticosteroid use and outcomes in pregnancy. *Ann Allergy Asthma Immunol* 2005; 95:234–238.
42. Murphy VE, Gibson PG, Talbot PI, *et al.* Asthma self-management skills and the use of asthma education during pregnancy. *Eur Respir J* 2005; 26:435–441.
43. Beckmann CA. A descriptive study of women's perceptions of their asthma during pregnancy. *MCN Am J Matern Child Nurs* 2002; 27:98–102.
44. Powell H, McCaffery K, Murphy VE, *et al.* Psychosocial outcomes are related to asthma control and quality of life in pregnant women with asthma. *J Asthma* 2011; 48:1032–1040.
- Cross-sectional survey of pregnant women with asthma that demonstrated that maintenance inhaled corticosteroid use in pregnancy is associated with negative illness beliefs and reduced QOL, and that women often overestimate the teratogenic risks of commonly prescribed asthma medications.
45. Chambers K. Asthma education and outcomes for women of childbearing age. *Case Manager* 2003; 14:58–61.
46. Apter AJ, Greenberger PA, Patterson R. Outcomes of pregnancy in adolescents with severe asthma. *Arch Intern Med* 1989; 149:2571–2575.
47. Murphy VE, Gibson P, Talbot PI, Clifton VL. Severe asthma exacerbations during pregnancy. *Obstet Gynecol* 2005; 106:1046–1054.
48. Kolarzyk E, Sztot WM, Lyszczyk J. Lung function and breathing regulation parameters during pregnancy. *Arch Gynecol Obstet* 2005; 272:53–58.
49. McAuliffe F, Kametas N, Costello J, *et al.* Respiratory function in singleton and twin pregnancy. *BJOG* 2002; 109:765–769.
50. Puranik BM, Kaore SB, Kurhade GA, *et al.* A longitudinal study of pulmonary function tests during pregnancy. *Indian J Physiol Pharmacol* 1994; 38:129–132.
51. Beckmann CA. Peak flow values by gestation in women with asthma. *Clin Nurs Res* 2008; 17:174–181.
52. Brancaccio LR, Laifer SA, Schwartz T. Peak expiratory flow rate in normal pregnancy. *Obstet Gynecol* 1997; 89:383–386.
53. Dweik RA, Boggs PB, Erzurum SC, *et al.* An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. *Am J Respir Crit Care Med* 2011; 184:602–615.
- Evidence-based clinical practice guideline which summarizes the currently available literature and provides parameters for using the F_eNO in clinical practice.
54. Morris NH, Carroll S, Nicolaides KH, *et al.* Exhaled nitric oxide concentration and amniotic fluid nitrite concentration during pregnancy. *Eur J Clin Invest* 1995; 25:138–141.
55. Tamasi L, Bohacs A, Bikov A, *et al.* Exhaled nitric oxide in pregnant healthy and asthmatic women. *J Asthma* 2009; 46:786–791.
56. Powell H, Murphy VE, Taylor DR, *et al.* Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial. *Lancet* 2011; 378:983–990.
- Double-blind, parallel-group, controlled trial comparing an algorithm with F_eNO to an algorithm using clinical symptoms to up- or down-titrate asthma therapies in pregnancy. Use of the F_eNO algorithm resulted in decreased asthma exacerbations when compared with the control group.
57. Barnes N, Greening A. Management of asthma in pregnancy. *Lancet* 2012; 379:e43.
58. Gibson PG, Coughlan J, Abramson M. Self-management education for adults with asthma improves health outcomes. *West J Med* 1999; 170:266.
59. Janson SL, McGrath KW, Covington JK, *et al.* Individualized asthma self-management improves medication adherence and markers of asthma control. *J Allergy Clin Immunol* 2009; 123:840–846.
60. Larson A, Ward J, Ross L, *et al.* Impact of structured education and self management on rural asthma outcomes. *Aust Fam Physician* 2010; 39:141–144.
61. Turner MO, Taylor D, Bennett R, Fitzgerald JM. A randomized trial comparing peak expiratory flow and symptom self-management plans for patients with asthma attending a primary care clinic. *Am J Respir Crit Care Med* 1998; 157:540–546.
62. Schatz M, Dombrowski MP, Wise R, *et al.* The relationship of asthma-specific quality of life during pregnancy to subsequent asthma and perinatal morbidity. *J Asthma* 2010; 47:46–50.
63. Dombrowski MP, Schatz M, Wise R, *et al.* Randomized trial of inhaled bclomethasone dipropionate versus theophylline for moderate asthma during pregnancy. *Am J Obstet Gynecol* 2004; 190:737–744.