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Review article

Review and appraisal of guidelines for the management of asthma during pregnancy

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ABSTRACT

Background: Asthma affects 12.7% of pregnancies in Australia. Poorly controlled asthma is associated with increased maternal and infant morbidity and mortality. Optimal antenatal management of asthma during pregnancy has the potential to reduce complications relating to asthma. Evidence-based clinical practice guidelines help to translate health research findings into practice and when implemented can improve health outcomes. National and International guidelines currently provide recommendations for optimal asthma care in pregnancy.

Aim: To appraise the existing asthma in pregnancy guidelines with respect to their evidence for recommendations, consistency of recommendations and appropriateness for clinical practice.

Method: The Appraisal of Guidelines for Research and Evaluation (AGREE II) tool was used to appraise four English language asthma in pregnancy guidelines, published or updated between 2007 and 2016. The recommendations, range and level of evidence was analysed.

Results: Two of the four guidelines scored highly in most domains of the appraisal. Many of the recommendations made in the appraised guidelines were consistent. Due to the lack of randomised controlled trials involving pregnant women with asthma, most recommendations were evidenced by consensus and expert opinion rather than high quality meta-analysis, systematic reviews of randomised controlled trials.

Conclusion: The recommended antenatal asthma management was generally consistent among the guidelines but lacked clarity in some areas which then leave them open to interpretation. More randomised controlled trials involving pregnant women with asthma are required to fortify the recommendations made and asthma management guidelines should be included in Australian Antenatal Care Guidelines as they currently are not.

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Statement of significance

Problem or issue

Poorly controlled asthma in pregnancy can lead to increased maternal and neonatal morbidity and mortality.

What is already known

Optimal management of asthma in pregnancy can reduce the risk of poor outcomes and guidelines exist outlining recommended management.

What this paper adds

An appraisal of the asthma in pregnancy guidelines showing consistency in recommendations but a need for more randomized controlled trials in the area of asthma management in pregnancy. An absence of asthma management guidelines in antenatal care guidelines was identified.

*practitioners to make decisions about appropriate health care for specific clinical circumstances”.*⁸

Clinical practice guidelines are important instruments for improving the quality of health care and should be based on the best available evidence and consider the woman's preferences and clinician's experience.⁹ It is suggested that high-quality evidence-based clinical practice guidelines can optimize outcomes by guiding diagnosis and treatment.¹⁰ Several National and International guidelines are available which outline optimal antenatal asthma management.^{11–14} However, it is not known whether these are consistent in their content, based on high quality evidence or suitable for use in clinical practice or antenatal care. Health professionals should have access to data which critically appraise these guidelines for their validity, impact, and applicability to the individual seeking care.¹⁵ An appraisal of asthma in pregnancy guidelines has not previously been documented. The aim of this review is to appraise existing asthma in pregnancy guidelines with respect to their evidence for recommendations, consistency of recommendations and appropriateness for clinical practice.

2. Method

Guidelines about asthma in pregnancy were sought purposively from the following organisations: The National Asthma Council (NAC, Australia); The National Heart Lung and Blood Institute–National Asthma Education and Prevention Program (NAEPP, USA); The Global Initiative for Asthma (GINA); the British Thoracic Society (BTS); The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG, Australia, New Zealand); National Health and Medical Research Council (NHMRC, Australia); National Institute for Health and Care Excellence (NICE, UK) and the Royal Australian College of General Practitioners (RACGP, Australia). This method of purposive guideline selection was previously used by Foureur et al.¹⁶ for the appraisal of guidelines related to vaginal birth after caesarean section. Our rationale was to obtain guidelines produced by leading national and international authorities on both antenatal care and asthma management. The most recent version of guidelines about asthma management in pregnancy were sought in January 2017 from these sources and the result of this initial search is shown as Table 1.

Each guideline found to include a section on the management of asthma in pregnancy was appraised by two appraisers, one being a clinical midwife specialist and the other a research fellow in

1. Introduction

Asthma is one of the most common chronic medical conditions affecting women during pregnancy. The prevalence of asthma in pregnancy in Australia is 12.7%¹; significantly higher than the USA rate of 7.8%.² Many studies have highlighted the increased maternal and neonatal morbidity associated with poorly controlled asthma during pregnancy.^{3–6} Adverse maternal and neonatal outcomes such as low birth weight and premature birth are increased further if the woman experiences an asthma exacerbation during pregnancy.⁷ Optimal management of asthma during pregnancy is essential to minimise the effects of poorly controlled asthma and asthma exacerbations on both maternal and neonatal health.³

Maternity carers such as midwives and obstetricians, and pregnant women engaging in shared decision-making should be supported by clinical practice guidelines. Clinical practice guidelines are defined as:

“Evidence based statements that include recommendations intended to optimize patient care and assist health care

Table 1
Guidelines examined for asthma in pregnancy recommendations.

Australia	The National Asthma Council Australia (NAC)	Australian Asthma Handbook 2016 ¹²
United States of America	The National Heart, Lung and Blood Institute – National Asthma Education and Prevention Program (NAEPP)	Asthma and Pregnancy Working Group 2004 ¹³
Global	The Global Initiative for Asthma (GINA)	Global Strategy for Asthma Management and Prevention 2016 ²³
United Kingdom	The British Thoracic Society (BTS)	British Guideline on the Management of Asthma: A National Clinical Guideline 2016 ¹⁴
Australia	The National Health and Medical research Council- Australian Health Ministers' Advisory Council (NHMRC-AHMAC)	Clinical Practice Guidelines: Antenatal Care – Module 1-2012 ⁵⁴
Australia/New Zealand	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)	College Statements & Guidelines (Medical Disorders in Pregnancy) ¹⁹
United Kingdom	National Institute for Health and Care Excellence (NICE)	Antenatal Care ²⁰
Australia	The Royal Australian College of General Practitioners (RACGP)	Clinical Guidelines ²¹

asthma and pregnancy (KMCL, VM), using the Appraisal of Guidelines for Research and Evaluation (AGREE II) (2001) instrument.⁹ The AGREE II instrument is considered the gold standard for the development and evaluation of guidelines and helps to evaluate the validity of guidelines. The AGREE II instrument consists of 23 items arranged into 6 domains, these include: Scope and Purpose; Stakeholder Involvement; Rigour of Development; Clarity of Presentation; Applicability; Editorial Independence; plus, an overall assessment and question about whether the assessor would recommend these guidelines for practice. Appraisers assessed each item using the online AGREE II tool and assigned a score from 1 (strongly disagree) to 7 (strongly agree). Two appraisers independently appraised each guideline and the appraisers' scores and comments were blinded until all appraisals were completed. Final domain scores (0–100%) were calculated based on the sum of ratings across both appraisers and scaled to include the maximum possible score as well as the difference between the maximum and minimum possible scores for that domain.⁹

Scope and Purpose (Domain 1), examines three aspects of the guideline: the specific descriptions of the objectives, health questions and population of the guideline. Stakeholder Involvement (Domain 2), examines the inclusion of relevant individuals on the guideline development group, the seeking of target population input and a clear definition of the target users of this guideline. Rigour of Development (Domain 3), examines 8 areas including: evidence of systematic methods for searching for evidence; clear description of selection criteria; strengths and limitations statements; recommendation formulation description; benefits, side effects and risks of recommendations; expert review of guideline prior to publication and procedure for update. Clarity of Presentation (Domain 4) examines the presence of clear and non-ambiguous recommendations; different options for management of the condition and clearly identifiable key recommendations. Applicability (Domain 5) consists of four items: description of the barriers and facilitators to the application of recommendations; the provision of advice and/or tools to aid putting the recommendations into practice; the potential resource implications of applying recommendations and the presence of monitoring and/or auditing criteria. Editorial Independence (Domain 6) examines disclosure of whether the views of the funding body have

influenced the content of the guideline and if any competing interests of the guideline development group have been recorded and addressed.

Guideline content was also reviewed and compared between guidelines for the following categories: (i) Assessment and monitoring of asthma symptoms and lung function; (ii) Health professional involvement in asthma management in pregnancy; (iii) Control of asthma triggers and comorbidities; (iv) Self-management education; (v) Pharmacologic treatment (vi) Inflammation-based management (using an objective marker of lung inflammation to adjust inhaled corticosteroid dosage).

3. Results

Eight clinical practice guidelines specific to antenatal care and/or asthma management were identified and examined (Table 1). Clinical practice guidelines for the management of asthma in pregnancy were not found in the antenatal care guidelines produced by the National Health and Medical Research Council–Australian Health Ministers' Advisory Council (NHMRC–AHMAC); Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG); National Institute for Health and Care Excellence (NICE) or Royal Australian College of General Practitioners (RACGP). Consequently, the AGREE II tool was not applied to these guidelines. However, some of these guidelines did contain mention of asthma in pregnancy. For example, the NHMRC–AHMAC clinical practice guidelines for antenatal care lists severe asthma as a condition requiring additional care to that detailed in the clinical guideline. No additional resources or references relating to asthma or asthma management are included. The RANZCOG–College Statements & Guidelines (Medical Disorders in Pregnancy)¹⁷ do not include any reference to asthma, despite having statements and guidelines relating to other medical disorders in pregnancy such as hypertension and gestational diabetes. The National Institute for Health and Care Excellence (NICE)–Antenatal Care (2017),¹⁸ does not mention asthma in the main guideline. Severe asthma is listed in an appendix under the heading: “Women requiring additional care”, with no further guidance as to the management of severe asthma in pregnancy. Additional guidelines are produced by NICE for: Diabetes in pregnancy; Hypertension in pregnancy; Multiple pregnancy and

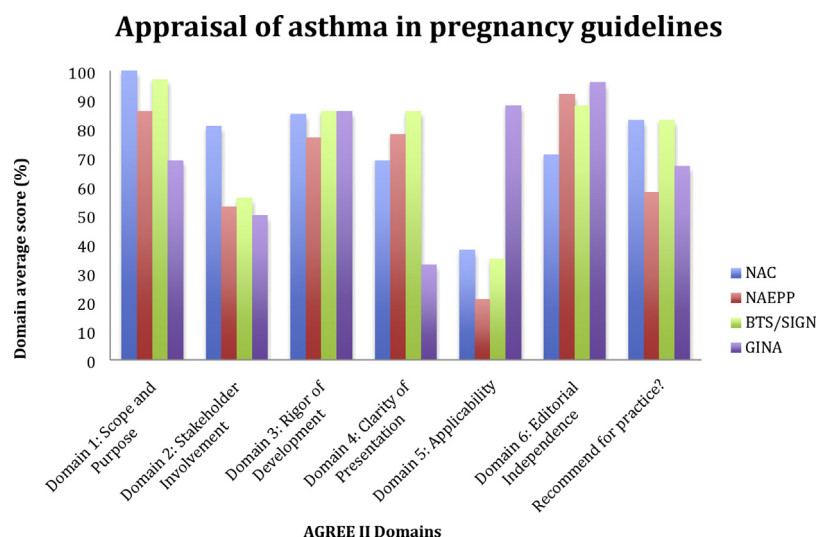


Fig. 1. Appraisal of asthma in pregnancy guidelines. NAC: The National Asthma Council Australia – Australian Asthma Handbook 2016¹²; NAEPP: The National Heart, Lung and Blood Institute – National Asthma Education and Prevention Program (Asthma and Pregnancy Working Group 2004¹³; GINA – The Global Initiative for Asthma – Global Strategy for Asthma Management and Prevention 2016²² and BTS: The British Thoracic Society – British Guideline on the Management of Asthma: A National Clinical Guideline 2016.

Ectopic pregnancy and Miscarriage. The Royal Australian College of General Practitioners (RACGP)–Clinical Guidelines¹⁹ also do not mention asthma management during pregnancy.

The four guidelines found to include asthma in pregnancy recommendations underwent appraisal using the AGREE II tool. These included: The National Asthma Council Australia (NAC) – Australian Asthma Handbook 2015¹¹; The National Heart, Lung and Blood Institute – National Asthma Education and Prevention Program (NAEPP)–Asthma and Pregnancy Working Group 2004²⁰; The Global Initiative for Asthma (GINA)–Global Strategy for Asthma Management and Prevention 2015²¹ and the British Thoracic Society (BTS)–British Guideline on the Management of Asthma: A National Clinical Guideline 2014.¹³

Fig. 1 shows the domain scores as percentages for each of the quality domains appraised using the AGREE II tool. A more comprehensive breakdown of the appraisal is detailed in Table 2, and shows the questions under each domain and the corresponding overall scores.

For Scope and Purpose (Domain 1), scores ranged from 69% for GINA to 100% for NAC. The NAC scored well with appraiser comments reflecting this, concluding that the aims and objectives were clearly stated, the scope of the guideline was defined, and the population to which the guideline applies was identified as pregnant women with asthma. Although GINA scored well for clear overall guideline objectives, they were not specifically defined in relation to asthma management during pregnancy, which reduced the overall domain score.

Most of the guidelines did not perform well in Stakeholder Involvement (Domain 2), with scores ranging from 50 to 81%. Overall NAC performed best in this domain as it was stated that

“patients’ views” had been sought via advocacy groups, such as Asthma Australia; however, pregnant women with asthma or pregnancy-related advocacy groups were not specifically mentioned as stakeholders. The NAC guidelines employed a multidisciplinary approach and provides a list of guideline development committee members and reviewers; however, this does not include or name an obstetric or midwifery expert. There was also no clear obstetric representation listed in the GINA guideline. A consultant obstetrician was noted in the BTS development committee and the NAEPP guideline included two obstetric and gynaecology representatives. The target users of all guidelines were noted as health professionals.

All appraised guidelines scored well in Rigour of Development (Domain 3), with BTS and GINA obtaining an overall score of 86%, NAC 85% and NAEPP 77%. A systematic review of the literature was evidenced in all guidelines, with clear inclusion and exclusion criteria; all guidelines stated that the majority of recommendations were formulated based on expert consensus. The risks and benefits of guideline recommendations were mentioned to various degrees in all guidelines. For example, the NAC guideline highlights the health benefits of remaining on prescribed asthma medications as a way of reducing the risk of an asthma exacerbation during pregnancy. It also provides evidence of the pregnancy safety categories for asthma and allergic rhinitis medicines. The risks and benefits surrounding medication use in pregnancy were clearly stated in the NAEPP guideline and also mentioned in the GINA guideline. BTS, NAC, GINA and NAEPP stated that an external review was conducted of the guideline prior to its publication. In regard to the process for updating the guidelines, GINA conducts a review of literature twice yearly and publishes updates annually in

Table 2
A comprehensive breakdown of the appraisal using the AGREE II tool.

Domain	NAC	NAEPP	BTS/SIGN	GINA
1. Scope and Purpose				
Item.1. Objectives of the guideline are specifically described	100%	93%	100%	93%
Item.2. Health question is specifically described.	100%	71%	100%	43%
Item.3. Population to whom guideline applies is specifically described.	100%	100%	93%	86%
2. Stakeholder Involvement				
Item.4. Guideline development group includes individuals from all relevant professional groups.	78%	57%	57%	64%
Item.5. Views and preferences of the target population have been sought	71%	71%	28%	14%
Item.6. Target users of the guideline are clearly defined	100%	50%	100%	93%
3. Rigour of Development				
Item.7. Systematic methods were used to search for evidence	86%	100%	93%	93%
Item.8. The criteria for selecting the evidence are clearly described	64%	100%	64%	93%
Item.9. The strengths and limitations of the body of evidence are clearly described.	93%	93%	93%	64%
Item.10. The methods for formulating the recommendations are clearly described.	93%	86%	93%	100%
Item.11. The health benefits, side effects and risks have been considered in formulating the recommendations.	86%	100%	86%	93%
Item.12. There is explicit link between the recommendations and the supporting evidence.	86%	57%	93%	86%
Item.13. The guideline has been externally reviewed by experts prior to publication.	100%	93%	86%	78%
Item.14. A procedure for updating the guideline is provided.	93%	14%	100%	100%
4. Clarity of Presentation				
Item. 15. The recommendations are specific and unambiguous	64%	64%	86%	50%
Item. 16. Different options for management of the condition or health issue are clearly presented.	57%	93%	78%	28%
Item. 17. Key recommendations are easily identifiable.	100%	86%	100%	50%
5. Applicability				
Item.18. The Guideline describes facilitators and barriers to its application.	57%	14%	71%	100%
Item.19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	71%	78%	78%	100%
Item.20. The potential resource implications of applying the recommendations have been considered.	43%	14%	14%	86%
Item.21. The guideline presents monitoring and/or auditing criteria.	14%	21%	14%	71%
6. Editorial Independence				
Item.22. The views of the funding body have not influenced the content of the guideline.	93%	93%	86%	93%
Item.23. Competing interests of the guideline development group members have been recorded and addressed.	57%	93%	93%	100%
Overall Guideline Assessment				
Rate the overall quality of the guideline.	86%	78%	86%	71%

December each year, BTS updates its guideline biennially, and NAC states that they have an ongoing review process, with updates every 3 years. An ongoing review process for NAEPP was not evident, with the last update in 2004.

There was a large discrepancy in scores for Clarity of Presentation (Domain 4), with GINA scoring 33%, BTS/SIGN scoring 86%, and NAC and NAEPP scoring 69% and 78%, respectively. GINA scored poorly due to recommendations being broad and not specific to asthma in pregnancy. In contrast, BTS, NAEPP and NAC contained recommendations specific to antenatal management of asthma, although NAC and NAEPP still used some ambiguous phrases such as ‘intervene early’, ‘preferred’ and ‘consider’. In regard to the presentation of different options for the management of asthma during pregnancy, NAC suggested a treatment trial if women were concerned about changing their treatment, while NAEPP suggested alternative, but not preferred, treatment options such as cromolyn, leukotriene receptor antagonists, and sustained release theophylline. However, given that the NAEPP guideline is now outdated, the safety and clinical utility of these alternate treatments is uncertain. Key recommendations relating to asthma in pregnancy were clearly outlined either as a table or highlighted under bolded headings in the BTS, NAC and NAEPP guidelines. Conversely, recommendations in the GINA guideline were suggested in text, not clearly shown as a table or listed for easy reference.

The overall scores for Applicability (Domain 5) were 88% for GINA compared to 35% for BTS/SIGN, 38% for NAC and 21% for NAEPP. GINA performed well in this domain as they dedicated a section to ‘implementing asthma management strategies into the health system’. Barriers to implementation are outlined and advice and tools are available to aid the implementation of guidelines into clinical practice, but not specifically into antenatal care. Resource implications are acknowledged and audits are described. In contrast, BTS mentioned some barriers to particular recommendations but not to the overall guideline or to the pregnancy section itself. There was some evidence of advice and tools for implementation of recommendations, but resource implications and auditing criteria were not found. NAC described dissemination strategies but does not mention barriers. A quick reference guide and tools are available for pregnant women, yet, potential resource implications and auditing process are not discussed. NAEPP provides a quick reference guide as a tool for application of the guideline but none of the other areas of this domain, such as discussion of barriers to implementation or implementation aids, are presented in this guideline.

Overall the guidelines scored well in Domain 6 (Editorial Independence) with scores ranging from 71% for NAC to 96% for GINA. It was clearly stated that group members were not paid to contribute to the guideline and all financial interests were disclosed. Competing interests were also clearly stated. Although GINA stated that the committee members did not receive payment for their work and disclosure statements are available for all members of the GINA committee, there was no mention of the influence of funding bodies on the content of the guideline. Statements made regarding views of funding bodies and declarations of interests are available in the supporting material section of the BTS guideline. NAC did not perform as well in this domain as it was not possible to determine the potential influence of the funding body over the content, and competing interests were declared, but not specified.

The final aspect of the appraisal centered around the overall quality of the guidelines. NAC and BTS scored highest on the overall quality of the guideline with 83%. Although both appraisers agreed that the four included guidelines should be used, it was suggested that NAEPP and GINA be recommended with some modifications. These modifications included clearer identification of the key

recommendations for pregnancy management in the GINA guideline and an updated version of the NAEPP guideline.

4. Review of asthma in pregnancy guideline content

The key content of the recommendations from the appraised guidelines is shown as Table 3.

4.1. Assessment and monitoring of asthma symptoms and lung function

The NAEPP report¹² suggests that women have a baseline spirometry assessment followed by monthly evaluations of their asthma symptoms and measurement of pulmonary function. The NAC also suggests regular review of asthma symptoms every 4 weeks during pregnancy, assessing asthma control consistently at each review using the same validated asthma assessment tool.¹¹ Assessment tools suggested are the Asthma Control Test [ACT]²² and the Asthma Control Questionnaire (ACQ).²³ NAC guidelines note the importance of using a version that has been validated for use in Australia. This recommendation is based on consensus of the panel of experts involved in the production of the Australian Asthma Handbook.¹¹ The GINA and BTS asthma in pregnancy guidelines are much less specific regarding asthma monitoring in pregnancy, with asthma management in pregnancy presented only as a subsection of the main guideline. The GINA guideline suggest that women could have monthly telephone monitoring for asthma control.²¹ The BTS guidelines also suggest that in order to keep their asthma well controlled, pregnant women with moderate/severe asthma should be monitored regularly. However, it is not specified in the GINA or BTS guidelines how often this monitoring should occur and what should be assessed at each visit.

4.2. Health professional involvement in asthma management in pregnancy

Health professional involvement in antenatal asthma management was covered by all the appraised guidelines, however, the recommendation of which specific health professionals should be involved was not consistent. NAEPP suggest that an obstetric care provider should be involved in antenatal asthma care and that a team approach would be helpful in managing a pregnant woman with asthma. NAC suggest that the obstetrician/midwife involved in the woman’s antenatal care should be informed of her asthma status. GINA suggests that antenatal asthma could be managed by pharmacist–clinician collaboration and BTS suggest a close liaison between the respiratory physician and the obstetrician.

4.3. Control of asthma triggers and comorbidities

NAEPP, BTS and NAC guidelines recommend advising pregnant women to avoid known asthma triggers during pregnancy and, if applicable, to quit smoking. NAC also suggests the management of comorbid conditions, such as allergic rhinitis and gastro-oesophageal reflux, which may mimic or contribute to asthma symptoms. GINA did not make any recommendations specifically relating to comorbidities contributing to asthma severity or symptom control in pregnant women. The level of evidence used to formulate this recommendation in NAEPP, BTS and NAC is stated to be consensus, based on clinical experience and expert opinion.

4.4. Self-management education

The education or suggested advice that should be offered to pregnant women with asthma during their pregnancy was consistent among the guidelines appraised. GINA, BTS and NAC

Table 3
Review of guideline content.

Practice	NAC	NAEPP	BTS/SIGN	GINA
<i>Assessment and monitoring of asthma and lung function</i>				
Frequency of review	4 weekly	Monthly	Not specified	Monthly
Type of review	Face-To Face in addition to regular antenatal visits	Face-to Face in conjunction with antenatal visits	Not specified	Telephone consult
Assessments required	Asthma control using ACQ or other validated tool	• Baseline spirometry • Monthly asthma history and pulmonary function • Serial ultrasounds from 32 weeks gestation.	Not specified	Not specified
<i>Health professional involvement in asthma management in pregnancy</i>				
Who should provide assessment	Obstetrician/Midwife should be informed of asthma status	Obstetrical care provider should be informed. A team approach is helpful.	Liaise between respiratory physician and obstetrician	Pharmacist–clinician collaboration
<i>Control of asthma triggers/comorbidities</i>				
Advise smoking cessation	✓	✓	✓	Not specifically stated in pregnancy guidelines but is stated in general population guideline.
Manage other co-morbidities such as allergic rhinitis.	✓ Rhinitis mentioned	✓ Allergens irritants (particularly cigarette smoke)	✓ Cigarette smoking	✓ Respiratory infections mentioned in relation to pregnancy
<i>Self-management education</i>				
Maintain good asthma control	✓	✓	✓	✓
Access to educational resources	✓	✓	Not mentioned	✓
Assess self management skills	✓	✓	Not mentioned	Not mentioned
Important to stay on prescribed asthma medication	✓	✓	✓	✓
<i>Pharmacologic treatment</i>				
Step-wise approach mentioned	✓	✓	Not mentioned	✓
Caution the stepping down of medication	✓	✓	Not mentioned	✓
Inflammation-Based Management	Mentioned as general diagnostic tool but not recommended in clinical management or pregnancy	Not mentioned	Not mentioned	Not recommended

all emphasise advising pregnant women on the importance of maintaining good asthma control and the possible risks to them and/or their baby if control is not maintained. NAEPP and NAC also discuss the importance of ensuring pregnant women have access to educational resources and have their self-management skills, such as symptom self-monitoring and inhaler technique assessed, and their asthma management plan revised. NAC also emphasises the importance of advising women to continue on prescribed asthma medications during pregnancy.

4.5. Pharmacologic treatment

A step-wise approach to pharmacologic therapy such as that used in the management of the non-pregnant adult is mentioned in the NAEPP, GINA and NAC asthma in pregnancy guidelines but is not mentioned in the BTS guidelines specifically in relation to pregnancy. In regard to the step-wise approach, it is suggested by NAEPP that the dose and frequency of medications should be increased and decreased as required to maintain asthma control. NAEPP state that the effectiveness of medication is assumed to be the same in pregnant women as in non-pregnant women, however this is not supported by evidence from RCT's. NAC and GINA both caution the stepping down of medication citing that this may increase the risk of exacerbation, but this recommendation is based on expert opinion rather than RCT's involving pregnant

women. BTS recommend giving drug therapy for acute asthma as for non-pregnant individuals, which is in line with the other guideline recommendations.

4.6. Inflammation-based management

GINA guidelines mention inflammation-based management of asthma during pregnancy. GINA cites one study where monthly Fractional Exhaled Nitric Oxide (FENO)-guided treatment in pregnancy was associated with fewer exacerbations and better fetal outcomes than the standard symptom-based algorithm.²⁴ However, the guideline does not recommend the approach due to concerns about the study design. Inflammation-based management is not mentioned in the other guidelines in relation to pregnancy care.

5. Discussion

This is the first examination of the quality of clinical guidelines for asthma management in pregnancy using the AGREE II assessment tool. Notably, only respiratory guidelines included any recommendations on the management of asthma during pregnancy; antenatal guidelines did not include recommendations for the clinical management of this population group, highlighting an area that requires urgent attention. Asthma affects more

Australian pregnancies (12.7%)¹ than diabetes (5%)²⁵ or hypertension (<10%)²⁶ and is also associated with adverse perinatal outcomes including preterm birth, low birth weight and pre-eclampsia.³ For these reasons, we call for the inclusion of asthma management recommendations within Australian antenatal care guidelines.

The quality of four asthma management guidelines, published or updated between 2004 and 2017, were appraised. The NAC and BTS guidelines used the AGREE II tool to guide the development of their guidelines and therefore scored highly in most domains of the appraisal. The domain in which all four guidelines generally performed well was Scope and Purpose with an overall average score of 87%. This appears to be common among appraisals of other guidelines which use the AGREE II tool, such as those for hypertensive disorders in pregnancy,¹⁰ occupational asthma guidelines,²⁷ the WHO guidelines in maternal health²⁸ and traditional medicine in Korea Guidelines.²⁹ This may be due to this aspect of the guideline being highly valued by guideline developers and easy to achieve.²⁷

Stakeholder Involvement scored modestly for the majority of the guidelines appraised indicating room for improvement in this area by involving more clinical experts and consumers in the development of guidelines targeting a particular population. This inclusion of relevant stakeholders would also help strengthen the applicability of the guideline recommendations to clinical practice as the stakeholders are aware of the barriers and practicality of implementing clinical guideline recommendations.

Rigour of Development was addressed well in the guidelines appraised, with clear inclusion and exclusion criteria noted for the systematic reviews conducted and grading systems presented for the quality of evidence and strength of recommendations. Only one guideline (NAEPP) did not have an ongoing review process, which is something that should be addressed.

Many of the recommendations made in the appraised guidelines were evidenced by consensus and expert opinion rather than high quality randomised controlled trials (RCTs), systematic reviews of RCTs or meta-analyses with a very low risk of bias. A 2014 Cochrane Review of RCTs examining interventions for managing asthma in pregnancy found 8 RCTs involving 1181 women and their babies³⁰: five trials assessed pharmacological agents and three assessed non-pharmacological interventions. The authors' concluded that the eight trials were of moderate quality overall and that firm conclusions about optimal interventions for managing asthma in pregnancy could not be made. High quality RCTs would further strengthen the evidence base and inform guidelines for asthma management in pregnancy however, careful consideration regarding the ethical concerns surrounding this target group is required.

Asthma symptoms are known to change with pregnancy, with one third of women experiencing symptom worsening, one third an improvement and one third no change.³¹ These changes are not necessarily consistent from one pregnancy to the next for the same woman. As a result, regular monitoring of symptoms is recommended. In addition, exacerbations are most likely to occur in the second trimester.⁷ New evidence supports the recommendation that pregnant women have their symptoms and lung function monitored regularly throughout pregnancy.³² This evidence came from a small study of 20 pregnant women with asthma and 20 pregnant women without asthma who had their pulmonary function tested via spirometry once during each trimester of their pregnancy. Those with asthma also completed the ACQ and mini Asthma Quality of Life Questionnaire (mAQLQ). This study concluded that pulmonary function changes were more pronounced in asthmatic women during the later stages of their pregnancy and that monitoring this with regular spirometry may assist in optimising asthma management.³² The small sample size

of 20 pregnant women with mild asthma means that the results may not be generalizable, and further work is needed to determine whether maternal lung function is influenced by gestational age.

Monthly telephone monitoring of asthma control was suggested in the GINA guideline. A recent RCT examined the efficacy of a telehealth programme for optimising asthma management in 72 pregnant women and concluded that participants in the intervention group, which was supported by a handheld respiratory device and a smart phone app, had significantly better asthma control asthma-related quality of life when compared to usual care at 6 months post intervention.³³

It has been demonstrated that women with severe asthma are more likely to experience a worsening of their asthma during pregnancy,^{31,34} however women with mild disease severity may also experience severe exacerbations of asthma during pregnancy³⁵ and for this reason all women with an asthma diagnosis, regardless of severity, should be monitored regularly during pregnancy. This potential for exacerbations in pregnant women with mild asthma and the need for regular asthma review, is not addressed well in all of the appraised guidelines and is something that needs to be made clearer to maternity care providers.

All of the appraised guidelines recommend that a multidisciplinary team of health professionals should be engaged to help monitor the pregnant woman's asthma symptoms and to provide self-management advice and education. The guidelines were not consistent with their recommendation of the type of health professional that should be engaged with different suggestions shown in Table 3. Pregnant women with asthma are at increased risk of not only maternal complications, related to both asthma (e.g. exacerbations) and pregnancy (e.g. pre-eclampsia), but also of adverse fetal/neonatal outcomes (e.g. low birth weight, preterm birth, neonatal intensive care unit admission). The inclusion of an obstetric health professional or a team of health professionals is important as previous research shows that 40% of women are more likely to continue with their asthma medication during pregnancy if directed to do so by their obstetrician³⁶ and 2 in 5 women will do so if directed by their General Practitioner (GP).³⁷ Adopting a team approach to optimise asthma management in pregnancy could improve asthma control during pregnancy and reduce adverse outcomes. However, previous studies show that midwives are uncertain about their role in antenatal asthma care.³⁸ GPs in Australia also reportedly lack confidence in providing optimal antenatal asthma management and following clinical guidelines related to asthma in pregnancy.³⁷ The inclusion of asthma management in antenatal care guidelines would enable Obstetricians, Midwives and GPs to be informed members of a multidisciplinary team caring for the pregnant woman with asthma and applying evidence-based recommendations.

Control of asthma triggers is highlighted in the guidelines as an important component of asthma management. Cigarette smoking is one example of an asthma trigger that could be modified. A study examining the effect of cigarette smoking on asthma control in pregnant women concluded that asthma exacerbations requiring medical intervention are more common (and more severe) in current smokers (52%) when compared to ex-smokers (48%) and never smokers (35%).³⁹ Moreover, maternal smoking in pregnancy has been linked to the development of asthma in her offspring.⁴⁰ The prevalence of co-morbidities that may influence asthma during pregnancy is high. A study was undertaken recently to describe the pattern and severity of rhinitis in pregnancy and the impact of rhinitis on asthma control and quality of life.⁴¹ Among 218 non-smoking pregnant women with asthma, 65% of the participants had rhinitis. Rhinitis was associated with poorer asthma control, quality of life impairment specific to sino-nasal and asthma symptoms and anxiety, but there was no association with adverse perinatal outcomes. A significant improvement in

rhinitis symptoms and severity was associated with active management of asthma and the progression of pregnancy,⁴¹ suggesting a link between well controlled asthma and improvements in rhinitis.

Previous research has demonstrated that self-management education is an important asthma management tool that can be delivered antenatally. One study aimed to determine the level of asthma self-management skills and knowledge among pregnant women with asthma.⁴² During this study women with asthma had lung function, asthma symptoms, medication use and adherence, knowledge and inhaler technique assessed at 20 weeks gestation ($n=211$) and 33 weeks gestation ($n=149$). The use of peak flow monitoring and possession of a written asthma action plan was also determined. The women were educated about asthma control, self-management skills, trigger avoidance and counseled regarding smoking cessation where appropriate. Improvement in self-management skills were observed with a significant reduction in inhaled corticosteroid (ICS) medication non-adherence and a significant improvement in both inhaler technique and asthma medication knowledge.⁴² Achieving asthma control is pertinent to maternal and fetal health as poorly controlled asthma has been associated with a higher risk of adverse maternal and neonatal outcomes such as premature birth, low birth weight and pregnancy-induced hypertension, compared with well-controlled asthma during pregnancy.⁴³

Health professionals with the authority to prescribe and monitor medications are advised to follow a step-wise approach to pharmacologic therapy during pregnancy. The recommendations in the included guidelines surrounding pharmacological therapy are based on systematic reviews (and meta-analysis) of RCT's involving adults with asthma, with only a few RCT's involving pregnant women available. This is in direct contrast to asthma management recommendations related to symptoms, health professional involvement, triggers and education, which are mainly based on consensus and expert opinion. Lim et al. included 33 studies in their systematic review of the safety of regular preventative asthma medications during pregnancy, concluding that preventer medication use during pregnancy is not significantly associated with any adverse events, such as congenital malformation or adverse perinatal outcomes.⁴⁴ However, the included studies were limited by small sample sizes, missing data, inadequate control for confounding factors and poorly documented dose ranges. Moreover, distinguishing between the effects of asthma medications on the fetus from the effects of maternal asthma itself is difficult. Therefore, further research is needed to strengthen the evidence of the safety of asthma medication use during pregnancy.

The question of stepping-down treatment once asthma is well controlled is discussed in the NAC guidelines. A systematic review of 5 RCTs involving non-pregnant adults is cited, which reports deterioration in asthma control after step-down of long-acting beta2 agonist (LABA) treatment in adults with asthma.⁴⁴ The LABA step-down regimen increased asthma impairment, with worse Asthma Quality of Life Questionnaire score (mean difference [95% CI], 0.32 [0.14–0.51] points lower); worse ACQ score (0.24 [0.13–0.35] points higher); fewer symptom-free days (9.15% [1.62%–16.69%] less); and greater risk of withdrawal from the study resulting from lack of efficacy or loss of asthma control (risk ratio, 3.27 [2.16–4.96]). There was no mention of pregnant women being involved in this study but many of the guidelines state that the pharmacological management of asthma in pregnancy should mimic that of non-pregnant adults with asthma. A study of an inflammation-based treatment approach, which included 220 pregnant women with asthma, adjusted ICS and LABA treatment up or down according to an algorithm using clinical symptoms or FENO measurement.²⁴ This RCT concluded that asthma control

could be improved even when ICS dosage was reduced and is the only RCT to successfully reduce the exacerbation rate in pregnancy. This area of research is ongoing with another large trial currently being conducted further examining the role and effectiveness of FENO-based asthma management in pregnancy, specifically for improving perinatal outcomes.⁴⁵

Application of asthma management recommendations to clinical practice remains an issue for clinicians and pregnant women with asthma. Studies show varied levels of compliance with the recommended asthma in pregnancy guidelines by both the pregnant women with asthma and the health professionals caring for them.^{37,46} These studies included a survey of 174 GPs in Australia which concluded that there was some compliance with evidence-based guidelines in the selection of preventative medications for pregnant women with asthma. However 25.8% of respondents to a scenario-based question, indicated that they would decrease the dose of ICS or advise the woman to stop it during her pregnancy even when she was well controlled on current therapy, despite this being contrary to guideline recommendations.³⁷ A study conducted in Spain surveyed 1000 health professionals in relation to asthma management in pregnant women and found that 64% of practitioners seldom followed the available asthma management guidelines despite 96.5% stating that they felt they were useful.⁴⁶ Further work surrounding the implementation of asthma management recommendations into clinical practice and the use of asthma management guidelines by health professionals is required.

In Australia, a nationally consistent collection of asthma management data in pregnant women does not exist. It is therefore difficult to assess the gaps that may exist between recommended clinical management of asthma antenatally and actual clinical practice.⁴⁷ In an attempt to develop a monitoring approach for asthma in pregnancy, the Australian Centre for Asthma Monitoring (ACAM),⁴⁸ have developed national indicators to monitor asthma indicators are the proportion of pregnant women who: have the presence or absence of current asthma documented; have a review of their asthma during their first trimester and have a 4–6 weekly review of their asthma symptoms. ACAM (2013) propose that enhancing data collection by midwives would be the most cost effective and feasible method of collecting data to monitor asthma prevalence and the management of asthma during pregnancy. Further research and development in this area is required.

The main identified limitation of this appraisal of the asthma in pregnancy guidelines is that guidelines were purposively selected, rather than via a systematic review. However, this method selected guidelines with a high profile which have the potential to be more widely used in clinical practice. As suggested by Fourer et al.,¹⁶ there is a high likelihood that other guidelines (produced locally or in other countries) are influenced by the guidelines appraised here. Indeed guidelines from Japan cite the GINA guidelines,⁴⁸ the Canadian asthma guidelines cite, GINA, BTS & NAEPP⁴⁹ and the New Zealand asthma guidelines cite NAC, GINA and BTS.⁵⁰ A further limitation of an appraisal of asthma in pregnancy guidelines is that this process does not identify the acceptance or use of these guidelines in clinical practice, and there is a need for further study in this area. While only two people appraised the guidelines, the use of a systematic tool reduces potential bias from an individual appraiser.

6. Conclusion

The lack of asthma management recommendations in antenatal care guidelines in Australia requires urgent attention, considering asthma is one of the most common complications of pregnancy and represents a significant risk to maternal and fetal health.

Recommendations for antenatal asthma management were generally consistent across the respiratory guidelines identified in this review, but lack clarity in some areas. This in turn leaves some recommendations open to interpretation. Although national and international asthma in pregnancy guidelines are available, their use among health professionals providing antenatal asthma management is unclear. Further work is required to determine how usual care in Australia compares to guideline recommendations.

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