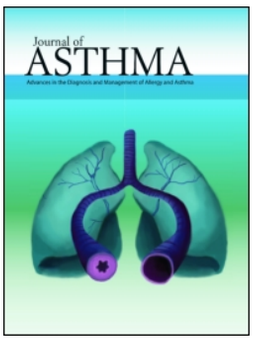

Journal of Asthma

ISSN: 0277-0903 (Print) 1532-4303 (Online) Journal homepage: http://www.tandfonline.com/loi/ijas20

Trends in asthma self-management skills and inhaled corticosteroid use during pregnancy and postpartum from 2004 to 2017

Annelies L. Robijn, Megan E. Jensen, Peter G. Gibson, Heather Powell, Warwick B. Giles, Vicki L. Clifton, Joerg Mattes, Michael J. Peek, Helen L. Barrett, Sean K. Seeho, Leonie K. Callaway, Alistair Abbott, John Attia, Peter A. Wark & Vanessa E. Murphy

To cite this article: Annelies L. Robijn, Megan E. Jensen, Peter G. Gibson, Heather Powell, Warwick B. Giles, Vicki L. Clifton, Joerg Mattes, Michael J. Peek, Helen L. Barrett, Sean K. Seeho, Leonie K. Callaway, Alistair Abbott, John Attia, Peter A. Wark & Vanessa E. Murphy (2018): Trends in asthma self-management skills and inhaled corticosteroid use during pregnancy and postpartum from 2004 to 2017, Journal of Asthma, DOI: 10.1080/02770903.2018.1471709

To link to this article: https://doi.org/10.1080/02770903.2018.1471709

JOURNAL OF ASTHMA
https://doi.org/10.1080/02770903.2018.1471709

Taylor & Francis
Taylor & Francis Group

Trends in asthma self-management skills and inhaled corticosteroid use during pregnancy and postpartum from 2004 to 2017

Annelies L. Robijn, BSc, MSc [a], Megan E. Jensen, BNutrDiet(Hons), PhD [a], Peter G. Gibson, MBBS [a,b,c], Heather Powell, MMedSc [b,c], Warwick B. Giles, MBBS, DDU, PhD [a], Vicki L. Clifton, BSc(Hons), PhD [d], Joerg Mattes, MD, PhD [a,e], Michael J. Peek, MBBS, BSc(Med), PhD, DDU [f], Helen L. Barrett, BSc, MBBS, PhD [g,h], Sean K. Seeho, MBBS, PhD [i], Leonie K. Callaway, MBBS, PhD [j,k], Alistair Abbott, MBBS [l,m], John Attia, BSc, MD, PhD, MSc [a], Peter A. Wark, BMed, PhD [b,c], and Vanessa E. Murphy, BMedChem(Hons), PhD [a]

[a]Priority Research Centre Grow Up Well, School of Medicine and Public Health, University of Newcastle, Hunter Medical Research Institute, New Lambton Heights, NSW, Australia; [b]Priority Research Centre for Healthy Lungs, University of Newcastle and Hunter Medical Research Institute, Newcastle, NSW, Australia; [c]Department of Respiratory and Sleep Medicine, John Hunter Hospital, Newcastle, NSW, Australia; [d]Department of Mothers', Babies and Women's Health, Mater Research Institute-University of Queensland, Translational Research Institute, South Brisbane, QLD, Australia; [e]Peadiatric Respiratory and Sleep Medicine Department, John Hunter Children's Hospital, Newcastle, NSW, Australia; [f]ANU Medical School, College of Health and Medicine, The Australian National University, Garran, ACT, Australia; [g]Chronic Disease Biology and Care, Mater Research Institute, University of Queensland, Brisbane, QLD, Australia; [h]Department of Endocrinology, Mater Adult Hospital, Mater Health Services, Brisbane, QLD, Australia; [i]Department of Obstetrics and Gynaecology, Sydney Medical School Northern, University of Sydney, Royal North Shore Hospital, St Leonards, Sydney, NSW, Australia; [j]Women's and Newborn Services, Royal Brisbane and Women's Hospital, Brisbane, QLD, Australia; [k]University of Queensland Centre for Clinical Research, Faculty of Medicine, The University of Queensland, Brisbane, QLD, Australia; [l]Department of Respiratory and Sleep Medicine, Nepean Hospital, Kingswood, NSW, Australia; [m]Nepean Clinical School, University of Sydney, Sydney, NSW, Australia

ABSTRACT

Objective: Asthma exacerbations and medication non-adherence are significant clinical problems during pregnancy. While asthma self-management education is effective, the number of education sessions required to maximise asthma management knowledge and inhaler technique and whether improvements persist postpartum, are unknown. This paper describes how asthma knowledge, skills, and inhaled corticosteroid (ICS) use have changed over time. *Methods*: Data were obtained from 3 cohorts of pregnant women with asthma recruited in Newcastle, Australia between 2004 and 2017 ($N = 895$). Medication use, adherence, knowledge, and inhaler technique were compared between cohorts. Changes in self-management knowledge/skills and women's perception of medication risk to the fetus were assessed in 685 women with 5 assessments during pregnancy, and 95 women who had a postpartum assessment. *Results*: At study entry, 41%, 29%, and 38% of participants used ICS in the 2004, 2007, and 2013 cohorts, respectively ($p = 0.017$), with 40% non-adherence in each cohort. Self-management skills of pregnant women with asthma did not improve between 2004 and 2017 and possession of a written action plan remained low. Maximum improvements were reached by 3 sessions for medications knowledge and one session for inhaler technique, and were maintained postpartum. ICS adherence was maximally improved after one session, but not maintained postpartum. Perceived risk of asthma medications on the fetus was highest for corticosteroid-containing medication; and was significantly reduced following education. *Conclusions*: There was a high prevalence of non-adherence and poor self-management skills in all cohorts. More awareness of the importance of optimal asthma management during pregnancy is warranted, since no improvements were observed over the past decade.

ARTICLE HISTORY
Received 4 March 2018
Revised 10 April 2018
Accepted 28 April 2018

KEYWORDS
Inhaler device technique; Knowledge; Non-adherence; Perceived risk

Abbreviations used

ACQ	Asthma Control Questionnaire
FENO	Fraction Exhaled Nitric Oxide
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
ICS	Inhaled Corticosteroids
OCS	Oral Corticosteroids

Introduction

Asthma is a common chronic condition affecting 12% of pregnant women in Australia, with an increasing prevalence over the past years (1). More than one-third of women with asthma will have an exacerbation requiring medical intervention during pregnancy (2,3), usually during the second trimester (4,5). Exacerbation of asthma

CONTACT Vanessa E. Murphy vanessa.murphy@newcastle.edu.au Level 2 West Wing, Hunter Medical Research Institute, University of Newcastle, University Drive, Callaghan, NSW 2308 Australia.

Supplemental data for this article can be accessed at www.tandfonline.com/ijas

and the use of oral corticosteroids (OCS) in pregnancy are associated with an increased risk of adverse perinatal outcomes including preterm delivery and low birth weight (6); however, active management of asthma during pregnancy can reduce this risk (7,8). International guidelines recommend a monthly review of asthma control during pregnancy and provision of self-management education (9). Our group has been conducting prospective studies of asthma in pregnancy in the Newcastle region, Australia since 2004 (10), and therefore, we have the available data to examine whether there have been any changes in baseline asthma self-management knowledge and skills, and inhaled corticosteroids (ICS) use among pregnant women with asthma over the past 13 years.

The recommended management of asthma during pregnancy is the same as for other adults, with ICS recommended as the predominant controller medication and short-acting beta-agonists (SABA) as reliever medication (11). However, medication non-adherence during pregnancy is a significant clinical problem. Previous research has demonstrated a decline in prescription filling for asthma medication in the first trimester, that returns to pre-pregnancy levels only by late pregnancy (12,13). The reason for this is unknown but it may be because of the cautious attitude of pregnant women and/or health professionals towards medication use during pregnancy.

We previously demonstrated that 29% of exacerbations requiring medical intervention were associated with self-reported non-adherence to ICS (4), with 40% of women non-adherent to ICS medication at study entry (approximately 20 weeks gestation) (10). The perception of medication risk can determine adherence and in pregnancy this in an important issue, since risk is shared by both the mother and the fetus. Provision of self-management education improves medication knowledge, inhaler technique, and adherence to controller medication (10). However, it is not known how many education sessions are required to maximize knowledge and self-management in this group, and whether these improvements persist postpartum.

The primary aim of this study was (i) to compare asthma self-management knowledge and skills, and ICS non-adherence rates, in 3 cohorts of pregnant women with asthma in Newcastle NSW, Australia from 2004 to 2017; secondary aims were (ii) to determine the number of repeat education sessions required for maximum improvement in self-management skills; (iii) to determine whether acquired self-management skills are maintained postpartum; and (iv) to determine whether education alters perceived risk of asthma medications on the fetus.

Methods

Population

The data presented come from 3 prospective cohort studies of pregnant women with asthma recruited via the antenatal clinic at the John Hunter Hospital, Newcastle, Australia:

1. The ***2004 cohort study*** was a prospective cohort study conducted between July 2004 and December 2006, which recruited pregnant women with asthma ($N = 85$) at approximately 18 weeks' gestation, as previously described (2).

2. The ***2007 cohort study*** included women ($N = 299$) from 2 related studies. The *Viral Exacerbations of Asthma during Pregnancy* (VEAP) study was conducted between April 2007 and November 2009, which recruited pregnant women with asthma ($n = 168$) between 12–20 weeks' gestation, as previously described (14). Of the 299 women in the 2007 cohort, 74% ($n = 220$) participated in a randomized controlled trial (RCT) of fractional exhaled nitric oxide (FENO)-based asthma management versus symptom-based management, known as the *Managing Asthma in Pregnancy* (MAP) Study (15).

3. The ***2013 cohort study*** is an ongoing RCT of asthma treatment adjustment with FENO-based asthma management versus usual care, known as the Breathing for Life Trial (BLT) (16). Pregnant women with asthma were recruited between 12 and 22 weeks' gestation. Data presented for this cohort come from women recruited between March 2013 and June 2017 ($N = 511$).

Details of the individual studies are provided in Supplement Table S1.

Ethical approval was obtained for all studies from the Hunter New England Health Human Research Ethics Committee and the University of Newcastle (2004 Cohort reference number 9709173.07, 2007 Cohort reference number 07/02/21/3.06 and 2013 Cohort reference number 12/10/17/3.04). Written informed consent was obtained from all women prior to participation.

Measurements

Baseline data from all three studies were collected prior to 23 completed weeks of gestation. This included current maternal age, body mass index (BMI, kg/m^2), gestational age, self-reported smoking status, asthma history (age at asthma diagnosis, and hospital admissions, emergency department visits, OCS use for asthma in the past 2 years), and current asthma symptoms and medication use. Forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were measured by spirometry (Spirotac IV, Vitalograph, Buckingham UK; the 2004

cohort, and EasyOne Spirometer, NicheMedical, North Sydney AU; the 2007 and 2013 cohorts) and age- and height-adjusted percent predicted FEV_1 and FVC values were calculated using the 2012 Global Lung Function equations (17). Airway inflammation was assessed by measuring FENO (see Supplement for details).

Asthma control was assessed in all women in the 2004 and 2007 cohorts, and the FENO-based asthma management group in the 2013 cohort, using the validated Asthma Control Questionnaire (ACQ) (18). Women with an ACQ7 >1.5 were considered to have uncontrolled asthma (19).

ICS adherence was assessed by asking the following question: "It can be difficult to remember all of your medicines when things get busy. How many times in the last week have you missed a dose of your controller?" Participants were considered to be adherent if they missed ≤20% of their prescribed medication doses.

General knowledge about asthma medications was assessed in the 2004 cohort, with knowledge about controller and reliever medications was assessed separately in BOTH the 2007 and 2013 cohorts, respectively. Medication knowledge was determined following direct questioning regarding how the controller and reliever medications worked, and when to use which type of medication. Answers were scored as correct or incorrect by a trained research nurse/midwife.

Participants were asked if they currently possessed a written asthma action plan (WAP). Women who did not possess a WAP were all provided one except for women in the usual care group in the 2013 cohort who were advised to obtain one from their treating physician.

Inhaler technique was assessed for pressurized Metered Dose Inhalers (pMDI) and turbuhalers following participant demonstration using their own inhaler or a placebo and using the criteria listed in Supplement Table S2.

Repeat data were available for the 2007 cohort and the 2013 cohort (FENO-based asthma management group only), where women ($n = 685$) attended repeat assessments (3–6 weeks apart) during pregnancy, plus one assessment at 6-months postpartum (the 2007 cohort only, $n = 95$). Self-management skills, medication knowledge, and inhaler technique were assessed at all visits, prior to the education session.

Perceived risk of asthma medications on the fetus was assessed using a 10-cm visual analogue scale at visits 1, 2, 3, and 5 (the 2007 cohort). Participants were instructed to do the following: "Please place a cross on the line between 0% and 100% where you think the medication may have side effects for your baby from no side effects to severe side effects (e.g., deformity)." Below the question, 3 visual analogue scales were presented, for controller medication, reliever medication, and OCS (e.g., prednisolone), with pictures of inhaler types or tablets shown.

Statistical analysis

All data were analyzed using Stata 15 (StataCorp, College Station, TX, USA) and presented as mean ± standard deviation, median [interquartile range] or *n* (%) unless otherwise stated. Dichotomous variables were analyzed with chi-square tests ($p < 0.05$) or pairwise chi-square post hoc analysis ($p < 0.017$) between the 3 cohorts. Non-parametric variables were analyzed using Kruskal–Wallis or Mann–Whitney tests, $p < 0.05$, with post hoc Dunn's test using Bonferroni correction ($p < 0.05$) between the 3 cohorts.

Proportions in the longitudinal analysis were compared pairwise between 4 sequential visits using pairwise chi-square tests ($p < 0.0125$). Perceived risk was analyzed using repeated measures one way analyses of variance (ANOVA), with post hoc pairwise comparison using Bonferroni adjustment ($p < 0.05$). The association between perceived risk of controller medication, correct controller knowledge, and optimal inhaler technique, with self-reported ICS adherence, was determined by a generalized estimated equation.

Since all studies were done in the same area, using the same recruiting method, some women participated in more than one study. We performed a sensitivity analysis by restricting to the first pregnancy, in order to evaluate the influence of participating multiple times in an asthma and pregnancy study.

Results

A total of 895 pregnant women were included in the analyses: 85, 299, and 511 women from the 2004, 2007, and 2013 cohorts, respectively. The median number of visits in the longitudinal analysis was 3 [2, 4]. Ninety-five women from the 2007 cohort underwent a minimum of 4 repeat assessments during pregnancy and an assessment at 6 months postpartum.

Baseline characteristics are shown in Table 1. Women participating in the 2013 cohort were older than the women in the 2004 cohort ($p < 0.001$) and the 2007 cohort ($p < 0.001$). Women in the 2013 cohort had a higher BMI compared to women in the 2004 cohort ($p = 0.003$). Women in the 2004 cohort were recruited later in gestation, and were more likely to smoke ($p < 0.001$), compared to the 2007 and 2013 cohort. In the 2013 cohort, the median ACQ7 score was higher than in the 2004 cohort ($p = 0.004$) and the 2007 cohort ($p < 0.001$), translating to a higher proportion of women with uncontrolled asthma compared to the 2004 cohort

Table 1. Baseline characteristics of women participating in the 2004 cohort, the 2007 cohort, and the 2013 cohort.

	2004 Cohort $N = 85$	2007 Cohort $N = 299$	2013 Cohort $N = 511$	P value*
Maternal age (years)	27.8 [24.2, 31.5]	28.2 [24.4, 32.2]	29.4 [25.1, 33.2]	**<0.001**[b c]
Maternal BMI (kg/m^2)	26.0 [23.1, 30.9]	27.9 [24.4, 32.4] $n = 298$	28.6 [24.5, 35.6] $n = 478$	**0.005**[b]
Gestational age (weeks)	19.4 [18.7, 20.4]	16.0 [14.0, 19.0]	19.0 [16.1, 21.1]	**<0.001**[a b c]
Gravidity	2.5 [1.0, 3.0] $n = 84$	2.0 [1.0, 3.0]	2.0 [1.0, 4.0] $n = 376$	0.220
Parity	1.0 [0, 2.0] 2.0 $n = 84$	1.0 [0, 1.0]	1.0 [0, 2.0] $n = 376$	0.590
Smoker	26 (30.6%)	46 (15.4%)	80 (15.7%)	**0.004**[a b]
Asthma History				
Age at diagnosis of asthma (years)	6 [2, 13] $n = 52$	7 [3, 14] $n = 284$	5 [2, 13] $n = 506$	0.092
≥1 hospital admissions for asthma past 2 years	6 (7.1%) $n = 84$	6 (2.0%)	28 (5.7%) $n = 489$	**0.027**[a c]
≥1 emergency department presentations for asthma past 2 years	14 (16.7%) $n = 84$	32 (10.7%)	66 (13.5%) $n = 489$	0.285
≥1 oral corticosteroid use for asthma past 2 years	15 (17.9%) $n = 84$	51 (17.1%)	103 (21.1%) $n = 489$	0.323
Asthma control (ACQ7)	0.86 [0.43, 1.43] $n = 81$	0.85 [0.29, 1.43] $n = 298$	1.29 [0.57, 2.14] $n = 259$	**<0.001**[b c]
Uncontrolled asthma (ACQ7 >1.5)	19 (23.5%)	73 (24.4%)	115 (44.4%)	**<0.001**[b c]
FENO (ppb)	11.5 [6.9, 20.2] $n = 70$	13.3 [6.1, 26.9] $n = 289$	10.6 [5.4, 27.3] $n = 256$	0.347
Spirometry‡				
FEV_1 % predicted	95.4 [84.3, 103.7]	95.3 [85.8, 103.8]	89.0 [80.5, 97.4]	**<0.001**[b c]
FVC % predicted	98.7 [91.1, 109.3]	103.2 [94.1, 112.4]	91.4 [84.7, 99.0]	**<0.001**[b c]
FEV_1/FVC (%)	81.9 [77.1, 87.3]	81.0 [74.9, 84.8]	83.3 [77.8, 86.6]	**<0.001**[a c]
Treatment				
Maintenance ICS use	35 (41.2%)	87 (29.1%)	195 (38.2%)	**0.017**[c]
ICS only	12 (34.3%)	24 (27.6%)	81 (41.5%)	
ICS/LABA combination	23 (65.7%)	63 (72.4%)	114 (58.5%)	0.076
Maintenance ICS dose among ICS users (BDP equivalent, µg/day)	1000 [800, 2000]	500 [400, 800] $n = 86$	500 [400, 1000] $n = 186$	**<0.001**[a b]

Note. ACQ = asthma control questionnaire; FENO = fractional exhaled nitric oxide; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; ICS = inhaled corticosteroids; LABA = long acting beta-agonists; BDP = beclomethasone diproprionate
Values are expressed as median [interquartile range] or n (%)
*Kruskaln–Wallis or chi-square appropriately
‡$n = 84$ the 2004 cohort, 296 the 2007 cohort and 441 (FEV_1 % predicted), 434 (FVC % predicted) and 438 (FEV_1/FVC) the 2013 cohort
[a]The 2004 cohort vs. the 2007 cohort
[b]The 2004 cohort vs. the 2013 cohort
[c]THE 2007 cohort vs. the 2013 cohort Dunn's test $p < 0.05$ or chi-square $p < 0.017$.

($p = 0.001$) and the 2007 cohort ($p < 0.001$). In addition, among the 2013 cohort participants, % predicted FEV_1 and FVC were lower compared to the 2004 cohort (both $p < 0.001$) and the 2007 cohort (both $p < 0.001$); however, FEV_1/FVC was lowest among women in the 2007 cohort (the 2004 cohort $p = 0.040$ and the 2013 cohort $p < 0.001$). In a regression analysis of the difference in baseline ACQ between cohorts, BMI was not identified as a confounder, while smoking and FEV1/FVC ratio were significant as confounders (data not shown). However, these results did not alter our conclusion that ACQ was different between the cohorts.

A smaller proportion of women were prescribed maintenance ICS at baseline in the 2007 cohort compared to the 2013 cohort ($p = 0.009$), while women in the 2004 cohort had higher ICS dose compared to the 2007 cohort and the 2013 cohort (both $p < 0.001$).

ICS non-adherence

Self-reported non-adherence to ICS at baseline was 40% in the 2004 cohort, 42% in the 2007 cohort, and 39% in the 2013 cohort ($p = 0.867$). During follow-up education sessions, ICS non-adherence decreased during pregnancy from 42% to 23% by visit 5, but increased to 56% postpartum (the 2007 cohort data only, ICS users $n = 45$, $p < 0.001$ compared to visit 5). ICS non-adherence was maximally improved after one education session ($p < 0.001$ between visits 1 and 2) (Figure 1A).

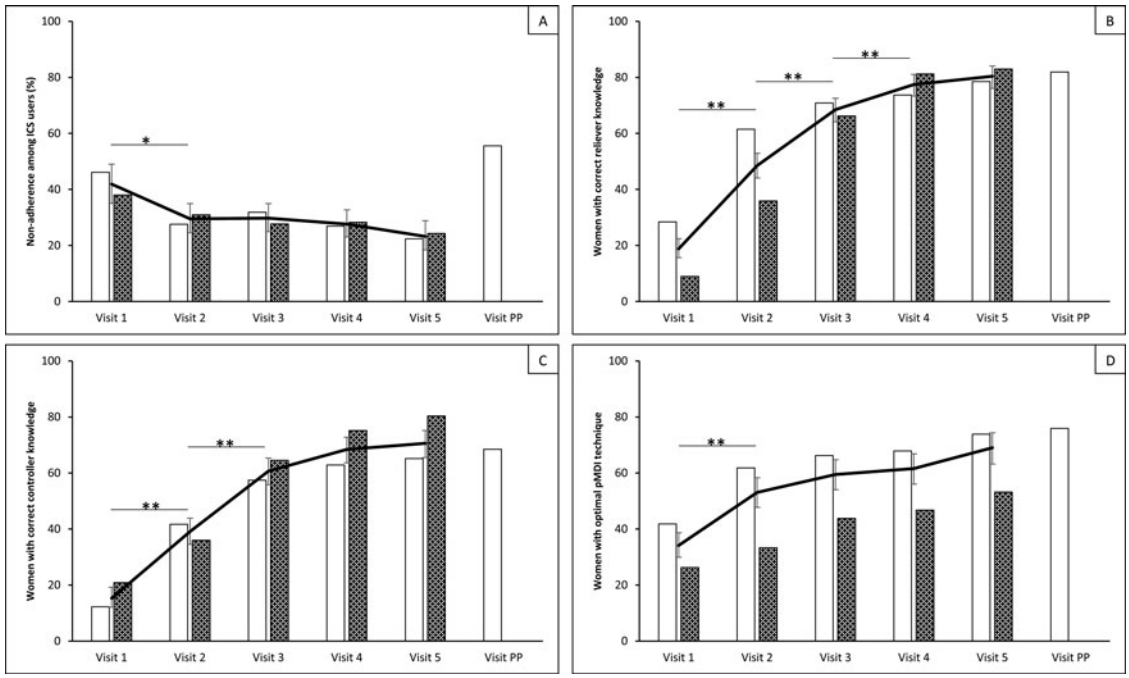

Figure 1. Proportion of ICS non-adherence (A), correct reliever (B) and controller (C) knowledge and optimal pMDI technique (D) among women in the 2007 cohort (open column), the 2013 cohort (closed column), and overall (line) at pregnancy visits 1 through 5 and at postpartum (PP) visit (2007 cohort only); gestational age in weeks at Visit 1 17 [15, 20], Visit 2 22 [20, 24], Visit 3 26 [24, 29], Visit 4 30 [28, 33] and Visit 5 34 [32, 36]; Weeks after delivery Visit PP 26 [25, 28]; $^{*}p < 0.01$, $^{**}p < 0.001$ between overall (line).

Medication knowledge

Correct medication knowledge at baseline was 29% in the 2004 cohort (controller and reliever combined). In the 2007 cohort correct medication knowledge was 12% (controller) and 29% (reliever) at baseline, and 14% (controller) and 13% (reliever) in the 2013 cohort ($p = 0.627$ controller and $p < 0.001$ reliever between the 2007 and 2013 cohorts). Correct medication knowledge for both reliever and controller medication increased from 19% and 15%, respectively, at the first visit to 80% and 71%, respectively, at the fifth visit ($p < 0.001$). Overall, correct knowledge increased significantly after the 2 educational sessions for controller medication and after the first 3 for reliever medication. Correct medication knowledge was sustained 6 months postpartum (2007 cohort data only) (Figure 1B, C).

Possession of a written asthma action plan

The possession of a WAP remained low between 2004 and 2017: 20% of study participants in 2004, 23% in 2007, and 17% in 2013 ($p = 0.136$).

Inhaler device technique

Baseline optimal inhaler technique was 48% in the 2004 cohort, 35% in the 2007 cohort, and 25% in the 2013 cohort ($p < 0.001$) for pMDIs, and 67%, 64%, and 65%, respectively, for turbuhalers ($p = 0.985$). Optimal pMDI technique among the 2013 cohort participants was significantly lower than the 2004 cohort ($p < 0.001$) and the 2007 cohort ($p = 0.002$). The proportion of inadequate use of pMDI at baseline increased from 37% in the 2004 cohort to 64% in the 2013 cohort. In the longitudinal analysis ($n = 448$), optimal pMDI technique increased from 34% at visit 1 to 69% at visit 5, with a significant increase between visits 1 and 2 ($p < 0.001$). Optimal pMDI technique was sustained 6 months postpartum (Figure 1D).

Perceived risk of asthma medications on the fetus

Perceived risk for reliever medication was lower than for controller medication, and highest for OCS across all 4 visits ($n = 299$, 2007 cohort). Baseline perceived risk was 31% $\pm$ 4 for controller medication, 14% $\pm$ 3 for reliever medication, and 48% $\pm$ 5 for OCS (Figure 2). After one education session, perceived risk was reduced significantly for all medications. Perceived risk for controller medication reduced to 19% $\pm$ 3, for reliever medication to 10% $\pm$ 2, and for OCS to 40% $\pm$ 5 ($p < 0.05$) at visit 2. Additional education sessions did not significantly lower the perceived risk for any of the asthma medications further.

Self-management skills and perceived risk in relation to adherence

Women with correct controller knowledge were 15% more likely to report ICS adherence (odds ratio = 1.15,

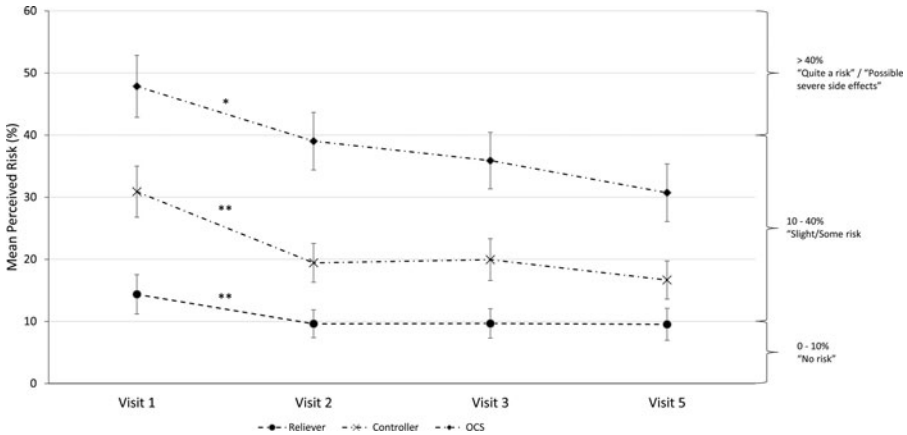

Figure 2. Mean perceived risk of adverse medication effects on the fetus during pregnancy. Graph displays perceived risk values for visits 1–3 and 5 during pregnancy in the 2007 cohort for 3 medication classes: reliever (circle), controller (cross), and OCS (diamond); 0% no side effect, 100% severe side effect (e.g., deformity), $^{*}p < 0.05$, $^{**}p < 0.001$.

$p < 0.001$) compared to women with incorrect controller knowledge. Inhaler technique and perceived risk of controller medication were not related to self-reported adherence (Supplement Table S3).

Sensitivity analyses

In a sensitivity analysis, we excluded 9 (3.0%) women from the 2007 cohort who had previously participated in the 2004 cohort and 27 (5.3%) women from the 2013 cohort (26 had participated in the 2007 cohort and 1 participated in the 2004 cohort). In the longitudinal analysis, 24 women were excluded, 5 (5.3%) women from the 2007 cohort who previously participated in the 2004 cohort were excluded, and 19 women from the 2013 cohort were excluded who previously participated in the 2007 cohort. Similar results in baseline data and in the longitudinal data were observed (Supplement Tables S4 and S5).

Discussion

The present study demonstrates that asthma self-management skills and ICS adherence did not improve in pregnant women with asthma between 2004 and 2017 in the Newcastle region, while asthma control worsened. In addition, the results demonstrate that asthma education improves self-management skills during pregnancy, with maximum benefit reaching after one to three education sessions. Optimal inhaler technique and medication knowledge were maintained 6 months postpartum. Asthma education lowers the mother's perceived risk of asthma medications on the fetus. However, optimizing self-management skills or lowering perceived risk of medication among pregnant women was not associated with an improvement in adherence.

To our knowledge this is the first study to report ICS adherence, asthma control, and asthma self-management skills in 3 cohorts of pregnant women with asthma from one center over more than a decade, and the first to report on the number of education sessions required to reach maximum benefit. Our data indicate that asthma control between 2004 and 2017 has significantly worsened in the Newcastle area, resulting in a greater proportion of pregnant women with uncontrolled asthma in early pregnancy, even though women with severe asthma were specifically excluded from the 2013 cohort. Moreover, the participant lung function has declined, with those in the 2013 cohort having significantly lower % predicted FEV_1 and FVC compared to women in the previous studies. Notably, this apparent asthma worsening was not reflected in the proportion of women taking controller medication or in ICS dose, nor adherence. Multiple studies have demonstrated that ICS non-adherence increases the risk of exacerbations during pregnancy (4,20,21) which may lead to poor maternal and neonatal outcomes (6). Our results likely represent the level of poor asthma skills in the community. The poor rate of WAP possession is clear evidence for the lack of adequate asthma management in the primary care setting. This could be the result of less community awareness campaigns or a poor implementation of the GP 3+ plan, currently known as the "Asthma Cycle of Care" (22). Despite national and international guidelines for asthma management in pregnancy (9,11), our results demonstrate apparent poor implementation into antenatal care.

Asthma medication non-adherence is not just a problem among pregnant women; the adherence rate among the asthmatic adult population in Australia is low. In 2015, Reddel et al. reported an ICS non-adherence rate of 43% among Australian asthmatics (adults of at least 16 years of age using ICS more than 5 days per week) (23). Similarly, we found that over all 3 studies the average non-adherence among pregnant women with asthma was 42%. In the study of Reddel et al., 61% of the participants used maintenance ICS in the past 12 months, of which 82% used

combination inhalers (23). Among our participants using ICS, the use of combination inhalers was 63%. Our results, however, represent current use in pregnancy whilst Reddel et al. report the use in the past 12 months in a broad population which may have included pregnant women. Women who are non-adherent pre-pregnancy might continue their medication behavior during pregnancy and beyond. Several other studies show a decrease in asthma medication prescriptions during pregnancy compared to pre-pregnancy, which may also reflect women decreasing their medication, and thereby lowering adherence, prior to discontinuation (12,13,24,25). Pre-pregnancy education is therefore needed to increase the proportion of women who are adherent during the first trimester.

In a previous study from our group which recruited pregnant women with asthma from the antenatal clinic in Newcastle prior to 2004 (pre-2004 cohort), Murphy et al. (2005) reported a significant improvement in medication knowledge after one visit (20 weeks vs. 33 weeks of gestation) (10). The percentage of improvement was similar to our results of the 2007 cohort between the first and second visit, 35% in the pre-2004 cohort versus 30% (controller) and 33% (reliever) among the 2007 cohort. However, the improvement among women in the 2013 cohort was lower than in the pre-2004 cohort, 15% (controller) and 27% (reliever).

A recent literature review by Bonham et al. surmised the components of effective asthma therapy in pregnancy, which includes inhaler technique, WAP possession, and an emphasis in education sessions on perceived risk of asthma medication on the fetus and the risks of discontinuing medication (26). This was the first study to report the effect of repeat education on self-management skills during pregnancy. We have demonstrated that repeat education sessions during pregnancy improved all asthma self-management skills: 3 sessions were needed for optimizing correct medication knowledge, 2 educational sessions for optimizing inhaler technique, and 1 educational session was sufficient to significantly lower perceived risk of asthma medications on the fetus. However, we were not able to reach complete benefit through education alone. Further research is needed to determine whether additional strategies enhance the effect of asthma education during pregnancy.

Several studies have reported on the influence of education on asthma medication adherence among non-pregnant adults (27). Normansell et al. recently performed a meta-analysis on 7 studies administering an educational intervention and reported an improvement in percentage of doses taken of 12% (3.7, 19.5) among adolescents and adults with asthma (follow-up varied between 10 and 26 weeks) (27). We found an improvement of 14% in doses taken between visits 1 and 4 (approximately 12 weeks' difference); however, between visit 4 and the postpartum visit (6 months after delivery), the adherence rate declined by 24%. The postpartum period is a unique time of life when a woman may be less likely to have the time or motivation to concentrate on her own health. Alternatively, asthma may improve postpartum leading to a perception of less need for medication (28). Further research is needed to determine reasons for this change in behavior and to determine strategies to improve adherence postpartum. Our results indicate that the prepartum and postpartum periods may be particularly vulnerable to non-adherence and poor asthma management skills.

Azzi et al. reported a 26% improvement in correct inhaler technique after one visit among non-pregnant adults with asthma (29). We found an improvement of 19% after one visit, with a total improvement during pregnancy of 35% in optimal use of the pMDI. Optimal inhaler technique was sustained 6 months after delivery. By combining adequate and optimal technique as correct inhaler technique, we found a similar improvement of 38% between baseline (49%) and visit 5 (87%). Optimal inhaler technique is a key component in reducing asthma symptoms and thereby increasing asthma control (30). Regular assessment of inhaler technique might contribute to better asthma control during pregnancy, as poor inhaler technique lowers drug delivery and thereby may lead to a reduced effect of the asthma medication (31).

Attitudes to asthma medication are believed to be an important factor influencing adherence behavior. Perceived risk for ICS was higher than for reliever medication at all visits, as we previously reported in a sub-group from the MAP study (32). Lim et al. conducted qualitative interviews with pregnant asthmatic women and reported that women would rather use more reliever medication and reduce ICS use than continue with their pre-pregnancy controller treatment (33). This suggests that attitudes towards steroid-based medications being unsafe during pregnancy still exist and are contributing towards non-adherence. Similarly, our data demonstrated that women had a higher perceived risk for corticosteroid-based medications (OCS, followed by ICS), compared to reliever medications. However, we did not find an association between perceived risk and self-reported non-adherence. Our adherence measure might be inadequate to detect such an association since it did not discriminate between the different adherence phenotypes, intentional and accidental non-adherence (34).

A strength of our analysis is that these data come from almost 900 pregnant women with asthma. By combining 3 cohorts from the same area, we were able to analyze

trends in time regarding asthma control and lung function among women in early-mid pregnancy. Throughout all 3 studies, inhaler technique and ICS non-adherence were assessed using the same methods, resulting in comparable outcomes. Furthermore, we were able to demonstrate that optimal inhaler technique and medication knowledge acquired during pregnancy are sustained for at least 6 months postpartum. We also were able to demonstrate that ICS use and adherence do not remain after pregnancy.

There were some limitations in this study; none of the studies were RCTs of an educational intervention, so there is no control group who did not receive education. In all 3 studies, adherence was self-reported; thus there is risk of social desirability bias which may have resulted in an overestimation of the adherence rate. Secondly, the decrease in lung function we observed may be partially explained by the increasing BMI over time. Among the women in the 2004 cohort study, there were more smokers than in the 2007 cohort and the 2013 cohort, which likely reflects reduced community smoking prevalence rather than a difference in socio-economic status between the cohorts (1). Thirdly, the number of women with a postpartum visit in the 2007 cohort was small ($n = 45$) so the results of the postpartum analysis should be interpreted with caution. Lastly, we cannot fully access the effect of education on the perceived risk of OCS on the fetus as this was not part of the educational session if the women in question did not receive OCS at that time.

In conclusion, asthma self-management skills including ICS adherence did not improve between 2004 and 2017 among pregnant women with asthma. Non-adherence remains high and written action plan possession remains low in this population of pregnant women with asthma. The use of maintenance ICS remained stable while asthma control and lung function declined. Asthma education in pregnancy is beneficial. Maximal improvement in self-management skills was reached after 3 repeat education sessions; however, further research is needed to investigate whether additional strategies can provide further benefit.

Acknowledgement

The authors would like to thank the staff of the antenatal clinics at the John Hunter Hospital (Newcastle) for assistance with patient recruitment and clinical assessment. Specifically, we thank Kelly Steel, Karen McLaughlin, and Philippa Talbot. We also thank all women who participated in one or more studies.

Funding

Project funding was received from Hunter Medical Research Institute, Port Waratah Coal Services, University of Newcastle, Asthma Foundation of NSW, National Health and Medical Research Council, the Singleton Foundation, John Hunter Hospital Charitable Trust, University of Newcastle Priority Research Centre GrowUpWell^{TM} and the Woodend Foundation.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

ORCID

Annelies L. Robijn http://orcid.org/0000-0001-5577-1118
Megan E. Jensen http://orcid.org/0000-0001-8653-4801
Peter G. Gibson http://orcid.org/0000-0001-5865-489X
Joerg Mattes http://orcid.org/0000-0003-3729-5722

Michael J. Peek http://orcid.org/0000-0001-6055-5129
Helen L. Barrett http://orcid.org/0000-0001-7141-2086
Peter A. Wark http://orcid.org/0000-0001-5676-6126
Vanessa E. Murphy http://orcid.org/0000-0003-3282-1324

References

1. Australian Bureau of Statistics. National Health Survey; First Results 2014–15. Belconnen, ACT; 2015.
2. Murphy VE, Clifton VL, Gibson PG. The effect of cigarette smoking on asthma control during exacerbations in pregnant women. Thorax. 2010;65(8):739–744. doi:10.1136/thx.2009.124941. PMID: 20627905.
3. Schatz M, Dombrowski MP, Wise R, Thom EA, Landon M, Mabie W, et al. Asthma morbidity during pregnancy can be predicted by severity classification. J Allergy Clin Immunol. 2003;112(2):283–288. doi:10.1067/mai.2003.1516. PMID: 12897733.
4. Murphy VE, Gibson P, Talbot PI, Clifton V. Severe asthma exacerbations during pregnancy. Obstet Gynecol. 2005;106(5):1046–1054. doi:10.1097/01.AOG.0000185281.21716.02. PMID: 16260524.
5. Stenius-Aarniala BS, Hedman J, Teramo KA. Acute asthma during pregnancy. Thorax. 1996;51:411–414. doi:10.1136/thx.51.4.411. PMID: 8733495.
6. Namazy JA, Murphy VE, Powell H, Gibson PG, Chambers C, Schatz M. Effects of asthma severity, exacerbations and oral corticosteroids on perinatal outcomes. Eur Respir J. 2013;41:1082–1090. doi:10.1183/09031936.00195111. PMID: 22903964.
7. Murphy VE, Namazy JA, Powell H, Schatz M, Chambers C, Attia J, et al. A meta-analysis of adverse perinatal outcomes in women with asthma. BJOG An Int J Obstet Gynaecol. 2011;118(11):1314–1323. doi:10.1111/j.1471-0528.2011.03055.x.
8. Murphy VE, Clifton VL, Gibson PG. Asthma exacerbations during pregnancy: incidence and association with adverse pregnancy outcomes. Thorax. 2006;61:169–176. doi:10.1136/thx.2005.049718. PMID: 16443708.
9. Global Initiative for Asthma. Global strategy for asthma management and prevention 2017. Available from: http://www.ginasthma.org [last accessed 25 January 2018]

10. Murphy VE, Gibson PG, Talbot PI, Kessel CG, Clifton VL. Asthma self-management skills and the use of asthma education during pregnancy. Eur Respir J. 2005;26(3):435–441. doi:10.1183/09031936.05.00135604. PMID: 16135724.
11. National Asthma Council Australia. Australian Asthma Handbook version 2017; Available from: http//www.asthmahandbook.org.au [last accessed 25 January 2018].
12. Enriquez R, Wu P, Griffin MR, Gebretsadik T, Shintani A, Mitchel E, et al. Cessation of asthma medication in early pregnancy. Am J Obstet Gynecol. 2006;195:149–153. doi:10.1016/j.ajog.2006.01.065. PMID: 16631099.
13. Charlton RA, Pierini A, Klungsøyr K, Neville AJ, Jordan S, de Jong-van den Berg LTW, et al. Asthma medication prescribing before, during and after pregnancy: a study in seven European regions. BMJ Open. 2016;6:e009237.
14. Murphy VE, Mattes J, Powell H, Baines KJ, Gibson PG. Respiratory viral infections in pregnant women with asthma are associated with wheezing in the first 12 months of life. Pediatr Allergy Immunol. 2014;25(2):151–158. doi:10.1111/pai.12156. PMID: 24329935.
15. Powell H, Murphy VE, Taylor DR, Hensley MJ, McCaffery K, Giles W, 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. doi:10.1016/S0140-6736(11)60971-9. PMID: 21907861.
16. Murphy VE, Jensen ME, Mattes J, Hensley MJ, Giles WB, Peek MJ, et al. The Breathing for Life Trial: a randomised controlled trial of fractional exhaled nitric oxide (FENO)-based management of asthma during pregnancy and its impact on perinatal outcomes and infant and childhood respiratory health. BMC Pregnancy Childbirth. 2016;16:111. doi:10.1186/s12884-016-0890-3. PMID: 27189595.
17. Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3–95 year age range: the global lung function 2012 equations: report of the global lung function initiative (GLI), ers task force to establish improved lung function reference values. Eur Respir J. 2012;40(6):1324–1343. doi:10.1183/09031936.00080312. PMID: 22743675.
18. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. Eur Respir J. 1999;14(4):902–907. doi:10.1034/j.1399-3003.1999.14d29.x. PMID: 10573240.
19. Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying "well-controlled" and "not well-controlled" asthma using the asthma control questionnaire. Respir Med. 2006 Apr;100(4):616–621. doi:10.1016/j.rmed.2005.08.012.
20. Williams DA. Asthma and pregnancy. Acta Allergol. 1967;22(3–4):311–323. doi: 10.1111/j.1398-9995.1967.tb03228.x.
21. Apter A, Greenberger P, Patterson R. Outcomes of pregnancy in adolescents with severe asthma. Arch Intern Med. 1989;149:2571–2575. doi:10.1001/archinte.1989.00390110121027. PMID: 2818116.
22. National Asthma Council Australia. Asthma Cycle of Care [Internet] 2018. https://www.nationalasthma.org.au/living-with-asthma/resources/health-professionals/reports-and-statistics/asthma-cycle-of-care [last accessed 23 January 2018].
23. Reddel HK, Sawyer SM, Everett PW, Flood PV, Peters MJ. Asthma control in Australia: a cross-sectional web-based survey in a nationally representative population. Med J Aust. 2015;202(9):492–498. doi:10.5694/mja14.01564. PMID: 25971575.
24. Beau A-B, Didier A, Hurault-Delarue C, Montastruc J-L, Lacroix I, Damase-Michel C. Prescription of asthma medications before and during pregnancy in France: an observational drug study using the EFEMERIS database. J Asthma. 2016;54(3):258–264. doi:10.1080/02770903.2016.1214731. PMID: 27657554.
25. Berard A, Sheehy O. The Quebec pregnancy cohort – Prevalence of medication use during gestation and pregnancy outcomes. PLoS One. 2014;9(4):e93870. doi:10.1371/journal.pone.0093870. PMID: 24705674.
26. Bonham CA, Patterson KC, Strek ME. Asthma outcomes and management during pregnancy. Chest. 2018;153(2):515–27. PMID: 28867295.
27. Normansell R, Kew KM, Stovold E. Interventions to improve adherence to inhaled steroids for asthma. Cochrane Libr or Syst Rev. 2017;4:CD012226.
28. Schatz M, Harden K, Forsythe A, Chilingar L, Hoffman C, Sperling W, 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. doi:10.1016/0091-6749(88)90187-X. PMID: 3346481.
29. Azzi E, Srour P, Armour C, Rand C, Bosnic-Anticevich S. Practice makes perfect: self-reported adherence a positive marker of inhaler technique maintenance. npj Prim Care Respir Med. 2017;27(1):29. doi:10.1038/s41533-017-0031-0. PMID: 28439076.
30. Haughney J, Price D, Barnes NC, Virchow JC, Roche N, Chrystyn H. Choosing inhaler devices for people with asthma: current knowledge and outstanding research needs. Respir Med. 2010;104(9):1237–1245. doi:10.1016/j.rmed.2010.04.012. PMID: 20472415.
31. Newman SP, Weisz AWB, Talaee N, Clarke SW. Improvement of drug delivery with a breath actuated pressurised aerosol for patients with poor inhaler technique. Thorax. 1991;46(10):712–716. doi:10.1136/thx.46.10.712. PMID: 1750017.
32. Powell H, McCaffery K, Murphy VE, Hensley MJ, Clifton VL, Giles W, et al. Psychosocial outcomes are related to asthma control and quality of life in pregnant women with asthma. J Asthma. 2011;48:1032–1040. doi:10.3109/02770903.2011.631239. PMID: 22091740.
33. Lim AS, Stewart K, Abramson MJ, Ryan K, George J. Asthma during pregnancy: the experiences, concerns and views of pregnant women with asthma. J Asthma. 2012;49(5):474–479. doi:10.3109/02770903.2012.678024. PMID: 22530982.
34. Hugtenburg JG, Timmers L, Elders PJM, Vervloet M, van Dijk L. Definitions, variants, and causes of nonadherence with medication: a challenge for tailored interventions. Patient Prefer Adherence. 2013;7:675–682. doi:10.2147/PPA.S29549. PMID: 23874088.