## CLINICAL REVIEW PEER-REVIEWED



What prompted my research in this area was a wish to further the role of the community pharmacist in the management of chronic diseases. There are fewer opportunities for patients in rural settings to be referred to specialized clinics regarding their condition, and pharmacists can help to close this gap in care. J'ai été amené à faire des recherches dans ce domaine parce que je voulais faire avancer le rôle du pharmacien communautaire dans la gestion des maladies chroniques. Les patients en milieu rural ont moins de chances d'être dirigés vers des cliniques spécialisées pour se faire traiter et les pharmaciens peuvent aider à combler ce fossé dans les soins.

# Improving asthma control in the rural setting: The BREATHE (Better Respiratory Education and Asthma Treatment in Hinton and Edson) study

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## Abstract

**Background:** Overuse of  $\beta$ -agonists is a risk factor for poor control of asthma. Pharmacists can identify high-risk patients through refill information and can then initiate disease-management programs for these patients.

Methods: The Better Respiratory Education and Asthma Treatment in Hinton and Edson (BREATHE) study was a randomized, controlled trial in high-risk asthma patients. The intervention included an educational program (with focus on development of a written action plan), assessment of asthma therapy, and referral to a respiratory therapist and primary care physician. The primary objective was to determine the effect of this program (initiated by community pharmacists) on asthma control, as measured by the Asthma Control Questionnaire. Secondary objectives included determining the effect of the program on numbers of emergency department visits and hospital admissions, use of inhaled corticosteroids, courses of oral steroids, and lung function. Endpoints were measured at baseline, 2 months, and 6 months.

**Results:** A total of 70 patients were randomized (34 to usual care, 36 to the intervention). At 6 months, there was no significant difference in asthma control between the usual care and intervention groups (change in ACQ score 0.33 and 0.43 respectively, p = 0.66). There were no significant differences in the secondary endpoints. Generally, pharmacist compliance with the intervention was poor.

Conclusions: Although no differences were found in asthma control, this model, which uses a multidisciplinary, community-based approach, offers a unique management strategy for rural asthma patients. *Can Pharm J* 2006;139(4):44-50.

Approximately 10% of Canadians have asthma.<sup>1,2</sup> Generally, control of asthma is poor, and in one study up to 28% of patients had visited the emergency department (ED) in the previous year.<sup>2</sup>

Less-than-optimal application of proven and effective asthma therapies can lead to poor patient outcomes, such as increased use of health care resources, decreased quality of life, and lost days at work or school.<sup>3,4</sup> Identification of these care gaps helps to target certain areas of management. Identified care gaps in asthma treatment include underuse of inhaled corticosteroids, poor education, and limited use of written action plans.<sup>5,8</sup>

Inhaled corticosteroids are the cornerstone of

asthma pharmacotherapeutic management.<sup>9,10</sup> However, approximately 30% to 40% of patients who should be taking an inhaled corticosteroid do not receive the necessary prescription,<sup>4,5</sup> and underuse of inhaled corticosteroids is associated with greater numbers of hospital admissions, ED visits, and deaths.<sup>11</sup>

Written action plans have been shown to reduce postdischarge morbidity, hospital admissions, and ED visits and to improve lung function and healthrelated quality of life.<sup>12,13</sup> The evidence for use of these plans is strong, but implementation in practice is poor.9 In the Alberta Strategy To Help Manage Asthma (ASTHMA) study of primary care clinics, only 2% of asthma patients had a written action plan.<sup>14</sup> In a survey of physician practices in Canada, only 14% of family physicians reported that they develop an action plan with "all" or "most" of their asthma patients.<sup>6</sup>

Overuse of  $\beta$ -agonists is an indicator of poorly controlled asthma and is associated with increased mortality.<sup>7,11,15</sup> Community pharmacists are able to identify high-risk patients through refill records. The benefit of the involvement of community pharmacists in the care of asthma patients has been previously demonstrated,<sup>16,17</sup> but a communitybased, interdisciplinary approach in the management of high-risk patients, with the participation of primary care physicians, respiratory therapists (RTs), and pharmacists, has not previously been studied. The goal of the Better Respiratory Education and Asthma Treatment in Hinton and Edson (BREATHE) study was to determine if community pharmacists, working with other primary care providers, could improve asthma control in a rural setting.

### Methods

Detailed methods of the study have been published previously.<sup>18</sup> In brief, the BREATHE study was a prospective, randomized, controlled trial. Patients were randomly assigned to a community management intervention (provided by pharmacists, RTs, and family physicians) or usual care. The primary objective of the study was to determine the effect of an education, assessment, and referral intervention program initiated by community pharmacists on asthma control in patients with poorly controlled asthma. The secondary objectives were to determine the effect of this program on numbers of emergency department visits and hospital admissions, use of inhaled corticosteroids, courses of oral steroids, and lung function as measured by forced expiratory volume in 1 second (FEV.).

The sample was derived from high-risk asthma

patients in Hinton and Edson, Alberta (identified through all 4 Hinton pharmacies and 1 pharmacy in Edson). Hinton and Edson are rural communities, both having populations of less than 10,000 people. Each community is more than 200 km from the nearest tertiary care centre.

The community pharmacists were responsible for recruiting patients who met the inclusion criteria. Patients were eligible for inclusion if they had a self-reported diagnosis of asthma, were 17 to 54 years of age, and were considered at high risk. High-risk asthma patients were defined as those who had had an ED visit or hospital admission due to asthma in the previous 12 months or who had used more than 2 canisters of inhaled  $\beta_2$ -agonist in the previous 6 months, which far exceeds the definition for asthma control as outlined by the Canadian guidelines.9,10 Patients were excluded if they were not responsible for administering their own asthma medications, were unable to understand English, were unavailable for 6-month follow-up, or did not provide written informed consent.

Randomization was accomplished through an Internet randomization service provided by the

Epidemiology Coordinating and Research (EPI-CORE) Centre and the Centre for Community Pharmacy Research and Interdisciplinary Strategies (COMPRIS) at the University of Alberta. Randomization was stratified by centre.

Subjects assigned to the intervention group received education on asthma, assessment, and optimization of drug therapy by the pharmacist, and referral to an RT and/or physician as needed. The education component included insFinancial support was provided by Canadian Institutes of Health Research, Institute of Health Economics, University Hospital Foundation, and ASTHMA Study (Alberta Strategy to Help Manage Asthma).

This study was presented in part at the Canadian Association for Population Therapeutics Annual Conference, Quebec City, Quebec, March 30 to April 1, 2003, and at the Canadian Pharmacists Association Annual Conference, Quebec City, Quebec, May 28–31, 2005.

## Key points

- This study examined whether pharmacists could make a difference in how patients with asthma manage their condition.
- The hypothesis was that pharmacists could identify patients at high risk for asthma-related morbidity through refill records and could improve care.
- All patients improved their asthma control, but there was no difference in control between the two groups.
- Patients in the intervention group used fewer courses of oral steroids.
- Patients who received a written action plan did better than those who did not.

truction on all asthma medications, with a focus on the development of a written action plan. Optimization of drug therapy included an assessment of medications by the study pharmacist in accordance with the Canadian asthma guidelines.<sup>9,10</sup> A physician referral form was faxed to the patient's family physician identifying the patient as being at high risk and providing recommendations regarding current asthma therapy; a copy of the patient's written action plan was included. Patients were referred to an RT within 1 week of randomization for administration of the Asthma Control Questionnaire (ACQ),<sup>19</sup> measurement of FEV<sub>1</sub>, and reinforcement of education. Patients in the intervention group had a follow-up visit with the pharmacist at 2 weeks and at 1, 2, 4, and 6 months. Follow-up appointments with the RT occurred at 2 and 6 months.

The usual care group was given an asthma education booklet and general advice as needed. Patients were referred to an RT within 1 week of randomization for measurement of FEV<sub>1</sub>. The usual care group had a follow-up visit with the pharmacist at 2 and 6 months. Follow-up in the usual care group included assessment of any outcome events and minimal education (assessment of inhaler technique and response to any questions). Administration of the ACQ and measurement of FEV<sub>1</sub> was performed at baseline and at 2 and 6 months.

The study protocol and consent forms were approved by the University of Alberta Health Research Ethics Board and the Community Research Ethics Board of Alberta.

The primary endpoint was a comparison of the difference between intervention and usual care groups in terms of the change in ACQ scores from baseline to 6 months.<sup>19</sup> The ACQ is comprised of 7 questions. The answers are summated and a total

score is calculated between 0 and 6 (0 indicating the best level of control, 6 indicating the poorest level of control). An improvement of 0.5 points or more is considered clinically significant. Secondary endpoints were comparisons between the intervention and usual care groups in terms of the number of ED visits and hospital admissions, the use of inhaled corticosteroid (at baseline and 6 months), the number of courses of oral steroid, and FEV<sub>1</sub> (at baseline and at 2 and 6 months).

All analyses were done using intention-to-treat principles. Univariate analyses were performed with Student's *t* test (for continuous dependent variables) and the Pearson chi-square test (for categorical dependent variables). For missing ACQ scores, the last value recorded was carried forward.

#### Results

A total of 70 patients were recruited, 34 in the usual care group and 36 in the intervention group (Figure 1). There were 9 early withdrawals from the study, 2 in the usual care group and 7 in the intervention group (p = 0.15, Fisher's exact test).

There were statistically significant differences between the 2 study groups with regard to the results of previous pulmonary function tests, inhaler technique, use of a peak flow meter at base-

> line, and unscheduled physician visits in the past 6 months (Table 1). Other commonly reported prognostic factors (age, sex) were not significantly different between the groups. Asthma was poorly controlled, as demonstrated by the baseline ACQ values (above 0.5).

> The mean change in ACQ at 6 months was 0.33 for the usual care group (standard error [SE] 0.17) and 0.43 in the intervention group (SE 0.15) (p = 0.66). In a multiple linear regression model controlling for age, sex, site, and factors not balanced at baseline, there was no statistically significant difference between usual care and intervention (Table 2).

None of the differences in secondary outcomes were statistically significant (Table 2). There were 6 ED visits or hospital admissions in each group during the study follow-up (p = 0.91). Use of inhaled corticosteroids increased in both groups to over 80% at 6 months, but there was no difference between the groups (82% in the usual care group, 83% in the intervention group, p =0.51). The difference in number of

#### Excluded n = 114Assessed for eligibility n = 185 Reasons: Not meeting inclusion criteria n = 92Randomization n = 71Refused to participate n = 22 Assigned to intervention n = 37Assigned to Received intervention usual care n = 34n = 36Received usual care Did not receive intervention n = 34 (patient did not sign consent) n = 1Incomplete data n = 2Incomplete data n = 7Reasons: Reasons No longer wished to No longer wished to continue n = 6continue n = 1Lost to follow-up n = 1Lost to follow-up n = 1Analyzed n = 36Excluded from analysis Analyzed n = 34

n = 1 (patient did not sign consent;

i.e., protocol violation)

## FIGURE 1 Flow of patients through the BREATHE study

courses of oral steroid prescribed approached statistical significance at 6 months (26.5% in the usual care group, 11.1% in the intervention group, p =0.08). There was minimal change in FEV1 from baseline to 6 months in both groups (change less than 3% in both groups, p = 0.22).

Compliance with some aspects of the intervention by the pharmacists and the RTs was poor. Only three-quarters of the intervention patients received a written action plan over the course of the study. Fewer than half of the patients received education about written plans at each pharmacy visit. Also, for more than half of the intervention patients, no treatment recommendations were made during the study. Follow-up was also poor, with less than twothirds of all patients completing the 6-month pharmacist and RT follow-up.

To determine if education about written action plans had an effect on outcome, we compared change in ACQ score among intervention patients who had been educated about action plans and those who had not. Intervention patients with a written plan (n = 27) had a greater improvement in ACQ than those who had not received a plan (n = 9) (p < 0.001).

#### Discussion

Previous research has revealed a number of care gaps associated with asthma management, including low use of inhaled corticosteroids and infrequent use of written action plans.<sup>48</sup> These care gaps represent areas that can be targeted with interventions to enhance asthma care.

The results of the BREATHE study were consistent for all measured endpoints, and there was no detectable difference in asthma outcomes between the intervention group and the usual care group. Supplementary analyses were conducted to explain the lack of differences. Reasons included imbalance between the study groups, contamination of usual care, and poor application of the intervention (low "dose").

The treatment groups appeared to be different at baseline. All unbalanced factors were controlled for in the multivariate analyses. These differences at baseline could be markers of various levels of asthma severity in the two groups. Despite statistical adjustment, there may be unknown prognostic factors, which could not be controlled for in the analysis, that played a role in the differences between the groups.

Contamination of the usual care group may have occurred, as the caregivers involved in the study were not blinded. As part of the study implementation, we met with all local physicians, RTs,

## TABLE 1Demographic characteristics and baseline<br/>data for patients in the BREATHE study

	No. (%) of patients or mean $\pm$ SD or SE	
Variable	Usual care ( <i>n</i> =34)	Intervention ( <i>n</i> =36)
Age (mean ± SD, yr)	38.7 ± 10.7	35.7 ± 10.2
Sex (no. and % females)	18 (52.9)	19 (52.8)
Achieved high school diploma or higher	27 (79.4)	27 (75.0)
Previous pulmonary function tests	22 (64.7)*	15 (44.1)*
Adequate inhaler technique	30 (88.2)*	24 (66.7)*
Use of a peak flow meter	11 (32.4) *	4 (11.1) *
Use of a spacer	8 (23.5)	8 (22.2)
Current smoker	10 (29.4)	11 (30.6)
Inhaled corticosteroid prescribed	26 (76.5)	25 (69.4)
Short course of oral steroids prescribed in previous 6 months	11 (32.4)	12 (33.3)
Unscheduled physician visit in previous 6 months	18 (52.9) *	10 (27.8)*
Hospital admission for asthma in previous 12 months	9 (26.5)	6 (16.7)
Baseline ACQ (mean $\pm$ SE)	1.91 (0.18)	1.45 (0.19)

SD = standard deviation, ACQ = asthma control questionnaire, SE = standard error. \*Statistically significant difference at p < 0.05.

and pharmacists to discuss the study design. As such, the intervention, or components of it, could have been administered to the usual care group or there may have been a Hawthorne effect (where knowledge of being studied influences behaviour). In particular, one site (where both pharmacists were certified asthma educators) probably had a high level of care for asthma patients before the study began. The benefits of the rigorous study design, most notably a higher causal inference, were

## Points clés

• Cette étude cherche à déterminer si les pharmaciens pourraient aider les patients souffrant d'asthme à mieux gérer leur maladie.

- L'étude s'appuyait sur l'hypothèse selon laquelle les pharmaciens pouvaient en examinant les renouvellements d'ordonnances repérer les patients asthmatiques à risque de morbidité élevé et améliorer les soins qui leur sont fournis.
- Tous les patients ont réussi à mieux contrôler leur asthme, mais il n'y avait aucune différence entre les deux groupes quant au contrôle de la maladie.
- Les patients du groupe d'intervention ont utilisé moins de stéroïdes oraux.
- Les patients qui ont reçu un plan d'action écrit ont obtenu de meilleurs résultats que ceux qui n'en avaient pas reçu un.

## Knowledge into practice

Use of written action plans, administered in a community pharmacy setting, appear to improve asthma control; however, further study in this area is needed. The results of this study can be used in future pharmacy practice research to improve study design, study implementation, and motivation of pharmacist involvement. felt to outweigh the risk of contamination.

The alternative to randomization by patient would have been randomization by site, to help reduce contamination by the pharmacist investigators. That method has been used in other health services research and studies of interventions performed by

pharmacists.<sup>16,20-22</sup> However, concerns would also arise with randomization by site. For example, controlling for differences in demographic characteristics and socioeconomic status would have been more difficult. In addition, from initial meetings, it was apparent that pharmacists would commit to involvement in the study only if given the opportunity to administer the intervention. Finally, randomization by site would not have controlled for contamination of usual care by physicians or RTs.

The sites did not apply the intervention uniformly. According to case report forms received, follow-up was poor, few asthma management rec-

Outcome	Crude analysis	Multivariate (MV) analysis	Variables controlled for in MV analysis
Change in ACQ at 6 months	<i>p</i> = 0.66	<i>p</i> = 0.91	Age, gender, site*
Inhaled steroid use at 6 months	OR 0.72 (95% CI 0.27–1.92) p = 0.51	OR 0.68 (95% CI 0.22–2.06) p = 0.50	Inhaler technique, ICS use at baseline
Change in FEV <sub>1</sub> (% of predicted)	<i>p</i> = 0.22	<i>p</i> = 0.40	Inhaler technique
Courses of oral steroids	OR 0.35 (95% CI 0.10–1.26) p = 0.11	OR 0.28 (95% CI 0.07–1.12) p = 0.08	Previous courses of oral steroid
ED visits or hospital admission	OR 0.93 (95% CI 0.27–3.24) p = 0.91	OR 1.08 (95% CI 0.27–3.24) p = 0.91	Previous ED visit or hospital admission

### TABLE 2 Results for primary and secondary endpoints

ACQ = asthma control questionnaire, OR = odds ratio, CI = confidence interval, ICS = inhaled corticosteroid, FEV<sub>1</sub> = forced expiratory volume in 1 second, ED = emergency department.

\*For the factors that were unbalanced at baseline (unscheduled physician visits, previous pulmonary function tests, inhaler technique, peak expiratory flow monitoring), only inhaler technique significantly added to the model (p = 0.04), and was therefore included in other multivariate models where it was clinically meaningful.

ommendations were made, and one-quarter of patients in the intervention group never received a written action plan, the focus of the intervention.

The follow-up completed at each site varied, with some sites having less than 30% follow-up at the time of the 6-month visit. The low rate of follow-up leads us to believe that the application of the intervention was also minimal at these sites. In a recent review of four studies of asthma care provided by community pharmacies, incomplete follow-up ranged from 18% to 45%.<sup>23</sup> Because research on pharmacy-based practice attempts to replicate real practice, slightly higher losses to follow-up would be anticipated than in an academic setting. However, poor follow-up makes the results more difficult to interpret and markedly reduces study power by reducing the effect size of the intervention.

Our analysis of another pharmacist intervention study showed that early recommendations have the most impact on outcomes.<sup>24</sup> The baseline and first follow-up visits are vital to achieving the desired outcome. The fact that for more than half of the intervention patients no other recommendations were made over the course of the study may have con-

tributed to the neutral findings of our study.

Patients in the intervention group who received a written action plan did significantly better than those who did not. During pharmacist training for the study, it was stressed that the standard doublingof-dose approach to inhaled corticosteroids should be applied in response to increasing symptoms. Recent data suggest that this approach may not be effective and that a quadrupling of inhaled steroid may be required for exacerbations.25 Other community pharmacy asthma interventions that have not included a written action plan have had poor outcomes.<sup>20,22</sup> Education-based interventions have been effective only if written plan and self-management components are included.26

Poor compliance with an asthma intervention among pharmacists was also reported by Weinberger et al.<sup>20</sup> In that study, the pharmacists did not effectively or consistently deliver the intervention. The authors of that study also published descriptions of the specific issues they encountered while working on their project.<sup>27,28</sup> They concluded that methods are available to help remove barriers to implementation of interventions; however, pharmacists need to take responsibility for delivering such programs as part of their jobs.<sup>28</sup> From our interactions with the pharmacists delivering the interventions in the present study, various degrees of commitment to the project were evident. This variation may have translated into poor application of the intervention.

In a logistic regression model controlling for previous courses of oral steroids, the difference between intervention and usual care approached statistical significance (odds ratio 0.28, 95% confidence interval 0.07-1.12, p = 0.08). This endpoint, which is a marker of asthma control, is not captured by the ACQ score. Courses of oral steroids reflect asthma exacerbations that may or may not have required an ED visit. One consideration in using courses of oral steroids as a marker is that intervention patients may receive steroids as part of their written action plan. Therefore, they may not have required the oral steroids for an exacerbation but might have had them on hand for future use. If this occurred in just one intervention patient, the true difference between the study groups in number of courses of oral steroids for asthma exacerbations would have been statistically significant (p = 0.04). Reduction in the use of oral steroids is often used as an outcome in clinical trials because it reflects urgent care needs.

#### Conclusion

In adult patients with a history of asthma, there was no difference in asthma control after a 6-month assessment, education, and referral program, relative to usual care. Overall, patients in both study groups improved their level of asthma control. There was an increase in the amount of inhaled corticosteroids prescribed for

teroids prescribed for patients in both the usual care and intervention groups. There was a trend toward a reduction in use of oral steroids among intervention patients.

La connaissance

L'utilisation de plans d'action écrits dans un

cadre de pharmacie communautaire semble

améliorer le contrôle de l'asthme; toutefois,

sont nécessaires. Les résultats de cette étude

peuvent être utilisés dans des travaux de

des études, ainsi que la participation des

des recherches plus poussées dans ce domaine

recherche futurs sur l'exercice de la pharmacie

pour rehausser la conception et la réalisation

en pratique

pharmaciens.

Although no differences were found between the study groups, the study had a number of positive outcomes. Unlike other community pharmacy interventions, this study was multidisciplinary in nature. This program allowed academics and primary health care providers from a rural setting to work together on a research project.

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