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Design paper

Improving asthma symptom control in rural communities: the design of the Better Respiratory Education and Asthma Treatment in Hinton and Edson study

Theresa Charrois[a], Stephen Newman[a], Don Sin[b], Ambikaipakan Senthilselvan[a], Ross T. Tsuyuki[b,*]

[a]*Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada*
[b]*Department of Medicine, University of Alberta, Edmonton, Alberta, Canada*

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Abstract

Methods: The prevalence of asthma in adults in the United States is approximately 7%, and 9% of asthma patients will require hospitalization each year. Many patients do not seek care, as they do not recognize overuse of beta-agonists as a risk factor for poorly controlled asthma. However, pharmacists are able to identify these patients through refill information on reliever medication prescriptions and potentially initiate community-management opportunities for these patients.
Design: The study is a randomized, controlled trial. Patients are randomized to intervention or usual care.
Study population: Patients are high-risk asthma patients (defined as having an ER visit or hospitalization in the previous year, or using >2 canisters of short-acting beta-agonist in the previous 6 months). They are identified through community pharmacies.
Objectives: The primary objective is to determine the effect of an education and referral intervention program initiated by community pharmacists, working with high-risk asthma patients, family physicians and respiratory therapists, on asthma control, as measured by the Asthma Control Questionnaire (ACQ). Secondary objectives include determining the effect of this program on ER visits/hospitalizations, inhaled corticosteroid use, courses of oral steroids and FEV_1.
Intervention: The intervention includes patient education, assessment and optimization of drug therapy, and physician referral as needed. Patients are referred to a respiratory therapist within 1 week of randomization

* Corresponding author. EPICORE Centre, Suite 220, College Plaza, 8215-112 Street, University of Alberta, Edmonton, Alberta, Canada T6G 2C8.

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for measurement of FEV_1 and reinforcement of education. Patients assigned to usual care receive written asthma information, referral to a respiratory therapist and usual pharmacy and physician care.
Unique aspects: The design of the Better Respiratory Education and Asthma Treatment in Hinton and Edson (BREATHE) study is unique, given the multidisciplinary involvement, rural and community based, pharmacist initiated and targets specifically high risk patients. We believe that this study will show that management of asthma patients, involving the major role-players in their asthma care, will improve their asthma control.

Keywords: Asthma; Outcomes research; Pharmacists; Patient education; Study design; Delivery of health care

1. Introduction

1.1. Burden of illness

In the United States, the prevalence of asthma in adults is estimated at 7%, and 26% of adults report wheezing in the previous 12 months [1]. Importantly, several studies have shown a significant trend in increasing asthma prevalence across all age groups [2–5].

Morbidity from asthma can be defined in several ways; however, it is most commonly described in the literature by emergency room visits and hospitalizations. In the US, 9% of people with asthma require hospitalization each year [1]. This contributes significantly to the direct health-care costs associated with asthma, which is estimated at over US$6 million a year [6]. Another important asthma morbidity measure is health-related quality of life. People with asthma have significantly poorer ratings of health status compared to non-asthmatics [7].

1.2. Care gaps

Less than optimal application of proven efficacious asthma therapies (care gaps) can lead to poor patient outcomes, such as increased health-care utilization, decreased quality of life and lost days at work or school [8,9].

Inhaled corticosteroids are the cornerstone of asthma management as the first-line controller medication for mild persistent to severe asthma [10]. Inhaled corticosteroid use has been shown to be much lower than the guidelines recommend for patients with a history of high-risk events and severe asthma. Inhaled corticosteroids are underused, with approximately 30–40% of patients not receiving them [9–12]. Underuse of inhaled corticosteroids is associated with poorer outcomes such as increased hospitalizations, emergency room (ER) visits and mortality [13–15].

Asthma education is an essential component of asthma therapy, however, is not consistently provided to patients [10]. Education provided by physicians is often lacking, and should be supplemented with educational support from other health-care professionals [8,10]. Education should include reinforcement of appropriate medication use, environmental controls and a written action plan [10,16].

A written action plan is a self-management plan that advises patients to adjust their medications in a predetermined manner, depending on their symptoms and/or peak flow measurements. Written action plans can decrease asthma-related morbidity and potentially mortality [16–18]. Patients without a written

action plan are up to four times more likely to be admitted to hospital [17]. Written action plans have been shown to reduce lost work and school days, unscheduled physician visits, ER visits, nighttime symptoms and improve lung function [16].

Another issue in providing asthma patients with optimal asthma therapy is the overestimation of asthma control by both providers and patients [19–23]. In one study 77% of family physicians believed they were usually able to achieve asthma control, however a survey of symptoms found that only 24% of patients were at acceptable levels of control, as defined by the Canadian consensus guidelines [21]. Patients' perception of asthma control does not match disease severity. In one survey, 50% of patients who had severe persistent symptoms believed their asthma was controlled [20]. This difference between patient perception and actual level of control may be due to a poor understanding of what can be expected from asthma medications and how asthma control is defined.

1.3. Pharmacist intervention

Within the last 15 years, the scope of pharmacy practice has changed from a primarily dispensing role to one of a primary health-care provider. Pharmacists are actively involved in therapy assessment, patient education and provision of drug information.

A number of studies have been published investigating the evolving role of pharmacists and their involvement with community-based asthma patients. Asthma patients are more satisfied with their pharmacy care if they believed their pharmacist was able to help them manage their asthma [24]. However, the primary goal of asthma therapy is not patient satisfaction, but rather, better control of symptoms and decreased hospitalizations. Several studies have been conducted that focus on asthma education and the role of the pharmacist. The majority of these studies have been non-experimental or quasi-experimental designs, the sample sizes are very small and the outcomes have primarily been non-clinical. Endpoints that have been considered in these studies include prescription costs, inhaler technique, peak expiratory flow (PEF) values and courses of oral steroids [25–28]. Most of these endpoints measure process and structure related outcomes, rather than clinical outcomes [29].

Recently, a large trial was published that included asthma patients in a community pharmacy setting [30]. Although the study was randomized, there were several weaknesses identified with this trial [31–35]. Firstly, the community pharmacy was the unit of randomization, therefore socioeconomic factors, which are important confounders in asthma control, may not be evenly distributed between the study groups. Secondly, the intervention was only an educational program, as the pharmacists made no recommendations regarding therapy. Thirdly, the endpoint included results for both chronic obstructive pulmonary disease (COPD) patients and asthma patients, a rather heterogeneous group of patients. Finally the pharmacists did not routinely administer the intervention (i.e., the 'dose' of the intervention was low and inconsistent).

Another trial conducted in community pharmacies in British Columbia, Canada has shown promising results; however, there are some issues with design and interpretation [36]. Although the outcomes selected for the study were primarily clinical (symptom scores, hospitalizations, peak flow readings), there were large losses to follow-up, which limit the ability to draw conclusions from this study. Of 631 patients who consented to participate in the study, only 225 patients were analyzed for outcomes. These lost patients may be systematically different from the participants who remained in the study. This study also had some design issues, such as limited generalizability (many of the pharmacists were certified asthma educators), a randomization scheme that included clustering some

pharmacists by geographic similarity, but not all, and finally utilizing a patient client survey that had not been previously validated.

To date, there have been no published randomized controlled trials of community pharmacist intervention that have been shown to impact positively on asthma control. To build upon the published research on pharmacist interventions in asthma care, we designed a community intervention study that included a multidisciplinary component, a clinical endpoint, both educational and therapeutic interventions, and randomization by patient.

2. Methods

2.1. Design

The study design is a prospective randomized, controlled trial. Patients are randomized to community-management intervention (including pharmacists, respiratory therapist and family physicians) or usual care.

2.2. Setting

The study is conducted in two rural communities in Alberta, Canada (Edson and Hinton). The communities both have populations of less than 10,000 and are over 200 km away from any tertiary care centres.

2.3. Study objectives

The primary objective of the study is to determine the effect of an education, assessment and referral intervention program initiated by community pharmacists, working with patients, family physicians and respiratory therapists, on asthma control, in patients with poorly controlled asthma.

The secondary objectives are to determine the effect of an education, assessment and referral intervention program by community pharmacists on ER visits/hospitalizations, inhaled corticosteroid use, courses of oral steroids and forced expiratory volume in 1 s (FEV_1).

2.4. Patients

The sample is derived from high-risk asthma patients in Hinton and Edson, Alberta, Canada (from all four local Hinton pharmacies and two pharmacies in Edson). Patients who have a diagnosis of asthma, are 17–54 years of age, and are considered high risk are eligible for participation in the study. High-risk asthma patients are defined as patients who have had an ER visit or hospitalization due to asthma in the previous 12 months, or use of more than two canisters of inhaled beta-2 agonist medication in the previous 6 months.

Patients are excluded if they are not responsible for administering their own asthma medications, unable to understand English, are unavailable for 6-month follow-up, or do not provide written informed consent.

2.5. Recruitment

The community pharmacists are responsible for recruiting their patients that fit the inclusion criteria. They screen patients by their pharmacy refill records to identify overusers of beta-2 agonists. The

hospital pharmacist identifies the patients who have been hospitalized or seen in the emergency room for asthma. With the patient's verbal consent, the hospital pharmacist then forwards this information to that patient's local community pharmacy for follow-up and potential recruitment into the study. The community pharmacist investigators are responsible for obtaining written consent prior to randomizing the patient to treatment groups.

After ensuring the patient meets the eligibility requirements for the study and written consent is obtained (as approved by the University of Alberta Research Ethics Board), the patient is randomized by an internet randomization service through the Epidemiology Coordinating and Research (EPICORE) Centre, University of Alberta. As 2 sites do not have internet access, sealed envelopes are provided for randomization. To help ensure balance, randomization is done in blocks of six and stratified by site.

2.6. Treatment Groups

2.6.1. Intervention

Subjects assigned to the intervention group receive education on asthma, assessment and optimization of drug therapy, respiratory therapist referral and physician referral as needed.

The education component includes medication teaching on all asthma medications, inhaler technique assessment/education, provision of written asthma education materials and development of a written action plan. The written action plan is based on the Canadian guidelines and has been developed and approved by the local pharmacists, physicians and respiratory therapist at the first investigators' meeting [10] (Fig. 1). The educational component is initiated by the pharmacists and reinforced by the respiratory therapist.

Optimization of drug therapy includes an assessment of medications by the study pharmacist in concordance with the Canadian asthma guidelines, in particular, ensuring all patients are prescribed an inhaled corticosteroid [10]. An assessment of adherence to current drug therapy helps determine if the patient is not taking their current therapy optimally.

Patients are referred to their physician if therapy adjustments are suggested, as determined by the drug therapy assessment. A physician referral form is faxed to the patient's family physician identifying patients as high-risk and includes any recommendations to the physician regarding current asthma therapy (based on the Canadian guidelines for the treatment of asthma) and the education being provided to the patient, including a copy of the patient's written action plan (Fig. 1). Furthermore, patients are referred to a respiratory therapist within 1 week of randomization for measurement of FEV_1 and reinforcement of education.

2.6.1.1. Follow-up by pharmacist. Follow-up for the intervention group includes a follow-up telephone call at 2 weeks by the pharmacist to determine if patients in the intervention group have made an appointment to see their family physician (if required) and to reinforce education. As well, they ensure that the patient has seen the respiratory therapist. The intervention group patients have follow-up, by the pharmacist, at 1, 2, 4 and 6 months for educational reinforcement, medication assessment, assessment of outcome events and reassessment of written action plan.

2.6.1.2. Follow-up by respiratory therapist. The respiratory therapist administers the Asthma Control Questionnaire at 2 and 6 months [37]. There are 2- and 6-month follow-up appointments with the

Reliever Medication: _____ **Preventor Medication:** _____

GREEN ZONE	YELLOW ZONE	RED ZONE
• I do not wheeze, cough or have trouble breathing with activity. • I do not wake at night because of my asthma. • I use my reliever medicine 4 times per week or less, except before exercise. • _____ Peak flow is above (80%) _____	• I wheeze, cough or have trouble breathing that goes away when I take my reliever medicine. • I have a cold or flu. • I wheeze, cough or have trouble breathing at night that goes away when I take my reliever medicine. • I use my reliever medicine once per day. • _____ Peak flow is above (60-80%) _____	• **Reliever medicine does not help, or last 4 hours.** • **Breathing is difficult.** • **I have trouble walking or talking.** • **My lips or nails turn blue.** • _____ **Peak flow is less than (60%)** _____
ACTIONS • Take preventor medicine _____ _____ puffs _____ times per day. • Take medicine _____ _____ puffs/pills _____ times per day. • Take reliever medicine _____ 1–2 puffs every 4–6 hours as needed. • Avoid triggers of asthma. • _____	**ACTIONS** • Take preventor medicine _____ _____ puffs _____ times per day. • Take medicine _____ _____ puffs/pills_____ times per day. • Take reliever medicine _____ 1–2 puffs every 4–6 hours as needed. • Avoid triggers of asthma. • _____	**ACTIONS** • Take preventor medicine _____ _____ puffs _____ times per day. • Take medicine _____ _____ puffs/pills _____ times per day. • Take reliever medicine _____ 1–2 puffs every 4–6 hours as needed. • ***Call 911* or go to the hospital, but donít drive yourself.** • _____ *My doctorís #* _____

		-		

Name _____ **Study #**

Date _____ **Dr.** _____

Fig. 1. Written action plan.

respiratory therapist for educational reinforcement, measurement of pulmonary function, and reassessment of the written action plan in conjunction with the pharmacist.

2.6.2. Usual care

The usual care group is provided with an asthma education booklet only and general advice as needed. The asthma education booklet entitled "Take a holiday from your asthma symptoms" (Astra Zeneca) was reviewed by asthma educators to ensure up-to-date, accurate information was included. Patients are referred to a respiratory therapist within 1 week of randomization for measurement of FEV_1.

2.6.2.1. Follow-up by pharmacist. The usual care group have follow-up with the pharmacist at 2 and 6 months. Follow-up includes assessment of any outcome events and minimal education (inhaler technique assessment). To address any concerns about provision of "usual care", the patients in the usual care group are offered the intervention after the 6 months of study.

2.6.2.2. Follow-up by respiratory therapist. Administration of the Asthma Control Questionnaire by the respiratory therapist occurs at 2 and 6 months. All patients have FEV_1 measured initially and at 2 and 6 months. The patients in the usual care group are offered the intervention after the 6 months of study.

2.7. Outcome measures

The primary endpoint will be a comparison of the difference in change in the Asthma Control Questionnaire (ACQ) scores from baseline to 6 months between intervention and usual care [37]. Secondary endpoints include comparison of the number of ER visits and hospitalizations, inhaled corticosteroid use (at baseline and 6 months), number of courses of oral steroid and FEV_1 (at baseline, 2 and 6 months) between the intervention and usual care groups.

2.8. Sample size

Sample size was calculated based on the standard deviation of scores for change in asthma control using the ACQ, a continuous response variable [37]. A clinically significant change in score is considered 0.5 (Juniper EF, personal communication) and a standard deviation of 0.24 was used in the calculation, based on the validation study (37). Therefore, for a power of 90% and a two-tailed alpha of 0.05, the required sample population is 25 patients per group. To account for losses to follow-up and to increase power for secondary endpoints, 35 patients per group will be recruited.

2.9. Pharmacist training and support

Training of pharmacists focuses on key concepts of self-management, appropriate drug therapy and patient monitoring. A previously developed and evaluated program called the Asthma Community Pharmacist Training Trial (ACTT) was utilized for the training [38]. In this trial, pharmacists were randomized to an interactive, activity and case-based program that focused on patient assessment, or delayed asthma education program. After the training session, standardized patient actors using standard patient scenarios approached pharmacists unknowingly in their pharmacy. The evaluation study showed that pharmacists who received the ACTT training were significantly better at facilitating plans for the

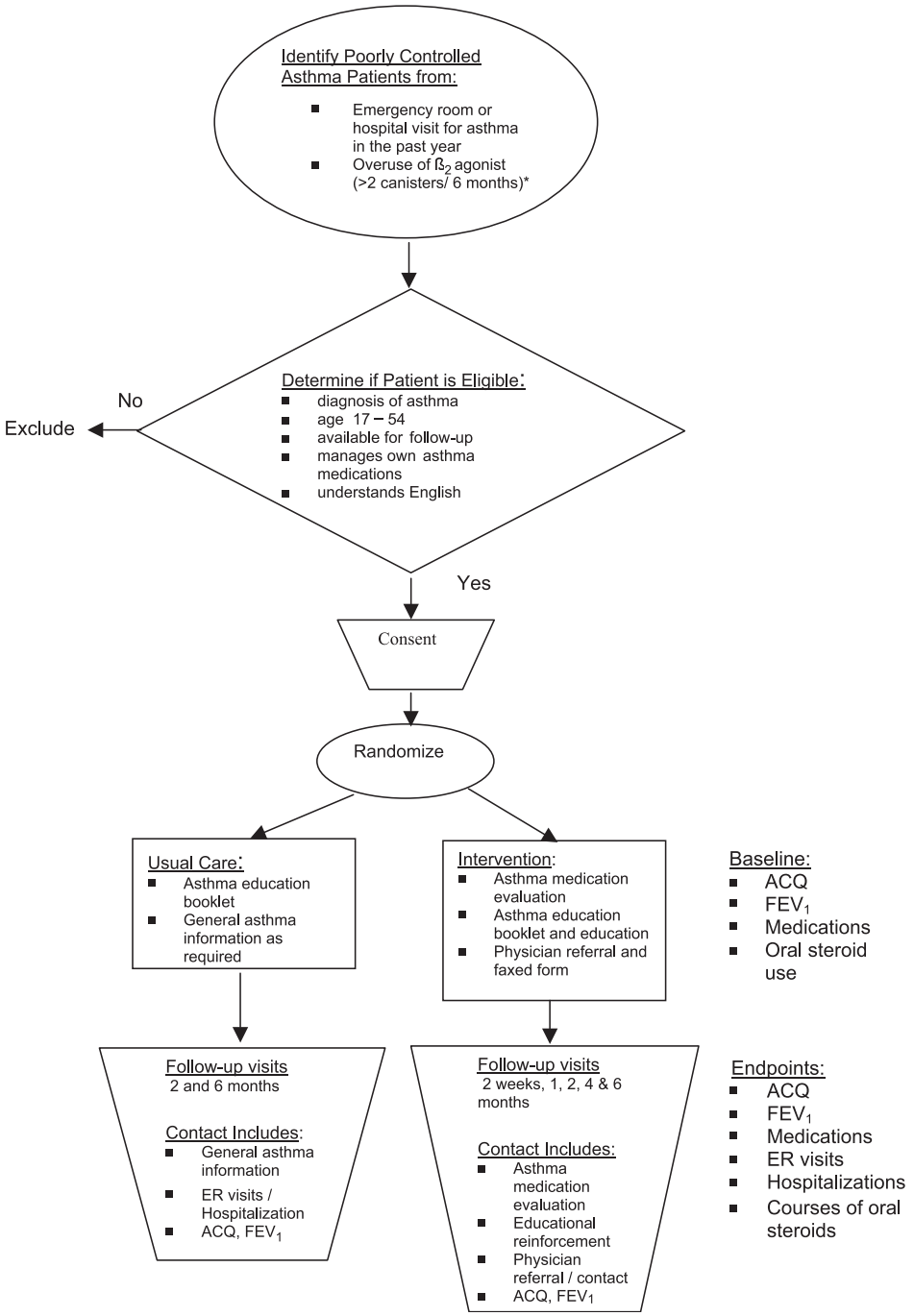

Fig. 2. Study flow diagram.

standardized patients, especially regarding the underuse of corticosteroids and overuse of short-acting beta-2 agonists. Better Respiratory Education and Asthma Treatment in Hinton and Edson (BREATHE) takes this study a step further to quantify this effect on a clinical measure, asthma control.

The training program does not focus on therapeutics, as do most continuing education programs. There is a therapeutic review and update; however, the main focus is patient assessment, patient interviewing and communication skills. Participants spend the afternoon involved in case scenarios with standard patient actors. Feedback, from trained reviewers and actors, is provided about the pharmacist's ability to identify drug-related problems in the case, as well as communication and interviewing techniques.

Pharmacists are offered a number of other support mechanisms during the course of the study. The research coordinator and assistant make periodic site visits to offer support, and ensure compliance with the protocol. Regular investigator meetings are scheduled to maintain contact between the study coordinators and all investigators, and update them on study progress. The study coordinator is available by pager. Newsletters are developed and mailed to all pharmacist investigators, respiratory therapist and physicians, on a monthly basis. The newsletters include updates regarding the study status, data quality and therapeutic reviews.

2.10. Study coordination

The study is coordinated and maintained through the Epidemiology Coordinating and Research (EPICORE) Centre, University of Alberta, and affiliated with COMPRIS (Centre for Community Pharmacy Research and Interdisciplinary Strategies). All data management, analysis and administrative support is coordinated through the study centre. See Fig. 2 for the study flow sheet.

3. Discussion

3.1. Design issues

3.1.1. Usual care

There is often expressed concern over the randomization of patients to "usual care". The patients who are randomized to usual care will actually be receiving better pharmacy care than usually provided to asthma patients in the pharmacy setting. Specifically, there will be an element of education, in the provision of written materials and assessment of inhaler technique, and there will also be follow-up and referral to a respiratory therapist, which is not a standard of care currently in pharmacy practice. All patients allocated to the usual care group will be offered the intervention at the end of the 6-month follow-up.

Any controversy over the ethics of randomization to usual care needs to be balanced with higher causal inference that can be concluded from the study results and resource implications of advocating a program of care that does not have proven efficacy. In this study, the usual care arm is unlikely to harm, as more care than usual is being offered.

3.1.2. Unit of randomization

Some investigators have used randomization by site rather than by patient. Even though the pharmacies are located in rural areas, there are still some demographic and socioeconomic differences in the populations served by each pharmacy. To control for these factors, randomization by patient, not pharmacy, was selected. Socioeconomic and demographic factors are associated with differences in

asthma control, therefore it is even more important to control for these known and unknown prognostic factors via randomization [39].

The pharmacists involved in the study felt it was unacceptable to be randomized to usual care. They are a motivated group of professionals, who all wanted to be involved in the intervention. Although there may be some risk of contamination of the usual care group, their level of usual care is at a higher level than what is normally provided. To offset this potential blunting of the treatment effect, the "dose" of the intervention provided needs to be high, therefore follow-up and reassessment is critical.

3.1.3. Primary outcome—ACQ

The ACQ is a clinically important endpoint as the patient's actual control of their disease is being measured. The ACQ incorporates both objective and subjective measures of control. Secondarily, the ACQ was selected over ER visits and hospitalizations, as the sample size required was more achievable. In discussion with pharmacists and physicians in Hinton, the rate of hospitalization and ER visits may be lower than anticipated, as the patients use the medical clinics often as a walk-in facility instead of going to ER. This highlights the importance of our preliminary meetings with pharmacists and physicians to learn about local practices. Therefore, by using a continuous variable (ACQ) as the primary endpoint, the sample size required is decreased.

3.1.4. Differential follow-up of the intervention group

The intervention group will be followed more closely than the usual care group. We anticipate that it is not just the education and assessment component that will improve asthma control, but the frequent contact with the patients. The differential follow-up is part of the intervention. Telephone follow-up as well as follow-up during refill visits to the pharmacy is relatively easy for pharmacists to do and will make the intervention easy to implement in community pharmacies.

3.1.5. Definition of high-risk

There is no standard definition of beta-agonist overuse in the literature, or definition of at what level of beta-agonist use a person is at higher risk of morbidity and mortality. Inappropriate beta-agonist use is associated with higher health-care utilization [40]. Our inclusion criteria for beta-agonist overuse far exceed what is in the current Canadian consensus guideline for the definition of asthma control (<4 puffs of reliever medication per week) [10]. Also, patients who have a prior ER visit or hospitalization have been shown to be at higher risk for a repeat ER visit [17].

3.2. Unique aspects of BREATHE

3.2.1. Rural, community based

Both Edson and Hinton are rural settings (Edson population 7800, Hinton population 9400), 200 and 300 km from the nearest tertiary care facilities in Edmonton. This offers a "closed" area in which to evaluate this intervention. Most patients are treated and followed up within the same town that they live and there is little involvement of any larger surrounding cities. Also, there are fewer health-care providers in a rural setting, which allows them to have good contact within the community.

If this model is proven to be beneficial in patients with asthma, it can be applied to other chronic disease states. Given the unique environment of rural communities, this model offers an alternative management system for patients, which involves a broader health-care concept.

3.2.2. Multidisciplinary

The physicians of the communities, as well as the hospital-based respiratory therapist were involved in development of the protocol and written action plan. Physicians approved the written action plan for initiation by the pharmacists. Given the multidisciplinary nature of the intervention, both respiratory therapist and physicians are integral in the provision of the intervention. Referral to other health-care professionals that can offer beneficial education and therapy to patients is unique in pharmaceutical care trials.

3.2.3. Pharmacist-initiated

Patients are primarily being identified based on refill information that is available and reviewed with prescription refills. This has tremendous potential as an entry point for patients into the health-care system. Physicians are often unaware of the amount of beta-agonist reliever being used and therefore are not necessarily aware of the patient's asthma control. Beta-agonist overuse provides an objective measure of control, as other methods of control assessment, such as self-reports of symptoms alone, have been shown to underestimate true determination of asthma severity [41]. This referral mechanism allows the physician to be aware of an important component in determining asthma control.

3.2.4. High-risk patient population

Patients included in the study are at higher-risk of morbidity and mortality then if all patients with a diagnosis of asthma were included [15,40]. Therefore, the program is targeted at affecting those patients who are the highest users of the health-care system in terms of asthma patients. Patients who present to ER for an asthma exacerbation often do not follow-up with their physician, and this program offers a system that attempts to overcome this care gap [8].

3.3. Study status

To date, over half of the study participants have been recruited. Ongoing support is offered to the study pharmacists through the research coordinating office to encourage continued recruitment and follow-up. Results are expected Fall 2004.

4. Conclusion

BREATHE offers an innovative research design and research support structure to investigate the role of pharmacists, as part of a multi-disciplinary team, in the management of high-risk asthma patients in the community on clinical outcomes.

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