



Drug-related problems and pharmacist interventions in a cohort of patients with asthma and chronic obstructive pulmonary disease



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ABSTRACT

Background: Asthma and chronic obstructive pulmonary disease are preventable and treatable chronic airway diseases with high incidence and prevalence. Pharmacists and clinical pharmacy based pharmaceutical care services have positive impact on therapy outcomes.

Objective: The aim of this study is to describe drug related problems in a cohort of patients with asthma and chronic obstructive pulmonary disease and to assess interventions provided by the pharmacist to address these problems in a community pharmacy. **Method:** Study population consisted of patients with asthma and chronic obstructive pulmonary disease older than 18 years who visited the study pharmacy during the pre-determined six-month period. The patients whose disease control states were “not fully controlled” were included in our study for further steps. On the first interview, present and potential drug related problems were addressed, interventions were provided. Follow-up interviews were held one month and two months later than the first interview. **Results:** For the 44 patients with asthma, 59 drug-related problems and 134 causes for these problems were identified. Eighty-four interventions were made to resolve the problems; and 54.2% of the problems were resolved. For the 37 patients with chronic obstructive pulmonary disease, 60 drug-related problems and 128 causes for these problems were identified. Ninety-five interventions were made to resolve the problems; and 63.3% of the problems were resolved.

Conclusion: Pharmacists taking part in therapy and management of asthma and chronic obstructive pulmonary disease can help patients be more educated about their disease and medications; and improve disease control and therapy outcomes.

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1. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) cases are of growing concern worldwide and have become a substantial burden for healthcare systems [1]. Although effective drugs and evidence-based guidelines have been developed, many factors affect the success of therapy, such as the route of administration, skill in using inhaler devices and medication adherence [2]. Patients with asthma and COPD are mainly treated with inhalers [3,4]. For many patients, proper use of inhalers is difficult. Several studies

have demonstrated that 50–80% of patients fail to use their inhaler devices correctly [2,5–10]. Patients are often not aware that they use their inhalers inadequately, and often overestimate their own abilities [11]. Incorrect use of inhalers may lead to uncontrolled disease states, unwanted side effects and higher treatment costs. According to Fink and Rubin, \$5–7 million are wasted annually in the United States of America (USA) because of inhaler misuse [8]. National and international guidelines for asthma and COPD management state that inhalation technique should be assessed regularly, and corrected if inadequate [3,4]. In light of these recommendations, there is a need for studies exploring the effectiveness and frequency of patient education, with appropriate consideration for improving inhalation technique. The pharmacist's role in asthma and COPD treatment includes evaluating therapy results and benefits, referring to a physician when there are worsening signs, giving patient education on disease and medications, evaluating all drugs used by patients, checking drug

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interactions, providing interventions, monitoring inhaler use technique, interviewing patients regarding medication adherence, advising regular exercising, immunization and smoking cessation. Recent studies demonstrated that pharmaceutical care services improve drug adherence and health outcomes by focusing on inhalation technique and patient education [11–24]. This may also lead to enhanced disease awareness, changes in patients' beliefs and attitudes towards treatment and improved self-efficacy and control [25].

The aim of this study was to describe drug-related problems in a cohort of Turkish patients with asthma and COPD who were not fully controlled and assess the interventions provided by pharmacists to address these problems.

2. Material and methods

2.1. Ethical approval

Ethical approval was obtained from the Ethics Committee of Marmara University, Institute of Health Sciences, prior to commencement of this study.

2.2. Study population

All adult patients with asthma and COPD who visited the study pharmacy (Hastaneler Pharmacy in Sivas, Turkey) for their prescribed medicines during the pre-determined 6-month period (5th September 2011 – 5th March 2012) were informed of the study. The study population consisted of the patients who accepted to be involved in the study and signed the informed consent form. The exclusion criteria were being unable to communicate, being illiterate, having cognitive impairment and serious psychiatric conditions. Also, participants who could not be contacted at 1 and 2 months following the first intervention visit were excluded from the study.

2.3. Tools

Disease states were assessed by the Asthma Control Test (ACT) [26] or the Clinical COPD Questionnaire (CCQ) [27]. Patients with asthma with an ACT score <20 and patients with COPD with a CCQ score ≥ 3 were considered to be “not fully controlled” and were included in the further stages of the study.

Medications used by the patients were accessed through the Social Security Institution Medula® Pharmacy Provision system and/or from the prescription records of the patients. The medications already being used by the patients, as well as the duration between the refills, were investigated.

The Morisky Medication Adherence Scale (MMAS) [28] was used to assess the medication adherence of the patients at the initial visit. The four-item MMAS consisted of the following questions: “Do you ever forget to take your medicine?; Are you careless at times about taking your medicine?; When you feel better do you sometimes stop taking your medicine?; Sometimes if you feel worse when you take the medicine, do you stop taking it?”. Each question was scored as 0 for ‘yes’ and 1 for ‘no’. The total score ranged from 0 (low adherence) to 4 (high adherence). A total score of 4 indicated ‘high adherence with medication regimen’.

Drug-related problems (DRPs) were identified at the initial visit using the Turkish version of the PCNE Classification scheme for Drug-Related Problems v6.2. (http://www.pcne.org/upload/files/11_PCNE_classification_V6-2.pdf). This instrument has four areas: problems; causes; interventions; and outcome of intervention. With its hierarchical design each area has its domains: problems (4 domains: treatment effectiveness; adverse reactions; treatment

costs; others); causes (8 domains: drug selection; drug form; dose selection; treatment duration; drug use/administration process; logistics; patient; other); interventions (5 domains: no intervention; at prescriber level; at patient (or carer) level; at drug level; other); and outcome of intervention (4 domains: outcome intervention unknown; problem totally solved; problem partially solved; problem not solved). For each problem identified, 1–3 causes can be applied, 1–3 interventions proposed and one outcome is chosen during follow-up.

The following data were collected on the DRP-Registration Form: demographic features (age, gender); number of drugs taken; duration of the first visit; whether the problem is potential or manifested; who identified the problem (patient, physician, pharmacist); the type and cause(s) of the problem; interventions provided to resolve the problem; and the outcomes of the interventions.

Participants were requested to fill in the patient satisfaction questionnaires to evaluate the service given by the pharmacist at the end of the second month. This self-administered questionnaire was developed by the authors for this study and was not piloted. It consisted of seven questions on items listed in Table 7. The response options for the Questions 1–6 were “Yes; No; or Uncertain”. The seventh question had response options as “Physician; Pharmacist; or Nurse”; this question might have more than one answer.

Other tools employed included smoking cessation leaflets for patients with asthma and COPD, and written instructions for the use of inhaler devices and inhaler demonstration aids.

2.4. Interventions

The reasons for non-adherence in participants with low medication adherence scores were further investigated. They were asked detailed questions regarding their opinions and attitudes toward the medications, and when and how they used the inhaler devices. They were requested to demonstrate the application of the inhaler device and the incorrect and/or missing steps were recorded. The possibility or presence of drug–drug interactions and smoking status were reviewed and recorded.

Interventions provided included those aimed at improvement of adherence and inhaler use, ameliorating adverse effects, counseling on medications and disease conditions as well as smoking cessation. Written and oral information was supplied to the patients and the interventions were recorded.

The pharmacist contacted the patients face-to-face at the pharmacy at 1 and 2 months following the first intervention visit to assess the outcome of the intervention. The initial visit, and the subsequent visits took place at a private counseling area in the pharmacy. The intervention was considered successful if the DRP was totally solved. When there were several factors affecting the outcome, and only some of them could be addressed, the problem was considered partially solved. The problem was considered not solved if the problem still existed.

2.5. Statistics

SPSS was used for all statistical analyses (v.11.5 SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), while the nominal and ordinal variables were expressed as median (25–75 percentile), numbers (n) and percentages (%), when appropriate.

3. Results

Seventy-two patients with asthma were interviewed at the beginning of the study. Sixty (83.3%) patients were not fully

controlled (ACT score < 20) and were subsequently included in the study. Forty-four (73.3%) patients could be reached at the 1- and 2-month follow-up, and were subsequently included in the final analyses.

The mean age of the patients with asthma ($n = 44$) was 52.4 ± 11.9 years (range: 30–84), with 79.5% female. The mean duration of the first visit was 16.2 ± 3.3 (range: 10–25) minutes. Four of the patients with asthma reported that they were smoking.

Seventy-nine patients with COPD were interviewed at the beginning of the study. Fifty-two patients (66%) were not fully controlled ($CCQ \geq 3$) and were included in the study. Thirty-seven of these patients (71.2%) could be reached at the 1- and 2-month follow-ups and so were included in the final analyses.

The mean age of the patients with COPD ($n = 37$) was 65.9 ± 10.5 years (range: 46–87), with 46% female. The mean duration of the first visit was 17.2 ± 6.2 (range: 10–50) minutes. Eight patients with COPD reported that they were smoking.

3.1. Patient medications

The total number of all medications including those prescribed for asthma was 4.6 ± 1.8 (range: 2–10) for patients with asthma (Table 1). All patients were on inhaled glucocorticoids: 27.3% high dose, 52.2% medium dose and 20.5% low dose. Approximately 57% of the patients were receiving a short-acting β_2 -agonist. The total number of all medications including those prescribed for COPD was 5.5 ± 2.0 (range: 3–11) for patients with COPD (Table 2). A majority (97.3%) of the patients were on inhaled glucocorticoids: 41.7% high dose and 58.3% medium dose. Seventy-three percent of the patients were receiving a short-acting β_2 -agonist.

3.2. Medication adherence

MMAS results for patients with asthma and COPD are presented in Table 3. The median (25–75 percentile) medication adherence score was 1 (1–3) for patients with asthma and 2 (1–3) for patients with COPD. Only five patients with asthma (11.4%) and four patients with COPD (10.8%) were highly adherent with their medication regimen.

3.3. Drug-related problems

3.3.1. Drug-related problems identified for patients with asthma

Fifty-nine DRPs were identified for 44 patients with asthma, of which 93% were manifested and 7% were potential. A majority of these problems (98%) were identified by the pharmacist, while the rest (one problem regarding adverse effects) was identified by the patient. A majority of the problems (96.6%) concerned 'treatment effectiveness' (not optimal drug treatment effect). The main causes of DRPs were related to drug use process ($n = 57$) and the patient ($n = 37$). Each problem could have more than one cause, and at most, three causes were identified for each problem. A total of 134 causes were identified for 59 problems (Table 4).

Table 1

Medications used for the control of asthma ($n = 44$).

Combination	n (%)
Montelukast + LABA + IGC + Theophylline	6 (13.6%)
Montelukast + LABA + IGC	25 (56.8%)
Montelukast + IGC	1 (2.3%)
Theophylline + IGC	1 (2.3%)
LABA + IGC	11 (25%)

LABA: long acting β_2 -agonist; IGC: inhaled glucocorticoid.

Table 2

Medications used for the control of chronic obstructive pulmonary disease ($n = 37$).

Combination	n (%)
Tiotropium + LABA + theophylline + IGC	17 (46%)
Tiotropium + LABA + IGC	14 (37.8%)
LABA + IGC + theophylline	1 (2.7%)
LABA + IGC	4 (10.8%)
Tiotropium + LABA	1 (2.7%)

LABA: long acting β_2 -agonist; IGC: inhaled glucocorticoid.

3.3.2. Drug-related problems identified for patients with COPD

Sixty drug-related problems were identified for 37 patients with COPD, with 88% of the problems manifested, while 12% were potential. A majority (95%) of these problems were identified by the pharmacist, while the rest (three problems regarding adverse effects) were identified by the patient. All of the DRPs concerned 'treatment effectiveness'. The main causes of the DRPs were related to drug use process ($n = 57$) and the patient ($n = 32$). Similarly, each problem could have more than one cause, and at most, three causes were identified for each problem. A total of 128 causes were identified for 60 problems (Table 4).

3.4. Interventions provided

Each problem could have received more than one intervention, and at most, three interventions were provided for each problem. Interventions attempted for patients with asthma and COPD are presented in Table 5. A total of 84 interventions were provided for the patients with asthma and 95 interventions were provided for the patients with COPD. The outcomes of those interventions are presented in Table 6.

3.5. Patient satisfaction

The response rate to the questionnaire was 86.4% for participants with asthma and 83.8% for participants with COPD. Answers to the questions were as presented in Table 7.

3.6. Smoking cessation

Pharmacist counseling consisting of effective referral helped one of the four smoker patients with asthma and two of the eight smoker patients with COPD quit smoking during the study.

4. Discussion

Asthma and COPD are highly prevalent and preventable chronic airway diseases. Given the role of pharmacists in health care, our aim was to describe the drug-related problems in patients with asthma and COPD who are not fully controlled, and assess the interventions provided by pharmacists to address these problems.

According to GOLD and GINA guidelines [3,4], every step of asthma and COPD treatments requires a short-acting β_2 -agonist bronchodilator on an as-needed basis. In our study, 43% of patients with asthma and 27% of patients with COPD were not prescribed a short-acting β_2 -agonist. As short-acting β_2 -agonists are reliever drugs (not the controllers), the "not fully controlled" status of the disease was not attributed to the lack of short-acting β_2 -agonist prescription; therefore this was not noted as a drug related problem (as an untreated indication). It is unlikely that the lack of short-acting β_2 -agonists is due to withheld treatment by the physician. Instead, this may be due to medications being checked on the Medula® Provision System records. As such, it is possible that a medication could have been purchased without a prescription,

Table 3

The answers to the questions in the Morisky Medication Adherence Scale.

	Patient with asthma (n = 44)	Patients with COPD (n = 37)
Do not ever forget to take her/his medicine.	15 (34.1%)	12 (32.4%)
Is not careless at times about taking her/his medicine.	15 (34.1%)	13 (35.1%)
When feels better do not stop taking her/his medicine.	12 (27.3%)	10 (27%)
If feels worse when she/he takes the medicine, she/he does not stop taking it.	33 (75%)	30 (81.1%)

Table 4

The causes of the drug related problems in asthma and chronic obstructive pulmonary disease patients.

DRP Causes	Asthma n* (%)	COPD n* (%)
Drug selection		
• Synergistic/preventive drug required and not given	—	2 (1.6%)
Dose selection		
• Deterioration/improvement of disease state requiring dose adjustment	1 (0.8%)	—
• Drug dose too low	—	1 (0.8%)
• Pharmacokinetic problem requiring dose adjustment	—	2 (1.6%)
Treatment duration		
• Duration of treatment too long	2 (1.5%)	—
Drug use process		
• Inappropriate timing of administration and/or dosing intervals	1 (0.8%)	1 (0.8%)
• Drug underused/under-administered (deliberately)	30 (22.4%)	20 (15.6%)
• Drug overused/over-administered (deliberately)	2 (1.5%)	2 (1.6%)
• Drug not taken/administered at all	20 (14.9%)	27 (21.1%)
• Patient unable to use drug/form as directed	25 (18.7%)	31 (24.2%)
Patient		
• Patient forgets to use/take drug	38 (28.4%)	32 (25%)
• Other cause	15 (11.2%)	10 (7.8%)

*Number of identified causes was n = 134 for patients with asthma and n = 128 for patients with COPD.

which is possible in Turkey. It is also possible that a medication could be present at a patient's home without appearing on the medication record. Other reasons include situations where patients do not refill their prescriptions on time, patients forget or skip some of their medications when refilling the prescriptions, and possible inadequate communication between physicians and patients.

Medication adherence is the voluntary cooperation with prescribed timing, dosage and frequency of medications. Assessment of patient medication adherence using the Morisky Medication Adherence Scale demonstrated the necessity of improving

medication adherence in most patients in the current study. Only about 10% of patients were highly adherent. A high level of adherence to treatment is critical, especially in management of chronic diseases. To obtain better therapeutic outcomes, pharmacists are required to determine the causes of poor adherence and provide interventions. Counseling patients, educating patients and encouraging patients to be more involved in the decision-making process are effective strategies in improving medication adherence [3,4]. The positive impact of pharmacist interventions on medication adherence and therapeutic outcomes has been reported in many studies [29–33]. As the primary focus of this study was identification and resolution of drug-related problems, we have not assessed this impact.

In patients with asthma and COPD, the most frequent causes of DRPs were those associated with drug use process and medication adherence-related causes such as forgetting to take the medication, using more/less than required or not using medication at all. In our study, “drug underused/-administered” was identified more frequently than “drug overused/-administered” among the causes of DRPs. During interviews with patients, it was observed that most of the patients did not have enough knowledge of the drug's

Table 5

Interventions to the drug related problems in asthma and chronic obstructive pulmonary disease patients.

Intervention	Asthma n* (%)	COPD n* (%)
No intervention	0	0
At prescriber level	2 (2.4%)	2 (2.1%)
• Intervention proposed, approved by prescriber	2 (2.4%)	—
• Intervention proposed, outcome unknown	—	2 (2.1%)
At patient (or carer) level	68 (81%)	76 (80%)
• Patient (medication) counseling	59 (70.2%)	58 (61.1%)
• Written information provided only	1 (1.2%)	—
• Patient referred to prescriber	1 (1.2%)	4 (4.2%)
• Spoken to family member/caregiver	7 (8.3%)	14 (14.7%)
At drug level	8 (9.5%)	9 (9.5%)
• Instructions for use changed	8 (9.5%)	8 (8.4%)
• Dosage changed	—	1 (1.1%)
Other	6 (7.1%)	8 (8.4%)
• Written/oral information provided for smoking cessation	4 (4.8%)	8 (8.4%)
• Patient was warned against potential interactions	2 (2.4%)	—

*Number of provided interventions was n = 84 for patients with asthma and n = 95 for patients with COPD.

Table 6

Outcomes of the interventions for asthma and chronic obstructive pulmonary disease patients.

	Asthma n* (%)	COPD n* (%)
Not known	0	0
Solved	32 (54.2%)	38 (63.3%)
Partially solved	6 (10.2%)	10 (16.7%)
Not solved	21 (35.6%)	12 (20%)
• Lack of cooperation of patient	20 (95.2%)	12 (100%)
• Intervention not effective	1 (4.8%)	—

*Number of identified drug-related problems was n = 59 for patients with asthma and n = 60 for patients with COPD.

Table 7

Answers to the patient satisfaction questionnaire.

	Asthma (n = 38)	COPD (n = 31)
1. Was satisfied with the service provided by the pharmacist.	37 (97.4%)	31 (100%)
2. Have not received such a service from a pharmacy before.	34 (89.2%)	27 (87.1%)
3. Knowledge about his/her disease improved after this service.	26 (68.4%)	22 (71%)
4. Knowledge about his/her medications improved after this service.	37 (97.4%)	30 (96.8%)
5. Wants to receive such a service for other diseases	22 (57.9%)	14 (45.2%)
6. Would suggest this service to others	28 (73.7%)	24 (77.4%)
7. Prefers to receive medication related counseling from ...		
Physician	34 (89.5%)	24 (77.4%)
Pharmacist	37 (97.4%)	30 (96.8%)
Nurse	15 (39.5%)	12 (38.7%)

purpose, whether the drugs were preventers or relievers, the importance of preventive medications and their long-term effects. Hence, it was observed that patients underused inhaled glucocorticoids and other preventive medications.

In our study, “Patient unable to use drug or form as directed” was the cause of DRPs in 18.7% of patients with asthma and 24.2% of patients with COPD. During the interviews with patients, we used inhaler use instruction leaflets prepared by GOLD and we checked every step. The latter is important given the discrepancy between a patient's perception of the inhaler technique and what they actually do in day-to-day life. In the ranking of causes of DRPs assessed in our study, “Patient unable to use drug or form as directed” was third among all causes in patients with asthma, and second among all causes in patients with COPD. This situation shows that although patients were treated appropriately according to their disease state, the main reasons for lack of full disease control included non-adherence, insufficient knowledge about disease/medications and poor inhaler use skills. This appears to be the result of inadequate education from healthcare professionals and the lack of therapy monitoring.

The majority of pharmacist interventions were at patient/carer level. In both patients with asthma and COPD, the most frequent intervention was counseling. Counseling included giving information about medications, disease and drug use, explaining correct inhaler use technique thoroughly and providing inhaler use instruction leaflets prepared by GOLD. Studies showed that written instructions are not sufficient alone for inhaler device use training and that oral instructions and demonstration are necessary as well [34]. In our study, the pharmacist gave oral instructions along with inhaler use instruction leaflets and demonstrated the use of each device that patients were using. Afterwards, the pharmacist asked the patient to repeat the process until ensuring that the patient was using the inhaler correctly. These steps were repeated at each encounter (initial and subsequent 2 visits).

The reason for an intervention not being effective was ‘lack of patients’ cooperation’ for almost all of the cases. It was subjectively observed that some of the patients, especially the older ones were not very motivated about their treatments. They refused to quit smoking and adhere to their controller therapy. Also, some patients were not caring about the correct inhalation technique. These people represent those of the general population who are persistent to change.

In our study, the mean duration of the first visit for patients with asthma was 16.2 ± 3.3 (range: 10–25) minutes and the mean duration of the first visit for patients with COPD was 17.2 ± 6.2 (range: 10–50) minutes. The range of 10–50 min seems to be a long time for counseling. It should be noted that the initial visit took this much time; the time spent was not merely for counseling/education. As the vast majority of the patients were involving in a such a practice for the first time in their lives, it was difficult to explain the

study, the rationale of this new service and anticipated benefits especially to the older patients. Although, we have not recorded the time periods of the following visits, none of them exceeded 15 min. In the current performance evaluation system of the Turkish Ministry of Health hospitals, Pulmonary Diseases Physicians are expected, and obliged, to examine and interview one patient per 10 min. Within this consult, physicians need to assess history, evaluate laboratory and other results, and physically examine the patient within 10 min. Therefore, some important steps in medication counseling, inhaler use technique and smoking cessation intervention might be omitted because of a lack of time. By spending an extra 10–15 min per patient, pharmacists would be in a better position to comprehensively cover asthma or COPD management and adherence.

Other causes of DRPs assessed in our study were “Patient gets/takes drug at the wrong time”, “Pharmacokinetic problem” and “Pharmacodynamic interaction”. Pharmacodynamic interactions observed in our study were between smoking and inhaled glucocorticoids.

The efficacy of inhaled corticosteroids might be reduced in patients with asthma who smoke [35]. It is suggested that patients with asthma who smoke might require higher doses of inhaled corticosteroids for asthma control [36], as the response to inhaled corticosteroids is attenuated [37]. The pharmacokinetic problem observed in our study was between smoking and theophylline. Smoking increases and accelerates the clearance of theophylline significantly. Since theophylline has a narrow therapeutic index, smoking status should be taken into consideration in dose adjustments.

Patients who smoked were encouraged to quit by explaining the negative impact of smoking on disease and drugs, and by providing informative leaflets on smoking cessation. Patients were informed about smoking cessation products and directed to smoking cessation clinics. Following these interventions 25% of the patients quit smoking. The American Cancer Society Guide to Quitting Smoking [38] indicates that about 25% of smokers who use medicines can stay smoke-free for over 6 months. Counseling and other types of emotional support can boost success rates higher than medicines alone. The rate of smoking cessation achieved in our study is consistent with data stated in the ACA guide, but was even higher than that reported for other various methodologies including physician advice, pharmacologic intervention (monotherapy and combination therapy), social support, behavioral interventions and telephone quitlines [39–41]. Therefore, pharmacists may be more efficient at achieving smoking cessation and there should be more studies in this regard in future.

Patient satisfaction can be defined as the overlap of a patient's experience compared with their expectations, and is also related to the degree to which general and specific health care needs are met. Satisfied patients are more likely to comply with medical treatment

and therefore ought to have a better outcome [42]. In our study, we had a high response rate to the satisfaction questionnaire. The vast majority of asthma (97.4%) and all of the patients with COPD were satisfied with the service provided by the pharmacist. Additionally, 87.1% of asthma and 89.2% of patients with COPD have not received such a service from a pharmacy before, and 73.7% of patients with asthma and 77.4% of patients with COPD reported that they would suggest this service to others. These results suggest that patients are in need of care provided by pharmacists and pharmaceutical care services.

This study has several limitations. The major limitation of the study is that; as the primary focus of this study was identification and resolution of drug-related problems, we have not assessed the impact of pharmacist's input on patient outcomes. Therefore, data on improvement of clinical parameters is lacking. Another limitation is that; as the study was conducted at a single pharmacy the results may not fully represent those of the other practice centers. Besides, the small sample size is another drawback limiting the generalizability of the results.

5. Conclusions

Clinical pharmacists have a significant role to play in improving asthma and COPD management, which not only impacts on patients' lives, but also reduces the burden on the healthcare system. Our study has identified that ensuring patient education and correct medication technique are key to improved disease management. Importantly, in light of time restraints with physicians, patients are happy for these interventions to occur within the pharmacy settings.

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