Improving Drug Therapy for Patients with Asthma—
Part 1: Patient Outcomes

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Objective: To evaluate the effects of a therapeutic outcomes monitoring (TOM) program on selected process and outcome measures.

Design: Prospective, controlled, multicenter study. Setting: Community pharmacies throughout Denmark (16 intervention, 15 control).

Patients: Five hundred patients with asthma aged 16 to 60 years and treated in primary care. Intervention: TOM is a community-based program for pharmaceutical care. Using a structured, seven-step, cyclical outcome improvement process, TOM pharmacists identify and resolve (or refer) problems with drug therapy that, if not addressed, might result in therapeutic failure or adverse effects. Equal emphasis is placed on the patient's perspective (e.g., coping, control, and empowerment) and the professional's perspective (e.g., adherence, patient knowledge, and therapeutic problems). TOM requires cooperation among pharmacists, patients, and physicians.

Main Outcome Measures: Asthma symptom status, days of sickness, health-related and asthma-specific quality of life, use of health care services and resources, and satisfaction with health care and pharmacy. Intermediate Outcome and Process Measures: Peak expiratory flow rate (PEFR), knowledge of asthma and asthma medications, inhalation errors, and drug therapy problems in the TOM group.

Results: The mean individual differences for TOM and control patients were tested. Beneficial effects were found for the following outcome measures: asthma symptom status, days of sickness, and health-related and asthma-related quality of life. Satisfaction with health care and pharmacy varied throughout the course of the project, with no significant difference between groups at the final evaluation. Although not statistically significant, differences in use of services were considered to be clinically significant and encouraging. Beneficial effects were found for knowledge of asthma and medications, inhalation errors, drug use and drug therapy problems. No significant differences were found for PEFR.

Conclusion: The project demonstrated that therapeutic outcomes monitoring by community pharmacists is an effective strategy for improving the quality of drug therapy for asthma patients in primary health care.


Uncontrolled asthma remains a serious problem worldwide, despite improvements in asthma medications and other methods for managing the disease. The problem’s persistence can be attributed in part to ineffective implementation of asthma therapy, which can be attributed to inappropriate prescribing, but also to ineffective management of therapeutic outcomes, patient nonadherence, and lack of knowledge and skills on the parts of patients and caregivers, including health care professionals.1–4 These difficulties, however, can be viewed as part of a larger problem: The medication use process is complex, and management of this disease by focusing on isolated factors within the process has not solved the implementation problem.

Studies have shown that therapeutic guidelines, patient education, adherence enhancement, written action plans, peak-flow monitoring, symptom diaries, and integrated programs for self-management of asthma can improve patients’ knowledge, beliefs, behaviors, and use of drugs and other health care resources.2,5,7–17 However, the studies have not demonstrated that such single interventions positively affect outcomes such as disease status and quality of life. Systems changes involving multiple aspects of the process may therefore be necessary to achieve the best outcomes.
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Patient problems cannot always be attributed to a lack of knowledge and/or lack of adherence. Adult patients and caregivers make decisions about drug therapy based on their perceptions, experiences, and preferences, and should therefore be viewed as active participants in care.1,3,5-12

This active involvement of both patients and caregivers is an integral element of any systems-based strategy. Increasing the pharmacist’s involvement in patient care has been shown to reduce the number of hospital admissions and emergency department visits and improve health status and quality of life.18,19 Therapeutic outcomes monitoring (TOM) is a model for increasing pharmacists’ role in primary health care. TOM is based on the concept of pharmaceutical care, a patient-specific, continuous quality improvement program for optimizing drug use.20-22

The purpose of the Danish TOM project was to implement and evaluate an adaptation of the TOM program originally developed at the University of Florida. The prototype has been described in detail elsewhere.22 In brief, to promote improved outcomes, pharmacists use the TOM strategy to identify and resolve (or refer) problems with drug therapy that, if not addressed, might result in therapeutic failure or adverse events. The major elements of the TOM program are a patient care process, clinical record system, educational materials for pharmacists and patients, and descriptive material for patients and physicians.

The general objectives of the Danish program were to improve drug therapy management and outcomes by increasing the participation of pharmacists in drug therapy management and by promoting cooperation among pharmacists, patients, and general practitioners (GPs). The overall research hypothesis was that providing TOM services in Danish community pharmacies could cost-effectively improve the overall health status, clinical and psychosocial outcomes, and quality of drug therapy for patients with moderate-to-severe asthma.

To test this hypothesis, we conducted a 12-month controlled study comparing (1) process variables and patient outcomes, (2) medication use, (3) cost-effectiveness, and (4) participants’ opinions. This article presents results from the patient outcomes study. In Part 2, also appearing in this issue of JAPhA,23 we compare medication use by patients in the control and experimental groups. The cost-effectiveness analysis has been reported elsewhere.24 In addition, a study of participants’ opinions25 and a qualitative study of patients’ perceptions26 were performed after the controlled study in order to explain and deepen understanding of the results, make methodologic triangulations, and inform the further development of TOM programs.

Objectives

Our objective was to evaluate the effects of TOM on selected outcome and process measures of asthma care. Our outcome measures were symptom status, days of sickness, quality of life, use of health care resources, and satisfaction with health care and pharmacy. Our intermediate outcome and process measures were peak expiratory flow rate (PEFR), knowledge of asthma and asthma medications, inhalation errors, and drug therapy problems.

Methods

Design

The Danish TOM project was carried out as a prospective, controlled, multicenter study from August 1994 through August 1995. Before the actual intervention study was initiated, a development project and a pilot study were completed. In the development project, a TOM manual, based on a manual developed by the original TOM research team at the University of Florida,22 was written and tested for use in the Danish program. A formative evaluation using action research methods was carried out in four pharmacies to identify obstacles to implementation of the project and to identify more effective structures and processes than suggested in the initial manual.27 A revised manual was produced for the main study. During the subsequent pilot study, outcome measures and administrative procedures for data collection28,29 were developed and tested. The instruments are described below.

TOM (intervention) and control groups were established as geographically distinct, nonoverlapping sets of pharmacies, physicians, and patients in a nested experimental design; that is, intervention pharmacies worked solely with intervention patients.

Pharmacies

Pharmacies responding to an advertisement in Farmaci, the journal of the Danish Pharmaceutical Association, were matched in pairs and then assigned to either the intervention or the control group. Assignment was not random, because the goal was to identify and match motivated pharmacies in each county. Criteria for matching were pharmacy size, workload, location, and experiences with extended professional activities.

Each pharmacy designated one pharmacist and one pharmacy assistant to be responsible for the TOM service. Pharmacy assistants, who in Denmark are licensed following 3 years of formal education, instructed patients in inhalation technique and performed administrative functions. The pharmacies were paid by the project.

General Practitioners

The project group chose four GPs at random from a list of GPs in each pharmacy’s local area. GPs were informed of the project by letter. Those GPs chosen at random for active participation were informed of the aim of the project and told whether their patient belonged to the TOM or the control group. When originally identified GPs were not interested in participating in the project, other GPs on the randomized list were asked to participate. Additional GPs were chosen from the list when four GPs could not identify the desired 20 patients per pharmacy. GPs participated in patient selection (see below) but had no other specific project duties.
Patients
Each participating GP received a list of their patients who had purchased asthma medications at the participating pharmacy in their area during the 3 months preceding the selection period. The GPs confirmed asthma diagnoses for patients and excluded patients who had mild asthma, bronchitis, dementia, cancer, or AIDS; were in the terminal phase of any disease; were under 16 or over 60 years of age; were being continuously monitored by a specialist; were following special programs for patient education; were unable to speak, read, and write Danish; and/or were unable or unwilling to cooperate.

Patients were then randomly selected from a list of those who met all inclusion criteria (16 to 60 years of age, with moderate-to-severe asthma, using antiasthma drugs, and speaking and reading Danish). These patients were contacted by the pharmacy in cooperation with the GP and invited to participate in the study. The patients were informed about the aim of the study and told whether they would belong to the TOM or the control group.

All patients provided written consent before enrollment into the study. Patients were not compensated, but, at the end of the study, control group patients were offered a free medication review or educational program. The project was approved by all of the regional ethics committees in Denmark, and permission was also obtained from the Danish Data Protection Agency.

Interventions
The principal adaptation of the Danish TOM program was its equal emphasis on the patient’s perspective (e.g., coping, control, and empowerment) and the professional’s perspective (e.g., adherence, patient knowledge, and therapeutic problems). The TOM program was designed to foster cooperation among pharmacists, patients, and physicians. It uses a structured, cyclical outcome improvement process consisting of the seven steps presented in Table 1. Of necessity, the specific activities under each step will vary according to the pharmacist’s and physician’s professional judgment of each patient’s needs.

Patients in the TOM group were asked to visit their pharmacist once a month during the study year. During each visit, pharmacists recorded the patient’s inhalation technique, PEFR, and asthma symptoms. Daily peak-flow measurements and symptoms experienced, which had been recorded in the patient’s PEFR diary, were monitored at these encounters. Patients discussed with pharmacists their daily experiences with the disease together with possible solutions to any subjective problems.

Pharmacists in the control group provided services according to the Danish professional standards existing at the time of the study. These services consisted of dispensing prescribed medications, advising patients about medications, and answering patients’ questions. Control pharmacists did not provide patient-specific pharmaceutical care services.

Pharmacists’ Competence Development
A long-term strategy for developing TOM pharmacists’ competence was formulated to build motivation and sustainable expertise in terms of theoretical and factual knowledge as well as personal experience and skills. Pharmacists received a TOM manual (which included lists of procedures and record forms), a textbook on asthma management, and a self-study manual on asthma pathophysiology, therapy, and management. Pharmacists attended a 2-day training course before starting the program. Intervention pharmacists studied asthma pathophysiology and therapy, the TOM process, organization of a TOM practice, and cooperation with partners in primary health care. They also participated in simulated patient care (case studies). Control pharmacists heard a description of the project, but did not participate in the training. TOM pharmacists were asked to practice the use of the TOM process and their counseling skills with volunteers in their private network before beginning the actual project, and they received a videotape that demonstrated the service for repetition and discussion in the pharmacy. During the project, TOM pharmacists met every 3 months in discussion groups to consider potential improvements in their practice.

Measures
Data for the evaluation were collected at baseline and after 6 and 12 months of the intervention. At each of these times, patients filled out evaluation questionnaires at the pharmacy during evaluation sessions that were separate from the TOM encounter. Pharmacists in both groups were instructed in their data collection responsibilities for the evaluation. Outcome and process measures are summarized below.

Outcome Measures
Asthma symptom status was measured at each time using a validated, three-item symptom score (asthma morbidty index), consisting of occurrence of symptoms, occurrence of days of sickness, and nocturnal shortness of breath. Symptom status was classified as mild (1), moderate (2), or severe (3). Patients were instructed to rate each symptom’s present status, not the general severity of the disease.

Patients used a calendar to record days of sickness (which days of the month they felt too ill from asthma to work or carry out planned activities) and asthma-related use of health care resources (scheduled and unscheduled physician visits and telephone contacts, emergency department visits, and hospitalizations). Calendars were reviewed during the evaluation sessions.

Health-related quality of life (HRQOL) was measured using the Nottingham Health Profile (NHP), in a validated Danish version. The instrument has six subdomains: physical mobility, emotional reactions, energy, pain, sleep, and social isolation. Patients are asked to respond yes or no to each question. Answers are subsequently scored on a scale from 0 to 100, with lower scores corresponding to higher quality of life.

Patients’ asthma-specific quality of life was measured using a validated, 29-item Danish version of the Living with Asthma
Table 1. Steps in the Danish TOM Program

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Establish patient-pharmacist-physician relationship</td>
<td>Discussion of pharmacist's new role in asthma management and expectations about the actions of each member of the partnership</td>
</tr>
</tbody>
</table>
| 2. Collect patient data (patient interview) | a. The patient's perspective:  
- Open-ended questions about  
  - Everyday life situation  
  - Social, medical, and therapeutic histories  
  - Patient-perceived problems  
  - Satisfaction and needs  
  - Health care, pharmacy service  
  - Illness and treatment  
- The professional's perspective:  
  - Checklist questions about  
    - Activities of daily living  
    - Knowledge and attitudes  
    - General health status, symptom status, allergies  
    - Clinical measurements  
    - Drug therapy, history of treatment  
    - Adherence and coping strategies, medication use |
| 3. Identify and analyze drug therapy problems ("SOATP") | Subjective information: described by patient, e.g., perceived problems with asthma symptoms  
- Objective information: e.g., drug use, PEFR, inhaler technique, specific symptoms such as coughing or waking at night  
- Assessment: initially, assessment of patient asthma status and prescribed drug therapy; on follow-up, assessment of progress toward therapeutic objectives, e.g., changes in drug use  
- Therapeutic objective: establishment or reconsideration of therapeutic objective based on patient information; on follow-up, assessment of information relative to achieving therapeutic objective  
- Plan to achieve therapeutic objective |
| 4. Outline therapeutic goals | Discussion of short- and long-term goals. Patient agreement with goals was given high priority. |
| 5. Choose individual intervention and monitoring plan | The intervention plan could include the following services:  
- Check of PEFR, inhaler technique, asthma symptoms, and patient-perceived problems  
- Assessment of the total drug therapy  
- Assessment and monitoring of drug use and compliance  
- Referral to GP  
- Counselling on problem solving in everyday life  
- Education on asthma, medication, and self-management |
| 6. Implement monitoring and follow-up | Implementation of referrals, counseling, patient education, written information, according to plan |
| 7. Document and report to physician and patient | Documentation on TOM monitoring form; report to patient; report to GP |

GP = general practitioner; PEFR = peak expiratory flow rate; TOM = therapeutic outcomes monitoring.

Questionnaire (LWAQ). The scale is from 1 to 3, with a low score corresponding to a higher quality of life.

Satisfaction with health care services was measured with a 28-item questionnaire developed and tested by researchers at the Danish College of Pharmacy Practice (DCPP) and the University of Florida. The scale was from 1 to 4, and, in contrast to the other two instruments, high scores corresponded to greater satisfaction. The questions were divided into two subdomains: satisfaction with health care and satisfaction with pharmacy. Cronbach α for the total satisfaction score was 0.85. Satisfaction with the program itself was measured using another questionnaire filled out by the patients at the end of the study.

Intermediate Outcome and Process Measures

PEFR was recorded as the best of three measures on each evaluation day. Because patients usually visited the pharmacy in the afternoon, the measure may often have represented "best peak flow of the day." Use of a β₂-agonist before the measurements was not recorded.

A 17-item questionnaire developed and tested by DCPP and the University of Florida measured patients' knowledge of asthma and asthma medications. The scale was from −100 to +100, with higher scores indicating greater knowledge. The questionnaire probed three factors: disease knowledge, drug knowledge, and disease management. The full questionnaire had an acceptable internal consistency, with a Cronbach α of 0.81.
Number of inhalation errors, the only direct measure of behavior used in this study, was scored with an eight-item instrument for each inhaler type.\textsuperscript{33}

Drug therapy problems among patients in the TOM group were identified through a review of pharmacy records.

**Statistical Analyses**

We entered data into two independent data sets, which we then compared and reconciled. The study used a hierarchic structure, as illustrated in Figure 1. At the top level, the factors considered were "group" (TOM versus control), "pharmacy," "physician," and "patient." The only factor that was considered deterministic was "group"; all of the others were considered random effects. A fifth factor, "time," was crossed with all of the effect variables and examined on three levels (baseline, 6 months, and 12 months).

In some patients older than age 45, asthma may be complicated by the presence of chronic obstructive pulmonary disease. Therefore, we carried out a preliminary analysis comparing outcomes in patients older than 45 with those in younger patients.

Changes in the outcome variables from baseline to 12 months were calculated for each patient. Group means were then statistically compared between the TOM and control groups, except for resource use data (e.g., GP visits) (see below). These analyses were performed using nested analysis of variance (ANOVA). As our outcome measures do not provide continuous normally distributed data, a parametric ANOVA technique is not the obvious choice. However, nonparametric techniques do not easily lend themselves to the hierarchic design in this study. The ANOVA included tests for differences among pharmacies and among physicians, and allowed isolation of patient effects. The ANOVA is, in theory, equivalent to the Student $t$ test if "pharmacy" and "physician" effects can be considered negligible. For all analyses, we also present results from ordinary Student $t$ tests or Mann-Whitney tests.

We calculated 6-month changes and considered whether any could be attributed to cyclic or seasonal effects. Except for the satisfaction measure, no cyclic effects were evident; therefore, 6-month differences are not presented.

Use of health care services is presented in actual numbers for patients in the TOM and control groups, as means per patient and as ratio of use (RU = number of events per patient from the TOM group divided by number of events per patient from the control group).

Significance was set at $P < .05$. All analyses were performed using SAS or SPSS statistical software.

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**Figure 1. Study Design**

39 pharmacies showed interest in participating

- Matching in pairs; no randomizing; distribution in all Danish regions
- Randomizing
- 16 TOM pharmacies
  - Randomizing
  - 75 TOM GPs
    - Randomizing
    - 264 TOM patients
  - Intervention: TOM program
  - Evaluation: Separate collection of evaluation data
- 15 control pharmacies
  - Randomizing
  - 64 control GPs
    - Randomizing
    - 236 control patients
  - Intervention: Normal practice
  - Evaluation: Separate collection of evaluation data

GP = general practitioner; TOM = therapeutic outcomes monitoring.
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Results

The study included 16 TOM and 15 control pharmacies. The average participation rate among the GPs across all pharmacies was 69.2%, and the total number of participating physicians was 139. Of the 870 patients invited, 500 (57.5%) agreed to participate. A higher proportion of patients agreed to enter the TOM group (62.7%) than the control group (54.8%). During the study year, 20.8% of the TOM group patients and 13.6% of controls dropped out. The majority of the dropouts were young (78.2% ≤ 45 years), and equal proportions had mild (36.8%) and severe (35.6%) asthma symptoms at baseline. One patient died from lung cancer during the year. We did not record patients’ reasons for declining to participate or for dropping out. Age and sex of participating patients are presented in Table 2. Because the conclusions on the effect variables did not differ for the two age groups compared with the sample as a whole, the results are not presented for separate age groups.

TOM pharmacies had 10.3 visits per patient on average. Visits lasted an average of 41 minutes each.

At baseline, the TOM group had a better general HRQOL (NHP) than the control group (8.68 versus 11.31) (again, with low scores corresponding to higher quality of life). Baseline difference in asthma-specific quality of life (LWAQ) was negligible (1.58 versus 1.67).

Correlations were calculated among effect variables (age, gender, asthma symptom status, NHP, LWAQ, knowledge, satisfaction with healthcare, PEFR) for TOM and control patients separately. There were negligible correlations between age and the effect variables (0.12 to 0.35); therefore, no adjustment was made for age in subsequent analyses. Because the correlation coefficient between the individual effect variables was small, except for NHP scores and LWAQ, each variable was considered as an independent measure. Data are presented separately for both quality of life measures, even though the correlation coefficients were 0.66 (NHP) and 0.67 (LWAQ).

According to the nested ANOVA, there was a significant “pharmacy” effect for asthma symptom status (P = .024) and inhalation technique (P = .0001) for the first 6 months. A pharmacy effect was also found for knowledge of asthma and asthma medications (P = .031) for the second half-year, meaning that there were significant differences between TOM and control pharmacies for these variables. For LWAQ scores, there was a significant “physician” effect (P = .04) in the second half-year. This implies that comparisons of means for these variables should employ the nested ANOVA, which takes the hierarchical research design into account.

Outcomes

The mean scores of the patient outcome effect variables are presented in Table 3 for TOM and control patients, together with the mean individual differences from 0 to 12 months and P values for the nested ANOVA and t test or Mann-Whitney test.

Final Outcomes

Both groups improved their asthma symptom status during the year (Table 3). Mean asthma symptom scores for TOM patients improved by 0.47 (23%) from baseline in 12 months. The 12-month difference between groups was statistically significant. The improvement for control patients was 49% of the improvement for TOM patients.

The total number of days of sickness was 793 in the TOM group and 1,249 in the control group during the year (see Table 4). TOM patients reported about 60% as many sick days as did controls, and the difference was present from the beginning of the study period. For TOM patients, proportion of sick days per patient per month (PPPM) relative to controls (sick days PPPM TOM/sick days PPPM control) tended to decrease over the 12 months by about 5% each month. Over the last 4 months of the study, TOM patients reported about 25% as many sick days as patients in the control group (see Figure 2).

HRQOL, as measured by the NHP, improved in the TOM group by 3.8 scale units over 12 months, significantly more than in the control group. The improvement for control patients was 28% of the improvement for TOM patients. Concerning the NHI subdomains, scores for TOM group patients improved significantly over controls during the 12-month period in energy, sleep, and social isolation.

Both groups had a better asthma-related quality of life after the study year, but the TOM patients improved over 12 months by 0.17, significantly more than controls. Improvement for control patients was 47% of that for TOM patients.

Satisfaction with healthcare services (not TOM program satisfaction for intervention patients) increased by about 4% in the TOM group in the first 6 months; after 12 months, however, it fell

<table>
<thead>
<tr>
<th>Table 2. Distribution of Patients by Age and Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td><strong>TOM</strong></td>
</tr>
<tr>
<td>(57.6% women)</td>
</tr>
<tr>
<td><strong>Control</strong></td>
</tr>
<tr>
<td>(54.7% women)</td>
</tr>
</tbody>
</table>

TOM = therapeutic outcomes monitoring.
by about 2%. The 6-month increase was significantly different from the corresponding change in the control group ($P = .041$). Both groups showed about the same small decrease in satisfaction over the study year.

Use of health care services is summarized in Table 4. The number of GP visits per TOM patient per month relative to controls showed that, on average, over 12 months, TOM patients made GP visits about 1.4 times more often than did control patients. This difference was significant ($P = .012$). However, this higher use occurred predominantly in the early months of the study. The relative rate of GP visits began to decline after the fifth month, then declined by about 0.13 each month from month 7 until the end of the study (by least squares fit to the second 6 months data). This pattern suggests that TOM patients were more often actively referred to GPs in the first 5 months.

TOM patients used fewer of the remaining services listed in Table 4 than did control patients, but none of the differences attained statistical significance. For all six types of services combined, control patients had 1.94 service events per patient per year. TOM patients had 1.45 events, 34% fewer than control patients ($P = .07$ by two-tailed Mann-Whitney test).

**Intermediate Outcome and Process Measures**

Mean PEFRs were essentially unchanged for patients in both groups. The 1% improvement over baseline in the TOM group was neither clinically nor statistically significant ($P = .989$).

Knowledge of asthma and asthma medications was greater in both groups after the study year, but TOM patients improved by about 21 scale units, significantly more so than did controls ($P < .001$), who improved by 7 scale units. The improvement for control patients was 33% of that for TOM patients. At 6 months, the improvement was also significantly larger in the intervention group than in the control group ($P < .001$). A separate analysis was performed on all individual questions at baseline and after 12 months. Both TOM and control patients had higher general knowledge about asthma, and increased knowledge of asthma and sports and asthma and smoking. Patients tended to have poorer knowledge on how to use the various kinds of asthma medications, how to predict an asthma attack, and how to manage an attack.

Number of inhalation errors decreased for both groups during the 12 months. The change in number of errors per patient was significantly different between the groups, though, with the TOM group improving by about 90% from baseline in 12 months ($P < .001$). The improvement for control patients was 30% of that for TOM patients. The 6-month evaluation also showed a significantly larger improvement in the intervention group compared with the control group ($P < .001$). Effects on drug use patterns are reported in Part 2.23

Figure 3 shows the distribution of unresolved drug-related problems in the TOM group at baseline and at 12 months. This number was sharply reduced in all 11 categories of DRPs. We did not collect corresponding data from control patients.

**Target Groups**

As an exploratory analysis, we looked for patient characteristics associated with better-than-average improvements from the TOM program. Our purpose was to determine whether we could
Table 3. Results of the TOM Project

<table>
<thead>
<tr>
<th>Measure</th>
<th>Score</th>
<th>PValue*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline Mean (SEM)</td>
<td>12 Months Mean (SEM)</td>
</tr>
<tr>
<td>Asthma symptom status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 208)</td>
<td>1.99 (0.057)</td>
<td>1.52 (0.047)</td>
</tr>
<tr>
<td>Control (n = 201)</td>
<td>2.10 (0.056)</td>
<td>1.88 (0.060)</td>
</tr>
<tr>
<td>NHP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 209)</td>
<td>8.76 (0.84)</td>
<td>4.97 (0.65)</td>
</tr>
<tr>
<td>Control (n = 204)</td>
<td>11.39 (1.08)</td>
<td>10.32 (1.13)</td>
</tr>
<tr>
<td>LWAQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 209)</td>
<td>1.58 (0.026)</td>
<td>1.41 (0.028)</td>
</tr>
<tr>
<td>Control (n = 204)</td>
<td>1.68 (0.027)</td>
<td>1.60 (0.031)</td>
</tr>
<tr>
<td>PEFR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 208)</td>
<td>467.71 (8.05)</td>
<td>476.25 (7.92)</td>
</tr>
<tr>
<td>Control (n = 201)</td>
<td>446.89 (8.55)</td>
<td>445.73 (8.70)</td>
</tr>
<tr>
<td>Knowledge of asthma and asthma medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 209)</td>
<td>52.10 (1.24)</td>
<td>72.98 (1.07)</td>
</tr>
<tr>
<td>Control (n = 203)</td>
<td>52.05 (1.14)</td>
<td>56.91 (1.29)</td>
</tr>
<tr>
<td>Satisfaction with health care</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 206)</td>
<td>2.78 (0.024)</td>
<td>2.46 (0.012)</td>
</tr>
<tr>
<td>Control (n = 203)</td>
<td>2.79 (0.023)</td>
<td>2.49 (0.012)</td>
</tr>
<tr>
<td>Inhalation errors per patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOM (n = 207)</td>
<td>1.71 (0.13)</td>
<td>0.17 (0.045)</td>
</tr>
<tr>
<td>Control (n = 190)</td>
<td>1.21 (0.096)</td>
<td>0.75 (0.088)</td>
</tr>
</tbody>
</table>

ANOVA = analysis of variance; LWAQ = Living with Asthma Questionnaire; MW = Mann-Whitney; NHP = Nottingham Health Profile; PEFR = peak expiratory flow rate; SEM = standard error of mean; TOM = therapeutic outcomes monitoring.

*P values refer to the significance of changes in mean individual differences between groups for the measures from baseline to 12 months.

recommend that future TOM-type programs or services target asthma patients with particular characteristics. Analyses were performed on knowledge, PEFR, HRQOL, and asthma-specific quality of life. During the first 6 months, both TOM and control patients who had an asthma symptom score of 3 at baseline increased their knowledge significantly more than did patients with a baseline score of 1. The same effect was not seen for the entire study period. No other target groups could be predicted from the baseline and outcome variables analyzed.

Discussion

Patients in the TOM group had better final outcomes than patients in the control group. TOM patients had better asthma symptom status, fewer days of sickness, higher quality of life, and lower use of health care services. They did not, however, have greater satisfaction with health care services. The effect of TOM on PEFR was in the hypothesized direction, but was not significant. The number of unresolved DRPs fell in the TOM group. Evidently, educational mechanisms contributed, as indicated by improved knowledge and fewer inhalation errors. Referrals of TOM patients to GPs increased in the first 6 months, followed by a steady decrease in referral rates until the end of the study. Use of other health care resources decreased in the TOM group, but the numbers in both groups were too small to show statistical significance. Although not statistically significant, the differences in use of health care services were considered to be clinically significant and encouraging.

Patients in the TOM group improved their symptom status to a greater extent than did patients in the control group. A similar result was found in a German study. Our final participants’ evaluation supported this finding, revealing that 60% of the TOM patients perceived a general improvement in their disease. Compared with control patients, TOM patients showed a diminishing risk of sick days during the study year. Results have been mixed in relation to risk of sick days in other studies on asthma programs. A Canadian study on self-management found a decreased number of days lost from work in their intervention group compared with their control group, but a British study on patient education found opposite results. The TOM approach has thus been relatively successful. In our participants’ evaluation, about one-third of TOM patients reported that illness due to asthma was improved during the TOM project, and 65% reported that it was unchanged.

Quality of life, both health-related and asthma-specific, improved more in the TOM group than in controls. This finding is similar to results on the NHP in the Swedish study of effects of asthma education by Ringsberg et al. The GRASSIC study, on the other hand, reported no changes in the LWAQ among their asthmatic patients. The German Asthma TOM Project showed improved asthma-specific quality of life as well as generic quality.
Figure 3. Percentage of TOM Patients with Drug Therapy Problems at Baseline and After 12 Months

of life, as measured using the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36). A TOM project conducted in the Netherlands also showed improved asthma-specific quality of life but no improvement on the SF-36. To assess practical significance, the 12-month change in NHP score in the present study spans only 3.8 points on the 100-point NHP scale; however, it represents a 43% improvement over baseline. Results from the participant evaluation suggest that these results were clinically significant: 50% of the TOM patients perceived an improved quality of life after participating in the TOM project.

Satisfaction with care is becoming an important outcome indicator. In our study, satisfaction with health care services decreased in both groups by about 2% over the 12-month period. The 4% increase in satisfaction among TOM patients in the first 6 months may reflect initial acceptance of the TOM program by patients who remained in the study. In the participant evaluation and the qualitative study, some TOM patients reported dissatisfaction with the health care they received before exposure to TOM. The interviews also suggested that TOM patients' expectations may have increased during the study, which affects perceived satisfaction. About 90% of the TOM patients expressed satisfaction with specific elements of the program and with the efforts of the pharmacists. Having a personal contact at the pharmacy, someone who took the time to listen, was mentioned as a positive feature of TOM. This finding is consistent with those of other studies of asthma TOM. Some patients, however, had more consultations than they felt they needed in the second half-year of the study. Furthermore, in the qualitative interviews, TOM patients reported more health care needs (giving more details) than did control patients. This finding implies that the program had an educational effect in terms of raising patients' awareness of quality in health care, and this may in turn have changed the expectations of the TOM patients. This implication may explain the initial improvement and subsequent decrease in satisfaction with health care and pharmacy in general.

TOM patients had more GP visits than did controls in the first 6 months, and this result is consistent with TOM program recommendations for physician referral based on symptom assessment. It is possible that TOM pharmacists referred patients too readily, but it is equally likely that the drug therapy problems they identified in fact required referral. The outcome of increased referral rates is improved asthma management, although it is nonetheless possible that fine-tuning the TOM program could lead to such improvements without the additional GP visits.

Otherwise, exposure to TOM was associated with lower use of health care services over the year. Although the numbers of patients were too small to confirm these differences statistically, lower use was evidenced by lower rates of hospital admissions and physician services. Furthermore, use of some services was lower in the second 6-month period, suggesting that, like sick days and GP visits, the rate might have continued to fall had the program continued past its 12-month cutoff. It would be worthwhile to follow up these results with a longer study, perhaps using continuous performance indicators.

We found no significant differences for PEFR. A small American study reported improvements in morning PEFR for the self-management groups compared with controls. The German Asthma TOM Project showed improvements in FEV1, although
other intervention programs with ambulatory patients with asthma showed no changes. However, our measurements were not well controlled (see Limitations), and the results may therefore be equivocal. Analysis of TOM patients’ daily measurements showed that the mean values of their lowest peak flow improved from 346 L/minute (October) to 415 L/minute (June). Also, the average percentage of days with peak flow values under 80% of the patient’s best value decreased from about 20% to 10%. (These data are not available for patients in the control group.) These results suggest that the variation in peak flow decreased during the year. Thus, our process evaluation data indicate that “peak flow of the day” may not have been the most appropriate pulmonary function measure for this sample.

Numbers of inhalation errors were significantly decreased and asthma knowledge was significantly improved in the TOM group, consistent with the improvement in outcomes. Other authors have reported smaller reductions in morbidity associated with significant improvements in asthma knowledge. However, the relationship between knowledge and morbidity may not be a simple one. For example, only the German study involved efforts to identify and resolve drug therapy problems as well as to improve knowledge. Our analysis of responses to individual questions showed that still more knowledge—concerning how to use asthma medications, how to predict an asthma attack, and how to manage an attack—would be desirable.

The sharp reduction in the frequency of unresolved DRPs from baseline to 12 months in the TOM group suggests that the process of care changed, at least among TOM pharmacists. Data requiring professional judgment were not collected for patients in the control group; therefore, data on pharmacist-assessed DRPs are only available for TOM patients. However, we hypothesize that pharmacists’ recognition and resolution (or referral) of DRPs was one important mechanism that led to the improved outcomes among TOM patients seen in this study. Other studies have associated improved patient outcomes with similar processes.

Theoretically, preventable drug-related morbidity results from inadequate management of therapy, specifically, failure to recognize and resolve drug therapy problems before the patient

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Table 4. Days of Sickness and Resource Use in TOM and Control Groups—Total and Relative Use

<table>
<thead>
<tr>
<th></th>
<th>TOM Group</th>
<th></th>
<th>Control Group</th>
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<tbody>
<tr>
<td></td>
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<td>Events per Patient</td>
<td>No. Events</td>
<td>Events per Patient</td>
<td>RU</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days of sickness</td>
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<td>GP visits</td>
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</tr>
<tr>
<td>12 months</td>
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<tr>
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<tr>
<td>12 months</td>
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<td>0.067</td>
<td>13</td>
<td>0.068</td>
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</tr>
<tr>
<td>First half-year</td>
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<td>0.034</td>
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<td>0.021</td>
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<td>0.011</td>
<td>0.89</td>
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<tr>
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<tr>
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<td>10</td>
<td>0.048</td>
<td>12</td>
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</tbody>
</table>

GP = general practitioner; RU = relative use. TOM versus control; TOM: therapeutic outcomes monitoring.

*P-value = test for difference between means of monthly ratios per patient in the first and second half-years.

b Value not calculated because number in cell was not adequate for each monthly record.
experiences overt therapeutic failure or an adverse effect. Therefore, improving isolated factors, such as prescribing or patient adherence, may be less effective than making fundamental system changes directed at preventing drug-related morbidity in patients with asthma.20,21

Our analyses of antiasthma medication use (see Part 2)23 showed changes in the TOM group that were consistent with consensus guidelines,43 which may have contributed to the final outcomes.

Limitations

The design of this study imposed certain limitations. Geographically separated TOM and control pharmacies were necessary to avoid any overlap between the intervention and control groups. This limited the number of pharmacies available and had the practical effect of preventing random selection. Also, use of a nested ANOVA may have reduced statistical power by reducing degrees of freedom from the number of patients to the number of pharmacies. It was impossible to blind patients to the TOM intervention.

Participation was voluntary, so selection bias was possible. The pharmacists in the study had responded to an advertisement, and so were self-selected. Pharmacists who did not volunteer may have lacked sufficient time, interest, and self-confidence, all of which were prerequisites for participation. While these factors might have increased the magnitude of the effects of TOM, they would have been equal for the TOM and control groups.

The substantial nonacceptance rate by patients may have introduced unpredictable sampling bias. Participating patients may have felt more in need of care, which would limit generalizability. We intended to study a realistic patient sample, based on GP diagnosis and evaluation of exclusion criteria, rather than an ideal sample based on hospital confirmation of asthma diagnosis and severity and strict exclusion of "unclear cases" (i.e., focusing on the effectiveness perspective rather than the efficacy perspective). Therefore, when some patients were later discovered to have met some exclusion criteria, our strategy was to retain them in the study.

The statistical assumption was that only "group" was a determinist factor. The baseline analysis and target group analysis supported this assumption. Although the baseline analysis revealed some differences between the TOM and control groups, there was no evidence that these differences affected our results. An analysis of how asthma symptom status influenced decisions to drop out of the study showed no difference in status between dropouts and those who remained in the study. Dropouts, however, were mostly younger. We also know from pharmacists' reports that some of the healthiest patients dropped out, stating they did not need the service for the full 12 months.

Control patients had more days of sickness than TOM patients, mainly due to a few patients with many days of sickness. However, because we could not identify any of the patients as statistical outliers, they were not excluded from our analyses.

Patients over age 45 might have a mixed disease (asthma and COPD) and might experience outcomes different from those in younger patients. The analyses of between-group differences showed no differences in results between those aged 45 years and younger and those over 45 years. Instead, the same differences were found between TOM and control patients in each age group. Hence, this probably did not affect the results in any appreciable way.

Both groups demonstrated improved outcomes during the 12-month period. This may have tended to reduce the apparent effect size of the TOM program. A number of mechanisms could be at work here. First, filling out questionnaires and meeting at evaluation sessions may be an educational intervention in itself. Second, some control pharmacists may have been more attentive to their asthma patients than they would otherwise have been, both through a Hawthorne effect and by casually including some new care practices. Third, during the study period there were many other asthma-related activities in Denmark that may have affected the process and outcomes of care in both groups.

Finally, daily peak flow readings did not account for time of day and prior use of β-agonist inhalers. This may have introduced an unknown amount of nonexperimental variation into this important clinical measurement.

Conclusion

Patients' participation in the Danish TOM project was associated with improved final outcomes of drug therapy, asthma symptom status, quality of life (health-related and asthma-specific), and days of sickness. Intermediate outcomes and process measures (knowledge, inhalation errors, drug therapy problems) also improved in the intervention group. Use of health care services was reduced, but not conclusively, perhaps because of limitations of sample size, study duration, or apparent effect size.

This study involved patients with relatively good lung function and few hospitalizations who were being treated in primary care. Although these patients are not normally considered at risk for serious drug-related morbidity and mortality, it appears that a TOM program can improve their outcomes.

We designed this study with a systems view of drug therapy. Taken together, our results are consistent with that view. For example, improved patient knowledge may have depended in part on other system changes aimed at improving outcomes (e.g., the pharmacist's identification and resolution of drug therapy problems). Our results also support the value of collaboration between health care professionals in primary care (e.g., GPs and pharmacists) in improving quality of care for patients with asthma. Future research should examine how changes in other aspects of the drug therapy system affect patient outcomes.

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