International Journal of Technology Assessment in Health Care, **23:2** (2007), 184–191.

DOI: 10.1017.S0266462307070298

Cost-utility of a disease management program for patients with asthma

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Objectives: The long-term cost-utility of a disease management program (DMP) for adults with asthma was assessed compared to usual care.
Methods: A DMP for patients with asthma has been developed and implemented in the region of Maastricht (The Netherlands). By integrating care, the program aims to continuously improve quality of care within existing budgets. A clinical trial was performed over a period of 15 months to collect data on costs and effects of the program and usual care. These data were used to inform a probabilistic decision-analytic model to estimate the 5-year impact of the program beyond follow-up. A societal perspective was adopted, with outcomes assessed in terms of costs per quality-adjusted life-year (QALY).
Results: The DMP is associated with a gain in QALYs compared to usual care ($2.7 \pm .2$ versus $3.4 \pm .8$), at lower costs (€$3{,}302 \pm 314$ versus €$2{,}973 \pm 304$), thus leading to dominance. The probability that disease management is the more cost-effective strategy is 76 percent at a societal willingness to pay (WTP) for an additional QALY of €0, reaching 95 percent probability at a WTP of €1,000 per additional QALY.
Conclusions: Organizing health care according to the principles of disease management for adults with asthma has a high probability of being cost-effective and is associated with a gain in QALYs at lower costs.

Keywords: Disease management, Economic evaluation, Decision analysis, Asthma

The Team for Economic Evaluation and Health Technology Assessment, within the Centre for Health Economics of the University of York, has been invaluable in teaching the principles and practical applications of decision-analytic modeling techniques and in providing critical feedback during the actual development of this decision-analytic model. The authors accept full responsibility for the views expressed in this paper as well as any errors or inaccuracies. The development of the decision-analytic model during an internship at the University of York (UK) has been supported by a travel grant from the Dutch Council for Scientific Research (NWO).

The economic burden of asthma is considerable both in terms of direct medical and indirect costs (18). A disproportionate amount of these costs are a consequence of unsuccessful asthma control (1). When the level of asthma control increases, the health-related quality of life of patients improves (28). Disease management programs (DMPs) that aim to improve asthma control by emphasizing coordinated, comprehensive care along the continuum of care and across healthcare delivery systems are expected to improve quality of life of patients and lower the economic burden of the disease (2;11).

After positive experiences with a diabetes DMP in the region of Maastricht, The Netherlands (31), a comparable program for patients with asthma was developed and implemented. Maastricht is located in the southern part of The Netherlands and contains a population of approximately 120,000 people, 90 general practitioners (GPs), and one hospital that functions as a regional as well as a teaching hospital.

By integrating care, the DMP aims to continuously improve the quality of care within existing budgets. The program is comprised of the six components of disease management distinguished by the Disease Management Association of America and has been described in detail before (25). In summary, care within the DMP was delivered by a collaborative practice team consisting of a pulmonologist, GPs, and respiratory nurse specialists (RNSs). Patients were assigned to one of the care providers based on disease severity, as defined in accordance with the international asthma guidelines (Global Initiative for Asthma [GINA]). Subject to approval of the patient, those with intermittent or mild asthma are assigned to the GP, those with moderate persistent asthma to the nurse specialist, and patients with severe persistent asthma to the pulmonologist. The RNSs independently provide protocolized care to the patients assigned to them, within the office of the GP. Tasks of the RNSs are concerned with direct patient care, organization and coordination of care for individual patients, and advancement of expertise (education of patients, themselves, and other care providers). The main differences compared to usual care are the extent to which the coordination is centralized and the position of the RNS as a liaison between primary and secondary care. Within usual care, patients are either managed by the GP (mild to moderate asthma) or the pulmonologist (moderate to severe asthma) and the responsibility for coordination of care lies with the patients and their GP.

To assess whether this DMP is an appropriate use of scarce healthcare resources, the costs and consequences of the program were compared to usual care (9). Historically, DMPs have had difficulty demonstrating the financial value of their programs using statistically rigorous methods (12;17). Several reasons for this have been suggested, including the relatively high levels of uncertainty around cost estimates and the fact that the major benefits of DMPs are expected to occur in the long-term (12;26). An increasingly common approach to assess cost-effectiveness of healthcare interventions and to assist in complex decision making is to use decision-analytic modeling techniques (10;14). The primary benefit of applying these techniques in this study is that they facilitate in linking the short-term results from the clinical trial (25) to a more appropriate time horizon for the economic analysis. The primary objective of this paper is to describe the expected long-term cost-utility of a DMP for adults with asthma compared to usual care.

METHODS

Overview

A clinical trial was performed over a period of 15 months to collect data on costs and effects of the DMP. To estimate the impact of the program beyond the study period, a probabilistic simulation model has been developed. The purpose was to assess the cost-utility of the DMP over a period of 5 years. The rationale for this time horizon lays in the assumption that, within this period, the DMP will not change substantially due to changes in the organization of health care or major changes within the evidence-based guidelines on which the DMP is based.

Data Source

Data from which the model inputs were derived came from a clinical trial using a pre/post-test design. Between May 2002 and March 2003, patients were recruited from sixteen general practices (twenty GPs) and the outpatient department of the hospital. Patients, 18 years of age and older, with a GP diagnosis of asthma were eligible for the study. Patients with comorbidity such as lung cancer or congestive heart failure were excluded. Data on clinical parameters, quality of life as well as direct and indirect costs were collected during 3 months before the DMP was implemented, and every 3 to 6 months afterward for a total period of 1 year (see Supplemental Table 1 at http://www.journals.cambridge.org/jid_thc). This design was chosen, as the program was implemented region-wide and a "fair" comparison region could not be found because, in all potential comparison-regions, innovations were being implemented that would bias the measure of usual care. Examples of these innovations include shared care arrangements, physician assistants working in primary care, or the implementation of self-management programs.

Development of the Model

To assess the cost-utility of the DMP in the long-term, a Markov model was developed (3). The structure of the model was based on a previously published model (22) and developed using Microsoft Excel 2000.

Model Structure: Markov Health States

Five mutually exclusive health states were defined in accordance with the model of Price and Briggs (22) and the international guidelines for asthma management (19). The

Table 1a. Transition Probabilities for Usual Care Strategy (Biweekly Data)

Usual care To From	Successful control	Suboptimal control	Primary care managed exacerbation	Hospital managed exacerbation
Successful control	.956	.024	.017	.003
Suboptimal control	.1	.885	.014	.001
Primary care managed exacerbation	.031	.225	.576	.168
Hospital managed exacerbation	.08	.442	.149	.329

Table 1b. Transition Probabilities for Disease Management Strategy (Biweekly Data)

Disease To management From	Successful control	Suboptimal control	Primary care managed exacerbation	Hospital managed exacerbation
Successful control	.972	.016	.010	.002
Suboptimal control	.300	.691	.008	.001
Primary care managed exacerbation	.146	.156	.568	.130
Hospital managed exacerbation	.222	.341	.228	.209

definitions as well as their implications for daily practice and/or the Markov model are clarified in Supplemental Table 2 (http://www.journals.cambridge.org/jid_thc). The model allows for movement of patients from one state to any other, except from the "all causes death" state (see Figure 1).

Data Inputs: Transition Probabilities

Transition probabilities (see Table 1) were calculated by dividing individual patient data from each strategy (i.e., disease management versus usual care) into biweekly segments. After the health state had been defined for each patient in each cycle, transitions from one state to another were counted for each patient, and the total for all patients in each strategy was calculated. For transitions that had a "zero count" in the observed data, an uninformative prior was used (22). The transition probability from any state to the "all causes death" state was calculated using the standardized age-dependent death rate from the Central Office of Statistics in the Netherlands, being .00013 (biweekly) for individuals between 45 and 54 years of age (7).

Data Inputs: Resource Utilization and Costs

Cost calculations are based on actual resource use as measured with a fifteen-item questionnaire and verified with administrative data from care providers. Collected data on resource use are number of planned consultations with GP, RNS, and pulmonologist; number of nonroutine

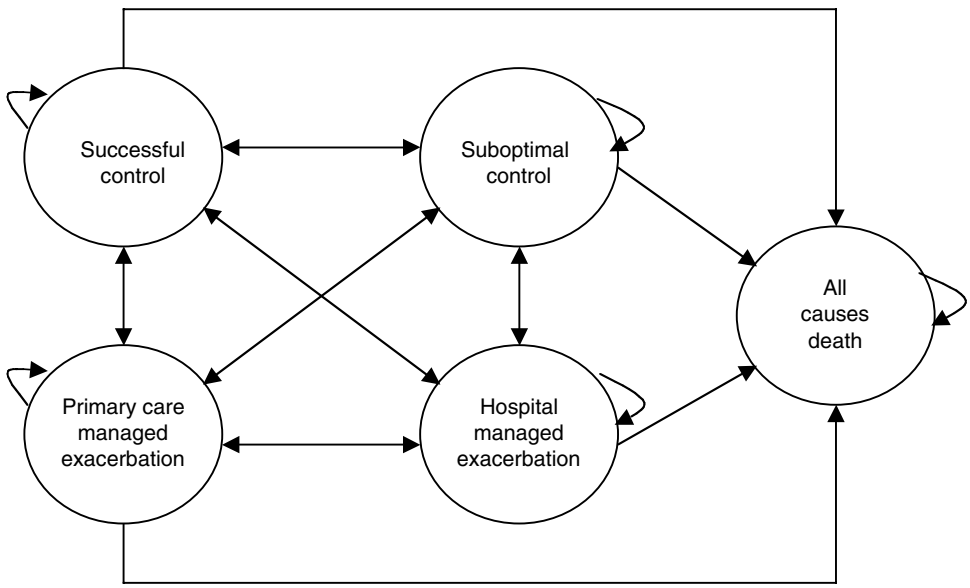

Figure 1. Markov model health state diagram showing the possible transitions between different health states in patients with asthma.

https://doi.org/10.1017/S0266462307070298 Published online by Cambridge University Press

consultations due to an exacerbation; amount and type of maintenance and emergency medication used; number and duration of hospital admissions; number of sick leave days due to asthma.

Data collected in the 3-month premeasurement period represent resource utilization within usual care. The data collected at 1-year follow-up were used to represent resource utilization within the DMP. Because patients from different GP practices entered the program gradually over a period of 10 months, both pre- and postmeasurement data collection was carried out across all seasons controlling for a seasonal effect at the group level. However, by using only 12-month data, learning costs that can potentially be caused by inefficient provision of care at the start of the program are ignored. To compensate for this finding, a sensitivity analysis was performed wherein total healthcare costs of the DMP were increased with 10 percent.

Costs of medications were calculated on a 2004 price base (€) taken from the Dutch Pharmacotherapeutic Compass 2004 (21). Costs for consultations with GPs or medical specialists, emergency stay, and hospital inpatient stay were derived from the Dutch guidelines for economic evaluations (20) and adjusted to 2004 price levels (7). Because no tariffs exist for consultations with the RNS, these costs were calculated using a bottom-up approach (23). Furthermore, overhead costs were included. These costs comprise costs for the employment of a medical and project coordinator, continuing education of the RNSs, the costs of an administrative support office, the maintenance costs of the electronic patient record system that the RNSs use, telephone and travel costs of the RNSs, and salary costs of the unit leader. Although in a different role, RNSs were previously employed in the healthcare system. Therefore, their training costs were not considered as developmental costs for the program. Because most program-specific costs have a continuous nature they are captured within the overhead costs and herewith included in the analysis.

Productivity losses were measured in terms of sick leave days, and costed using the age-dependent friction costs method (20). All costs are discounted at a 4 percent discount rate (20). The direct and indirect cost data for each strategy are presented in Supplemental Table 3 (http://www.journals.cambridge.org/jid_thc).

Data Inputs: Health Outcomes

The quality of life (utility) associated with disease management and usual care was measured using the EQ-5D (29). With the exception of the "death" state, all health states are assigned a specific utility value obtained from the underlying data set. The number of QALYs relating to a health outcome is expressed as the utility value given to a particular health state multiplied by the length of time spent in that state. Within the model, a discount rate of 4 percent was applied (20). Utilities are presented in Table 4 (http://www.journals.cambridge.org/jid_thc).

Perspective

A societal perspective on costs and outcomes was adopted. Because there is some debate about how productivity costs would have to be included in cost-utility analysis (6;15;32), we present the analysis both with and without productivity costs included in the numerator of the cost-effectiveness ratio. The analysis without productivity costs is the base case.

Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis (PSA), using second-order Monte-Carlo simulation with 5,000 iterations, was employed to handle uncertainty in the model by obtaining distributions of costs, health outcomes, and the resulting cost-effectiveness estimates (8). Distributions were fitted to the transition probabilities and parameters evaluating resource use, number of sick leave days, and utilities. The estimates were presented graphically on a cost-effectiveness plane, to show the estimated joint distribution of incremental costs against incremental effects, and evaluated using net benefit analysis (27). Subsequently, a cost-effectiveness acceptability curve (30) was derived from these data.

Fitting Distributions

Transition probabilities from one state to another were assumed to follow a Dirichlet distribution (5;13). Costs are a mixture of resource use and unit costs and are constrained to be zero or positive. This suggests the fitting of a gamma distribution to represent uncertainty in cost data, because this distribution is also constrained on the interval zero to positive infinity.

The theoretical constraints on utility parameters are negative infinity at the one end (representing the worst possible health state) and 1 at the upper end (representing perfect health). However, because the utility data obtained from the patients in the trial indicated that values less than zero were implausible, a beta distribution was used to reflect uncertainty in this input. Parameters of the gamma and beta distributions are analyzed using method-of-moments fitting (4) and are reported in Table 1 and Supplemental Table 3 (http://www.journals.cambridge.org/jid_thc), respectively.

Subgroup Analyses

In addition to the main analysis comparing the disease management strategy with usual care, a series of separate subgroup analyses were undertaken for each of the three patient groups assigned to the GP, the RNS, or the pulmonologist. The purpose of these subgroup analyses was to gain more insight into the relative contribution of each of the patient groups to the overall cost-utility of the disease management strategy. The same model structure was applied as that used

for the main analysis, but each of the subgroup analyses was performed using subgroup-specific input data.

RESULTS

Patients and Response Rates

Of 707 patients eligible for the study, 658 participated (93.1 percent). Of the included patients, 10 percent were assigned to the pulmonologist, 65 percent to the RNS, and 25 percent to the GP. Response rates on both quality of life questionnaires and cost questionnaires were moderate to high (ranging from 55 percent to 96 percent) as was the availability of clinical data (ranging from 80 percent to 100 percent). The most common reason for dropping out of the study was unwillingness to fill out questionnaires. Other reasons were having problems with the Dutch language ($n = 10$), moving away ($n = 7$), or illiteracy ($n = 4$).

Patients who were assigned to the GP were less likely to complete data collection compared to patients who were assigned to the RNS or pulmonologist. Therefore, lung function values of patients not completing follow-up were on average higher compared to patients that completed all questionnaires. Also, patients with missing data had significantly less pack years of smoking than patients with complete follow-up. When comparing baseline characteristics within the GP subgroup of patients with missing data to those of patients with complete follow-up, no selective follow-up in this subgroup was found (25).

Markov Model Results

Differences in transition probabilities between usual care and disease management show that the probability of moving into one of the exacerbation states is lower in the disease management strategy. The probability for moving back toward the health state "successful control" is higher compared to usual care. Overall, costs for routine consultations and regular medication increased after implementation of the DMP. Costs for nonroutine consultations, emergency medication, hospital stay, and lost productivity of the patients decreased. Annual overhead costs amounted to €101 per patient. Quality of life improved as demonstrated by a gain of .69 QALYs within 5 years.

The results for the base case model show that the disease management strategy led to a gain in QALYs compared to the usual care strategy (usual care $2.7 \pm .2$ versus disease management $3.4 \pm .8$), at lower costs (€$3{,}302 \pm 314$ versus €$2{,}973 \pm 304$). Hence, the disease management strategy dominates usual care (i.e., it is more effective and less costly). When productivity costs are included, the finding of dominancy is even strengthened (costs usual care €$3{,}833 \pm 410$ versus costs disease management €$3{,}242 \pm 241$; difference in QALYs remains .69).

Probabilistic Sensitivity Analysis

Base Case Results. The results of the PSA for the base case model are graphically presented in Figure 2, showing the results of 5,000 simulations on the cost-effectiveness plane. For 76 percent of simulations, the disease management strategy is associated with increased QALYs and lower costs, compared to usual care.

However, 22 percent of simulations lie in the northeast quadrant, indicating a gain of QALYs at higher costs for the disease management strategy. The remaining 2 percent of simulations ended up in one of the western quadrants, indicating a loss of QALYs at either lower (1.5 percent) or higher (0.5 percent) costs compared to usual care. To better understand the uncertainty around the point estimate of the incremental cost-effectiveness ratio (ICER), a cost-effectiveness

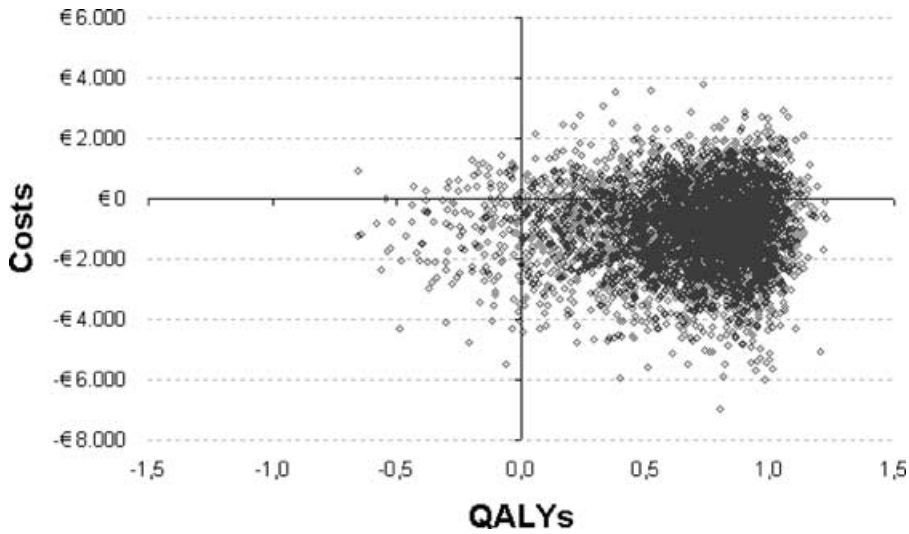

Figure 2. Incremental cost-effectiveness plane comparing disease management with usual care (results of 5,000 Monte Carlo simulations): base case model. QALYs, quality-adjusted life-years.

https://doi.org/10.1017/S0266462307070298 Published online by Cambridge University Press

acceptability curve (CEAC) was plotted (See Supplemental Figure 1 at http://www.journals.cambridge.org/jid_thc). It shows that, if decision makers are willing to pay approximately €1,000 for an additional QALY, the disease management strategy will be the preferred strategy in this patient population 95 percent of the time.

Results Including Productivity Costs. The results of the PSA for the model that includes productivity costs show that 90 percent of the simulations indicate dominance for the disease management strategy (Supplemental Figure 1). This 90 percent certainty is reached without any additional investments.

Sensitivity for Learning Costs. After increasing total healthcare costs of the base case analysis with 10 percent to account for learning costs, the DMP remains dominant in 64 percent of simulations. At a willingness to pay (WTP) of €3,000 per additional QALY, this probability reaches 95 percent.

Results Subgroup Analyses. For patients assigned to the RNS, the disease management strategy is associated with a gain in QALYs ($+1.2 \pm .05$) at higher costs ($+€757 \pm 612$). The expected costs and outcomes for patients assigned to the pulmonologist ($+.2 \pm .38$ QALY; $-€3{,}687 \pm 6{,}378$) or the GP ($+.1 \pm .2$ QALY; $+€23 \pm 1{,}020$) remain largely the same after implementation of the DMP. Furthermore, the CEACs of these subgroups indicate that there is much more uncertainty around the cost/effect ratio compared to the RNS subgroup that, unlike the others, shows a steep rise when the WTP for one additional QALY increases (Figure 3). The same pattern of effect is seen when productivity costs are included.

DISCUSSION

The DMP under study is associated with a gain in QALYs at lower costs in a population of adult asthmatics as compared to usual care. Given the current information, the probability of disease management being the more cost-effective strategy is 76 percent at a societal WTP for an additional QALY of €0, reaching 95 percent certainty at a WTP of €1,000 per additional QALY. The finding of dominancy remains when accounting for learning costs that might have been missed in the base case analysis.

The result is mainly driven by the increase in asthma control that is gained within the disease management strategy. In the DMP, patients who are better controlled continue to be better controlled than in usual care and patients experiencing exacerbations or being in a state of "suboptimal control" are more likely to be successfully controlled again. From the subgroup analyses, it can be concluded that the relative contribution to the observed gain in QALYs is highest within the RNS subgroup, whereas the major part of the overall cost savings seems to occur from the pulmonologist subgroup. However, uncertainty around costs is relatively high in this subgroup as well as in the overall analysis, which might be due to the fact that only data of 3-month measurement periods were used to inform the model. Although any adoption decision should be made by policy makers, an intervention that produces results of this magnitude would generally be considered to be extremely cost-effective (22). However, there are some limitations to this study that need to be taken into account when interpreting these results. First, by using a before–after study design, no causal relationship between the introduction of the DMP and the observed changes in costs and effects can be demonstrated. The results from this study might be biased by, for example, regression to the mean. However, this finding would have biased the results

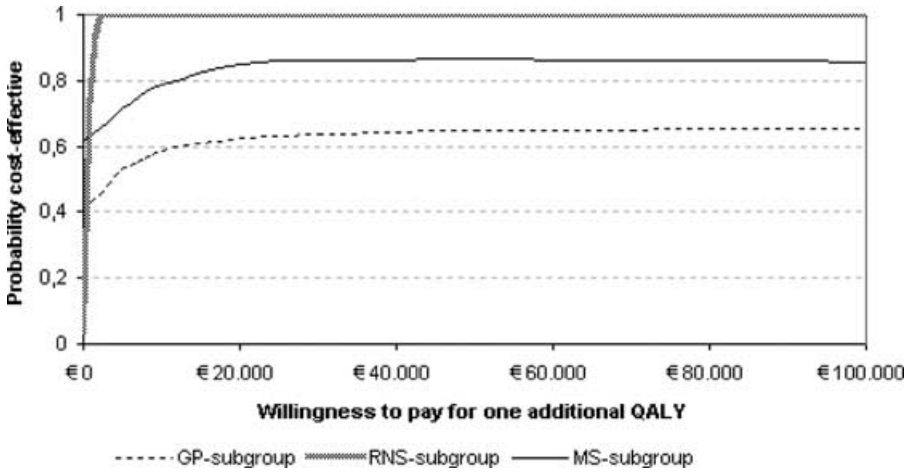

Figure 3. Cost-effectiveness acceptability curves for each subgroup. QALY, quality-adjusted life-year; GP, general practitioner; RNS, respiratory nurse specialists; MS, medical specialist.

https://doi.org/10.1017/S0266462307070298 Published online by Cambridge University Press

in all patients, not selectively affecting utilities in patients assigned to the RNS or costs for patients assigned to the pulmonologist. Second, measurement periods of 3 months are quite vulnerable to bias caused by, for example, seasonality or, coincidentally high or low estimates of certain parameters. To check if our data are likely to be biased, we sought literature against which to compare our findings. Although not optimally comparable due to different settings (Hungary versus The Netherlands), the most recently published study of health-related quality of life of patients with asthma measured with the EQ-5D (28) suggested a mean score of .70 in usual care, which is quite comparable to our findings within usual care being an overall average of .72. Concerning costs, Schermer et al. found annual direct costs within usual care to be circa €400 per patient in the Netherlands, excluding costs for hospital admissions or emergency room visits (24). Our estimate of overall direct costs within the usual care strategy lies within €660 per patient per year, reasonably higher given that we did include costs for hospital or emergency room admissions. Another similarity between our study and the study of Schermer et al. regards indirect costs. Both studies showed a substantial reduction in sick leave or limited activity days after respectively implementing a DMP that has a strong self-management component (25) or guided self-management in primary care (24). Another source of potential bias are the missing values that mainly occurred within the follow-up period, herewith selectively affecting measures of the disease management strategy. Because patients with missing data were more likely to be those patients with relatively good asthma control (i.e., patients assigned to the GP), the estimate of cost-effectiveness of the disease management strategy is more likely to be underestimated than overestimated.

One of our models strengths is the PSA component, which enables the estimation of the joint uncertainty around incremental costs and effects, and the construction of cost-effectiveness acceptability curves using net benefit analysis. Another strength of the presented model is the use of the QALY construct as a generic measure of effectiveness, permitting its value to be assessed in a wider healthcare context (10). A limitation of the presented model is that, as in all Markov models, transition probabilities are considered constant over time (14), which in reality will not be the case. Since there is a lack of studies reporting long-term effects of DMPs (16) for asthma, data informing the magnitude and direction of any adjustment of those probabilities over time are scarce. Thus, allowing for time dependent transitions would increase the complexity of the model enormously.

CONCLUSION

This study reports on one of the first probabilistic decision-analytic models to assess the cost-utility of a DMP for adults with asthma in the long-term. We conclude that organizing health care according to the principles of disease management for adults with asthma is associated with a gain in QALYs at lower costs compared to usual care. When productivity costs are included, the cost savings are even higher, indicating that employers may also benefit from the program.

POLICY IMPLICATIONS

Based on the results, we recommend implementing DMPs, featuring a collaborative practice model, on a wider scale. However, decision makers should continue to look critically to the different programs that currently exist to find the optimal DMP given the organizational context of the region in which it is implemented. Scenario studies should be done to support this decision making and assess the generalizability of results. Furthermore, the methodological quality of disease management evaluation studies is still limited (17;26) and needs continuous attention. The application of decision-analytic modeling techniques is likely to take research and decision making in the complex field of chronic disease management a step further.

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