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Internet-based self-management in asthma

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Internet-based self-management in asthma

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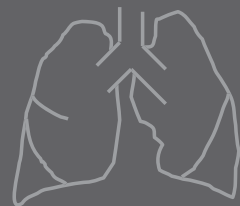
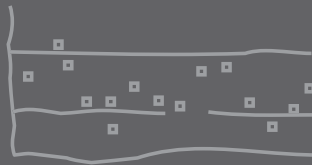
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CONTENTS

Chapter 1	General introduction and aims of the studies	7
Chapter 2	Compliance and reliability of electronic PEF monitoring in adolescents with asthma	27
Chapter 3	Internet-based self-management offers an opportunity to achieve better asthma control in adolescents	33
Chapter 4	Internet-based self-management plus education compared with usual care in asthma: a randomized controlled trial	49
Chapter 5	Weekly self-monitoring and treatment adjustment benefit patients with partly controlled and uncontrolled asthma	73
Chapter 6	Cost-effectiveness of internet-based self-management compared with usual care in asthma	89
Chapter 7	Summary and general discussion	103
Chapter 8	Dutch summary / Nederlandse samenvatting	117
	Dankwoord	127
	Curriculum Vitae	128
	Bibliography	129

CHAPTER 1

General introduction and aims of the studies



INTRODUCTION

Asthma is a chronic respiratory disease, typically characterized by recurrent symptoms such as wheeze and breathlessness. The Global Initiative for Asthma has described asthma as follows (1): asthma is a chronic inflammatory disorder of the airways. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.

This chapter successively describes the epidemiology of asthma, the establishment of a diagnosis of asthma and the emphasis is on the self-management of asthma. The topic of this thesis is the development and evaluation of an internet-based self-management support program. The aims of the studies are presented in the last section.

EPIDEMIOLOGY

Asthma is a common disease, affecting about 300 million people worldwide. The global prevalence ranges from 1 to 18% of the population in different countries (2). Based on Dutch primary care registries, the prevalence of asthma in the Netherlands is 3% in men and 3.5% in women, which represents more than 500 000 people. The number of newly diagnosed asthma patients in Dutch primary care is 7 per 1000 per year (3).

Prevalence rates in children and adolescents are higher than in adults. Based on a positive answer to the question: "Have you (has your child) had wheezing or whistling in the chest in the past 12 months?", the prevalence of asthma symptoms in Western Europe is 7-20% among children aged 6-7 years, and 8-30% in the 13-14 year age group (4). The prevalence of asthma in children seems to decrease. A Dutch study showed that wheeze in 8-9 year old children decreased from 13.4% in 1989 to 9.1% in 2001 (5).

The global burden of asthma is considerable. Surveys, conducted in 29 countries worldwide, revealed that over 50% of patients experienced asthma symptoms during the day and more than 40% had nighttime awakenings due asthma (6). A telephonic survey in Western Europe showed that only 5.3 % of all patients met all the criteria for asthma control (7). Over one third of children and half of the adults reported daytime symptoms at least once a week and about one third of all patients required an unscheduled urgent care visit in the past 12 months. Furthermore, 30% and 50% of children and adults, respectively, reported limitation of activities such as sports, social activities and school or work absence (7). More recently, a questionnaire survey in the Netherlands showed similar characteristics with regard to asthma control (8). The validated Asthma

Control Questionnaire (ACQ) showed poor asthma control in 54% of patients and well or moderately controlled asthma in the remaining 46% (9, 10). The former group had twice as much hospitalizations and urgent primary care visits as the latter group (8).

DIAGNOSIS OF ASTHMA

History taking and physical examination are the basis for diagnosing any disease, as it is in asthma. A clinical diagnosis of asthma is prompted by symptoms such as recurrent wheeze, breathlessness, shortness of breath, cough, and chest tightness. Typically, asthma is characterized by variable, intermittent symptoms, which may be exacerbated by exercise, viral infection and exposure to irritant or allergen. (1, 11). On physical examination, expiratory wheeze and increased expiratory time may indicate airflow obstruction, however these physical signs are often not present (12).

The presence of asthma may be identified correctly by a combination of specific symptoms and signs such as wheeze, dyspnoea, allergen induced symptoms and prolonged expiration (13). However, often non-specific symptoms such as coughing, chest tightness and fatigue occur and may lead to underdiagnosis of the disease due to unawareness by physicians. Patient-related factors such as non-attendance and acceptance or poor perception of symptoms may be another cause of underdiagnosis (14). On the other hand overdiagnosis is described. A minority of patients in primary care is treated with asthma medication without proper indication (15), which stresses the need for objective testing to enhance diagnostic confidence. Tests on airflow obstruction, variability or reversibility such as peak flow examinations or spirometry are recommended. Spirometry is the preferred test in general practice to establish a diagnosis of asthma (16). About two third of the Dutch general practitioners have an own office spirometer and are capable to diagnose asthma accurately (17).

The studies reported in this thesis include patients with a physician diagnosis of asthma. So-called physician-diagnosed asthma is a conglomerate of patients with positive spirometric tests and patients with empirically and successfully prescribed medication, who are presumed to have asthma and treated as such. This pragmatic approach reflects the heterogeneity of a primary care population and enhances the generalisibility of the studies presented.

ASTHMA SELF-MANAGEMENT

The goal of asthma management is to minimize asthma symptoms and short-acting bronchodilator therapy, to prevent exacerbations and to achieve and maintain optimal

lung function. These goals are to be reached at the lowest possible dose of inhaled corticosteroids in order to minimize the risk of side effects and optimize user friendliness of therapy. Important components of asthma self-management are 1) the assessment and monitoring of asthma control, 2) education for a partnership in asthma care, 3) the use of an asthma action plan, including pharmacological treatment, and 4) regular medical review (18, 19).

In a Cochrane review of 36 randomised controlled trials, self-management programs that included all these four components were considered optimal. Optimal self-management showed reductions in unscheduled health care visits and nocturnal symptoms, but only small changes in lung function. A few studies evaluated the effect of optimal self-management on asthma related quality of life. Some found significant improvements in quality of life measured with the Asthma Quality of Life Questionnaire or St George Respiratory Questionnaire (20, 21), however, others reported only minor improvements in asthma related quality of life assessed by these scales (22, 23).

Despite substantial evidence of the beneficial effects of self-management plans in asthma, implementation of these plans is poor (24, 25). Patients, as well as health care providers, may be reluctant to use asthma action plans, viewing them as time consuming, impractical and complex (26). Time and distance from a medical centre have been shown to be barriers to participate in self-management education (27) and significant start-up costs may impair the implementation of education programs in daily practice (28).

Internet-based self-management might overcome these barriers. Internet is widely available and on-line communication with health care providers is possible asynchronously (i.e. patient and health care provider need not be present at the same time) without travel time. Moreover, internet has the possibility of incorporating complex treatment algorithms or action plans which may be presented clearly and may be easy to use and incorporate into daily clinical practice.

Asthma self-management and the internet

Three studies have evaluated the effects of asthma management using internet technology (29, 30, 31). Rasmussen et al. conducted a 6-month randomised controlled trial in 300 adults with asthma. Patients in the internet group daily reported symptoms and peak flow on an internet diary. An on-line decision support system advised the physician to increase, decrease or continue the usual treatment. The investigators reported improved asthma related quality of life, asthma symptoms and lung function after 6 months for the internet-based physician-managed care group compared to specialist or general practitioner care (30).

Two studies evaluated the effect of internet-based self-management in children with asthma (29, 31). In a 3-month randomised controlled trial comparing an internet-based

interactive telemonitoring system with a written asthma diary and self-management instructions in children aged 6-12 years, beneficial effects on asthma related quality of life, symptoms and peak flow were found (29). However, the only long term randomised controlled trial conducted in children aged 6 to 17 years, revealed similar outcomes in the internet group and conventional diary group for asthma related quality of life, asthma control and lung function after 1 year (31). Therefore, the evidence has shown to be inconclusive and incomplete. Internet-based self-management programs so far have not included all cardinal components of optimal self-management.

The development and evaluation of an internet-based self-management support program, including self-monitoring, education, an asthma action plan, and medical review is the topic of this thesis. The next four sections describe each component in detail; its implementation into our internet-based program is revealed in the last paragraph of each section.

Assessment and monitoring

Severity and control

Monitoring of asthma requires understanding of the concepts of asthma severity and asthma control. Asthma severity refers to the intrinsic intensity of the disease process. The assessment of severity takes into account not only the current symptoms and lung function, but also the level of treatment that is required to achieve treatment goals (32, 33). Severe asthma is defined as the requirement for (not necessarily just the prescription or use of) high-intensity treatment.

Asthma control refers to the degree to which manifestations of asthma are minimized and the goals for therapy are met. Two domains of asthma control can be distinguished: current impairment and future risk. Current impairment refers to the level of asthma symptoms such as wheeze, cough, breathlessness, chest tightness and functional limitations. Future risk includes the risk for exacerbations, progressive lung function decline or adverse effects from medication (18, 32).

The emphasis for asthma management is on asthma control, not on severity. The level of asthma control guides decisions to maintain or adjust therapy in order to minimize the clinical manifestations of asthma (both impairment and risk) at the lowest possible level of medication. Several measures are available for assessing (components of) asthma control: lung function monitoring, symptom monitoring or self-assessment questionnaires which include several elements of asthma control such as symptoms, activity limitations, need for quick relief medication and/or lung function (9, 34, 35).

Lung function monitoring

Monitoring of peak expiratory flow (PEF) or forced expiratory volume in the first second (FEV₁) potentially provides valuable information on asthma control, future risk of asthma episodes and for evaluation of the effectiveness of therapy (36, 37). López-Vina et al. showed that PEF monitoring increased adherence to prescribed treatment compared to symptoms only as a guide to self-management (38). However, effects of PEF monitoring on clinical outcomes have proved to be inconsistent; a meta-analysis of peak-flow versus symptom based asthma plans showed no differences in hospitalizations, ER visits, days lost from school or work, FEV₁ and only a slight beneficial effect of peak-flow based plans on unscheduled doctor visits and oral corticosteroid courses (39). Moreover, knowledge of peak flow did not improve quality of life and symptom scores in a randomised controlled trial exploring the effect of PEF recordings in addition to symptom-based self-management (40).

The use of conventional, written diaries for lung function reporting is impaired by poor adherence and reliability (data falsification). Studies suggest that over 20% of reported written lung function recordings are not actually measured, and therefore self-invented (41, 42). The number of incorrectly reported written lung function data is also considerable, leaving only about 50% of all recordings being correctly reported (41). These unsatisfying reports call for novel ways to monitor and report lung function in asthma self-management plans in order to guide treatment appropriately.

Technical innovation has led to the advent of electronic home spirometers. These spirometers have shown to provide accurate lung function data, which match the criteria of standardized spirometry, even in unsupervised settings (43-46). Subsequent reporting of the data can be established either by direct downloads to a PC or manually to an internet website or by mobile phone text messaging. Obviously, direct downloads to PC or palmtop of spirometric data have the advantage of less incorrect data and no self-invented values (29, 46), but implementation of this feature into self-management plans is not available yet.

We therefore evaluated the compliance and reliability of electronic PEF recordings, manually reported on the internet or by mobile phone text messaging.

Symptom monitoring and self-assessment questionnaires

Symptom monitoring needs to be valid, reliable, responsive and, if used as part of asthma self-management plans, patients must be sufficiently adherent in order to guide treatment. For many years, questionnaires have been used in clinical trials to measure symptoms in terms of their intensity, duration and characteristic of an episode and the frequency of episodes (47-49). However, until recently, the validity and responsiveness of symptom monitoring instruments was poorly studied (47, 50).

The development of self-assessment questionnaires with properly evaluated psychometric aspects to assess asthma symptoms and asthma control has evolved rapidly in the past decade. International guidelines recommend the use of validated self-assessment measures to assess the extent of asthma control such as the Asthma Control Questionnaire (ACQ), the Asthma Control Test (ACT) and the Asthma Therapy Assessment Questionnaire (ATAQ) (1, 18). The ACQ and ACT have shown to be responsive to changing asthma control (51, 52). The ACT covers frequency and intensity of asthma symptoms during the past 4 weeks and includes questions on activity limitation and rescue medication (52). Similar to the ACT, the ACQ includes items on frequency and intensity of symptoms and questions on activity limitations and rescue medication. However, it additionally provides information on the characteristics of asthma symptoms (wheeze and shortness of breath) and lung function. The ACQ items relate to asthma control in the past week and a minimally important difference was estimated to be 0.5 on the 7-point scale (51). These features (symptom and lung function assessment; weekly questionnaire; responsiveness to change) provide the possibility to incorporate the ACQ into an asthma self-management program.

Despite the recommendation by international guidelines to use this validated measure on asthma control over time in clinical research and patient care, its value as a guide to adjust treatment in order to improve asthma control has not been shown yet. In our internet-based self-management program, we have therefore incorporated ACQ self-monitoring and evaluated the effects of treatment guidance according to an algorithm based on weekly, consecutive ACQ assessments.

Education for a partnership in asthma care

Effective asthma management requires a partnership between the patient with asthma and the professionals that deliver asthma health care. This partnership is aimed at empowering the patient to manage his or her asthma with guidance from the health care professional. By gaining essential knowledge, skills and confidence, patients should be able to minimize impairment due to asthma and to maintain normal activity levels (1, 18).

Asthma education may take many forms. Limited patient education only consists of the transfer of information about asthma and its causes and treatment. Although the need for providing information to asthma patients is undisputed, mere transfer of information is insufficient to consistently improve asthma symptoms and lung function or to reduce doctor visits and hospitalization (53). Therefore, more complex educational programs have been developed as an integral part of patient self-care. These educational programs have been shown to be successful if they are directed toward behavioral change and focus on patient empowerment (e.g. patient self-confidence and self-efficacy) beyond patient knowledge (19, 54, 55). Thus, as an additive to improving

asthma knowledge, the content of educational programs should comprise skills training (lung function measurements and inhalation technique), pharmacological and non-pharmacological treatment instructions, and self-management education with regard to the use of an asthma action plan (19, 28, 56). Conversely, provision of an asthma action plan without adequate patient education is unlikely to improve patient outcomes (39).

Some randomized controlled trials have specifically focused on cognitive-behavioral change as an outcome of asthma education programs. Cognitive-behavioral outcomes such as knowledge, attitudes and self-efficacy with regard to managing asthma are improved by self-management education (57-59). Self-management skills such as monitoring and adherence to asthma medication, can be influenced positively by tailored asthma management programs (57-60).

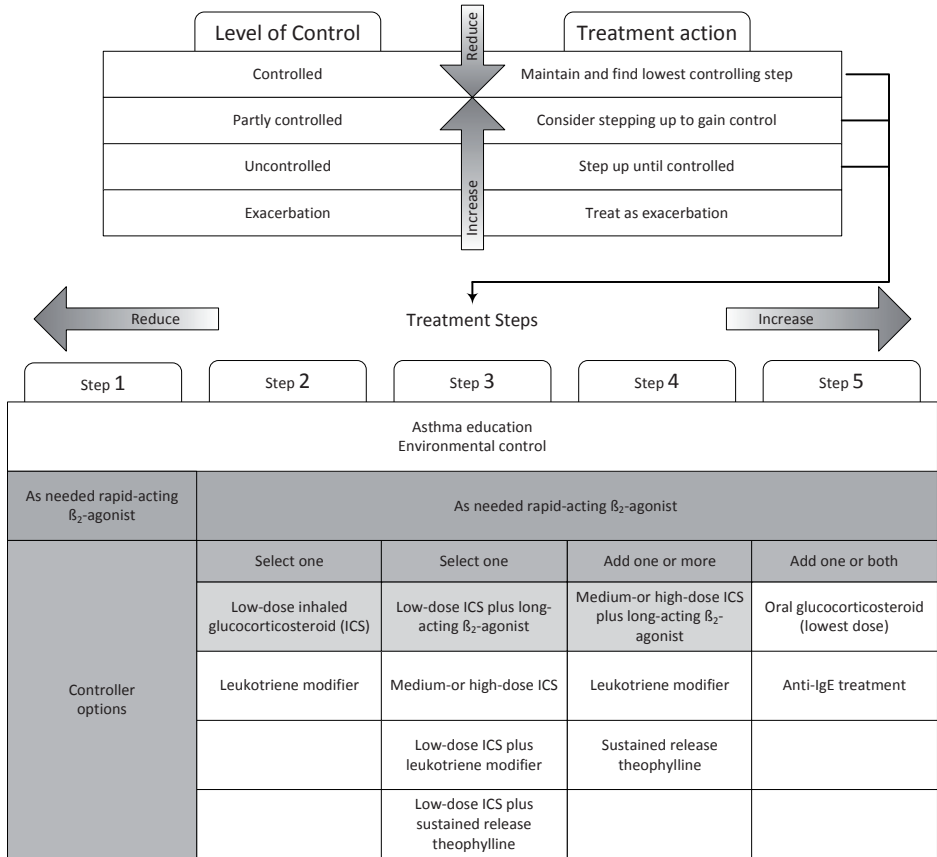
In our asthma self-management support program we offered education in two ways; 1) three group-based sessions focusing on patient empowerment to adopt tailored and adequate asthma management behavior, and 2) web-based education including all core content areas of asthma information. The development of an active partnership between patient and health care provider was fostered by on-line web communication. The effect of the educational components was assessed and evaluated as part of the process evaluation of our program.

Asthma action plans and pharmacological treatment

Step-wise approach

There are two main categories of asthma medications: relievers and controllers. Pharmacological treatment in asthma is characterized by a step-wise approach (1, 11, 16, 18) (figure 1). At each treatment step, reliever medication (usually a short-acting β_2 -agonist) is recommended for quick relief of symptoms. At step 1 this is the only necessary treatment. Patient who present with more frequent symptoms, arbitrarily more than 2 times a week, should be provided with controller medication. At step 2 the preferred controller medication is a low-dose inhaled corticosteroid. If the treatment goals are not reached with step 2 inhaled corticosteroids and appropriate compliance and inhaler device use, addition of a long-acting β_2 -agonist is recommended. Alternative treatment options are to increase the dose of inhaled corticosteroids or to add a leukotriene modifier. The choice of controller medication to be added in step 4 depends on prior selections at steps 2 and 3. The preferred treatment is to combine a medium- or high-dose of inhaled corticosteroid with a long-acting β_2 -agonist (61), but alternative or multiple add-on treatment possibilities may be considered. If treatment goals continue to fail with step 4 therapy oral glucocorticosteroids added to other controller medications may be effective (62). This option should only be considered after referral to or consultation of a chest physician (16).

Figure 1. Stepwise asthma management approach - adapted from GINA guidelines, figure 4.3-2 (1) -



The step-wise pharmacological approach to gain and maintain asthma control in patients with persistent symptoms should be distinguished from acute treatment changes in patients during an asthma exacerbation. The former (step-wise approach to gain and maintain control) provide an ideal strategy against the variable and intermittent course of asthma symptoms. The latter (acute treatment changes during an exacerbation) requires immediate consultation (not necessarily face-to-face) of a health care provider. Asthma exacerbations are clinically characterized by episodes of increased symptoms such as shortness of breath, wheezing, cough or chest tightness and may be defined on the basis of symptoms or rapid lung function decline (63, 64). They require the administration of rapid-acting inhaled β_2 -agonist and early administration of oral glucocorticosteroids to reduce the number of hospitalizations (65).

Treatment instruction in asthma action plans

Personal asthma action plans help individuals with asthma to make changes to their pharmacological treatment in response to worsening symptoms or lung function and to contact a health care provider in case of emergencies. When incorporated in a complete asthma self-management program, which additionally includes monitoring, asthma education and regular medical review, asthma action plans have shown to reduce hospital admissions and asthma symptoms (19). The way action thresholds are determined vary and the various approaches differ in their results. If treatment instructions are given based on fall in personal best peak flow, also beneficial effects on mean peak flow were seen, in contrast to treatment instructions based on fall in percentage of predicted peak flow (66). Symptom-based action plans produce equivalent results compared to peak flow based action plans (66). Action plans based on FEV₁ measurements have not been studied yet, which is not surprising, since home spirometry has only become available recently (43).

Asthma action plans not only need to specify when, but also how to increase treatment and for how long (66). Almost all evaluated action plans recommend a doubling of the dose of inhaled corticosteroids in case of deteriorating peak flow or symptoms (20, 22, 23, 58, 67-71). Many of these studies report reduced exacerbations (20, 67, 70), reduced asthma symptoms (22, 23, 70), improved quality of life (20, 23, 58) or improved lung function (22, 69, 70). Remarkably, a study on doubling the dose of inhaled corticosteroid as a sole intervention revealed no effect on the number of exacerbations, and peak flow or symptom scores (72), suggesting that other factors than only this doubling contribute to the observed beneficial results in asthma action plan studies.

Almost all asthma action plans focus on instructions to increase treatment, but do not provide instructions when and how to decrease medication. There is, however, some experimental evidence that reducing the dose of inhaled corticosteroid is safe without comprising asthma control in patients with stable asthma (73, 74). Guidelines recommend that a 50% reduction in inhaled corticosteroid dose should be attempted at 3 month intervals (1, 11, 16, 18). The interval of 3 months, however, is arbitrary; the asthma action plan in the study of Thoonen e.a. advised the inhaled corticosteroid to be halved when peak flow was more than 80% for a period of 6 weeks (23). Although the effects of this specific advice were not analysed in detail, the study overall showed that the self-management program lowered the perceived burden of asthma and was at least as effective as usually provided care (23).

In our self-management support program patients were provided an action plan based on the well validated Asthma Control Questionnaire (ACQ). We therefore aimed at detecting and managing uncontrolled asthma, rather than at preventing asthma exacerbations. Advices on when, how and for how long to adjust (i.e. increase or decrease) treatment were given according to an ACQ based algorithm based on (inter)national asthma management guidelines.

Medical review

The accuracy of asthma self-management behavior has been shown to decline over time (18, 75). Therefore, medical follow-up and review is recommended to take place at regular intervals, in order to keep self-management at the required level. In case asthma is insufficiently controlled, medical review should be scheduled at 2 to 6 week intervals. When asthma is controlled follow-up visits are recommended once or twice each year (16, 18). At each visit asthma control, medication technique, use and understanding of the asthma action plan and patient adherence should be assessed.

Our self-management program included regular follow-up visits according to the national guideline on asthma management (16). Additionally, medical review was available by on-line communication with our asthma nurse specialist.

COST-EFFECTIVENESS OF ASTHMA SELF-MANAGEMENT

Since health care resources are scarce it is important to evaluate not only the clinical effectiveness of new disease management programs, but also the cost-effectiveness. The benefits of a new self-management program should be evaluated against the costs in order to justify its implementation.

The direct costs of asthma, defined as resources consumed, include drugs and devices, consultations with physicians and other health care professionals and hospital costs (76, 77). Drug costs make up over 50% of the total direct costs of asthma (77). Non-medical direct costs consist of time and travel costs (78). The indirect costs of asthma, defined as resources that are lost, consist of loss of productive work as a result of the ill health of the patient and premature retirement or death (76).

It has been estimated that approximately three quarters of the total asthma-related costs are a result of inadequately controlled disease (76). New asthma self-management strategies that aim for good asthma control may therefore reduce asthma costs related to uncontrolled disease. However the implementation of the self-management program itself will be accompanied by additional, or incremental, costs, which need to be related to expected benefits of the program.

A recent systematic review on the cost-effectiveness of peak-flow based asthma self-management programs identified 21 studies of which 18 self-management interventions led to net savings compared with usual care (79). Moreover, 14 out of 17 full economic evaluations reported that the new self-management strategy was dominant, i.e. more effective and less costly compared with usual care (79). The methodological quality, types of costs and different outcomes, however, made it difficult to compare the studies and to draw definite conclusions regarding the cost-effectiveness of peak-flow based self-management programs.

To compare the cost-effectiveness of different programs across different diseases it is recommended to use a generic measure of outcome, such as quality-adjusted life-years (QALYs) gained (80). Only one study evaluated the cost-effectiveness of an asthma self-management program in terms of QALYs gained (81). Schermer et al. reported an average effect of 0.015 QALYs gained per patient and incremental costs per QALY gained of €13,267. At a willingness-to-pay level of €22,500 to gain one additional QALY, the probability that self-management was cost-effective compared with usual care was 52%. In this thesis, we report the results of our cost-effectiveness analysis evaluating the costs and QALYs gained by internet-based self-management compared with usual care.

AIMS OF THE STUDIES

The studies in this thesis explore the potential role of internet-based self-management support in the management of asthma and are presented in five chapters. The content of these chapters is summarized below.

CHAPTER 2. Peak-flow recordings potentially provide valuable information on risk prediction of asthma episodes and effectiveness of treatment, but the use of conventional, written peak-flow diary cards is impaired by poor compliance and reliability. In this study, 97 adolescents with asthma were provided with electronic spirometers and reported daily peak-flow recordings by using internet or SMS (short message service). We examined compliance and reliability of electronic peak-flow recordings for a period of four weeks.

CHAPTER 3. Written self-management plans are poorly disseminated and used in primary care patients with asthma. In a focus group study following the four week lung function monitoring study of chapter 2 we explored 1) the intrinsic barriers to current asthma management and 2) the barriers and benefits of internet-based asthma management perceived by adolescents with asthma.

CHAPTER 4. This chapter reports the design and results of a randomised, controlled trial, comparing internet-based self-management with usual physician provided care for 200 adults with asthma, who were followed for one year. Outcomes of the study were related to the self-management process and to its clinical effects.

The process evaluation compared internet-based self-management with usual care with regard to educational outcomes (asthma related knowledge, inhaler technique and medication adherence), the number of health care provider contacts and medication changes.

With regard to the clinical effectiveness we evaluated whether internet-based self-management led to improvements in asthma related quality of life, asthma control, symptom-free days, lung function and to a reduction in exacerbations compared with usual care.

CHAPTER 5. The level of asthma control at baseline of the study presented in chapter 4 differed between individuals. About 40% had well controlled asthma, 35% partly controlled asthma and 25% poorly controlled asthma. In this study we evaluated the monitoring adherence, pharmacological treatment and asthma control changes for the three groups with different levels of asthma control at baseline.

CHAPTER 6. New disease management strategies, such as internet-based self-management in asthma, require not only an evaluation of the clinical effectiveness, but also of their cost-effectiveness. The economic evaluation presented in this chapter investigated whether the benefits of internet-based asthma self-management in terms of QALYs (quality adjusted life years) were attained at reasonable costs.

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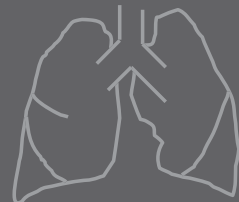
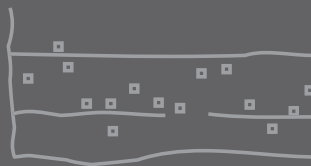
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CHAPTER 2

Compliance and reliability of electronic PEF monitoring in adolescents with asthma

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Self-management education is the cornerstone of modern asthma care and consists of self-monitoring, transfer of information, a written action plan, and regular medical review (1). Current international guidelines recommend the use of home monitoring of peak expiratory flow (PEF) as a part of self-monitoring (2). PEF recordings potentially provide valuable information on risk prediction of asthma episodes and effectiveness of treatment (3). However, compliance and reliability of written PEF diaries is poor (4). Information and communication technologies (ICT) such as the internet and mobile phone short message service (SMS) are potentially powerful tools in the management of asthma. The use of these technologies enables adolescents to fit asthma management into their daily life activities. We therefore investigated the compliance and reliability of daily PEF measurements by adolescents with controlled and uncontrolled asthma symptoms using a handheld electronic spirometer and reporting the data via the internet or SMS.

Ninety seven adolescents aged 12–17 years with physician diagnosed asthma and regular prescriptions of low or medium dose inhaled corticosteroids for at least 3 months in the previous year were recruited from general practices and from the outpatient clinic of the department of paediatrics. Patients using systemic steroids, having no access to the internet, and those with serious co-morbidities were excluded. Participants and their parents gave written informed consent and the study was approved by the medical ethics committee of the Leiden University Medical Center, Leiden, the Netherlands. All participants received an electronic spirometer (PiKo1; Ferraris, UK) and were trained to perform a forced expiratory manoeuvre. They were asked to perform three manoeuvres every morning before taking medication and to report PEF values by typing these daily on a designated web application or via SMS for 4 weeks. Participants instantly received a receipt message with the PEF value expressed as a percentage of their personal best value. They were unaware that the spirometer also stored the values in a memory chip. The participants completed the Asthma Control Questionnaire (ACQ) weekly (5). Reported compliance was defined as the proportion of reported PEF entries to the number of expected entries. Actual compliance was calculated as the proportion of entries in the spirometer memory to the number of expected entries. In order to evaluate reliability, the reported PEF values were compared with the spirometer memory: correctly reported values were identical to the spirometer memory values on the same day. We distinguished between controlled and uncontrolled asthma symptoms on the basis of the mean ACQ score over 4 weeks, a score of ≤ 0.5 indicating controlled asthma and a score of > 0.5 indicating uncontrolled asthma. Repeated measures analysis of variance was used to assess differences between the 4 weeks and between the two ACQ groups. Mean (SD) PEF values were 419 (97) l/min and 378 (86) l/min for the controlled and uncontrolled groups, respectively ($p=0.052$).

Overall reported compliance was 90.6% and actual compliance was 91.5%. Actual compliance significantly decreased between week 1 (97.2%) and week 4 (83.7%; $p < 0.01$, ANOVA). Correctly reported PEF values were found on 79.2% of the days; 2.2% of the PEF values were self-invented (table 1). There were no differences between ACQ groups.

Table 1. Reliability of PEF values: mean (SD) percentages of correct, incorrect, self-invented, and missing values for patients with controlled and uncontrolled asthma symptoms

	Week 1	Week 2	Week 3	Week 4
Patients with controlled asthma symptoms (n=25)*				
Correct (%)	93.1 (13.1)	89.7 (14.6)	81.1 (25.0)	67.4 (30.2)
Incorrect (%)	4.0 (9.7)	8.0 (13.7)	9.1 (15.4)	16.0 (24.2)
Self-invented (%)	0.0 (0.0)	0.6 (2.9)	2.9 (7.1)	4.6 (9.0)
Missing (%)	2.9 (7.1)	1.7 (6.3)	6.9 (14.9)	12.0 (17.3)
Patients with uncontrolled asthma symptoms (n=72)†				
Correct (%)	86.1 (18.4)	82.1 (21.3)	76.8 (24.4)	69.2 (29.1)
Incorrect (%)	7.5 (12.5)	7.9 (13.3)	9.3 (14.2)	10.1 (12.3)
Self-invented (%)	1.2 (5.7)	1.2 (4.0)	2.0 (5.5)	4.0 (11.3)
Missing (%)	5.2 (11.3)	8.7 (15.5)	11.9 (20.9)	16.7 (26.5)

*Mean (SD) Asthma Control Questionnaire (ACQ) score 0.28 (0.15).

† Mean (SD) Asthma Control Questionnaire (ACQ) score 1.17 (0.56).

Correct, reported PEF values that were identical to memory values on the same day as % of expected entries; incorrect, reported PEF values that differed from memory values on the same day; self-invented, reported PEF values without a memory value on the same day; missing, expected entries where there was no PEF value reported.

We conclude that the compliance and reliability of home PEF measurements by adolescents using the internet or SMS is high over a 4 week period. Actual compliance was over 83% during the whole period. Compared with conventional written diary cards, electronic monitoring and reporting seems to result in better compliance and reliability (4). The internet and SMS are both well established communication tools in the daily lives of adolescents, and this probably accounts for these remarkably good results. We observed a modest decline in compliance and an increase in erroneous reports over time which had not reached a plateau by week 4. The feasibility of long term ICT based monitoring by adolescents is therefore uncertain. In our observational study lung function monitoring was not followed by feedback and/or therapeutic consequences which might have negatively influenced compliance over time. Implementation of electronic monitoring into an asthma management programme in adults has shown continuing high compliance rates (6). This study supports the implementation and evaluation of electronic PEF monitoring as part of ICT based asthma management programmes in adolescents.

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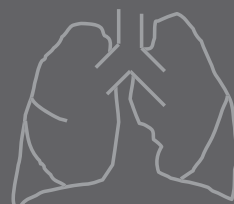
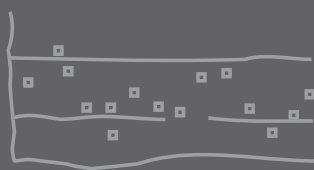
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CHAPTER 3

Internet-based self-management offers an opportunity to achieve better asthma control in adolescents

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ABSTRACT

Background

Internet and short message service are emerging tools in chronic disease management of adolescents, but few data exist on barriers and benefits of internet-based asthma self-management. Our objective was to reveal the barriers and benefits by adolescents with well controlled and poorly controlled asthma to current and internet-based asthma management.

Methods

Ninety-seven adolescents with mild to moderate persistent asthma monitored asthma control on a designated website. After 4 weeks, 35 adolescents participated in eight focus groups. Participants were stratified in terms of age, gender, and asthma control level. We used qualitative and quantitative methods to analyze the written focus group transcripts.

Results

Limited self-efficacy to control asthma was a significant barrier to current asthma management in adolescents with poor asthma control (65%) compared to adolescents with good asthma control (17%) ($p < 0.01$). The former group revealed the following several benefits from internet-based asthma self-management: feasible electronic monitoring, easily accessible information, email communication and use of an electronic action plan. Personal benefits included the ability to react to change and to optimize asthma control. Patients with poor asthma control were able and ready to incorporate internet-based asthma self-management for a long period of time (65%), whereas patients with good control were not (11%) ($p < 0.01$).

Conclusions

Our findings reveal a need for the support of self-management in adolescents with poorly controlled asthma that can be met by the application of novel information and communication technologies. Internet-based self-management should therefore target adolescents with poor asthma control.

INTRODUCTION

Asthma is the most common chronic disease among adolescents. Its prevalence in this age group is about 11% worldwide (1). Despite the availability of potent medical treatment, there is a significant burden of asthma in children and teenagers (2, 3).

Guided self-management strategies including self-monitoring, continuous education, regular medical review, and a written action plan have been shown effective in clinical trials (4, 5). The recently updated Global Initiative for Asthma guidelines advocate ongoing self-assessment of asthma control as part of a written personal asthma action plan (6). However, patients and doctors are not enthusiastic about paper and pencil self-management programs and participation rates are low (7, 8). Structural barriers to participate in a self-management program should be overcome and personal benefits should be appreciated (8, 9). Lemaigre et al. have demonstrated the importance of external barriers such as time and distance from a medical center to predict the intention to participate in self-management programs (9). The role of intrinsic barriers such as attitude and perceived ability to manage asthma is unknown.

Internet and short message service (SMS) are potentially powerful tools through which guided self-management programs can be delivered to adolescents with chronic disease (10-14). To date, it is unknown whether internet and SMS can help to overcome intrinsic barriers and can reveal personal benefits of asthma self-management in adolescents. Since asthma control predicts acute health care utilization (15), the level of asthma control might identify those patients who benefit most from a self-management intervention program.

We conducted focus group interviews with adolescents with asthma. Our aim was 1) to reveal intrinsic barriers to current asthma management and 2) to explore the barriers and benefits of internet-based self-management in patients with good and poor asthma control, stratified by gender and age.

METHODS AND MATERIALS

Subjects

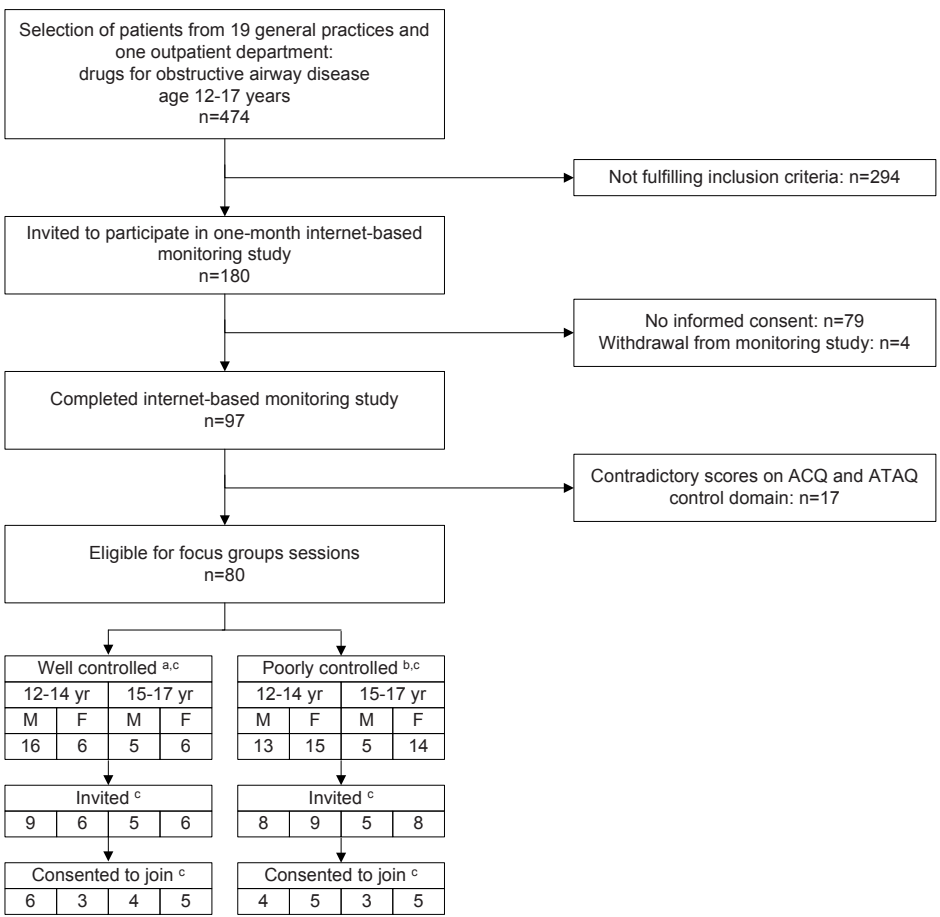
Prior to the focus group sessions, we invited adolescents with asthma to participate in a one-month observational study on internet-based lung function and symptom monitoring. Participants were recruited from 19 general practices (44 general practitioners) in and around Leiden, The Netherlands, and from the outpatient clinic of the department of pediatrics of the Leiden University Medical Center. Inclusion criteria were physician-diagnosed asthma, age 12-17 years, use of inhaled corticosteroids at least three months in the previous year, no serious co-morbid conditions that interfered with asthma treatment, access to internet at home and able to understand Dutch. The study

was approved by the medical ethics committee of the Leiden University Medical Center. All participants gave written informed consent.

Design

Ninety-seven adolescents consented to participate in the observational internet-based monitoring study (figure 1). All participants received a hand-held electronic spirometer (PiKo1; Ferraris, UK) and were trained to perform three maneuvers every morning before taking medication and to report FEV₁ (lung volume in the first second of a forced expira-

Figure 1. Flow diagram of focus group participants



ACQ: Asthma Control Questionnaire

ATAQ: Asthma Therapy Assessment Questionnaire

^a ACQ maximum score < 1.0 and ATAQ control score = 0

^b ACQ maximum score ≥ 1.0 and ATAQ control score ≥ 1

^c numbers per age group and gender (M=male, F=female)

tion) and PEF (peak expiratory flow) values by typing these daily on a designated web application or via SMS during a one-month period. Participants instantly received a return message with the FEV₁ and PEF values expressed as a percentage of expected or personal best value, respectively. These electronic return messages were not accompanied by any interpretation or treatment advice. The methods have been described previously (13). Weekly, the participants completed the Asthma Control Questionnaire (ACQ) via the internet. The Asthma Therapy Assessment Questionnaire (ATAQ) was filled in once.

In March and April 2005, following the electronic monitoring study, we conducted eight focus group sessions lasting 1 to 1.5 hour. The goal was to recruit four to eight participants per focus group. We stratified the focus groups on the basis of asthma control, gender and age (figure 1).

Questionnaires

Asthma control was measured through the ACQ and the control domain of the ATAQ (16, 17). The ACQ contains six questions on asthma symptoms and includes one lung function measurement (FEV₁). Scores range from 0 (well controlled asthma) to 6. The control domain of the ATAQ for adolescents contains seven items; sum scores range from 0 (no control problems) to 7. Participants with well controlled asthma were identified by low scores on both the ACQ (maximum ACQ score during one month <1.0) and the ATAQ (control score = 0). Participants with poorly controlled asthma were identified by a maximum ACQ score of >1.0 and an ATAQ control score of ≥1 or higher (18-20).

Attitude and self-efficacy were measured using the Knowledge, Attitude and Self-Efficacy Asthma Questionnaire (KASE-AQ) (21). Mean scores range from 1 to 5 with higher scores indicating a more positive attitude and higher self-efficacy toward asthma management.

Focus groups

We used the focus group procedures of Morgan and colleagues in preparing and conducting the sessions (22). One moderator and one observer guided the interviews according to a carefully constructed protocol (table 1).

With regard to our first objective (adolescents' intrinsic barriers to current asthma management) we used the Theory of Planned Behaviour as a theoretical framework (23, 24). It assumes that attitude, perceived social norm and self-efficacy (*i.e.*, perceived ability) expectations determine a person's intention to perform a specific behaviour, in our case asthma management behaviour.

In order to explore adolescents' views on barriers and benefits of internet-based self-management we addressed the four major elements of asthma self-management in the focus group discussions. These elements are self-monitoring of lung function and symptoms, transfer of information about asthma, regular medical review and the use of an individualized action plan (7).

Table 1. Focus group protocol

<i>Intrinsic barriers regarding self-management</i>	
1.	How do you perceive your asthma? Probes: When do you feel your asthma is under control? How do you know your asthma is/is not under control? <i>self-efficacy</i>
2.	Do you mind if your asthma is not under control? Probes: Why do / don't you mind? <i>attitude</i>
3.	What is easy about controlling your asthma? What is difficult about controlling your asthma? Probes: What about medication? What about triggers? What about friends, family, doctors? <i>self-efficacy / social norm</i>
4.	How do you appreciate asthma management? Probe: Do you take it positively / negatively? <i>attitude</i>
<i>Explanation about monitoring / information / regular medical review / action plan.</i>	
5.	How do you appreciate (electronic) monitoring? Probe: How would you feel about monitoring your lung function / symptoms daily?
6.	How do you evaluate obtaining information (via the internet / via leaflets or books)? Probe: In which way would you like to obtain information?
7.	How do you appraise visiting a medical practitioner or asthma nurse? Probe: Why is it (not) necessary for you to visit your general practitioner / specialist / nurse?
8.	How do you value an (internet-based) action plan? Probe: How confident are you to develop your own action plan with your doctor / nurse?

Statistical analysis

All focus group sessions were audio-taped and transcribed in full for analysis. We analyzed the transcripts using methods of theory-based and data-based analysis style. In theory based analysis the text is organized according to pre-existing theoretical categories. In data-based analysis units in the text are identified to form data developed categories (25). We coded the transcribed text into categories using a software program for qualitative data analysis (Nvivo version 1.3; QSR International, Doncaster, Australia). The first two transcriptions were independently coded by two researchers (HvS and VvdM). Disagreements were solved after discussion. One author (HvS) coded the remaining transcriptions (25).

We counted the number of participants who made comments fitting a specific category. If a participant made many similar comments, these comments were counted only once. We present frequencies of categories and comparative statistics (Fisher's exact test) to support our qualitative analysis and to provide insight in the representativeness of the statements (26, 27).

RESULTS

Eighty patients were eligible for participating in the focus groups (well controlled asthma, 33 patients; poorly controlled asthma, 47 patients). On the basis of asthma control, age and gender 56 adolescents with asthma were invited to participate and

35 (62.5%) attended the focus group sessions. Sessions lasted on average 71 minutes (range, 40 to 100 minutes).

Patient characteristics are listed in table 2. Participants with poorly controlled asthma had significantly lower self-efficacy scores on the KASE-AQ self-efficacy subscale than participants with well controlled asthma. Attitude towards asthma did not differ between the groups (table 2).

Table 2. Patient characteristics

	Well controlled asthma (n=18)	Poorly controlled asthma (n=17)	Group comparisons (<i>P</i> values)
Clinical characteristics			
Age; years (SD)	14.2 (1.7)	14.7 (1.5)	0.36 ^e
Sex; M/F	10/8	7/10	0.51 ^f
Duration of asthma; years (SD)	7.4 (4.9)	8.8 (5.1)	0.41 ^e
Current prescription inhaled corticosteroids; no. (%)	17 (94.4%)	17 (100%)	1.00 ^f
Care provider			0.73 ^f
primary care; no. (%)	13 (72.2%)	11 (64.7%)	
secondary care; no. (%)	5 (27.8%)	6 (35.3%)	
ACQ score (SD) ^a	0.6 (0.3)	1.9 (0.5)	<0.01 ^e
ATAQ control score (SD) ^b	0 (0)	2 (1.8)	<0.01 ^e
KASE-AQ: attitude (SD) ^c	3.7 ^g	3.8	0.55 ^e
KASE-AQ: self-efficacy (SD) ^d	4.0 ^g	3.6	0.046 ^e
Pre-bronchodilator FEV ₁ (% predicted); mean (SD)	100.7 (20.9)	90.7 (17.7)	0.14 ^e
Electronic characteristics			
Internet connection			1.00 ^f
broadband; no. (%)	17 (94.4%)	16 (94.1%)	
dial-up; no. (%)	1 (5.6%)	1 (5.9%)	
Owns mobile phone; no. (%)	17 (94.4%)	14 (82.4%)	0.34 ^f
Lung function reports			1.00 ^f
by website only	10 (55.6%)	9 (52.9%)	
by SMS only	2 (11.1%)	2 (11.8%)	
both by website and SMS	6 (33.3%)	6 (35.3%)	

^a Asthma Control Questionnaire ranges from 0 (optimal asthma control) to 6. The mean of all maximum ACQ scores was calculated.

^b Asthma Therapy Assessment Questionnaire; control domain ranges from 0 (optimal control) to 7.

^c Knowledge, Attitude and Self-efficacy Asthma Questionnaire; attitude subscale ranges from 1 (negative attitude toward asthma) to 5 (positive attitude toward asthma).

^d Knowledge, Attitude and Self-efficacy Asthma Questionnaire; self-efficacy subscale ranges from 1 (poor perceived ability to control asthma) to 5 (well perceived ability to control asthma).

^e Unpaired *t* tests.

^f Fisher's exact test.

^g One missing observation.

INTRINSIC BARRIERS TO CURRENT ASTHMA MANAGEMENT

Attitude toward asthma management: Participants experienced symptoms as annoying; however, nobody perceived asthma as a serious disease. A minority expressed a negative attitude toward current asthma management. Two participants with well controlled asthma expressed attitudes of laziness and unwillingness to take medications; three participants with poor asthma control were bothered by the face-to-face medical reviews, since they learnt to live with their symptoms and saw no need for regular consultations (table 3, panel 1).

Table 3. Frequency of categories of statements in the focus group sessions and comparative statistics between participants with well and poorly controlled asthma

	Well controlled asthma: No. (%)	Poorly controlled asthma: No. (%)	Group comparison (<i>P</i> values) ^a
Panel 1: Intrinsic barriers to current asthma management			
Negative attitude toward asthma management	2 (11%)	3 (18%)	0.66
Negative social influences	0 (0%)	3 (18%)	0.11
Limited perceived ability to manage asthma	3 (17%)	11 (65%)	< 0.01
Panel 2: Barriers and benefits of internet-based self-management ^b			
2.1 <i>Internet-based monitoring</i>			
Electronic monitoring is feasible	15 (83%)	15 (88%)	1.00
Recognize benefits of electronic monitoring	1 (6%)	4 (24%)	0.18
2.2 <i>Internet information</i>			
Need for comprehensive information	3 (17%)	5 (29%)	0.44
Positive features of internet information	11 (61%)	12 (71%)	0.73
2.3 <i>Internet-based medical review</i>			
Positive attitude toward electronic consultation	8 (44%)	10 (59%)	0.51
Negative attitude toward electronic consultation	2 (11%)	2 (12%)	1.00
2.4 <i>Internet-based action plan</i>			
Able and ready to use internet-based action plan	2 (11%)	11 (65%)	< 0.01
No need to use action plan at all	14 (78%)	3 (18%)	< 0.01

^a Fisher's exact test.

^b Four components of asthma self-management programs (Gibson et al. *Respir Med* 2003).

Social norm: Only three participants with poorly controlled asthma reported negative social influences during sports and social activities (table 3, panel 1). They experienced social rejection by teachers or peers at school, who took no account of the patient's asthmatic symptoms.

Self-efficacy to manage asthma: About two-third of the participants with poor asthma control expressed limited perceived ability to control asthma (table 3, panel 1). There were situations in which they felt helpless with regard to gaining asthma control. They thought nothing could be done about symptoms or about an attack. Patients said they experienced symptoms or an attack even after administering medication. The majority of these participants experienced symptoms, but said that they were used to symptoms as a part of everyday life and that they had learnt to live with them (table 4).

Table 4. Expressions of acceptance of asthma symptoms

'It's just something you've got. Medications do help, but you just have these symptoms. So I think it's something that is just a part of it'

'You accept it and learn to live with it. I've got it since I was a kid, so I don't know any better.'

'I don't think when I'm short of breath: oh dear, I've asthma, how bad! Some have a bloody nose, others have asthma. I've had it for such a long time, so I get used to it.'

'There are others with more serious problems. Then I think...I've just got asthma and if it stays like this, I'm satisfied.'

Views on barriers and benefits of internet-based asthma self-management

Monitoring: The majority of participants held the view that internet-based monitoring and reporting was feasible (table 3, panel 2.1). They mentioned that it was not time consuming and did not interfere with their daily activities. Sending lung function values and symptom scores via the internet or SMS was easy and fast.

Patients in the well controlled group had fun doing the measurements, but did not think it was very useful. They felt able to personally register deteriorating symptoms without using electronic lung function measurements or symptom scores. They did not observe benefits from daily electronic monitoring and feedback, since they did not experience any symptoms at the moment.

About a quarter of patients with poor asthma control did report the usefulness of measuring their lung function daily and getting instant feedback (table 3, panel 2.1). Observing symptoms and lung function over time and being able to react to changes in asthma were mentioned as personal benefits of internet-based monitoring, reporting and feedback. Almost nobody with poorly controlled asthma worried about monitoring for a long time (*ie*, > 1 year).

Information: In general, participants noted that they had not obtained much information on asthma or asthma medication in the past. Some said they had got some information many years ago, but could not remember which information or only remembered that they did not understand.

A quarter of all participants expressed a need for information about asthma. Participants wanted to obtain information about the cause of asthma, functioning of the lungs and mechanisms of asthma medication. We did not observe differences between participants with good and poor asthma control (table 3, panel 2.2).

The majority of participants did not express a need for extra information about asthma. They believed they had sufficient knowledge regarding how and when to use controller and reliever puffs. Some participants with well controlled asthma thought it would be useful to provide information about asthma to patients with more severe symptoms, but not to themselves. All patients agreed that if information was offered it should be offered through the internet and not through, for instance, leaflets or books from the asthma foundation. Internet is easy to use, easily accessible ('I have a computer with internet connection in my bedroom') and provides the opportunity to show graphics and short films. Most participants felt that just plain text was rather boring.

Regular medical review: Most participants thought it was not necessary to visit their physician if their asthma was under control. Three patients even mentioned that doctor visits were annoying. During doctor visits, lung values were measured, and if these were acceptable, you could leave. Patients preferred to visit their doctor only when symptoms were getting worse.

Participants were enthusiastic about the internet-based review by sending lung values and symptom scores via the internet or SMS, with the possibility to add comments or questions (table 3, panel 2.3). Patients with poorly and well controlled asthma mentioned that e-mail communication and electronic consultation was useful (table 5). Almost everyone used the computer daily. Most participants felt no need to see their physician or nurse in person for regular review.

Table 5. Participants' views on electronic communication

<i>Participant with well controlled asthma :</i>
'I don't need to see a doctor or nurse personally. If I know she [doctor or nurse] sees my values, then it's okay for me. Maybe when things go worse, I'd like to be examined, but if things go just normally, I don't mind to be in contact just by email.'
<i>Participant with poorly controlled asthma:</i>
'I don't need personal contact. One should just trust the advice. It's about the advice not about the nurse or doctor. So I think electronic consultation is rather useful.'

Individualized action plan: Almost 80% of the patients with well controlled asthma saw no need for an individualized written action plan (table 3, panel 2.4). They mentioned that they did not need it, that they already managed their asthma themselves and that it was unpleasant or difficult to develop a personalized action plan with a health-care professional on how to adjust treatment in response to worsening asthma control. Some

said that it may be useful for others but not for themselves. Only two participants were willing to use an electronic action plan, which involved daily monitoring, for a long period of time.

In contrast, two third of participants with poor asthma control mentioned that it was useful to formulate an action plan on the internet (table 3, panel 2.4). They appreciated messages when lung function or symptoms deteriorated and they valued advice on how and when to change asthma medication. Participants with poorly controlled asthma were able and ready to use an internet-based asthma self-management plan for a long period of time (*ie*, at least a year).

DISCUSSION

We conducted focus group interviews with adolescent asthma patients to reveal the intrinsic barriers in current asthma management and to explore barriers and benefits of internet-based asthma self-management. A limited perceived ability to control asthma was the most striking barrier to current asthma self-management in adolescents with poor asthma control. Patients indicated their inability to adequately manage symptoms and, therefore, accepted symptoms to a large extent. This particular group clearly expressed several benefits from internet-based asthma self-management: electronic monitoring and feedback, easily accessible information, email communication and an electronic action plan.

Our study protocol was unique in its design. Since we performed an observational study on electronic lung function and symptom monitoring prior to the focus groups we were able to identify patients with poorly and well controlled asthma and to focus on differences between these groups. The most striking difference in intrinsic barriers to current asthma management between patients with poorly and well controlled asthma was the fact that the former group did currently not feel able to manage asthma and accepted asthma symptoms as part of their everyday life. It is, however, well known that there is no need to accept asthma symptoms, since good asthma control can be achieved in the vast majority of patients (28). In the context of guided asthma self-management it is important for patients to become aware of achievable asthma control through information and education and to empower patients in self-managing their asthma by using feasible management programs.

Another advantage of the study design is that patients participated in electronic monitoring via the internet and SMS prior to the focus group sessions, which informed their opinions. In contrast to a questionnaire survey and a recent study using discrete choice experiments with hypothetical scenarios which raised concerns about workload and interference with day to day lives (14, 29), we learnt that electronic monitoring

and reporting was no burden at all and easy to incorporate in the daily activities of adolescents. Previous studies have doubted the compliance and reliability of home monitoring by asthmatic patients when they were also required to keep a conventional paper diary (30, 31). However, use of electronic monitoring alone appears to improve outcomes of compliance and reliability and may thus provide a useful tool in guided self-management (13, 32).

Some patients expressed a need for information on, for example, the cause of asthma, the functioning of the lungs and mechanisms of asthma medication. From the intrinsic barriers to manage asthma, mentioned by participants with poorly controlled asthma, we learnt that there is room for improvement of self-efficacy activities. Inaccurate beliefs about the need to accept asthma symptoms and the cause of asthma can be addressed during information or education sessions. Participants indicate that the internet is the most convenient way for obtaining information on asthma matters rather than, for instance, the leaflets of the asthma foundation. The preference for internet-based information over leaflets is likely to relate to the existing practices of this particular age group, but would not necessarily be reported by elderly patients. (11)

Adolescents' views on regular medical review are in concordance with what we know from adult interviews (33). Face-to-face consultations are appropriate in those with deteriorating asthma but are not accepted for reviewing well controlled asthma. Participants did not mind communicating by e-mail or SMS without having face-to-face contact with a health care provider.

In accordance with previously published focus group research in which patients did not appear to be enthusiastic about guided self-management plans (8), we observed that patients with good asthma control are not willing to use self-management plans. They did not think these plans are useful for them or they believed that they were already managing their asthma competently. In contrast, most participants with poorly controlled asthma favored the further use of electronic self-management plans.

A limitation of our study is that we counted only verbal statements made in the focus groups. A drawback of this analysis is that non-verbal expressions are not counted (*e.g.*, nodding agreement with a statement made by another participant) (25). Nevertheless, to our opinion these quantitative counts of verbal utterances support our qualitative findings.

A second limitation concerns the selection of patients. Since 63% responded to our invitation to join the focus groups, we must be cautious in generalizing our results. We may have observed the opinions of a selected group of patients willing to participate in asthma self-management programs. On the other hand this assumption does not hold in patients with well controlled asthma who were reluctant to use guided self management plans.

Our findings reveal that there is a need to overcome limited perceived ability in current asthma management of adolescents with poor asthma control. Internet-based self-management appears to be a powerful tool to overcome limited self-efficacy in this group of patients. Adolescents with poorly controlled asthma recognize the extensive potential benefits of internet-based self-management and are ready and able to use a guided self-management program including internet and short message service over a long period of time (*ie*, at least 1 year). This group can be easily identified by administering short questionnaires on asthma control. Adolescents with well controlled asthma are unlikely to use internet-based self-management programs. Internet-based self-management should therefore target adolescents with poor asthma control.

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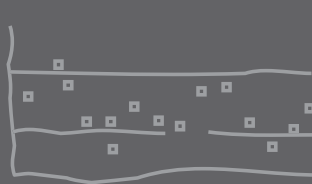
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CHAPTER 4

Internet-based self-management plus education compared with usual care in asthma: a randomized controlled trial

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ABSTRACT

Background

The Internet may support patient self-management of chronic conditions, such as asthma.

Objective

To evaluate the effectiveness of Internet-based asthma self-management.

Design

Randomized controlled trial.

Setting

37 general practices and 1 academic outpatient department in The Netherlands

Patients

200 adults with asthma who were treated with inhaled corticosteroids for 3 months or more during the previous year and had access to the Internet.

Measurements

Asthma related quality of life at 12 months (minimal clinically significant difference of 0.5 on the 7-point scale), asthma control, symptom-free days, lung function, and exacerbations.

Intervention

Participants were randomly assigned by using a computer-generated permuted block scheme to Internet-based self-management (n=101) or usual care (n=99). The Internet-based self-management program included weekly asthma control monitoring and treatment advice, on-line and group education, and remote Web communications.

Results

Asthma related quality of life improved by 0.56 and 0.18 points in the Internet and usual care groups, respectively (adjusted between-group difference, 0.38 [95% CI, 0.20 to 0.56]). An improvement of 0.5 point or more occurred in 54% and 27% of Internet and usual care patients, respectively (adjusted relative risk, 2.00 [CI 1.38 to 3.04]). Asthma control improved more in the Internet group than in the usual care group (adjusted difference -0.47 [CI, -0.64 to -0.30]). At 12 months, 63% of Internet patients and 52% of usual care patients reported symptom-free days in the previous 2 weeks (adjusted absolute difference, 10.9% [CI 0.05% to 21.3%]). Pre-bronchodilator FEV₁ changed with

0.24 L and -0.01 L for Internet and usual care patients, respectively (adjusted difference, 0.25 L [CI, 0.03 to 0.46 L]). Exacerbations did not differ between groups.

Limitations

The study was unblinded and lasted only 12 months.

Conclusion

Internet-based self-management resulted in improvements in asthma control and lung function, but did not reduce exacerbations, and improvement in asthma-related quality of life was slightly less than clinically significant.

INTRODUCTION

Asthma is a chronic disorder of the airways that is characterized by recurring respiratory symptoms, variable airflow obstruction, airway hyperresponsiveness, and underlying inflammation (1, 2). Recent clinical guidelines for the management of asthma distinguish four essential components of asthma care: assessment and monitoring, patients' education, control of environmental and co-morbid factors that affect asthma, and drug treatment. With appropriate medical care, well-informed and empowered patients can control their asthma and live full active lives (1, 2). However, despite the availability of monitoring tools and effective therapy, asthma control is suboptimal in many patients worldwide, and long-term management falls far short of the goals set in the guidelines (3).

Self-monitoring, education and specific medical care are important aspects in improving the lives of asthma patients (1, 2). However, many patients with mild or moderate persistent asthma do not attend check-ups regularly or visit their doctor with symptoms of the disease (4). In addition, in practice, both patients and their health care providers are reluctant to use written self-management plans (5).

Internet technology is increasingly being seen as an appealing tool to support self-management for patients with chronic disease in remote and underserved populations (6-8). However, to date, studies on Internet-based asthma self-management show only short-term improvements in asthma control, lung function and quality of life (9-11). Long-term studies on the effect of Internet-based self-management, including all its essential features, are not available.

Therefore, we developed a guided self-management tool for adult patients with asthma that included Internet-based home monitoring and treatment advice (action plan), on-line education and remote Web communication with a specialized asthma nurse. The goal of our study was to assess the long-term clinical effectiveness of Internet-based self-management education compared with usual physician-provided care alone.

METHODS

Design Overview

We conducted a 12-month, multicenter, nonblinded, randomized, controlled trial. We randomly assigned patients to Internet-based self-management (Internet group) as an adjunct to usual care or to usual physician-provided care alone (usual care group). The Internet-based self-management program included weekly asthma control monitoring and treatment advice, online and group education, and remote Web communications with a specialized asthma nurse. The intervention continued for 12 months after enrollment. The Medical Ethics Committee of the Leiden University Medical Center, Leiden, the Netherlands, approved the study.

Setting and Participants

We recruited patients from 37 general practices (69 general practitioners) in the Leiden and The Hague area and the Outpatient Clinic of the Department of Pulmonology at the Leiden University Medical Center from September 2005 to September 2006. Inclusion criteria were physician-diagnosed asthma coded according to the International Classification of Primary Care in the electronic medical record (12), age 18 to 50 years, prescription of inhaled corticosteroids for at least 3 months in the previous year, no serious co-morbid conditions that interfered with asthma treatment, access to the Internet at home, and mastery of the Dutch language. We excluded patients who were receiving maintenance oral glucocorticosteroid treatment. On the basis of diagnosis, age, prescribed asthma medication, and co-morbid conditions, we sent eligible patients an invitation letter followed by 1 reminder letter after 2 to 4 weeks if they did not respond to the first. We continued this process until a total of 200 patients had entered the study (September 2006). All participants gave written consent.

Randomization and Intervention

In a 2-week baseline period before randomization, we collected data on patient demographic characteristics, asthma-related quality of life, symptom control, lung function, and medication level. We provided basic education about core information on asthma, action of medications, and inhaler technique instructions to all patients. We trained all participants to measure FEV₁ daily with a hand-held electronic spirometer (PiKo-1, Ferraris Respiratory, Hertford, United Kingdom) and to report the highest value of 3 measurements in the morning before taking medication (2, 13). They were shown how to report these values on a personal page on a secure Web application by using a login password (or how to report by mobile telephone text message). Patients were also asked to report their nighttime and daytime asthma symptom scores on this Internet page or by text message. We asked all participants to complete the Asthma Control Ques-

tionnaire on their personal Internet page each week (14). We did not give any patients feedback about lung function or asthma control.

After the 2-week baseline period, we randomly assigned participants to either the Internet group or the usual care group. We stratified according to care provider (primary vs. subspecialty care) and asthma control at baseline (15). We randomly assigned patients to the 2 groups (1:1 ratio) by using a computer-generated, permuted-block scheme. Allocation took place by computer after collection of the baseline data, ensuring concealment of allocation.

The Internet-based self-management program consisted of the 4 principal components of asthma self-management and was accessed through the specially designed Web site, which allowed monitoring through the Web site (or text message on a mobile telephone), use of an Internet-based treatment plan, online education, and Web communications with a specialized asthma nurse (16). Patients monitored their asthma weekly by completing an electronic version of the Asthma Control Questionnaire on the Web site and instantly received feedback on the current state of their asthma control along with advice on how to adjust their treatment according to a predefined algorithm and treatment plan (Table 1 and Appendix Figures 1, 2, 3, 4, and 5). Depending on the scores submitted, patients received 4 types of self-treatment advice. When 4 consecutive Asthma Control Questionnaire scores were 0.5 or less, patients were advised to decrease treatment according to treatment plan. When 2 consecutive scores were greater than 0.5 but less than 1.0, patients were advised to increase treatment according to treatment plan. When 1 score was 1.0 or more but less than 1.5, patients were advised to immediately increase treatment according to treatment plan. Finally, when 1 score was 1.5 or more, patients were advised to immediately increase treatment and contact the asthma nurse.

Table 1. Treatment plan

Step*	Medication
1	As needed rapid-acting β_2 -agonist†
2	Low-dose inhaled glucocorticosteroids
3a	Low-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
3b	Medium-dose inhaled glucocorticosteroids
3c	High-dose inhaled glucocorticosteroids
4a	Medium-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
4b	High-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
4c	Contact asthma nurse‡ : consider addition of leukotriene modifier
5	Contact asthma nurse‡ : consider addition of oral glucocorticosteroid

* Step numbers correspond with recommended steps in the Global Initiative for Asthma guidelines (1).

† Applies to all treatment steps.

‡ Or other health care provider.

We advised no medication changes during the 4 weeks after treatment was stepped up (evaluation period). In addition to weekly assessments, patients could optionally report daily symptoms and lung function and were able to contact our asthma nurse through the Web or by telephone. Thus, any acute deterioration warranting a visit to the general practitioner or hospital could be detected (Appendix Figures 2 and 3).

We aimed to empower patients to use the Internet-based self-management tool and to develop a patient–provider partnership in asthma care (2). Self-management education consisted of both Web-based and face-to-face, group-based education. Web-based education included asthma information, news, frequently asked questions, and interactive communication with a respiratory nurse specialist. We scheduled 2 group-based education sessions, which lasted 45 to 60 minutes, for patients in the Internet-based self-management group within 6 weeks after entering the trial. Both sessions included exploration of a patient’s interests and previous knowledge (negotiating an agenda and patient-centered education), personalized feedback, and empowerment of self-management (self-efficacy and implementing a plan for change) (2, 17). The first educational session also included pathophysiology of asthma, information on the Web-based action plan, and information and review of inhalation technique. The second educational session gave information about the mechanisms and side effects of medication and explained trigger avoidance.

Patients in the usual care group received asthma care according to the Dutch general practice guidelines on asthma management in adults, which recommend a medical review and treatment adjustment every 2 to 4 weeks in unstable asthma and medical review once or twice yearly for patients whose asthma is under control (18). These national guidelines are based on international guidelines, such as the Global Initiative for Asthma guidelines (1, 18).

Outcomes, Measurements and Follow-up Procedures

Process Evaluation

The process evaluation included educational outcomes (asthma knowledge, inhaler technique, and self-reported medication adherence), health care provider contacts for asthma, use of the Internet-based monitoring tool, and medication changes. We assessed asthma knowledge with the 12-item Consumer Asthma Knowledge Questionnaire (19, 20) and inhalation technique with the standardized checklist of the Dutch Asthma Foundation (21). We assessed knowledge, inhaler technique, and medication adherence at baseline and 12 months.

Health care provider contacts included physician visits, telephone contacts (quarterly questionnaire), and remote Web communications with a specialized asthma nurse.

We extracted the frequency of Internet-based monitoring from Web site log files and included optional daily lung function and symptom monitoring and weekly Asthma Control Questionnaire monitoring.

Medication use was reported at baseline, 3 months, and 12 months. For each patient, we measured the number of medication changes (or steps) by comparing treatment step at 3 months with treatment step at baseline (number of medication changes in first 3 months) and treatment step at 12 months with treatment step at 3 months (number of medication changes in the next 9 months). We totaled the numbers of medication changes in the first 3 months and next 9 months and reported averages per patient.

Clinical Outcomes

The primary clinical outcome measure was asthma-related quality of life, as measured by the 32-item Asthma Quality of Life Questionnaire (22). The minimal important difference is 0.5 on a 7-point scale. We assessed 5 secondary clinical outcomes: asthma control (minimal important difference is 0.5 on the 7-point Asthma Control Questionnaire scale), symptom-free days, prebronchodilator FEV₁, daily inhaled corticosteroid dose, and exacerbations. We assessed all outcomes except for exacerbations over 2 weeks, at 3 months, after the baseline period, and again at 12 months. During these assessments, all patients kept Internet-based daily diaries as they had during the baseline period. We restricted Web site access for usual care patients to this diary page. We defined symptom-free days as a night and day without asthma symptoms or being awakened by asthma symptoms, as measured by the TRUST (The Regular Use of Salbutamol Trial) diary card (23). We measured prebronchodilator FEV₁ during each 2-week assessment period (the end value used for analysis). We calculated daily inhaled corticosteroid dose as fluticasone equivalents. We defined exacerbations as deterioration in asthma that required emergency treatment or hospitalization (collected by quarterly questionnaire) or the need for oral steroids for 3 days or more (collected by pharmacy records), as judged by the attending physician, and assessed them over the whole year (24). We collected all outcome data similarly in both groups. Participants provided the Asthma Control Questionnaires, symptom-free days, and prebronchodilator FEV₁ through the Internet (the usual care group had limited access to the Web site for 2 weeks at baseline, 3 months, and 12 months). We collected the other outcomes by written questionnaires.

Statistical Analysis (including power calculation)

Our primary objective was to determine whether changes in asthma-related quality of life (Asthma Quality of Life Questionnaire score) differed between the Internet group and the usual care group. With a total of 100 patients per group, an SD of 0.75 (17), and a correlation coefficient of 0.5, our repeated-measures analysis had a statistical power

of 80% (at the 2-tailed 5% significance level) to detect a 0.26-point difference in Asthma Quality of Life Questionnaire score.

We analyzed the differences in the demographic characteristics between participants and non-participants and differences in baseline characteristics between the 2 randomization groups by using Fisher exact tests and unpaired Student *t* tests for proportions and continuous data, respectively. We analyzed within- and between-group differences in the process outcomes with paired and unpaired Student *t* tests, respectively.

We analyzed changes in the Asthma Quality of Life Questionnaire scores, Asthma Control Questionnaire scores, percentage of symptom-free days, and lung function by using linear mixed-effects models. We added a random intercept at the patient level to adjust for repeated measurements over time (25). We added 6 covariates (sex, age, education level, smoking status, type of care provider, and number of control problems in the previous year) to the models. We entered time to the models as a categorical covariate. We aimed the primary analysis at treatment effects after 12 months. In addition, we analyzed differences in treatment effects between 3 and 12 months. We compared exacerbations between the 2 groups with a Cox proportional hazards model, including the same 6 covariates as added to the linear mixed-effects model.

To estimate the number of patients who gained a clinically important benefit from treatment, we used logistic regression analysis with “clinical improvement at 12 months” as a dichotomized outcome and the same 6 covariates, as previously described (26). We analyzed complete cases and did not impute missing values. Clinical improvements in Asthma Quality of Life Questionnaire and Asthma Control Questionnaire scores were changes from baseline of 0.5 or more and changes from baseline of –0.5 or less, respectively (27, 28). As the outcomes of interest were common, odds ratios were inappropriate to estimate relative risks (RRs); therefore, we recalculated them into RRs with CIs on the basis of marginal standardization by using a bootstrap method (29).

We did all analyses on an intention-to-treat basis. We did not impute missing values. We used Stata, version 9.0 (StataCorp, College Station, Texas), for all analyses.

RESULTS

We invited the 930 patients who met the selection criteria to participate in the study. Patients who consented to participate ($n = 200$ [21.5%]) did not differ from non-participants in age (mean age, 36.6 years vs. 35.8 years; $P = 0.27$) or socioeconomic status (living in an underprivileged area, 5.0% vs. 7.1%; $P = 0.29$), but they did differ in sex (women, 69.5% vs. 59.7%; $P = 0.012$). Baseline characteristics of the randomization groups were similar (Table 2).

Table 2. Baseline characteristics

	Usual care group (n=99)	Internet group (n=101)
Men, %	29%	32%
Mean age (range), y	37 (18-50)	36 (19-50)
Mean asthma duration (range), y	18 (0-47)	15 (1-47)
Education level, %		
Low	14%	11%
Middle	33%	37%
High	53%	52%
Smoking status, %		
Never	53%	58%
Former	33%	30%
Current	14%	12%
Care provider, %		
General practitioner	80%	79%
Chest physician	20%	21%
Mean FEV ₁ (pre-bronchodilator) (range), L	3.13 (1.56-5.23)	3.08 (1.14-5.19)
Mean FEV ₁ (pre-bronchodilator) (range), % predicted	90 (53-118)	88 (34-133)
Mean daily inhaled corticosteroid dose (range), µg	517 (0-2000)	497 (0-1000)
Inhaled long-acting β ₂ -agonist use, %	60%	59%
Leukotriene modifier use, %	2%	3%
Mean educational outcomes (range) *		
Asthma knowledge †	8.32 (3-12)	8.74 (2-12)
Inhaler technique ‡	4.11 (1-5)	4.34 (3-5)
Self-reported medication adherence §	6.19 (0-7)	6.46 (0-7)
Clinical outcomes		
Mean Asthma Quality of Life Questionnaire score (range)	5.79 (3.03-7.00)	5.73 (3.66-6.94)
Mean Asthma Control Questionnaire score (range)	1.11 (0-3.86)	1.12 (0.07-3.22)
Symptom-free days (range), %	44.5 (0-100)	44.9 (0-100)

Data are mean (range) or percentage unless otherwise indicated.

FEV₁ = Forced expiratory volume in 1 second.

* Baseline data for asthma knowledge and self-reported medication adherence were available for 91 and 99 patients in the usual care and Internet groups, respectively. † Consumer Asthma Knowledge Questionnaire score range (worst – best), 0 – 12. ‡ Checklist of the Dutch Asthma Foundation score range (worst – best), 0 – 5. § Range: 0 – 7 d/wk.

Process Evaluation

Asthma knowledge improved in the Internet group (0.42 [95% CI, 0.05 to 0.79]) and the usual care group (0.86 [CI, 0.35 to 1.36]), but the improvements did not differ between the groups ($P = 0.70$) (Table 3). Similarly, inhalation technique improved in the Internet group (0.21 [CI, 0.04 to 0.38]) and the usual care group (0.32 [CI, 0.15 to 0.50]), but the improvements did not differ between the groups ($P = 0.143$) (Table 3). There were no within- or between-group differences in self-reported medication adherence.

Patients in the Internet group had 5.9 (CI, 4.8 to 7.1) online contacts with the asthma nurse during the 1-year follow-up. The Internet group had slightly fewer physician visits than the usual care group (−0.74 physician visits [CI, −1.55 to 0.06 physician visits]). Patients in the Internet group reported optional daily lung function and symptom scores at 108 days (CI, 98 to 126 days) and Asthma Control Questionnaire scores at 35 weeks (CI, 31 to 38 weeks). Treatment increases (step-up) and decreases (step-down) both occurred more often in the Internet group than in the usual care group (Table 3).

Table 3. Process outcomes for usual care and Internet-based self-management groups after 12 months

	Usual care group (n = 92)	Internet group (n = 91)	Difference (95% CI)	P Value
Educational outcomes				
Asthma knowledge *	9.10	9.21	0.11 (−0.44 to 0.66)	0.70
Inhaler technique †	4.49	4.63	0.15 (−0.05 to 0.34)	0.14
Self-reported medication adherence ‡	6.37	6.32	−0.05 (−0.59 to 0.49)	0.86
Health care provider contacts for asthma, average number per patient				
Physician visits	1.86	1.11	−0.74 (−1.55 to −0.06)	0.071
Telephone contacts with health care provider	2.35	2.39	0.04 (−0.75 to 0.84)	0.91
Online contacts with asthma nurse §	NA	5.93	-	-
Use of Internet-based monitoring tool §				
Optional daily lung function scores, average days per patient	NA	107.8	-	-
Asthma Control Questionnaire monitoring, average weeks per patient	NA	34.8	-	-
Medication changes, average number per patient				
Step-up in treatment	0.39	0.90	0.51 (0.30 to 0.72)	<0.001
Step-down in treatment	0.44	0.75	0.31 (0.09 to 0.53)	0.006

NA = not applicable. * Consumer Asthma Knowledge Questionnaire score range (worst – best), 0 – 12. † Checklist of the Dutch Asthma Foundation score range (worst – best), 0 – 5. ‡ Range: 0 – 7 days a week. § Obtained from Web site log files available for all patients in the Internet group (n = 101).

Clinical Outcomes

Participants did not deviate from the study protocol. We obtained 90% and 91.5% of primary outcome data during the assessment periods at 3 and 12 months, respectively (Figure 1). The analysis set included all randomly assigned patients who provided any data during the study.

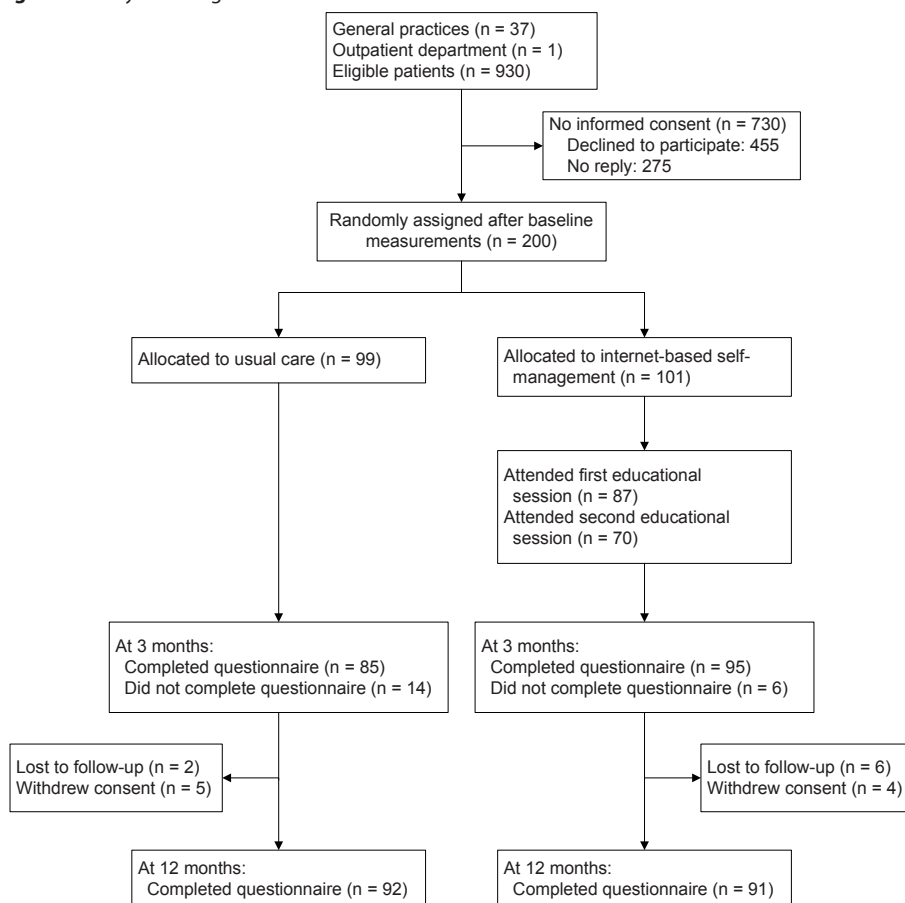
Table 4 summarizes the results of the primary and secondary clinical outcomes (table 4).

Asthma-related quality of life (Asthma Quality of Life Questionnaire) improved more in the Internet group than in the usual care group (change from baseline, 0.56 vs. 0.18; adjusted

Table 4. Primary and secondary clinical outcomes in usual care and Internet-based self-management groups *

	Usual care group (n = 99)				Internet group (n = 101)				Between-group comparisons	
	Baseline	3 Months	12 Months	Change From Baseline to 12 Months (95% CI)	Baseline	3 Months	12 Months	Change From Baseline to 12 Months (95% CI)	Difference in Changes (95% CI)	P value
Primary outcome										
Asthma Quality of Life Questionnaire †	5.79	5.96	5.97	0.18 (0.05 to 0.31)	5.73	6.15	6.29	0.56 (0.43 to 0.68)	0.38 (0.20 to 0.56)	<0.001
Secondary outcomes										
Asthma Control Questionnaire ‡	1.11	1.05	1.04	-0.06 (-0.18 to 0.05)	1.12	0.67	0.59	-0.54 (-0.65 to -0.42)	-0.47 (-0.64 to -0.30)	<0.001
Symptom-free days, %	44.5	47.5	51.8	7.3 (0.0 to 14.6)	44.9	63.4	63.1	18.2 (10.8 to 25.6)	10.9 (0.05 to 21.3)	0.039
FEV ₁ , L	3.13	3.10	3.12	-0.01 (-0.16 to 0.14)	3.08	3.20	3.32	0.24 (0.08 to 0.39)	0.25 (0.03 to 0.46)	0.025
Daily inhaled corticosteroid dose, µg	517	494	470	-48 (-115 to 20)	497	638	506	9 (-58 to 76)	57 (-38 to 152)	0.24

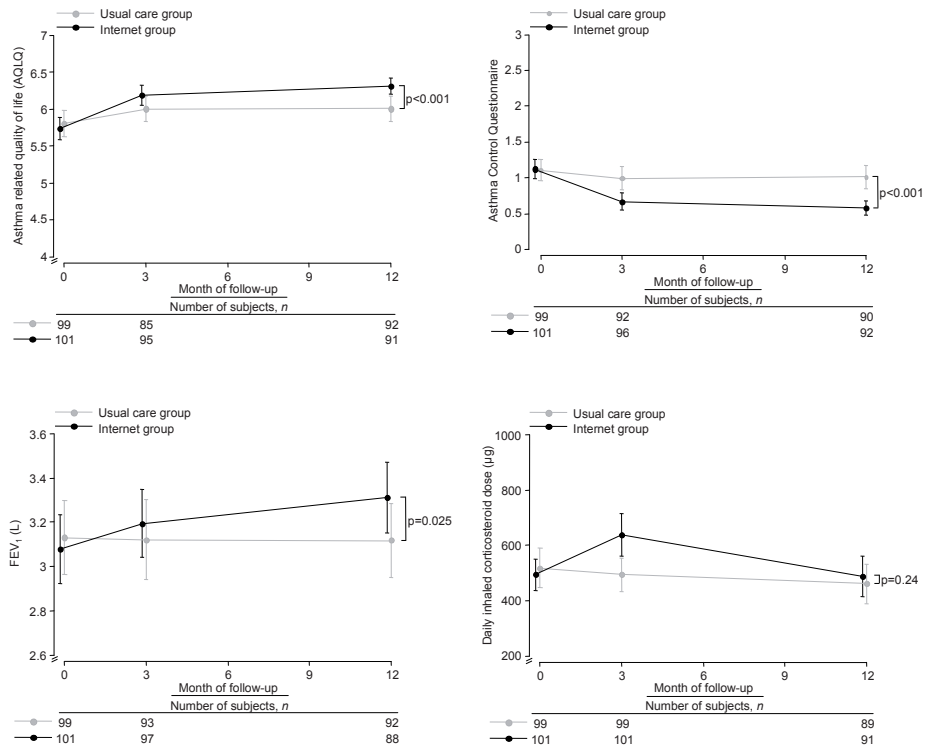
* Values are model estimates of linear mixed-effects models with a random intercept, adjusted for sex, age, education level, smoking status, type of care provider and number of control problems in the previous year. † Score range (worst – best), 1 – 7. ‡ Score range (worst – best), 6 – 0.

Figure 1. Study flow diagram

difference, 0.38 [CI, 0.20 to 0.56]) (Figure 2 A). This treatment effect was not statistically different between 3 and 12 months. Patients assigned to the Internet group more often had a clinically relevant improvement (≥ 0.5) in asthma-related quality of life than did those in the usual care group (54% vs. 27%; adjusted RR, 2.00 [CI, 1.38 to 3.04]) (Figure 3, *top*).

The Internet group showed greater improvement of asthma control (Asthma Control Questionnaire) than did the usual care group (change from baseline, -0.54 vs. -0.06 ; adjusted difference, -0.47 [CI, -0.64 to -0.30]) (Figure 2 B, and Table 4). This treatment effect was not statistically different between 3 and 12 months. Patients assigned to the Internet group had a clinically relevant improvement (-0.5 or less) in asthma control more often than those in the usual care group (48% vs. 17%; adjusted RR, 2.87 [CI, 1.86 to 5.14]) (Figure 3, *bottom*).

Figure 2. Changes in mean Asthma Quality of Life Questionnaire score (A), Asthma Control Questionnaire score (B), FEV₁ (C), and daily inhaled corticosteroid dose (D) during 1-year follow-up for the Internet group and usual care group.

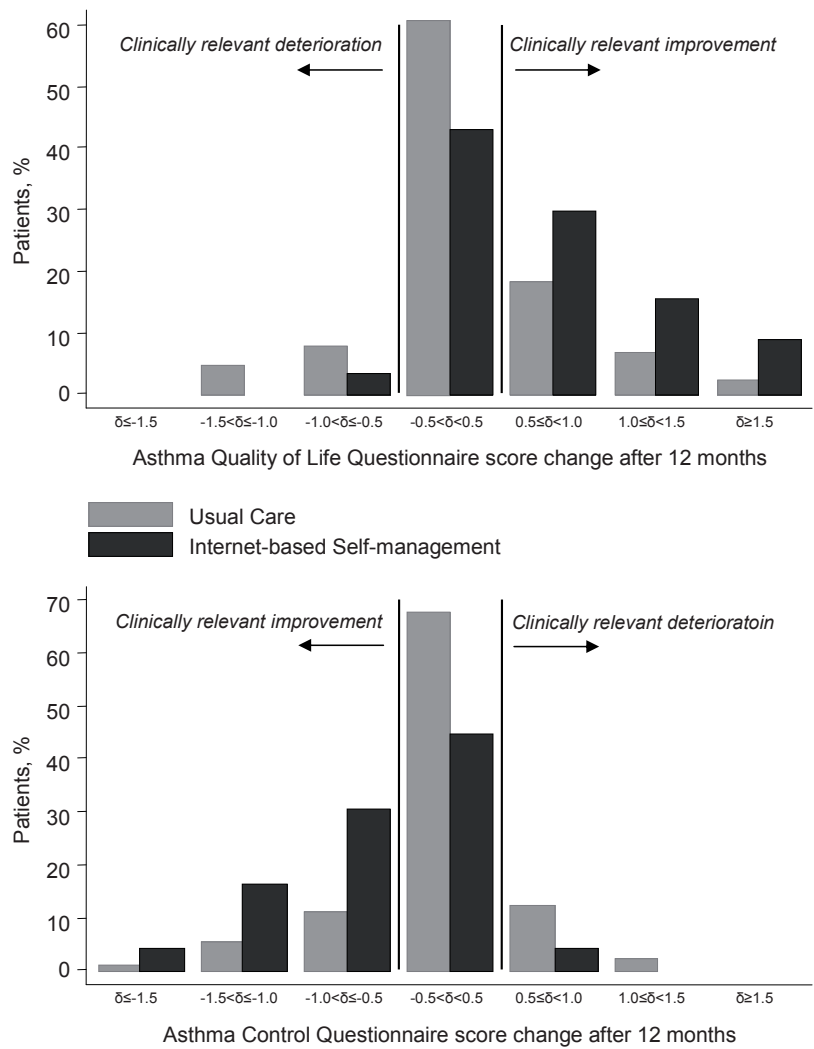


The minimal important difference for the Asthma Quality of Life Questionnaire score is 0.5, with higher scores indicating better quality of life. The minimal important difference for the Asthma Control Questionnaire is 0.5, with lower scores indicating better asthma control. Plotted values are based on complete cases. Error bars indicate 95% CIs. P values are shown for between-group differences in change scores at 12 months and are from linear mixed-effects models.

After 12 months, the proportion of symptom-free days reported for the previous 2 weeks increased by an absolute 18.2% and 7.3% (adjusted difference, 10.9% [CI, 0.05% to 21.3%]) in the Internet and usual care groups, respectively. Prebronchodilator FEV₁ changed by 0.24 L and –0.01 L (adjusted difference, 0.25 L [CI, 0.03 to 0.47 L]) for the Internet and usual care groups, respectively (Figure 2 C). Daily inhaled corticosteroid dose did not statistically significantly differ after 12 months (difference, 57 µg [CI, –38 to 152 µg]) (Figure 2 D). However, a statistically significant time-by-intervention effect occurred during the first 3 months when the daily inhaled corticosteroid dose increased by 164 µg (*P* < 0.001) in the Internet group followed by a change of –107 µg (CI, –202 to –12 µg; *P* = 0.027) in the next 9 months in the Internet group compared with the usual care group. During follow-up, 17 exacerbations occurred in 11 patients in the Internet

group compared with 20 exacerbations in 10 patients in the usual care group (hazard ratio, 1.18 [CI, 0.51 to 2.74]).

Figure 3. Distribution of change in scores for Asthma Quality of Life Questionnaire (top) and Asthma Control Questionnaire (bottom).



δ = 12-month score minus baseline score. The minimal important difference for the Asthma Quality of Life Questionnaire is 0.5, with higher scores indicating better quality of life. The minimal important difference for the Asthma Control Questionnaire is 0.5, with lower scores indicating better asthma control.

DISCUSSION

We compared the clinical effectiveness of Internet-based self-management (as an adjunct to physician care) with usual physician-provided care alone. We offered all the components for optimal self-management (monitoring, education, medical review, and an action plan) through the Internet: electronic Internet-based symptom and lung function monitoring, access to an online personalized action plan, online education, and professional review using e-mail and private messaging. Our results suggest that Internet-based self-management of asthma improves quality of life, asthma control, and lung function and increases the number of symptom-free days compared with usual physician-provided care.

To our knowledge, this is the first randomized, controlled evaluation of Internet-based asthma self-management that shows sustained improvement in asthma-related quality of life. The improvement achieved in the Internet group was as large as the minimal important difference with patients who reached optimal scores for asthma-related quality of life during 1-year follow-up (27). Two previous trials on Internet-based asthma management in adults and children, respectively, reported only short-term improvements on asthma-related quality of life (10, 11), whereas a 1-year, randomized, controlled trial that compared Internet-based and office-based asthma care in children did not show any changes in quality of life (9). Previous trials of paper-and-pencil self-management programs showed only moderate and inconsistent improvements on asthma-related quality of life (16, 17).

For secondary end points, we consistently demonstrated clinically relevant improvements in asthma control, lung function, and the percentage of symptom-free days. The beneficial clinical effects were reached without an increase in inhaled corticosteroid dose at 12 months. In the first 3 months, many patients had uncontrolled asthma and were advised to increase their inhaled corticosteroid doses. The improvement in asthma control seen after 3 months allowed a decrease in inhaled corticosteroid medication over the next 9 months without loss of asthma control. This pattern suggests tailoring medication to patients' needs rather than increasing medication for the whole study sample.

The process evaluation included outcomes on the principal components of asthma self-management. We showed improvements in asthma knowledge and inhalation technique in both groups for asthma education but without between-group differences. The improvements in the usual care group may be explained by the baseline meeting and measurements, which triggered patients to improve their asthma knowledge and inhalation skills. Other studies that assessed the behavioral effect of self-management programs found a similar result (9, 30). Basic education only, therefore, did not seem to be the key component explaining the positive effects of the Internet-based self-

management intervention. The Internet group tended to have fewer annual physician visits. This was due to either increased asthma control in this group and therefore fewer requirements for medical review or physician visits may have been substituted by online contacts with our asthma nurse. By protocol, Internet-based monitoring only occurred in the intervention group. Patients reported symptoms and lung function once in 3 days and reported weekly asthma control in 35 of 52 weeks. The difference in the number of treatment changes between the groups may be explained by this frequency of monitoring and subsequent treatment advice.

Differences in the baseline characteristics, patient selection, participation rate, or underperformance of usual care do not seem to influence the results of this study. First, we found no statistically significant differences in the baseline characteristics between the 2 groups. Second, we selected patients from primary care practices and an outpatient subspecialty practice on the basis of a physician's diagnosis of asthma. We cannot exclude the possibility that some patients did not meet the lung function or airway responsiveness criteria for a diagnosis of asthma, according to recent guidelines. However, in our study, as in a realistic routine care setting, we identified patients who were eligible for an asthma Internet-based self-management intervention through a physician's diagnosis of asthma. Consequently, this might have diluted the effect of the Internet-based self-management intervention but enhanced the external validity of our study (31). Third, the participation rate was 21.5%, which is similar to rates in other asthma education and management studies (17, 32, 33). Age and socioeconomic status of non-participants were similar to those of participants, and women were only slightly overrepresented in the study sample. Demographic characteristics would suggest broad applicability in the general population; however, other important determinants of the non-participants were unknown. Patients with previously uncontrolled asthma are more likely to participate in a self-management program than are patients with well-controlled asthma (7). Structural barriers, such as lack of time; living too far; and social behavioral factors, such as self-efficacy, belief in personal benefits, and social influence, also predict participation in a self-management program (34). These clinical and psychological factors could have differed in participants and non-participants and might therefore have bearing on generalizability. In addition, about 20% of the population in the Netherlands does not have access to the Internet, which is an obvious reason for nonparticipation in our study. However, because Internet access is increasing worldwide, this barrier might disappear. Fourth, because we also saw improvements in asthma-related quality of life and control in the usual care group, although these did not reach statistical significance, it seems unlikely that our results can be explained by underperformance of physician-provided care during the study compared with prestudy standards.

A potential limitation of our study was that the patients and physicians were aware of the allocation group. Because asthma-related quality of life, asthma control, and

symptom-free days were self-reported, the improvements may have resulted from increased awareness rather than the Internet-based intervention. Furthermore, because the Asthma Control Questionnaire score was the target measurement that drove the treatment algorithm, we expected improvements. In addition, the absence of a difference in an objective outcome, such as exacerbations, does not support our positive findings in patient-reported outcomes. However, this study was not designed or powered to detect a difference in exacerbation rate in patients with mild-to-moderate persistent asthma (24). Moreover, the improvement in lung function, as an objective measurement, provides a fair basis for our findings in quality of life, asthma control, and symptom-free days.

The implications of our findings show that self-management of asthma guided by a validated, short questionnaire on asthma control, as recommended by recent guidelines, is feasible and improves quality of life. In addition, we demonstrate that the Internet is an effective way to disseminate knowledge to patients with asthma and a successful tool that can empower patients to achieve and maintain control of their asthma by adjusting treatment with effective medication. Our study further supports the emphasis that recent guidelines have placed on monitoring asthma control and illustrates that a relatively simple validated instrument, such as the Asthma Control Questionnaire, can be used to operationalize asthma control in guided self-management (1, 2, 14). Taken together, Internet-based self-management provides new ways to tailor monitoring and education continuously to patients' needs, which empowers patients to control their asthma and to live full, normal, and active lives, even potentially in remote and underserved populations in developed and developing countries (35).

In conclusion, Internet-based self-management improves asthma-related quality of life, asthma control, and lung function and increases the number of symptom-free days. The challenge is implementing Internet-based self-management on a wider scale within routine asthma care.

ACKNOWLEDGMENT

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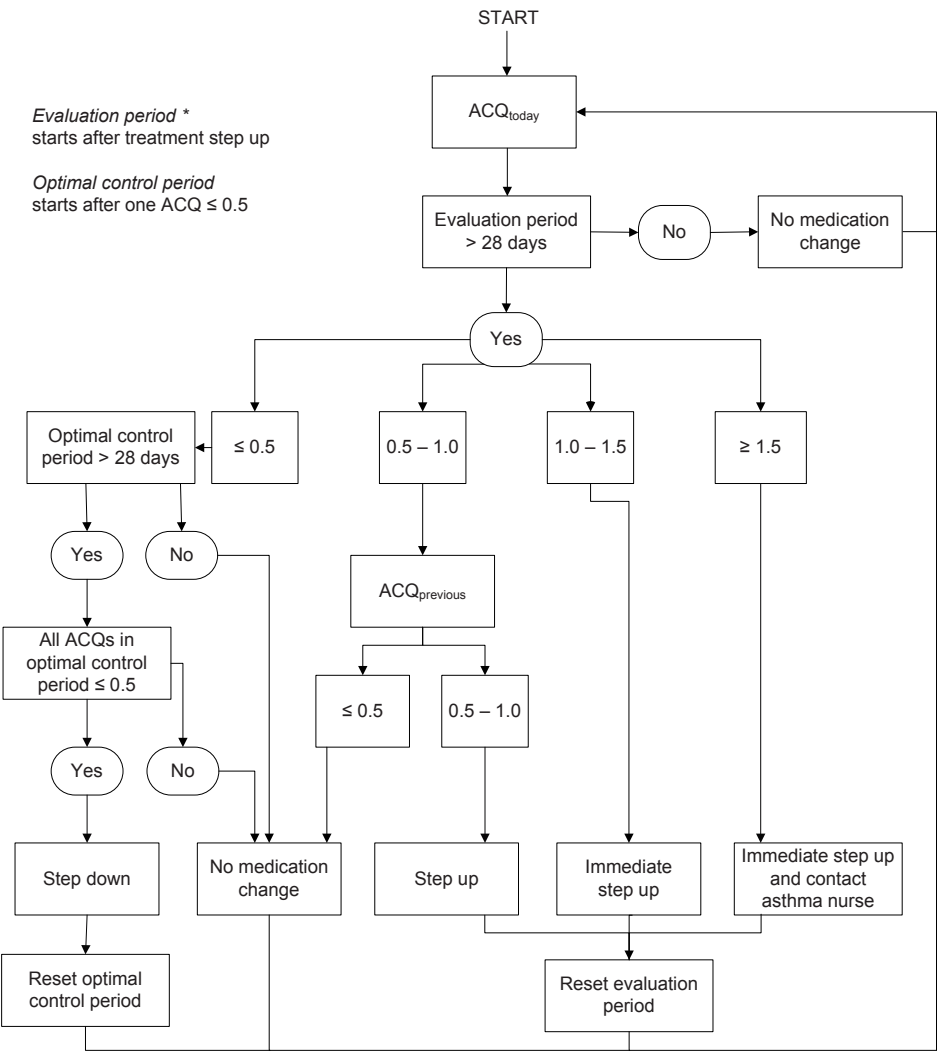
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APPENDIX

Appendix Figure 1. Algorithm based on consecutive ACQ scores to adjust medical treatment.



ACQ = Asthma Control Questionnaire

*At entry of the algorithm, the evaluation period is bypassed.

Appendix Figure 2. Screen shot of daily lung function and symptom monitoring.

@stma.nu

ICT self-management asthma

User menu

- measurements
- private messages
- forum
- F.A.Q.
- contact
- log out

Asthma information

- all about asthma
 - what is asthma?
 - monitoring
 - treatment
- self-management
- presentations
- video instruction about inhaler technique
- useful links

Measurements and questionnaires

Enter lung function Enter ACQ Show results Print

Week: 46
Last FEV1: 13-11-2007, 08h03

FEV1
2.78

Night time symptom score
Symptoms are chest tightness, wheezing, breathlessness and cough.

- ☐ No symptoms during the night.
- ☐ Symptoms on waking but not causing you to wake early.
- ☐ Symptoms causing you to wake once or to wake early.
- ☐ Symptoms causing you to wake twice or more (including waking early).
- ☒ Symptoms causing you to be awake most of the night.
- ☐ Symptoms so severe that you did not sleep at all.

Daytime symptom score
Symptoms are chest tightness, wheezing, breathlessness and cough.

- ☐ No symptoms
- ☐ Symptoms for one short period during the day.
- ☒ Symptoms for two ore more short periods during the day.
- ☐ Symptoms for most of the day, which did not interfere with usual daytime activities.
- ☐ Symptoms for most of the day, which did interfere wiht usual daytime activities.
- ☐ Symptoms so severe that you could not perform your usual daytime activities.

Add comments

Restore Save

Search

Search

News

- 11/04 New York marathon
- 10/31 getting the flu
- 10/10 asthma in Japan
- 09/25 expensive health care
- 08/28 fatter and fatter
- 07/19 sun tanning
- 07/01 smog
- 06/07 smoking prohibited
- 05/29 apples and fish
- 05/01 World Asthma Day
- 04/19 asthma in New York
- 04/10 hay fever
- 03/15 grandma smokes
- 02/20 Spider Award
- 01/01 happy new year

Poll

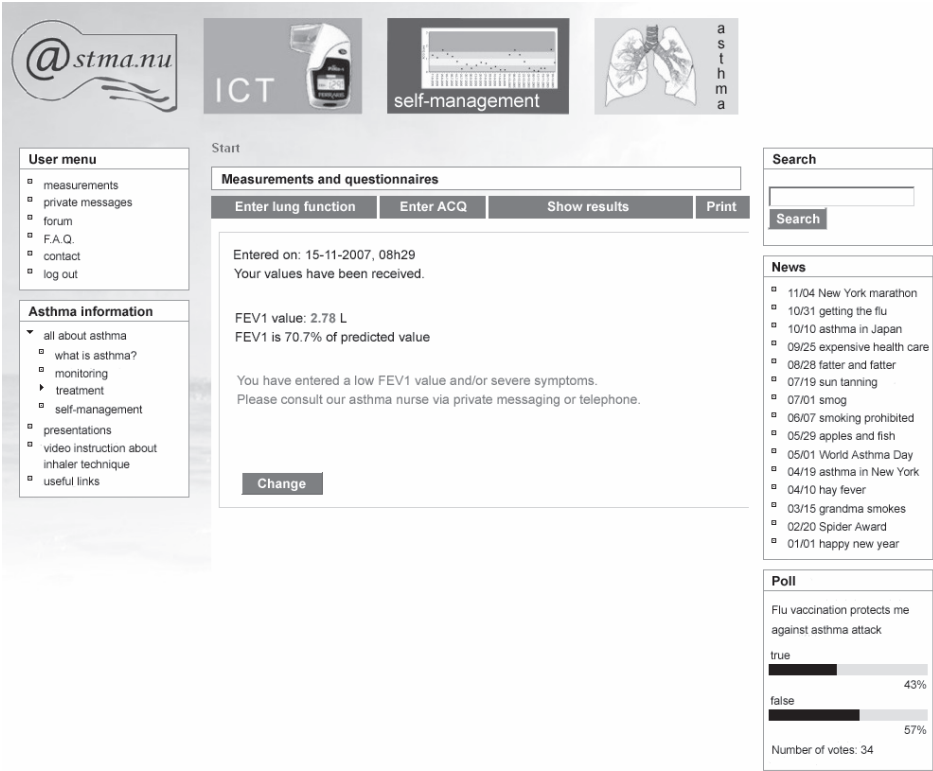
Flu vaccination protects me against asthma attack

true 43%

false 57%

Number of votes: 34

Appendix Figure 3. Screen shot of feedback on daily lung function and symptom monitoring.



Appendix Figure 4. Screen shot of weekly Asthma Control Questionnaire monitoring.

@stma.nu

ICT self-management

asthma

User menu

- measurements
- private messages
- forum
- F.A.Q.
- contact
- log out

Asthma information

- all about asthma
- what is asthma?
- monitoring
- treatment
- self-management
- presentations
- video instruction about inhaler technique
- useful links

Measurements and questionnaires

Enter lung function Enter ACQ Show results Print

Week: 46
Last entered ACQ: 06-11-2007

Restore Save

1. On average, during the past week, how often were you **woken by your asthma** during the night?

- ☐ Never
- ☐ Hardly ever
- ☒ A few times
- ☐ Several times
- ☐ Many times
- ☐ A great many times
- ☐ Unable to sleep because of asthma

2. On average, during the past week, how **bad were your asthma symptoms when you woke up** in the morning?

- ☐ No symptoms
- ☐ Very mild symptoms
- ☒ Mild symptoms
- ☐ Moderate symptoms
- ☐ Quite severe symptoms
- ☐ Severe symptoms
- ☐ Very severe symptoms

3. In general, during the past week, how **limited were you in your activities** because of your asthma?

- ☒ Not limited at all
- ☐ Very slightly limited
- ☐ Slightly limited
- ☐ Moderately limited
- ☐ Very limited
- ☐ Extremely limited
- ☐ Totally limited

Search

Search

News

- 11/04 New York marathon
- 10/31 getting the flu
- 10/10 asthma in Japan
- 09/25 expensive health care
- 08/28 fatter and fatter
- 07/19 sun tanning
- 07/01 smog
- 06/07 smoking prohibited
- 05/29 apples and fish
- 05/01 World Asthma Day
- 04/19 asthma in New York
- 04/10 hay fever
- 03/15 grandma smokes
- 02/20 Spider Award
- 01/01 happy new year

Poll

Flu vaccination protects me against asthma attack

true

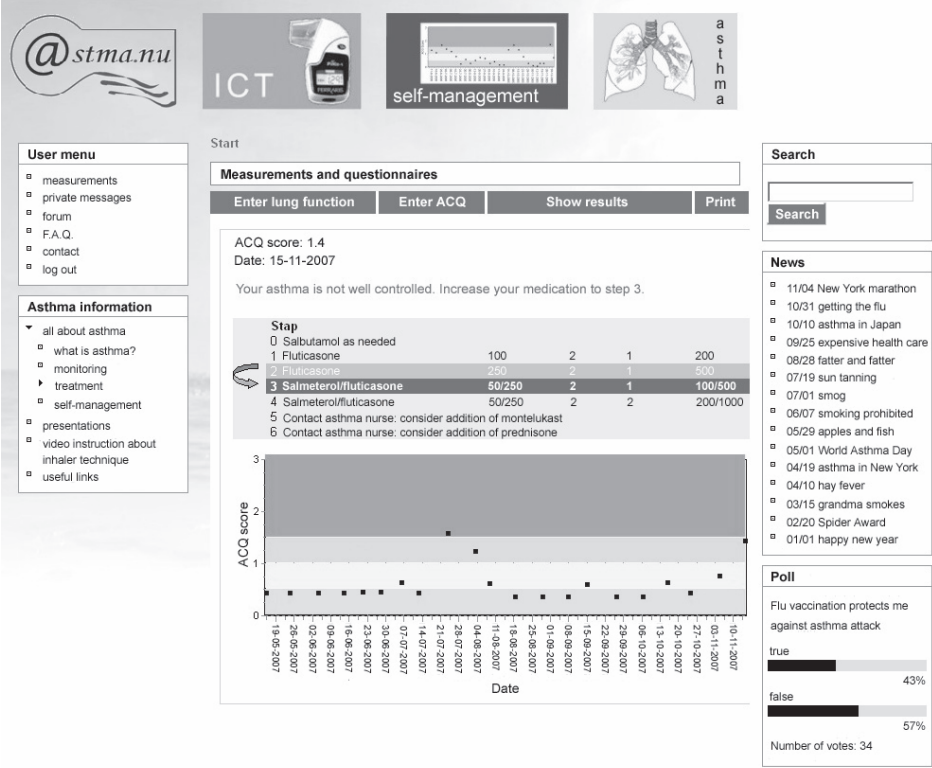
false

43%

57%

Number of votes: 34

Appendix Figure 5. Screen shot of feedback on Asthma Control Questionnaire, treatment advice according to personalized treatment plan and results of past 6 months.

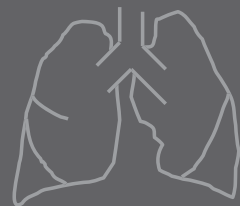
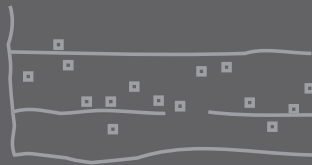


CHAPTER 5

Weekly self-monitoring and treatment adjustment benefit patients with partly controlled and uncontrolled asthma

Victor van der Meer, Henk F. van Stel, Moira J. Bakker, Albert C. Roldaan,
Willem J.J. Assendelft, Peter J. Sterk, Klaus F. Rabe, Jacob K. Sont

Under revision



ABSTRACT

Background

Internet-based self-management has shown to improve asthma control and asthma related quality of life, but the improvements were only marginally clinically relevant for the group as a whole.

Objective

We hypothesized that self-management guided by weekly monitoring of asthma control tailors pharmacological therapy to individual needs and improves asthma control for patients with partly controlled or uncontrolled asthma.

Methods

In a 1-year randomised controlled trial involving 200 adults (18-50 years) with mild to moderate persistent asthma we evaluated the adherence with weekly monitoring and effect on asthma control and pharmacological treatment of a self-management algorithm based on the Asthma Control Questionnaire (ACQ). Participants were assigned either to the internet group (n=101) that monitored asthma control weekly with the ACQ on the internet and adjusted treatment using a self-management algorithm supervised by an asthma nurse specialist or to the usual care group (UC) (n=99). We analysed 3 subgroups: patients with well controlled ($ACQ \leq 0.75$), partly controlled ($0.75 < ACQ \leq 1.5$) or uncontrolled ($ACQ > 1.5$) asthma at baseline.

Results

Overall monitoring adherence was 67% (95% CI, 60% to 74%). Improvements in ACQ score after 12 months were -0.14 ($p=0.23$), -0.52 ($p<0.001$) and -0.82 ($p<0.001$) in the internet group compared with usual care for patients with well, partly and uncontrolled asthma at baseline, respectively. Daily inhaled corticosteroid dose significantly increased in the internet group compared with usual care in the first 3 months in patients with uncontrolled asthma (+278 μg , $p=0.001$), but not in patients with well or partly controlled asthma. After one year there were no differences in daily inhaled corticosteroid use or long-acting β_2 -agonists between the internet group and usual care.

Conclusions

Weekly self-monitoring and subsequent treatment adjustment leads to improved asthma control in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs.

INTRODUCTION

Recent international guidelines define asthma control in terms of two domains: impairment and risk (1, 2). The distinction between these two domains for assessing asthma control emphasizes the need to consider separately patients' functional capacity on an ongoing basis in the present and the risks for adverse events, such as side effects of medication, progressive lung function loss or exacerbations in the future.

Ongoing monitoring of asthma control (both impairment and risk) is required to determine whether the goals of therapy are met (1, 3). Well-validated self-assessment questionnaires are available to periodically monitor the level of asthma control (4, 5, 6). Each of these instruments assess the impairment domain by measuring asthma symptoms, limitation of activities and need for rescue medication. However, lung function is only included in the Asthma Control Questionnaire (ACQ) (4). The periodic assessment of lung function is important, since it captures both asthma impairment at present and may detect future risk of progressive lung function and exacerbations (7, 8).

The frequency of periodic monitoring depends on the phase of treatment (9). At the initial phase intensive monitoring is required to evaluate the effect of treatment titration in order to achieve better asthma control. Once control has been achieved, the monitoring interval may be longer (9). Monitoring frequency and subsequent treatment decisions therefore depend on the level of asthma control and vice versa.

We have conducted a trial in which the ACQ was used as a weekly monitoring tool and participants made treatment decisions according to an ACQ-based algorithm (10). Asthma control and asthma related quality of life improved compared with usual physician-guided care, but the improvements were only marginally clinically relevant for the group as a whole (10). In the present pre-planned analysis we investigated whether a simple index of asthma control can be used to predict the outcomes of internet-based self-management. We hypothesized that self-management guided by weekly monitoring of asthma control tailors pharmacological therapy to individual needs and improves asthma control for patients with partly controlled or uncontrolled asthma.

METHODS

Patients

Full details of the study methodology and subjects for the Self-Management of Asthma Supported by Hospitals, ICT, Nurses and General Practitioners (SMASHING) project at baseline have previously been published (10). Briefly, the study enrolled 200 adults with asthma who were recruited from 37 general practices (69 general practitioners) in and around Leiden, The Netherlands, and from the outpatient department of Pulmonology

of the Leiden University Medical Center. We included patients with physician diagnosed asthma, aged between 18 and 50 years who had a prescription of inhaled corticosteroids for at least three months in the previous year. We excluded patients on continuous oral glucocorticosteroids. The study was approved by the Medical Ethics Committee of the Leiden University Medical Center. All participants gave written informed consent.

Design

This analysis is part of a prospective, randomised controlled cost-effectiveness trial (ISRCTN79864465) (10). Participants collected baseline data during a period of 2 weeks. They were trained to measure forced expiratory volume in 1 second (FEV_1) daily with a hand-held electronic spirometer (PiKo1; Ferraris, UK) and were asked to report the highest value of three measurements in the morning on a designated Web application or by mobile phone text messaging. Along with the FEV_1 value participants reported night time and daytime symptom scores. All participants were asked to complete the Asthma Control Questionnaire (ACQ) weekly on the Web application. During the baseline period participants received no feedback on lung function or clinical status.

After the baseline period, patients were randomised to either internet-based self-management (internet group) or usual physician-provided care (usual care group). The internet group was instructed to use a personal internet-based asthma action plan. This action plan required weekly completion of the ACQ via the internet for a period of 1 year. After reporting the ACQ, participants instantly received a return message on the Website including advice on how to adjust treatment and a graphical representation of lung function and ACQ over time.

Patients in the usual care group received asthma care according to the Dutch general practice guidelines on adult asthma management, which recommend follow-up consultations every 2-4 weeks if asthma is not well controlled and medical review every year in well controlled asthma (11). These national guidelines are based on international recommendations such as the GINA guidelines for asthma management and prevention (3).

After 3 months and 1 year both the internet and the usual care group collected asthma control data for a period of 2 weeks similar to the baseline period.

Asthma Control Questionnaire

The ACQ is a 7-item questionnaire that has been validated to measure asthma control (4). The items refer to asthma symptoms, rescue bronchodilator use and FEV_1 % of predicted normal. Responses are given on a 7-point scale and the overall score is the mean of the responses where 0 = totally controlled and 6 = severely uncontrolled.

Asthma Therapy Assessment Questionnaire – control index

The ATAQ is a 20-item questionnaire that generates indicators of problems in asthma care. The control index of the ATAQ contains 4 items that refer to asthma symptoms, activity limitation and rescue bronchodilator use in the past 4 weeks. Sum scores range from 0 (no control problems) to 4 control problems (1, 5).

Treatment algorithm

Five pulmonologists, two general practitioners with special interest in respiratory disease and two respiratory epidemiologists participated in the development of the algorithm for the internet-based asthma action plan. This algorithm was based on consecutive weekly ACQ scores. Two previous studies identified cut-off points for levels of asthma control. Juniper et al reported a cut-point of 0.75 for patients with well controlled asthma and a cut-point of 1.50 for patients with uncontrolled asthma (13). Van den Nieuwenhof et al described cut-off points of 0.5, 1.0 and 1.5 to differentiate between the four severity levels of asthma in accordance with the GINA guidelines, although omitting the FEV₁% of predicted normal (14).

Based on a clinically important difference of 0.5 the algorithm in our study uses three cut-points with 0.5 points differences: 0.5, 1.0 and 1.5 including the FEV₁% of predicted normal (15). It provides instructions to increase treatment (step-up) or decrease treatment (step-down) according to a pre-defined action plan. Figure 1 and table 1 show the treatment algorithm and action plan respectively. In brief, treatment step-up is advised when the ACQ score is above 1.0 once or between 0.5 and 1.0 twice consecutively and treatment step-down is advised after four weeks of ACQ scores below 0.5. When the ACQ score is above 1.5 the algorithm additionally advises to contact the asthma nurse or other health care provider. An evaluation period of four weeks without treatment

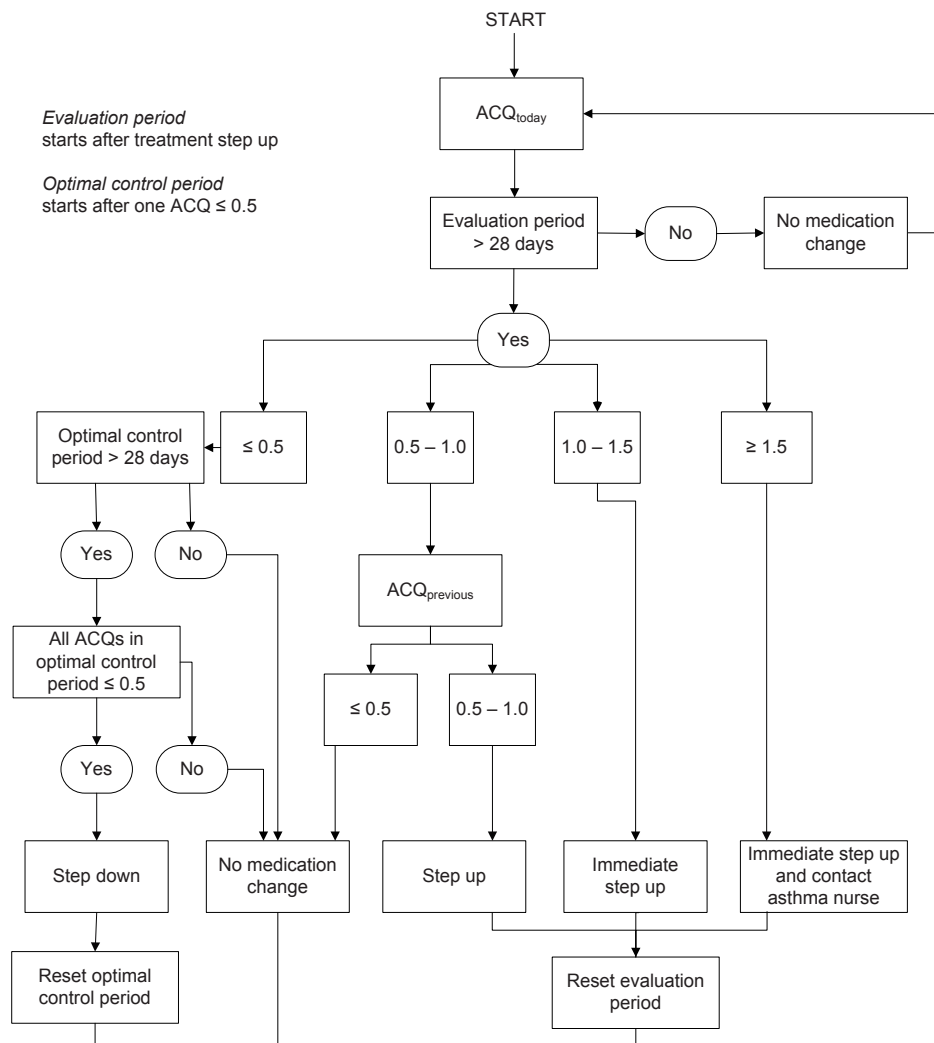
Table 1. Treatment steps for the internet-based asthma action plan (10)

Step*	Medication
1	As needed rapid-acting β_2 -agonist†
2	Low-dose inhaled glucocorticosteroids
3a	Low-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
3b	Medium-dose inhaled glucocorticosteroids
3c	High-dose inhaled glucocorticosteroids
4a	Medium-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
4b	High-dose inhaled glucocorticosteroids plus long-acting β_2 -agonist
4c	Contact asthma nurse‡ : consider addition of leukotriene modifier
5	Contact asthma nurse‡ : consider addition of oral glucocorticosteroid

* Step numbers correspond with recommended steps in GINA guidelines figure 4.3-2.(3).

† Applies to all treatment steps.

‡ Or other health care provider.

Figure 1. Algorithm based on consecutive ACQ scores to adjust medical treatment (10).

changes follows after step-up instruction. Step-down instruction is followed by a period of four weeks (step-down period) in which no second step-down can be advised, but in case of deteriorating asthma, a treatment step-up is possible in this period.

Monitoring adherence

Monitoring adherence was defined as the proportion of weekly completed internet-based ACQs in the internet group in each month of follow-up. We analyzed three subgroups of patients to allow evaluation of adherence for different levels of asthma

control at baseline: well controlled ($ACQ < 0.75$), partly controlled ($ACQ \geq 0.75$ to < 1.5) or uncontrolled asthma ($ACQ \geq 1.5$) (1, 13).

Outcome measures

Asthma control was the primary outcome. Asthma control was calculated as the average of ACQ scores during the two-week baseline and two-week end periods. The ATAQ control index acted as a measure of construct validity.

Secondary outcome measures were the mean daily dose of inhaled corticosteroid (ICS), and the proportion of participants using long-acting β_2 -agonists (LABA) or leukotriene receptor antagonists (LTRA). Inhaled corticosteroid doses were reported as fluticasone equivalents. Data on pharmacological treatment were obtained from self-reports at baseline and after 3 months and 1 year.

We analyzed three subgroups of patients to allow evaluation of the treatment algorithm for different levels of asthma control at baseline: well controlled ($ACQ < 0.75$), partly controlled ($ACQ \geq 0.75$ to < 1.5) or uncontrolled asthma ($ACQ \geq 1.5$) (3, 13).

Sample size

With the 100 participants per study group and a standard deviation of changes in ACQ score of 0.69 we were able to detect at least a 0.28 difference between ACQ score changes in the two study groups (significance level 0.05 two-sided; power 0.80 one-sided) (16). A clinically important decrease in ACQ score of at least 0.50 could thus be detected if at least 30 participants were present per subgroup (15).

Statistical analysis

Differences in ACQ scores and inhaled corticosteroid doses between internet and UC groups at two time points (3 and 12 months) were analyzed using multivariate linear regression modelling with a random intercept to adjust for repeated measures (17). The construct validity of the ACQ as an outcome measure was evaluated by Pearson's correlation coefficients: 1) between ACQ and ATAQ control index at baseline and 12 months and 2) between change scores (12 months minus baseline value) of ACQ and ATAQ control index.

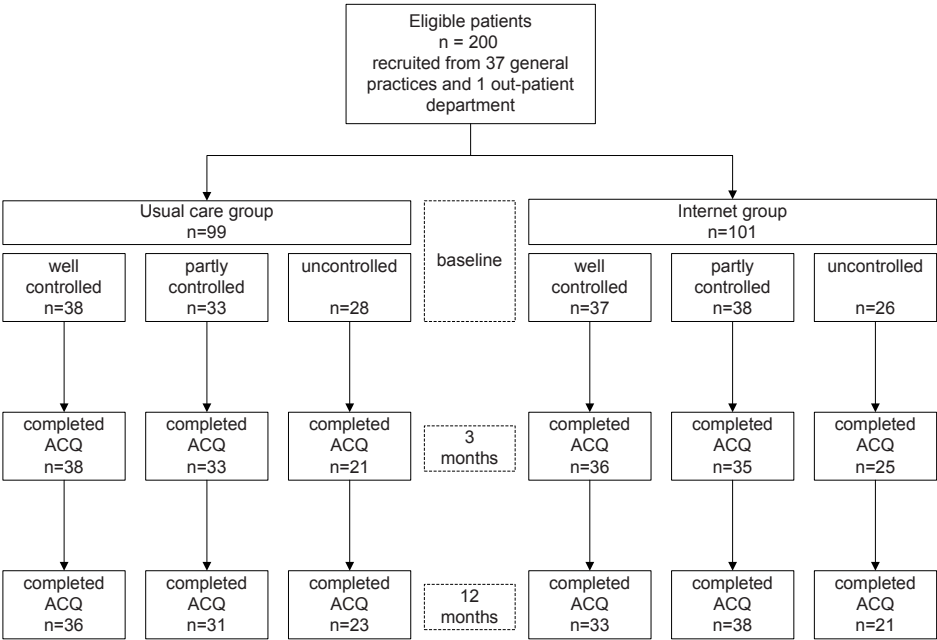
Differences in the proportion of patients using long-acting β_2 -agonists or leukotriene receptor antagonists between the two groups and at the two different time point were analyzed using multivariate population averaged logistic regression analysis with a random intercept (17). Covariates in both regression models were baseline values of the appropriate outcome parameter, sex, age, education level, smoking status and type of care provider.

All analyses were carried out on an intention-to-treat basis. We used the statistical software package STATA 9.0 (StataCorp; College Station TX, US).

RESULTS

Figure 2 summarizes the participant flow during enrolment, allocation and follow-up (figure 2). A total of 200 consented to participate in the randomised controlled study: 75 patients had well controlled asthma, 71 had partly controlled asthma and 54 had uncontrolled asthma at baseline (table 2). Mean age was 36.3 and 31% was male. Smoking was reported more often in patients with uncontrolled asthma (33% current smokers) than in patients with partly controlled (8%) or well controlled asthma (3%). The ACQ at baseline was 0.43, 1.10 and 2.09 for the three groups, respectively. Inhaled corticosteroid use at baseline was 448, 483 and 620 µg/day, respectively. The use of long-acting β_2 -agonists was similar for the groups with partly and uncontrolled asthma (62% and 63%), and only slightly higher than in patients with well controlled asthma (55% long-acting β_2 -agonists use). Five patients used leukotriene receptor antagonists: one in the group with well controlled asthma, two in the group with partly controlled asthma and two in the group with uncontrolled asthma.

Figure 2. Flow diagram of subject progress through the study.



Monitoring adherence

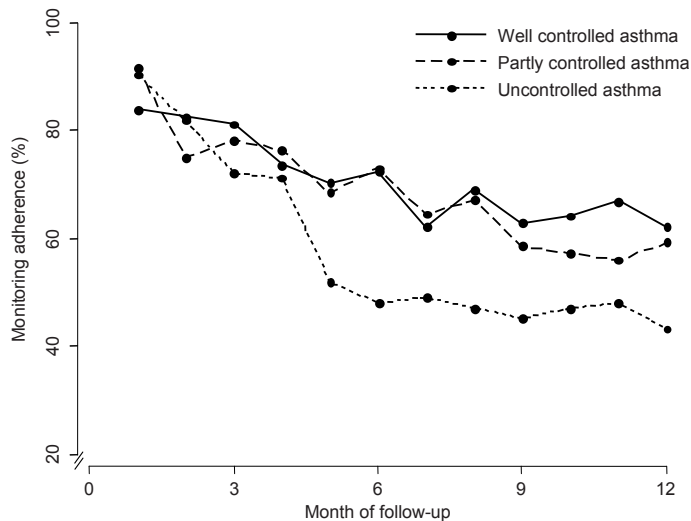
Overall monitoring adherence was 67% (95% CI, 60 to 74%). Adherence to ACQ monitoring gradually declined from the first month (88%) to the seventh month (60%) and then

Table 2. Baseline characteristics of 200 patients with mild to moderate persistent asthma who were randomised to the internet group or usual care group

	Well controlled asthma		Partly controlled asthma		Uncontrolled asthma	
	Usual Care group (n = 38)	Internet group (n = 37)	Usual Care group (n = 33)	Internet group (n = 38)	Usual Care group (n = 28)	Internet group (n = 26)
Age, mean yr (SD)	37.6 (7.5)	35.8 (8.9)	36.3 (10.1)	35.5 (9.7)	36.0 (6.9)	36.9 (7.6)
Male, no. (%)	12 (31.6)	11 (29.7)	10 (30.3)	8 (21.1)	7 (25.0)	13 (50.0)
Lower education, no. (%)	4 (10.5)	2 (5.4)	2 (6.1)	4 (10.5)	8 (28.6)	5 (19.2)
Current smoker, no. (%)	1 (2.6)	1 (2.7)	4 (12.1)	2 (5.3)	9 (32.1)	9 (34.6)
Subspecialty care, no. (%)	6 (15.8)	6 (16.2)	6 (18.2)	11 (29.0)	8 (28.6)	4 (15.4)
Duration of asthma, mean yr (SD)	16.8 (11.4)	15.5 (14.0)	20.4 (13.3)	16.1 (12.6)	15.8 (14.5)	14.2 (9.9)
Pre-bronchodilator FEV ₁ (% predicted), mean (SD)	96.1 (11.4)	102.3 (13.4)	89.6 (13.6)	86.5 (9.6)	83.2 (14.9)	70.9 (15.9)
ACQ, mean (SD)	0.40 (0.23)	0.46 (0.18)	1.08 (0.22)	1.12 (0.23)	2.11 (0.55)	2.07 (0.44)
ATAQ control index, median (range)	1 (0-3)	1 (0-3)	1 (0-3)	1 (0-3)	2 (0-3)	2.5 (0-4)
Inhaled corticosteroids, mean µg/day (SD)	480 (368)	416 (236)	475 (377)	489 (309)	618 (311)	623 (316)
Long-acting β ₂ -agonist, no. (%)	23 (60.5)	18 (48.7)	17 (51.5)	27 (71.1)	19 (67.9)	15 (57.7)
Leukotriene modifier, no. (%)	0 (0)	1 (2.7)	0 (0)	2 (5.3)	2 (7.1)	0 (0)

remained stable up to 1 year. Monitoring in the three subgroups was 71%, 68% and 58% during the one-year follow-up for well, partly and uncontrolled asthma, respectively (figure 3).

Figure 3. Monitoring adherence (percentages) for patients with well controlled (n=75), partly controlled (n=71) or uncontrolled asthma at baseline (n=54)

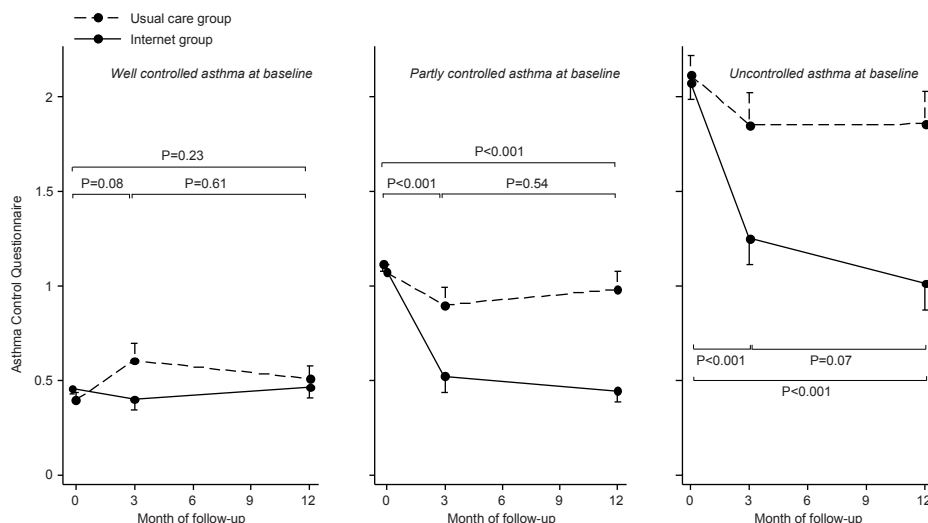


Asthma control

There were no deviations from random allocation. At baseline 75 participants had well controlled asthma, 71 partly controlled and 54 participants had uncontrolled asthma. ACQ scores at 12 months were provided by 69 (92%), 69 (97%) and 44 (81%) participants, respectively.

Figure 4 shows the ACQ scores at baseline, 3 and 12 months of follow-up in the UC and internet group for each baseline control level (figure 4). In patients with well controlled asthma at baseline ACQ scores were not significantly different between the usual care and internet group during follow-up. In patients with partly controlled asthma at baseline ACQ scores in the internet group improved with -0.44 (95% CI, -0.67 to -0.22) and -0.51 (-0.73 to -0.29) after 3 and 12 months, respectively, compared with usual care. In patients with uncontrolled asthma at baseline ACQ scores in the internet group improved with -0.57 (95% CI, -0.84 to -0.31) and -0.82 (-1.10 to -0.55) after 3 and 12 months, respectively, compared with usual care. Correlations between ACQ and ATAQ control index were 0.57 ($p < 0.001$) and 0.64 ($p < 0.001$) at baseline and 12 months, respectively. The correlation of change scores was 0.52 ($p < 0.001$).

Figure 4. ACQ scores during study follow-up for patients with well controlled (panel I; n=75), partly controlled (panel II; n=71) or uncontrolled asthma at baseline (panel III; n=54).



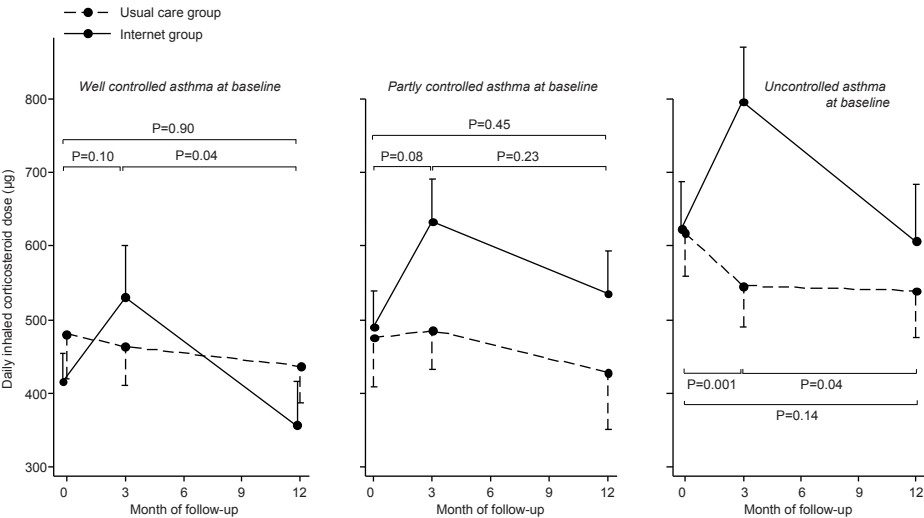
P-values represent statistical significance of change scores between internet group and usual care. Error bars indicate the standard error of the mean.

Pharmacological therapy

Figure 5 shows the daily dose of inhaled corticosteroid (ICS) at baseline, 3 and 12 months of follow-up in the usual care and internet group for each baseline control level (figure 5). In patients with well controlled asthma at baseline the ICS dose increased non-significantly, followed by a significant decrease from 3 to 12 months ($p=0.042$). At 12 months the ICS dose was similar for both groups: difference $-9 \mu\text{g}$ (95% CI, -147 to 130). In patients with partly controlled asthma at baseline the ICS dose increased in the first 3 months and decreased in the next 9 months in the internet compared to the usual care group, both changes being non-significant. At 12 months the ICS dose did not differ between the groups: difference $54 \mu\text{g}$ (95% CI, -86 to 194). Patients with uncontrolled asthma showed a significant increase in the first 3 months ($278 \mu\text{g}$, $p=0.001$) followed by a significant decrease in the next 9 months ($-149 \mu\text{g}$, $p=0.043$) in the internet group compared with usual care. At 12 months the ICS dose was not significantly higher in the internet group compared with usual care: difference $130 \mu\text{g}$ (95% CI, -43 to 303).

The number of patients using LABA or LTRA was not significantly different between the three baseline control levels and are therefore presented altogether (figure 6). The proportion of patients using LABA was similar for the internet and usual care group at 3 months (63% internet and 62% usual care; $p = 0.60$) and 12 months (64% internet and 58% usual care, $p = 0.11$), adjusted OR: 1.61 (95% CI, 0.74 to 3.48).

Figure 5. Mean daily dose of inhaled corticosteroids (μg) during study follow-up for patients with well controlled (panel I; $n=75$), partly controlled (panel II; $n=71$) or uncontrolled asthma at baseline (panel III; $n=54$).



P-values represent statistical significance of change scores between internet group and usual care. Error bars indicate the standard error of the mean.

Figure 6. Percentage of patients using long-acting β_2 -agonists (laba) or leukotriene receptor antagonists (ltra) at baseline, 3 and 12 months for the internet and usual care groups as a whole.

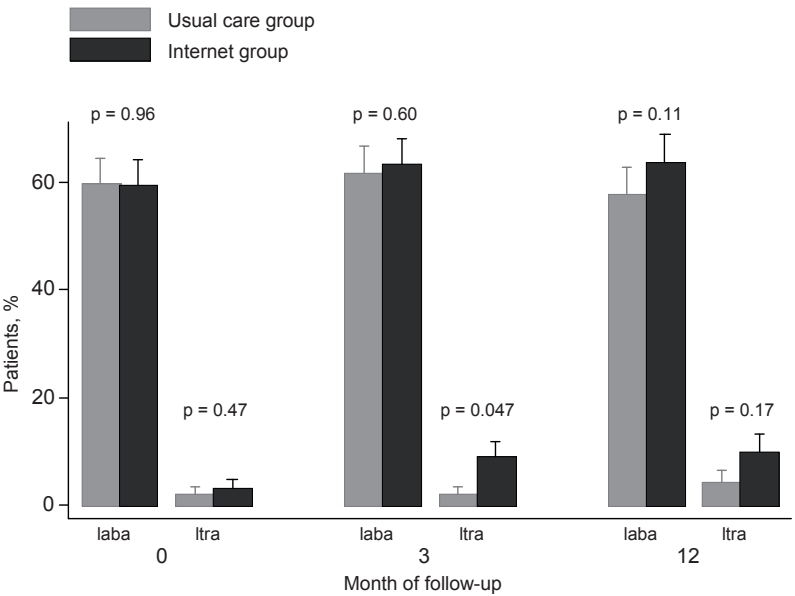


Figure 6 shows that only a few patients used LTRA. The proportion of patients using LTRA was significantly higher for the internet group than usual care at 3 months (9% vs 2%, adjusted OR: 6.03 (95% CI, 1.03 to 35.4)), but not at 12 months (10% vs 4%, adjusted OR: 2.63 (95% CI, 0.67 to 10.3)).

DISCUSSION

This analysis provides insight into the effects of internet-based self-management guided by an electronic algorithm based on weekly assessment of asthma impairment on process outcomes for three different levels of asthma control at baseline. Adherence to the internet-based monitoring instrument was 67%. The results show a considerable improvement in asthma control for patients with partly controlled or uncontrolled asthma at baseline without significant increases in inhaled corticosteroids, long-acting β_2 -agonists or leukotriene receptor antagonist use at 12 months.

This is the first randomised controlled evaluation of asthma self-management guided by a short validated questionnaire on asthma control. By guiding treatment on the basis of short interval monitoring of asthma control we were able to adopt recommended treatment strategies into an asthma action plan (1, 3). The current analysis reveals three important findings regarding asthma control, pharmacological therapy and monitoring adherence in the three subgroups of patients with different levels of asthma control at baseline.

First, the improvements in asthma control scores for patients with partly or uncontrolled asthma at baseline suggest a significant reduction of current functional impairment. Remarkably, control scores stabilised or even continued to improve after 3 months, while ICS doses decreased in patients with well or uncontrolled asthma at baseline. A possible explanation is that to achieve asthma control higher doses of anti-inflammatory therapy are needed than to maintain asthma control (3). The reduced need for ICS may decrease future risk for side effects of medication.

Second, this asthma action plan is one of few that not only specifies action points to increase, but also to decrease treatment, which provides the possibility to tailor medication to individual needs. All three baseline control level groups showed a similar pattern of pharmacological therapy over time: an increase in inhaled corticosteroids in the first three months, followed by a decrease in the next 9 months. However, the different magnitudes of the increases and decreases reflected tailoring of medication to individual patients' needs rather than a mere increase of medication for the whole population. It can be seen that only for patients with uncontrolled asthma at baseline the inhaled corticosteroid dose significantly increased after three months.

Third, this study showed that weekly internet-based monitoring is feasible in terms of monitoring adherence. In the groups with well and partly controlled asthma at baseline monitoring adherence of about 80% in the first 3 months decreased to 60% during the last months of follow-up. Despite declining monitoring adherence, asthma remained adequately controlled. This reflects the reduced need for monitoring once control of the disease has been achieved (9). Patients with uncontrolled asthma at baseline monitored asthma control in 80% during the first 3 months (similar to patients with well and partly controlled asthma). However, in this group monitoring adherence declined to below 50% and asthma control did not reach the good control scores (below 0.75) as it did in the well and partly controlled groups. Efforts to optimise monitoring adherence may further increase asthma control.

Two methodological issues are of particular interest. The outcomes of our study were patient reported. Patient reported outcomes may have a risk of reduced validity compared to objective outcomes. We therefore evaluated the correlations of our outcome measure of asthma control with another asthma control index (5). The moderate to good correlations of both cross-sectional scores and change scores not only illustrated the effectiveness of a potent algorithm, but also demonstrated a satisfactory construct validity of this algorithm. With regard to medication reports, we asked patients to bring their inhalers at baseline and end visits, which enhanced the validity. However, patients may have reported different numbers of puffs than actually used or other types of inhalers than they actually brought to the visits. Second, we recognize that the effect of the internet-based self-management intervention can not solely be attributed to our treatment algorithm. We emphasize that, except for asthma monitoring and a medical treatment plan, a self-management asthma support programme should consist of asthma education, environmental control and medical review (18).

To conclude, weekly self-monitoring and subsequent treatment adjustment leads to improved asthma control in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs. Future asthma treatment strategies should incorporate continuous self-monitoring with use of a short validated questionnaire on asthma control.

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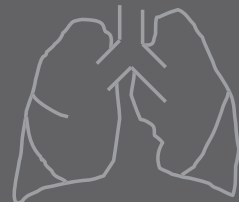
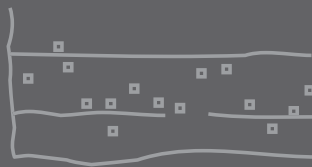
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CHAPTER 6

Cost-effectiveness of internet-based self-management compared with usual care in asthma

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Submitted



ABSTRACT

Background

Effectiveness of internet-based self-management in patients with asthma has been shown, but its cost-effectiveness is unknown. We conducted a cost-effectiveness analysis of internet-based asthma self-management compared with usual care.

Methods

Cost-effectiveness analysis alongside a randomized controlled trial, with 12 months follow-up. Patients were aged 18 to 50 year and had physician diagnosed asthma. The internet-based self-management program involved weekly on-line monitoring of asthma control with self-treatment advice, remote Web communications, and internet-based information. We determined quality adjusted life years (QALYs) as measured by the EuroQol-5D and costs for health care use and absenteeism. We performed a detailed cost price analysis for the primary intervention.

Results

QALYs improved for internet-based self-management compared with usual care with 0.024 (-0.016 to 0.065). Costs of the internet-based intervention were \$254 (\$243 to \$265) during the period of 1 year. From a societal perspective, costs were \$641 (95% CI, \$-1957 to \$3240) higher in the intervention group, with a cost-utility ratio of \$26700 per QALY. From a health care perspective, total costs were \$37 (95% CI, \$-874 to \$950) higher in the intervention group, with a cost-utility ratio of \$1500 per QALY. At a willingness-to-pay of \$50000 per QALY, the probability that internet-based self-management was cost-effective compared with usual care was 62% and 82% from a societal and health care perspective, respectively.

Conclusions

The results suggest that internet-based self-management in asthma is cost-effective compared with usual care, even more so from a health care perspective than from a societal perspective.

INTRODUCTION

Asthma is a chronic, inflammatory disorder of the airways clinically characterized by respiratory symptoms such as wheeze, cough, dyspnoea, chest tightness and impaired lung function (1, 2). Treatment for asthma is aimed at improving asthma control, i.e. reducing current symptoms and need for short-acting bronchodilation, improving lung function and preventing future exacerbations (1-3).

In the past decade, the care for asthma patients has shifted from physician-managed care to guided self-management. Guided self-management includes asthma education, self-monitoring of symptoms and/or lung function and adjustment of treatment according to an action plan guided by a health care professional (not necessarily a physician). Self-management has been shown to improve asthma control and quality of life and reduce health care utilization and sometimes improve lung function (4).

Besides clinical effectiveness, the implementation of new disease management strategies requires an economic evaluation to determine whether the clinical benefits are gained at reasonable costs. Several cost evaluations have compared paper-and-pencil self-management plans to usual care in asthma (5-11), but only a few compared costs to quality of life (10-11). Most of these economic evaluations found that written self-management plans for asthma were likely to be cost-effective compared with usual physician provided care. However, the implementation of paper-and-pencil self-management plans is hampered by patients' and doctors' reluctance to use written diaries (12).

Implementation of guided self-management programs may be enhanced by the use of internet-based technologies, particularly in remote and underserved areas. In a recently conducted randomized controlled trial we have shown that internet-based self-management is feasible and provides better clinical outcomes compared with usual physician provided care with regard to asthma related quality of life, asthma control, symptom-free days and lung function (13). Although previous trials have also evaluated the clinical effects of internet-based self-management in adults (14) and children (15, 16), so far, no economic evaluations have been conducted. We therefore carried out a cost-utility analysis, comparing quality of life with societal and health care costs during one year, to determine whether the clinical benefits gained with internet-based self-management are attained at reasonable costs.

METHODS

Setting and participants

Two hundred patients participated in a 12-month multicenter, non-blinded, randomized controlled trial. Patients were recruited from 37 general practices (69 general practitio-

ners) in the Leiden and The Hague area and the Outpatient Clinic of the Department of Pulmonology at the Leiden University Medical Center, The Netherlands over the period from September 2005 to September 2006 (13). We included patients with physician diagnosed asthma as coded according to the International Classification of Primary Care in the electronic medical record (17), aged 18-50 years, with a prescription of inhaled corticosteroids for at least three months in the previous year, access to internet at home, mastery of the Dutch language and without serious co-morbid conditions that interfered with asthma treatment. Patients on maintenance oral glucocorticosteroid treatment were excluded. All participants gave their written consent. The study was approved by the Medical Ethics Committee of the Leiden University Medical Center.

Details of the randomization and intervention have been described previously (13). Briefly, the 200 patients were randomly assigned to internet-based self-management as an adjunct to usual care (internet group: 101 patients) or to usual physician-provided care alone (usual care group: 99 patients). Allocation took place by computer after collection of the baseline data, ensuring concealment of allocation. The internet-based self-management program included weekly monitoring of asthma control and lung function, immediate treatment advice according to a computerized personal action plan after completing the validated Asthma Control Questionnaire on the internet (18), on-line education and group-based education, and remote Web communication with a specialized asthma nurse. After one year, asthma related quality of life (Asthma Quality of Life Questionnaire (19)), asthma control and lung function showed a clinically relevant and statistically significant improvement in the internet group compared to the usual care group (13).

Utilities and QALYs

Utilities express the valuation of health-related quality of life on a scale from zero (death) to one (perfect health). Patients described their health-related quality of life using the EuroQol classification system (EQ-5D) (20), from which we calculated their utilities over time using the British tariff (21). The area under the utility curve is known as quality-adjusted life years (QALY) and was used as the primary outcome measure for the cost-effectiveness analysis. Patients additionally valued their own health status on a visual analogue scale (VAS). This scale from the patient perspective is potentially more responsive to change than other generic quality of life instruments, but is not the best choice for economic evaluations from a societal perspective (22). The VAS scale was transformed to a utility scale using the power transformation $1 - (1 - \text{VAS}/100)^{1.61}$ (23).

We obtained utility measurements at baseline, 3 and 12 months. For EQ-5D measurements 6.5%, 10% and 8.5% were missing and for visual analogue measurements 7%, 10% and 9% were missing at 0, 3 and 12 months, respectively. To correct for possibly selective non-response, missing measurements were replaced by 5 imputed values

based on switching regression (24, 25) with regression variables randomisation group, age, sex, asthma control at baseline and available utility measures at all time points. We estimated the intervention effect for each of the 5 data sets by a linear regression model with randomisation group as only independent variable, combining the multiple imputation sets using Rubin's rules (26).

Costs

We distinguished three major cost categories: intervention costs, other health care costs and productivity costs (10, 11). Intervention costs consisted of materials (software support, electronic spirometer), personnel and patient costs (travel, time, internet and text messaging costs). Other health care costs included contacts (including face-to-face, telephonic and home contacts) with health care professionals (general practitioners, chest physician, other specialists, physiotherapists, psychologists, complementary care and other paramedical professionals), emergency room visits, hospital admissions and both asthma and non-asthma medication.

Patients reported their use of health care resources and the hours of absence from work using a quarterly cost-questionnaire. Details of the drugs used were derived from pharmacy records. We used standard prices for units of resource use and hours of absenteeism (27, 28), which were converted to the price level of 2007 according to the general Dutch consumer price index (29) and converted to US dollars using the purchasing power parity index ($\text{€}1 = \$1.131$) (30). Because of the one-year time horizon, costs were not discounted.

Cost-questionnaires were scheduled to be handed in at 3, 6, 9 and 12 months. Of these quarterly questionnaires, 10%, 14%, 19% and 9% were missing, respectively. Pharmacy records were available for 182 patients (91%). Missing cost-questionnaire and pharmacy record were imputed using multiple imputation, as previously described under 'Utilities and QALYs'.

Statistical analysis

The base case cost-effectiveness analysis compared societal costs with QALYs gained based on the British EQ-5D over the period of one year. Because of the limited degree of modelling in this cost utility analysis, we carried out sensitivity analyses only on the use of different utility measures (British EQ-5D or Visual Analogue Scale) and on the included cost categories (societal or health care perspective).

Differences and statistical uncertainty of QALYs and costs were calculated using non-parametric bootstrap estimation with 5000 random samples (1000 from each of the 5 imputations). Statistical uncertainty of the cost-effectiveness was analyzed using the net benefit approach (31). The net benefit (NB) is defined as $\text{WTP} \times \Delta\text{QALY} - \Delta\text{costs}$, where WTP is the willingness to pay for a QALY gained. This approach reformulates the QALY

difference into a monetary difference. In a cost-effectiveness acceptability curve we graphed the probability that the internet-based self-management program was cost-effective compared with usual care as a function of WTP and reported this probability at commonly cited WTP values of \$50000 and \$100000 per QALY (32).

Analyses were carried out with Stata 9.0 (StataCorp, College Station, TX).

RESULTS

The internet group and usual care group consisted of 101 and 99 participants, respectively. Mean age of the sample was 37 years and 70% of the participants were women (table 1). At baseline, asthma related quality of life, asthma control and medication use were similar for the two randomization groups.

Table 1. Baseline characteristics

	Usual care group (n=99)	Internet group (n=101)
Women	71%	68%
Age, years	37 (18-50)	36 (19-50)
Asthma duration, years	18 (0-47)	15 (1-47)
Education level		
Low	14%	11%
Middle	33%	37%
High	53%	52%
Care provider		
General practitioner	80%	79%
Chest physician	20%	21%
FEV ₁ (pre-bronchodilator), L	3.13 (1.56-5.23)	3.08 (1.14-5.19)
FEV ₁ (pre-bronchodilator), % predicted	90 (53-118)	88 (34-133)
Inhaled corticosteroid dose, µg/day	517 (0-2000)	494 (0-1000)
Inhaled long-acting β ₂ -agonist, % of patients	60%	59%
Leukotriene modifier, % of patients	2%	3%
Clinical outcomes		
Asthma Quality of Life Questionnaire *	5.79 (3.03-7.00)	5.73 (3.66-6.94)
Asthma Control Questionnaire †	1.11 (0-3.86)	1.12 (0.07-3.22)
Patient utilities ‡		
EQ-5D utility	0.89 (-0.06-1.00)	0.91 (0.49-1.00)
EQ-5D visual analogue scale	74 (35-100)	73 (20-100)

Data are mean (range) unless otherwise indicated. * Range 1 (worst) – 7 (best) (19). † Range 0 (best) – 6 (worst) (18). ‡ EQ-5D = EuroQol questionnaire, 5 dimensions (20). Parts of this table were published previously (13).

Utilities and QALYs

At baseline, the utilities according to the EQ-5D were non-statistically significantly higher for the internet group than for the usual care group. EQ-5D utilities did not reach a statistical significant difference throughout the study. At 3 months and 12 months the difference in EQ-5D utility was 0.037 (-0.007 to 0.081) and 0.006 (-0.042 to 0.054), respectively, in favour of the internet group. Quality adjusted life years gained in the internet group were estimated to be 0.024 (-0.016 to 0.065) compared to the usual care group (table 2).

Similarly, visual analogue scale utilities were not statistically significantly different throughout the study. At 3 and 12 months the difference in visual analogue scale utility was 0.012 (-0.026 to 0.050) and 0.013 (-0.015 to 0.040), respectively, in favour of the internet group. Quality of life years gained based on the visual analogue scale were estimated to be 0.007 (-0.017 to 0.032) in favour of the internet group (table 2).

Table 2. Utilities at 0, 3 and 12 months and QALYs *

Variable	Usual care group	Internet group	Difference (95% CI)	P value
EQ-5D				
0 months	0.89	0.91	0.026 (-0.024 to 0.076)	0.31
3 months	0.89	0.93	0.037 (-0.007 to 0.081)	0.099
12 months	0.91	0.92	0.006 (-0.042 to 0.054)	0.80
QALYs	0.90	0.92	0.024 (-0.016 to 0.065)	0.25
Visual analogue scale †				
0 months	0.87	0.86	-0.013 (-0.045 to 0.019)	0.43
3 months	0.87	0.89	0.012 (-0.026 to 0.050)	0.54
12 months	0.88	0.89	0.013 (-0.015 to 0.040)	0.37
QALYs	0.88	0.88	0.007 (-0.017 to 0.032)	0.57

* Values are summary estimates of the 5 data sets obtained by multiple imputation, combined using Rubin's rules. † Transformed using the power transformation $1 - (1 - \text{VAS}/100)^{1.61}$ (23)

Costs

The total intervention costs were estimated at \$25675, which is \$254 (95% CI, \$243 to \$265) per patient (table 3). The highest cost components of the internet-based intervention were software support (\$7917) and the patients' time costs (\$5380 for monitoring time and \$5106 for attending the education sessions).

The difference in other health care costs amounted to \$-217 (95% CI, \$-1117 to \$682) per patient indicating (non-significant) cost savings for the internet group (table 4). Patients in the internet group had fewer contacts with health care providers than patients in the usual care group. Particularly, reductions in contacts with physiotherapists (\$-120,

Table 3. Implementation costs (\$) of internet-based self-management intervention

Component of cost	Cost per unit	Number of units	Total cost
Materials			
software support	7917 / yr	1	7917
electronic spirometer	19.22 / device	101	1942
Personnel			
development educational aids	26 / hr	16	412
education sessions	26 / hr	30	780
data review and patient communication	26 / hr	91	2351
Patient costs			
travel costs for sessions	6 / session	258	1465
time costs for sessions (incl. travel time)	20 / session	258	5106
time costs for monitoring *	0.50 / log in	10873	5380
internet log in costs †	0.0016 / log in	9374	15
mobile phone costs ‡	0.20 / message	1499	305
Total implementation costs			25675
Total implementation costs per patient			254

* Monitoring time was estimated at 3 minutes per log in and valued at \$10 per hour, i.e. the Dutch standard price for unpaid labour (27). Number of units was obtained from internet log files. † Internet costs were valued at \$23 per month. ‡ Mobile phone costs were valued at \$0.20 per message.

$p=0.03$) and contacts with general practitioners (\$-69, $p=0.18$) resulted in cost reductions for the internet group. In contrast, costs for medication were higher in the internet group due to increased use of inhaled corticosteroid/long-acting β_2 agonist combinations (\$82, $p=0.09$) and leukotriene antagonists (\$25, $p=0.12$). The difference in other health care costs was similar in size to the opposite difference in intervention costs, resulting in a negligible difference in health care costs of \$37 (95% CI, \$-874 to \$950), slightly in favour of usual care.

Patients in the internet group reported 114 hours of absence from work compared to 98 hours for patients in the usual care group. The 16 hours difference in absenteeism was estimated to be equivalent to \$604 (95% CI, \$-1430 to \$2637) in monetary terms. The difference in societal costs (i.e. health care costs plus costs due to absenteeism) was therefore estimated at \$641 (95% CI, \$-1957 to \$3240) in favour of usual care.

Cost-utility analysis

From a societal perspective, costs were in favour of usual care and QALYs, based on the EQ-5D, were in favour of internet-based self-management. According to this base case analysis, the cost-utility ratio was \$26700 per QALY. Due to statistical uncertainty of both costs and QALYs, the probability that internet-based self-management is cost-effective compared with usual care depends on the willingness-to-pay per QALY. This probability was 62% at \$50000 per QALY and 74% at \$100000 per QALY (figure 1). From a health care perspective, the lower health care costs result in a cost-utility ratio of \$1500 per QALY.

Table 4. Average health care costs and societal costs per patient (\$)

	Usual care group		Internet group		Difference	
	Volume	Costs	Volume	Costs	Costs	P Value
Intervention costs	-	-	1	254	254	<0.001
Other health care costs						
General practitioner	12.2	294	10.0	225	-69	0.18
Chest physician	0.9	63	0.6	42	-21	0.20
Other specialist	2.5	167	2.3	155	-12	0.75
Physiotherapist	8.6	234	4.2	114	-120	0.03
Psychologist	1.1	161	1.2	180	18	0.78
Complementary care	1.4	87	1.2	75	-12	0.66
Other paramed. professionals	1.5	43	0.8	24	-19	0.28
Emergency room	0.3	45	0.2	35	-10	0.47
Day admissions	0.3	92	0.3	86	-6	0.88
Hospitalizations	1.5	589	1.4	571	-17	0.95
Drugs *						
Short-acting β_2 -agonists	54%	28	50%	20	-8	0.26
Inhaled corticosteroids (ICS)	50%	89	52%	77	-12	0.47
Long-acting β_2 -agonists (LABA)	10%	26	11%	20	-6	0.67
Combination ICS + LABA	55%	264	71%	345	82	0.09
Leukotriene antagonists	8%	21	23%	46	25	0.12
Oral corticosteroids	12%	2	13%	2	-1	0.50
Non-asthma medication	99%	312	97%	285	-27	0.71
Subtotal other health care costs		2518		2300	-217	0.63
Total health care costs		2518		2555	37	0.94
Productivity costs †	98 hr	3131	114 hr	3735	604	0.56
Total societal costs		5647		6289	641	0.63

* Volumes of drugs represent percentage of patients. † Volumes of productivity costs are number of hours of absence from work

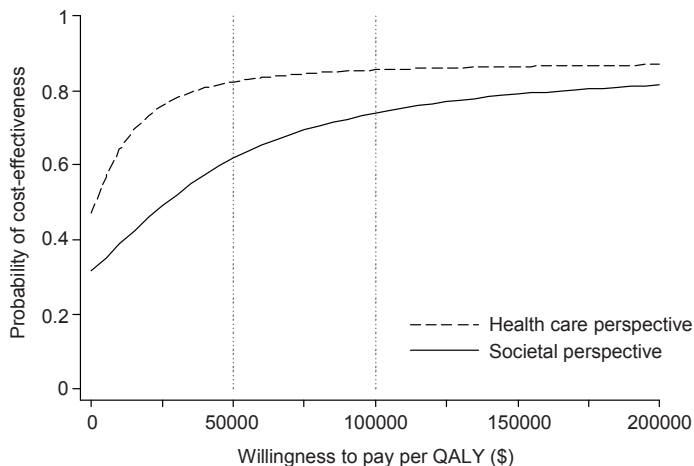
The probability that internet-based self-management is cost-effective from a health care perspective was 82% at \$50000 per QALY and 86% at \$100000 per QALY (figure 1).

QALYs gained, based on the visual analogue scale, were less than those based on the EQ-5D. In this case cost-utility ratios were \$91600 per QALY and \$5300 per QALY from a societal and health care perspective, respectively.

DISCUSSION

In this study we evaluated the cost-effectiveness of a new disease management strategy, internet-based self-management, for patients with asthma. The internet group non-statistically significantly gained 0.024 QALY during a follow-up period of 1 year compared with usual care. Costs were \$641 higher from a societal perspective, with an estimated

Figure 1. Cost-effectiveness acceptability curves, i.e. the probability that internet-based self-management is cost-effective compared with usual care depending on the willingness-to-pay per QALY from a societal perspective and health care perspective.



cost-utility ratio of \$26700 per QALY, which is generally considered acceptable. Both the estimation of QALYs gained and the calculated expenses showed considerable uncertainty, which is displayed by the probability curves. At a commonly cited willingness-to-pay threshold of \$50000 per QALY (32) the internet-based self-management intervention had a probability of 62% and 82% to be cost-effective compared with usual care from a societal perspective and health care perspective, respectively.

We have previously shown substantial and statistically significant clinical effects in favour of internet-based self-management with regard to asthma related quality of life, asthma control and lung function (13). Although the utility outcomes presented in the current study point in the same direction (i.e. in favor of internet-based self-management) as the clinical outcomes, their statistical significance is less evident. There are two main reasons that may explain this finding. First, generic quality of life measures, such as the EQ-5D, must be distinguished from disease-specific quality of life measures, such as the Asthma Quality of Life Questionnaire (19). The latter is well known to be responsive to change (22). However, generic preference-based instruments may differentiate between the highest and lowest levels of asthma control, but are less able to discriminate between moderate levels (33, 34). The baseline asthma control scores found in our primary care study population can be classified as moderately or partly controlled asthma and substantial improvements in disease-specific quality of life may have been missed by the generic instruments. Second, the absence of a statistically significant difference in our primary utility measure may reflect a lack of statistical power, since our trial was powered to detect a statistical difference in the primary outcome

measure, asthma related quality of life, and not explicitly to detect differences in generic preference-based utility measures (13, 35).

The intervention costs of \$254 per patient were similar to intervention costs of a paper-and-pencil asthma self-management program (10), but were half of the costs of intensive nurse-led telemonitoring in asthma reported by others (11). The costs of the technological innovation (software support, electronic spirometer, internet and mobile phone costs) were only about 40% of the total intervention costs. The fixed technological costs of software support constituted about one third of the intervention costs, so a considerable increase in the number of users could reduce the cost per user by one third. Moreover, the calculations were based on costs during the one-year randomized controlled trial. Asthma self-management cost-effectiveness studies with a longer time horizon have shown that intervention costs decrease after the first year (10, 36). In our study, costs for education sessions only apply to the first year, thus reducing costs in later years by about a quarter.

The other health care costs show a reduction of contacts with health care providers in the internet group. Although this reduction is consistently observed in 9 out of 10 health care providers, only the reduction in contacts with physiotherapists were statistically significant, suggesting that patients with better asthma control are less in need for physiotherapy. The cost of drugs for asthma show small decreases in short-acting β_2 -agonists and inhaled corticosteroids along, but increases in combination therapy (inhaled corticosteroids plus long-acting β_2 -agonists) and leukotriene antagonists in the self-management group. This finding, in combination with favorable clinical outcomes of the internet-based self-management group, suggests that asthma medication was used more efficiently by those in the internet group.

Our study had several limitations. First, quality adjusted life year estimates were calculated from only two follow-up measurements. More measurements would possibly have resulted in more accurate QALY estimates, but we limited the number of follow-up measures in order to minimize the awareness of participating in a clinical trial among patients in the usual care group. Second, patients were inevitably aware of the allocated group, which may have influenced their utility ratings. Third, our economic evaluation was limited to one year. As pointed out above a longer duration would probably have resulted in reduced intervention cost estimates after one year. It is, however, unknown how EQ-5D utility scores will progress after one year.

New cost-effective disease management strategies for asthma are required to face up to the global burden of asthma. Internet-based self-management is an innovative and effective management strategy in adults with asthma that improves clinical outcome. The results of the current study suggest that internet-based self-management is cost-effective compared with usual care, even more so from a health care perspective than from a societal perspective.

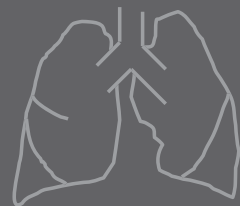
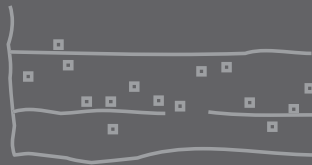
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CHAPTER 7

Summary and general discussion



SUMMARY

This thesis describes the role of internet-based support in the delivery of an asthma self-management program. First, the compliance and reliability of home lung function monitoring, one of the key features of asthma self-management, was studied. Second, we explored intrinsic barriers to current asthma management and revealed possible benefits from internet-based asthma self-management. Third, we assessed the clinical effectiveness and cost-effectiveness of an internet-based asthma self-management program over a period of 1 year. The conclusions from our studies are summarised below.

- Compliance and reliability of home peak flow measurements by adolescents using the internet or short message service is high over a 4-week period (chapter 2).
- Limited self-efficacy to control asthma is the main barrier to current asthma management in adolescents with poor asthma control (chapter 3).
- Adolescents consider feasible electronic monitoring, easily accessible information, e-mail communication and the use of an electronic action plan to be the main benefits of internet-based self-management (chapter 3).
- Asthma knowledge, inhaler technique and self-reported medication adherence are similarly improved by internet-based self-management as compared with usual physician-provided care. Internet-based self-management may reduce doctor visits and the number of medication changes is increased (chapter 4).
- Internet-based self-management improves asthma related quality of life, asthma control, symptom-free days and lung function, but does not decrease the number of exacerbations (chapter 4).
- Self-management based on weekly assessments of asthma control leads to improved asthma control in patients with partly and uncontrolled asthma at baseline and tailors asthma medication to individual patients' needs (chapter 5).
- Internet-based self-management is cost-effective compared with usual care, even more so from a health care perspective than from a societal perspective (chapter 6).

GENERAL DISCUSSION

Telemonitoring; how, what and how often?

How?

In all presented studies home telemonitoring played a pivotal role. Previous reports on paper-and-pencil peak flow diaries showed poor compliance and more than 40% erroneous reports (1, 2). We intended to use an electronic spirometer as part of the

self-management program. Therefore, we evaluated the compliance and reliability of electronic home peak flow monitoring and reporting. The adolescents in our observational study reported peak flow values on 90% of the days during 4 weeks (chapter 2). Comparison of the values with those in the memory of the electronic spirometer revealed that about 80% of reported values were correct. However, we observed a decrease in compliance and increase in erroneous reports over time which had not reached a plateau by week 4. Most likely this course over time was due to the lack of feedback or therapeutic consequences following peak flow reporting. Previous studies, using electronic monitoring in order to guide therapy, showed continuing high compliance rates compared to paper-and-pencil diaries (3, 4). Therefore, we recommend electronic monitoring rather than written diaries in order to evaluate lung function in research and clinical practice settings.

What?

The electronic spirometer used in our studies (PiKo; Ferraris, UK) also measures FEV₁. Compliance and reliability of the FEV₁ reports were similar to the peak flow reports in our 4-week observational study. Its good validity had been shown earlier (5). The availability of a home lung function device which measures not only peak flow, but also FEV₁, opened up ways to measure validated composite control scores, such as the Asthma Control Questionnaire (ACQ), at home (6). Several studies have compared written versus electronic respiratory questionnaires and generally found high concordance (7-9).

How often?

The use of composite control scores, such as the ACQ, has the advantage of not only capturing one or more (randomly chosen) elements of asthma control, but providing one single score for the level of asthma control, taking into account asthma symptoms, limitations in activity, quick reliever use and lung function. Since the ACQ addresses asthma symptoms and quick reliever use during the past week, we created an asthma action plan algorithm based on weekly consecutive ACQ measurements. Overall, ACQ monitoring adherence was 67%. We observed a decline in monitoring adherence from 88% in the first month to 60% in the seventh month and after that adherence remained stable (chapter 5). Despite the decline in monitoring adherence, asthma remained adequately controlled in the majority of patients.

The optimal frequency of monitoring has not been established yet. Obviously, there is a difference between episodes of uncontrolled asthma where asthma control is to be gained and episodes of adequately controlled asthma where asthma control must be maintained. The former episodes require a higher monitoring and feedback frequency than the latter episodes.

This theory is reflected by the reduced need for monitoring, observed in our study, once control of the disease had been achieved (10).

Our algorithm was based on weekly measurements, since the ACQ captures the previous week. However, post-hoc analysis of our study data showed a good agreement between a single ACQ and the lowest level of asthma control in the previous month, with less than 11% unobserved loss in asthma control (11). In addition, daily symptom or lung function monitoring may be advised. In research settings, daily monitoring may be feasible and indicated in order to guide and evaluate treatment (3, 12). However in routine clinical practice it is questionable whether daily monitoring is necessary and accepted, especially by those patients with well controlled asthma (chapter 3). Therefore, the advantage of daily monitoring additional to weekly asthma control assessment as part of an internet-based self-management support program is questionable.

Understanding participation in internet-based self-management; users and health care professionals

Users

Self-management of chronic diseases usually requires individual behaviour change. In contrast to traditional education, where patients are offered information and inhaler technique skills, self-management education teaches problem-solving skills and requires collaborative care. Previously, researchers have studied intentions to participate in asthma self-management and found that patients with less structural barriers, such as no time, living too far away and financial barriers were twelve times more likely to participate (13). In addition to these well-known external barriers, we conducted a semi-quantitative focus group study to elicit intrinsic barriers. The theory of planned behaviour, which assumes that attitude, social norm and self-efficacy expectations determine a person's intention to perform a specific behaviour, was used as a theoretical framework (chapter 3). Of these three determinants, limited self-efficacy (i.e. perceived ability to perform a specific action in a specific situation), turned out to be the main barrier in current asthma management, particularly for those patients with uncontrolled asthma. These patients in particular expressed several benefits from internet-based asthma self-management: electronic monitoring and feedback; easily accessible information; e-mail communication; and an electronic action plan. These characteristic features of an internet-based program may also eliminate external barriers such as time and distance constraints.

Health care professionals

Not only users, but also health care professionals, should be encouraged to use these new technologies in order to make implementation succeed. Previous research suggests

that health care professionals are resistant to adopt internet-based technologies into routine practice (14). At baseline, only 10 participants (5%) in our study reported to possess a written action plan, despite the availability of an effective asthma action plan for the Dutch primary care setting (15, 16), which seems to confirm physicians' reluctance to incorporate asthma self-management plans. Nevertheless, 37 out of 43 general practices (86%) we approached consented to participate in our study. Participation was not time-consuming for the health care professionals in these practices, mainly because the study team organised the education sessions and our asthma nurse specialist took care of the web-based follow-up. Obviously, successful implementation of internet-based asthma self-management requires professional roles and ways of working to be redefined including the delegation of particular tasks to other (medical) personnel, patients and carers (17).

The evidence-base; methodology, effectiveness and economic consequences

Methodology

How strong is the evidence of effectiveness of internet-based self-management in asthma? To answer this question, we have to consider the design and attitude of our trial. In contrast to explanatory trials, designed to test causal research hypotheses, our trial had a highly pragmatic attitude. Pragmatic trials are designed to help choose between options for care. Therefore, the choice of the design should maximise applicability of the trial results to usual care settings and are tested in a wide range of participants (18). Key features of pragmatic trials are the setting of a normal practice, little or no selection of participants beyond the clinical indication of interest, a flexibly applied intervention as it would be in normal practice and outcomes that are directly relevant to participants, healthcare practitioners and communities (19). In our trial, participants were recruited from routine practice settings and exclusion criteria were set to a minimum, which enhances generalisability. The outcomes were both patient-centred (e.g. asthma related quality of life, asthma control) (20) and relevant to the community and policy makers (utilities and costs).

We applied important dimensions of methodological quality such as randomisation and concealment of allocation to the design of our trial. However, blinding of participants and health care providers was not only impossible, but also not desirable. As opposed to explanatory trials, where blinding prevents belief in the effectiveness of the intervention from confounding the causal link between intervention and outcome, in pragmatic trials, as in the routine care setting, belief in or enthusiasm for an intervention may add to the effects of the intervention. Moreover, even in pragmatic trials, it is possible to support patient-centred outcomes with an objective source of data, in our case lung function (19).

Obviously, a placebo self-management program was not available. Therefore, we had to use another comparator; either a written self-management program or usual physician-provided care. The latter comparator, usual care, was most appropriate for two reasons. First, our research question was whether internet-based self-management led to improved asthma-related outcomes compared to the current routine practice. This current practice has incorporated written self-management plans only to a very limited degree. Second, we aimed to conduct an economic analysis, which requires a comparator which is most relevant for the policy question being addressed (21). In our case this question concerned the economic evaluation of internet-based asthma self-management against the current standard of care.

Effectiveness

We evaluated processes as well as clinical outcomes (chapter 4). Since the principal components of asthma self-management have been shown to be self-monitoring, education, drug treatment and medical review, we have focused on these 4 process outcomes. Self-monitoring has been discussed previously. Interestingly, the educational outcomes (knowledge, inhaler technique and adherence to medication) improved for both groups without differences between groups. This finding corresponds with a Cochrane review which showed that limited patient education did not appear to improve health outcomes in adults with asthma (22). The provision of asthma information may be a necessary, but not a sufficient condition for improved outcomes in asthma self-management programs.

We found significant differences in process outcomes between the study groups with regard to medication changes. Participants in the internet group had twice as many treatment increases and almost twice as many treatment decreases as participants in the usual care group. This suggests that the frequent medication changes (undoubtedly the consequence of self-monitoring and treatment advice) is the key feature of successful internet-based self-management. The rise in inhaled corticosteroid use during the first 3 months in which asthma outcomes improved markedly, was followed by a decrease in the next 9 months without deteriorating outcomes, which suggests that higher doses of inhaled corticosteroids are necessary to gain than to maintain asthma control and optimal asthma related quality of life.

The correlation between for instance lung function and quality of life has been shown to be weak (20, 23). Therefore, we evaluated patient-centred (Asthma Control Questionnaire (ACQ), Asthma Quality of Life Questionnaire (AQLQ)) and traditional outcomes (lung function, symptoms). The minimal important difference for the ACQ and AQLQ scores is 0.5 on a 7-point scale. However, it is important to realize that, although the mean difference between a treatment and a control is appreciably less than the smallest change that is important for the group as a whole, treatment may have an important im-

impact on many patients (24). Our study showed that even with a mean difference in AQLQ of 0.38 at a group-level, the proportion of participants with a clinically important benefit (>0.5) in the internet group (54%) was twice as high compared to the usual care group (27%). In other words, 4 patients need to participate in internet-based self-management in order to improve asthma related quality of life for 1 patient. Similarly, the ACQ clinically improved in 48% versus 17%; number needed to treat is 3. Lung function (FEV_1), as the only objective outcome, improved markedly, which supports the validity of the patient-reported outcomes.

We did not observe any differences in the rate of exacerbations between the two groups. This may be due to three reasons. First, the self-management program did not have any impact on asthma exacerbations. Second, the self-management program did have impact on exacerbations, but the number of participants was too small to detect this effect. Our sample size calculation was not aimed at detecting a reduction in exacerbations, but an improvement in asthma related quality of life. Third, we defined an exacerbation as a deterioration in asthma that required emergency treatment or hospitalization or the need for oral steroids. These severe exacerbations occurred in only 21 out of 200 patients (0.1 per patient per year) in our study. Defining mild exacerbations for instance as a fall in peak flow of 20% below the base-line value or awakening at night on two consecutive days would probably have resulted in more reported exacerbations (25). However, a definition of mild exacerbation would have required close, daily monitoring in both groups, which would highly have disturbed routine clinical practice in the usual care group. This was not our intention, so we refrained from interfering into daily routine care in order to identify mild exacerbations and only monitored severe exacerbations.

Economic consequences

Studies on innovative treatment strategies should ideally be accompanied by an economic evaluation in order to justify its implementation in the health care system. Preferably, a cost-utility analysis is performed, which measures costs from a societal or health care perspective and utilities as a generic outcome measure. These measures allow comparison of the economic consequences of different treatment strategies across a wide range of health care problems (21).

We performed a cost-utility analysis using data from our randomised, controlled trial and found a cost-utility ratio of \$26700 per QALY (quality adjusted life year) (chapter 6). Some issues regarding this result need to be addressed. First, the calculations were based on costs during the one-year trial. The fixed technological costs of software development constituted about one third of the intervention costs (\$254 per patient). A longer time horizon is likely to reduce intervention costs by a third. Second, the calculations were based on 101 participants. Use of the internet-based program by more

participants would substantially reduce intervention costs per patient. Third, costs of the intervention should be set off against the cost reduction by reduced health care provider contact. Either the participants in the internet-group were less in need for health care provider contacts, because of better asthma control, or face-to-face consultations were replaced by on-line asthma nurse contacts (chapter 4). The latter contacts were captured by the intervention costs. Fourth, it is remarkable that the differences in utilities were not statistically significant, whereas the differences in most clinical outcomes were. Most likely, the EQ-5D as a generic preference-based instrument may be able to differentiate between the highest and lowest levels of asthma control, but may be less able to discriminate between moderate levels (26, 27).

The point estimates of both costs and utilities were rather uncertain. To quantify this uncertainty we used the net benefit approach, which allowed us to report the probability that our intervention was cost-effective at certain willingness-to-pay thresholds (28). These willingness-to-pay thresholds are arbitrary and subject of debate. In the literature, a commonly cited value is \$ 50000 per QALY (29). The probability that internet-based self-management was cost-effective at this threshold was 62%. This result provides a fair basis to investigate the possibility of implementing internet-based self-management support of asthma into routine clinical care.

Implications and directions for future research; internet, chronic disease, self-management

Internet

The studies in this thesis have addressed the role of the internet in the delivery of an asthma self-management program. Patients have favourably accepted this innovation in health care technology. Importantly, internet is available for the majority of patients: eighty-seven percent of the population has internet access at home (30).

The use of internet adds to, rather than replaces ways of communication in current health care practices. Asynchronous communication, i.e. the fact that patient and health care provider need not be present at the same time, facilitates contact with the health care provider. Moreover, email or private message contacts may be time-saving compared to visits to the health care centre.

Within several years, it will probably be possible for patients to interact with their medical information using web portals. Ideally, the portal is integrated into existing electronic medical records. Patients will be able to view (parts of) their records and might be able to add information to their personal health record. In recent decades we have witnessed the evolution of e-banking and e-learning; now the ways are paved to implement interactive e-health technology into routine clinical practice.

Chronic disease

Not only asthma, but also other conditions such as COPD, diabetes, heart failure, depression, arthritis or inflammatory bowel syndrome may be suitable for self-management interventions. These diseases share the characteristics of being chronic with recurrent and episodic deteriorations, and the effectiveness of self-management programs has been demonstrated (31, 32).

Patients often have co-morbid conditions: COPD may coexist with heart failure, diabetes with depression, and asthma with COPD. Moreover, drugs for different diseases may interact. This interaction may go unnoticed, as the number of health care providers increases with the number of co-morbid diseases and more than one medical record may exist without mutual communication between health care providers. This may impair patient safety and quality of care. The challenge is to integrate existing and effective self-management programs into one comprehensive disease management program for each patient.

Self-management

Although our internet-based self-management program has proved to be effective and seems to provide value for money, several issues need to be considered (33).

Long-term effectiveness: The one-year results of our internet-based asthma self-management program are promising and the benefits seem to outweigh the costs. But what are the long-term consequences of implementation into current routine care; will the benefits still outweigh the costs in the long run? Economic evaluations over an extended period of time, using modelling techniques wherever necessary, are needed to convince policy makers and health care insurers of the necessity to implement self-management support programs for asthma or other chronic diseases into routine care.

Targeting self-management: We have demonstrated the effectiveness of internet-based self-management for asthma patients. At subgroup level we have been able to differentiate between patients who did and did not benefit from the program on the basis of current asthma control. Probably, other individual factors, such as self-efficacy or attitude, may predict the individual's response to an internet-based self-management program. These factors should be identified in order to better target the self-management intervention, and maximize its efficiency.

Organizational issues: Well conducted trials and modelling studies are not sufficient to ensure successful implementation. Self-management programs need to fit seamlessly within routine daily practice. In the past decade, primary care has faced and facilitated the advent of nurse practitioners, who have been responsible for improved quality of care for patients with chronic diseases such as diabetes, asthma and COPD. With the introduction of internet-based self-management programs tasks of health care professionals and personnel again need to be redefined. Are health care professionals able,

willing and ready to adopt these programs? The new care system in 2006 introduced many new parties in the market. We now witness the rise of companies who develop and promote internet-based self-care programs and products, such as Personal Medical Records. These initiatives may add to the adoption of self-management programs, but financial and personal interests need to be considered. The future for telemedicine, including internet-based self-management support, is promising, but should go hand in hand with a careful evaluation of its consequences, both health-wise and financial, along with all parties involved.

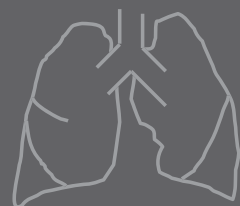
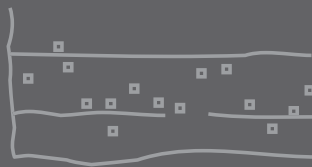
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CHAPTER 8

Dutch summary / Nederlandse samenvatting



ACHTERGROND

Astma is een aandoening van de luchtwegen en wordt gekenmerkt door een piepende ademhaling, kortademigheid, hoesten en soms een beknellend gevoel op de borst. De klachten zijn niet continu aanwezig, maar treden episodegewijs op. Patiënten met astma reageren versterkt op prikkels waarop mensen zonder astma niet reageren. Het gaat daarbij om allergische prikkels zoals huisstofmijt, honden, katten, gras- of boompollen en om niet-allergische prikkels zoals mist, kou, rook of parfum. Dit fenomeen wordt bronchiale hyperreactiviteit genoemd.

De klinische kenmerken van astma zijn het gevolg van een ontstekingsproces in de longen. Door deze ontsteking treedt slijmvlieszwelling (oedeem) op, wordt meer slijm in de luchtwegen geproduceerd (hypersecretie) en trekken de spieren rondom de luchtwegen samen (bronchospasme). Dit ontstekingsproces veroorzaakt luchtwegvernauwing met de daarbij optredende klachten en symptomen.

Ruim 3% van de Nederlanders heeft astma. De diagnose wordt gesteld door middel van anamnese en lichamelijk onderzoek. Longfunctietesten, bij voorkeur spirometrie, ondersteunen de diagnose. Een spirometrisch onderzoek bestaat uit een geforceerde uitademing vanuit volledige inademing. De voor astma belangrijkste maat die zo verkregen wordt, is de FEV_1 (forced expiratory volume in 1 second ofwel het éénsecondevolume). Wanneer de FEV_1 na het toedienen van een luchtwegverwijdend middel meer dan 12% is toegenomen ten opzichte van de uitgangswaarde (reversibiliteit) dan ondersteunt dit de diagnose. De laatste jaren is het gebruik van spirometrie in de huisartspraktijk fors toegenomen. Ongeveer tweederde van de Nederlandse huisartsen beschikt momenteel over spirometrie. Indien spirometrie niet beschikbaar is, kan een piekstroommeter aanvullende waarde hebben. De piekstroom is de maximale volumestroom bij een geforceerde uitademing vanuit volledige inademing. Toegenomen reversibiliteit of variabiliteit (het verschil tussen piekstroomwaarden op verschillende dagen of binnen één dag) ondersteunen de diagnose.

Behalve voor het stellen van de diagnose astma worden FEV_1 - en piekstroommetingen ook gebruikt om de behandeling te evalueren. Een toename van de longfunctieparameters en een afname in reversibiliteit of variabiliteit duiden op een betere astmacontrole.

BEHANDELING

De behandeling van astma richt zich op het verbeteren van de huidige astmacontrole en op het voorkomen van complicaties in de toekomst. De behandeldoelen voor astmacontrole bestaan uit het verminderen van klachten en symptomen, het minimaliseren van het gebruik van kortwerkende luchtwegverwijders en het optimaliseren van de

longfunctie. Bij het voorkomen van complicaties in de toekomst gaat het om het voorkomen van exacerbaties, het behoud van een goede longfunctie op de lange termijn en het voorkomen van bijwerkingen van medicatie.

Belangrijke componenten van de behandeling van astma zijn 1) voorlichting en niet-medicamenteuze adviezen vanuit een goede arts-patiëntrelatie, 2) metingen van astmacontrole, 3) medicamenteuze therapie en 4) reguliere medische controle. Juist bij zelfmanagement van astma zijn dit de belangrijkste pijlers van de behandeling. Kenmerkend voor zelfmanagement is de actieve betrokkenheid van de patiënt bij zijn behandeling. Dit kan door het verrichten van zelfmetingen van astmacontrole (klachten en longfunctie) en het gebruik van een vooraf opgesteld behandelplan. De patiënt maakt aan de hand van het behandelplan zelf keuzes in zijn behandeling en wordt niet zozeer behandeld, maar eerder begeleid.

DIT PROEFSCHRIFT

Hoewel nationale en internationale richtlijnen de gunstige effecten van astma-zelfmanagement onderschrijven en professionals aanbevelen patiënten te ondersteunen bij zelfmanagement, wordt hier in de praktijk weinig gebruik van gemaakt. Een van de oorzaken is dat bestaande schriftelijke behandelplannen als bewerkelijk en tijdrovend worden gezien. Zowel patiënten als zorgverleners zijn daardoor niet erg enthousiast over het gebruik van dergelijke schriftelijke astmabehandelplannen. Met de komst van nieuwe media als het internet is het mogelijk om deze behandelplannen niet alleen op papier, maar ook elektronisch aan te bieden. Dit biedt mogelijk voordelen ten aanzien van de voorlichting, communicatie en het gebruik van zelfmetingen en zelfbehandelplannen, maar de opbrengst is niet eerder onderzocht. Dit proefschrift beschrijft onderzoeken naar verschillende aspecten van zelfmanagement bij astma via internet: compliantie en betrouwbaarheid van elektronische piekstroommetingen, barrières bij huidige astmabehandeling en voordelen, effectiviteit en kosten-effectiviteit van zelfmanagement via internet.

Compliantie en betrouwbaarheid van elektronische piekstroommetingen

Compliantie is de mate waarin patiënten het advies van hun zorgverlener opvolgen. In het geval van geschreven piekstroomdagboeken blijken patiënten met astma vaak niet dagelijks een piekstroom te blazen en te noteren, ook als de zorgverlener daar om vraagt. De compliantie laat dus te wensen over. Ook zijn de genoteerde piekstroomwaarden vaak niet betrouwbaar. Patiënten schrijven de waarde van de piekstroommeter verkeerd over of verzinnen zelf een waarde. Het is onbekend wat de compliantie en betrouwbaarheid van elektronische piekstroommetingen zijn, waarbij de patiënt de piekstroomwaarden rapporteert via SMS of via een website.

Onderzoeksvraag

Hoe is de compliantie en betrouwbaarheid van elektronische piekstroommetingen?

Methode

We vroegen 97 adolescenten met astma tussen de 12 en 17 jaar om gedurende 4 weken dagelijks een piekstroom te blazen en de piekstroomwaarde te rapporteren via SMS of via een speciaal ontworpen website. Direct na het rapporteren ontvingen de deelnemers een ontvangstbericht met informatie over hun piekstroomwaarde als percentage van de persoonlijk beste waarde. De deelnemers waren niet op de hoogte dat de elektronische piekstroommeter de waarden in het geheugen opsloeg.

Resultaten

De compliantie bedroeg in de eerste week ruim 90% en daalde tot ruim 80% in de vierde week. Het percentage correct gerapporteerde metingen was 80% over de hele periode, ruim 90% in de eerste week dalend naar bijna 70% in de laatste week. Twee procent van alle gerapporteerde metingen bleek te zijn verzonnen.

Conclusie

De compliantie en betrouwbaarheid van elektronische piekstroommetingen zijn hoog gedurende een periode van 4 weken. Dit onderzoek ondersteunt de invoer van elektronische longfunctiemetingen bij zelfmanagementprogramma's voor adolescenten met astma via internet.

Barrières bij huidige astmabehandeling en voordelen van zelfmanagement via internet

Hoewel zelfmanagement bij astma een effectieve behandelstrategie is, maken weinig patiënten en zorgverleners gebruik van zelfmanagementprogramma's. Patiëntfactoren die uit eerder onderzoek van belang zijn gebleken voor deelname aan dergelijke programma's zijn tijd en afstand tot de zorgverlener. Weinig is echter bekend over de rol van intrinsieke barrières zoals negatieve attitude en beperkte eigen-effectiviteit. Daarnaast is niet bekend welke mogelijke voordelen zelfmanagement via internet biedt in de ogen van adolescenten (met goed of slecht gecontroleerd astma).

Onderzoeksvragen

Wat zijn intrinsieke barrières bij de behandeling van astma?

Wat zijn de voordelen van zelfmanagement via internet bij patiënten met goed of slecht gecontroleerd astma?

Methode

De patiënten die hadden deelgenomen aan het hiervoor beschreven onderzoek naar elektronische piekstroommetingen werden na de periode van 4 weken zelfmetingen uitgenodigd voor focusgroepinterviews. We vormden 8 groepen (in totaal 35 deelnemers) en stratificeerde deze groepen naar leeftijd, geslacht en mate van astmacontrole.

Resultaten

Beperkte eigen-effectiviteit, dat wil zeggen vertrouwen in eigen kunnen, was de belangrijkste barrière bij de behandeling van astma bij patiënten met slecht gecontroleerd astma. De adolescenten gaven meerdere voordelen aan van zelfmanagement via internet: de haalbaarheid van elektronische zelfmetingen, toegankelijke informatie, e-mailcommunicatie en het gebruik van een onlinebehandelplan. De groep met slecht gecontroleerd astma zag het nut in van zelfmanagement via internet en was er klaar voor om dit in het dagelijks leven in te passen. De groep met goed gecontroleerd astma noemde dit niet.

Conclusie

Beperkte eigen-effectiviteit is de belangrijkste intrinsieke barrière bij de behandeling van astma. Voordelen van zelfmanagement via internet zijn de elektronische zelfmetingen, toegankelijke informatie, e-mailcommunicatie en het gebruik van een onlinebehandelplan. Zelfmanagement via internet dient gericht te zijn op patiënten met slechte astmacontrole.

Effectiviteit van zelfmanagement bij astma via internet

Bij meer dan de helft van de patiënten met astma zijn klachten en symptomen onvoldoende gecontroleerd. In de praktijk komen deze patiënten vaak niet voor controle op het spreekuur. Internet lijkt een aantrekkelijk medium om zelfmanagement van patiënten met astma te ondersteunen. Onderzoek naar zelfmanagement van astma via internet heeft op de korte termijn gunstige resultaten laten zien wat betreft astmacontrole, longfunctie en kwaliteit van leven. Langetermijnstudies naar zelfmanagement van astma zijn nog niet verricht. We ontwikkelden met behulp van internet een zelfmanagementprogramma voor coaching van volwassen patiënten met astma. Het programma omvatte alle essentiële aspecten van zelfmanagement: zelfmetingen met daaraan gekoppelde behandeladviezen (behandelplan), online educatie en coaching door een longverpleegkundige.

Onderzoeksvraag

Is zelfmanagement via internet gedurende 1 jaar effectief wat betreft procesuitkomsten en klinische uitkomsten bij astma?

Methode

Via 37 huisartspraktijken en een polikliniek longziekten rekruteerden we 200 astmapatiënten met een voorschrift van inhalatiecorticosteroiden gedurende tenminste 3 maanden in het afgelopen jaar en toegang tot internet. Patiënten werden at random toegewezen aan de internetgroep (n = 101) of de gebruikelijkezorggroep (n = 99). Deelnemers in de internetgroep verrichtten wekelijks zelfmetingen van astmacontrole via internet en kregen onlinebehandeladvies, educatie en coaching door een longverpleegkundige. Procesuitkomsten waren kennis, inhalatietechniek, therapietrouw, aantal contacten met zorgverleners en aantal medicatieveranderingen. Klinische uitkomsten waren astmagerelateerde kwaliteit van leven, astmacontrole, klachtenvrije dagen, longfunctie en tijd tot eerste exacerbatie.

Resultaten

De kennis over astma en inhalatietechniek verbeterde iets in beide groepen, maar er was geen verschil tussen de 2 groepen. Therapietrouw bleef in beide groepen hetzelfde. Het aantal doktersbezoeken vanwege astma was in de internetgroep iets meer dan 1 per patiënt en bijna 2 per patiënt in de gebruikelijkezorggroep. Patiënten in de internetgroep hadden ongeveer tweemaal zo vaak een verandering in medicatie dan patiënten in de gebruikelijkezorggroep.

Astmagerelateerde kwaliteit van leven verbeterde meer in de internetgroep dan in de gebruikelijkezorggroep. In de internetgroep had 54% een klinisch relevante verbetering ten opzichte van 27% in de gebruikelijkezorggroep. Ook astmacontrole verbeterde meer in de internetgroep dan in de gebruikelijkezorggroep. Na 12 maanden was het percentage klachtenvrije dagen ruim 10% hoger in de internetgroep dan in de gebruikelijkezorggroep en was de longfunctie in eerstgenoemde groep beter. Er was geen verschil tussen de groepen wat betreft tijd tot eerste exacerbatie.

Conclusie

Vergeleken met gebruikelijke zorg verbeteren de kennis over astma, inhalatietechniek en therapietrouw niet door zelfmanagement via internet. Wel vermindert het aantal doktersbezoeken en stijgt het aantal aanpassingen van medicatie. Zelfmanagement via internet verbetert de astmagerelateerde kwaliteit van leven, astmacontrole, aantal klachtenvrije dagen en longfunctie. De tijd tot de eerste exacerbatie verandert niet. Zelfmanagement bij astma via internet is effectief en biedt nieuwe mogelijkheden in de behandeling van astma.

Verskil in effectiviteit tussen patiënten met verschillende mate van astmacontrole bij de start

Het effect van zelfmanagement via internet op astmacontrole dat gevonden werd in bovenstaand onderzoek was weliswaar statistisch significant, maar voor de groep als geheel niet erg groot. In de huidige studie bestudeerden we het effect op medicatiegebruik en astmacontrole van zelfmanagement via internet voor drie subgroepen van astmacontrole bij de start van het onderzoek (baseline): goed gecontroleerd, matig gecontroleerd en slecht gecontroleerd astma.

Onderzoeksvraag

Wat is het effect op astmacontrole en medicatiegebruik van zelfmanagement via internet voor groepen met verschillende mate van astmacontrole op baseline?

Methode

De patiënten uit het hiervoor beschreven gerandomiseerde onderzoek deelden we in in de groepen goed, matig en slecht gecontroleerd astma op baseline. Vervolgens onderzochten we bij deze drie groepen gedurende 1 jaar de veranderingen in medicatiegebruik en astmacontrole.

Resultaten

Astmacontrole was verbeterd in de groepen met matig en slecht gecontroleerd astma, maar niet in de groep met goed gecontroleerd astma. In de groep met slecht gecontroleerd astma was het gebruik van inhalatiecorticosteroïden in de eerste 3 maanden toegenomen. Na een jaar was er in geen van de 3 groepen een statistisch significante verandering in medicatiegebruik.

Conclusie

Zelfmanagement via internet verbetert de astmacontrole bij patiënten met matig en slecht gecontroleerd astma op baseline. Medicatiegebruik wordt toegesneden op de behoefte van iedere individuele patiënt.

Kosten-effectiviteit van zelfmanagement bij astma via internet

In de bovenstaande twee onderzoeken hebben we laten zien dat zelfmanagement bij astma via internet een effectieve behandelstrategie is om klachten en symptomen te doen verminderen en de astmagerelateerde kwaliteit van leven te verbeteren. Nieuwe behandelstrategieën vereisen behalve een evaluatie van de effectiviteit ook een evaluatie van de kosten-effectiviteit om te bepalen of de gunstige resultaten bereikt worden tegen acceptabele kosten. Een kosten-effectiviteitsanalyse helpt richtlijnontwikkelaars, beleidsmakers en verzekeraars om de nieuwe behandelstrategie al dan niet aan te

bevelen of te vergoeden. Daarom verrichtten wij een kosten-effectiviteitsanalyse van zelfmanagement bij astma via internet.

Onderzoeksvraag

Is zelfmanagement bij astma via internet kosten-effectief vergeleken met de gebruikelijke zorg?

Methode

De data voor deze analyse werden verkregen via het gerandomiseerde onderzoek bij 200 patiënten met astma, beschreven in de vorige twee onderzoeken. De effectiviteit in deze analyse betrof het aantal gewonnen QALYs. Een QALY (quality adjusted life years) is een maat die zowel de kwaliteit als de kwantiteit van leven omvat. Een gewonnen levensjaar in perfecte gezondheid wordt gewaardeerd met 1 QALY, maar wanneer een levensjaar wordt gewonnen dat gepaard gaat met ziektelast dan is de QALY kleiner dan 1. De kosten van zelfmanagement bij astma via internet bestonden uit de kosten voor de interventie, de kosten voor zorggebruik (zoals doktersbezoek en gebruik van medicatie) en productiviteitsverlies door absentie van werk. We berekenden de waarschijnlijkheid dat zelfmanagement bij astma via internet kosten-effectief is vanuit maatschappelijk perspectief en vanuit het perspectief van de gezondheidszorg.

Resultaten

Ten opzichte van gebruikelijke zorg was er een lichte toename in QALYs bij zelfmanagement via internet. Deze toename was niet statistisch significant. De kosten voor de interventie waren \$254 per persoon per jaar. De kosten voor zorggebruik waren \$217 lager in de internetgroep dan in de gebruikelijkezorggroep, met name vanwege minder contacten met zorgverleners. Wanneer de maatschappij bereid is om voor 1 QALY \$50000 te betalen (willingness to pay) dan is de waarschijnlijkheid dat zelfmanagement kosten-effectief is ten opzichte van gebruikelijke zorg 62% vanuit maatschappelijk perspectief en 82% vanuit het perspectief van de gezondheidszorg.

Conclusie

Zelfmanagement bij astma via internet is waarschijnlijk kosten-effectief. Implementatie van deze nieuwe behandelstrategie is aan te bevelen, zeker vanuit het perspectief van de gezondheidszorg.

CONCLUSIES

- De compliantie en betrouwbaarheid van elektronische piekstroommetingen zijn hoog gedurende een periode van 4 weken.
- Beperkte eigen-effectiviteit is de belangrijkste intrinsieke barrière bij de behandeling van astma.
- Voordelen van zelfmanagement via internet zijn de elektronische zelfmetingen, toegankelijke informatie, e-mailcommunicatie en het gebruik van een onlinebehandelplan.
- Vergeleken met gebruikelijke zorg verbeteren de kennis over astma, inhalatietechniek en therapietrouw niet door zelfmanagement via internet.
- Zelfmanagement via internet verbetert de astmagerelateerde kwaliteit van leven, astmacontrole, aantal klachtenvrije dagen en longfunctie, maar de tijd tot de eerste exacerbatie verandert niet.
- Zelfmanagement via internet verbetert astmacontrole bij patiënten met matig en slecht gecontroleerd astma op baseline. Medicatiegebruik wordt toegesneden op de behoefte van iedere individuele patiënt.
- Zelfmanagement bij astma via internet is waarschijnlijk kosten-effectief.

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Curriculum Vitae

Victor van der Meer was born on July 3rd 1977 in Rotterdam, the Netherlands. He received secondary education at the Regionale Scholengemeenschap in Oud-Beijerland, where he passed his Gymnasium exam in 1995. He studied medicine at the University of Leiden and followed additional courses on medical ethics, medical law and history of medicine. He graduated from medical school in 2002 (*cum laude*).

The first year of his medical career, he worked as a resident at the department of Internal Medicine, Red Cross Hospital, the Hague (dr. R.M. Valentijn). In 2003 he started the vocational training for general practice at the department of Public Health and Primary Care of the Leiden University Medical Centre (LUMC) (prof. dr. W.J.J. Assendelft). One year later he started the research project described in this thesis at the department of Medical Decision Making of the LUMC (prof. dr. J. Kievit) in a combined vocational and research-training program (AIOTHO: arts in opleiding tot huisarts-onderzoeker). In 2006 he received an International Trainee Travel Award from the behavioural science assembly of the American Thoracic Society.

In 2004 and 2005 Victor was board member and vice-president of the LOVAH, the Dutch organisation of general practitioner trainees.

From 2005 until 2008 he followed several courses in epidemiology at the VU University, Amsterdam, and at the London School of Hygiene and Tropical Medicine, London, United Kingdom, and obtained his registration as an epidemiologist upon completion of this thesis.

From 2007 onwards he works as a general practitioner in health care centre Stevenshof in the city of Leiden and continues his clinical epidemiological research work in the fields of self-management and prevention at the department of Public Health and Primary Care (LUMC).

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