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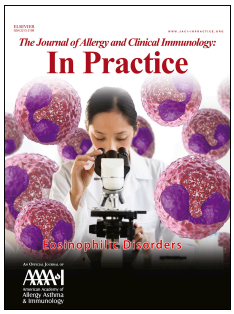

Effectiveness of myAirCoach: a mHealth self-management system in asthma

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Effectiveness of myAirCoach: a mHealth self-management system in asthma

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Take home message: use of mHealth assisted self-management of asthma leads to improved control, quality of life and reduced amount of severe exacerbations.

The trial was approved by the Medical Ethics Committee of Leiden University Medical Center and North West - Greater Manchester South Research Ethics Committee. The trial was registered at http://www.trialregister.nl/trialreg/admin/rctview.asp?TC=7200 with trial code NTR7200.

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Conflict of interest

Mr. Khusial has nothing to disclose. Dr. Chung reports grants and personal fees from GlaxoSmithKline, personal fees from Astra-Zeneca, personal fees from Novartis, grants and personal fees from Merck, personal fees from Boehringer Ingelheim, personal fees from TEVA, outside the submitted work. Dr. Usmani reports grants and personal fees from Astra Zeneca, grants and personal fees from Boehringer Ingelheim, grants and personal fees from Chiesi, personal fees from Aerocrine, grants from GlaxoSmithKline, personal fees from napp, personal fees from Mundipharma, personal fees from Sandoz, personal fees from Takeda, personal fees from Zentiva, grants from Edmond pharma, personal fees from Cipla, outside the submitted work. Dr. Honkoop reports personal fees from E-wise, outside the submitted work. Dr. Ortmann reports grants from European Commission, during the conduct of the study; In addition, Dr. Ortmann, Dr. Votis and Dr. Tzovaras have a patent DE 10 2016 219 759.2 pending. Ms. Meah has nothing to disclose. Dr. Simpson has nothing to disclose. Dr. Biddiscombe has nothing to disclose. Dr. Koopmans has nothing to disclose. Dr. Fowler has nothing to disclose.. Dr. Lalas has nothing to disclose. Dr. Polychronidou has nothing to disclose. Dr. Moustakas has nothing to disclose. Dr. Snoeck-Stroband has nothing to disclose. Dr. Soares has nothing to disclose. Dr. Sont research grants from AstraZeneca, outside the submitted work.

Abstract

Background

Self-management programs have beneficial effects on asthma control, but their implementation in clinical practice is poor. Mobile health (mHealth) could play an important role in enhancing self-management.

Objective

To assess the clinical effectiveness and technology acceptance of myAirCoach supported self-management on top of usual care in asthma patients using inhalation medication .

Methods

Patients were recruited in two separate studies. The myAirCoach system consisted of an inhaler adapter, an indoor air-quality monitor, a physical activity tracker, a portable spirometer, a Fraction exhaled Nitric Oxide (FeNO) device and an app. The primary outcome was asthma control; secondary outcomes were exacerbations, quality of life, and technology acceptance. In study 1, 30 participants were randomized to either usual care or myAirCoach support for 3-6 months; in study 2, 12 participants were provided with the myAirCoach system in a 3 month before-after study.

Results

In study 1 asthma control improved in the intervention group compared to controls (ACQ difference 0.70, p=0.006). A total of six exacerbations occurred in the intervention group compared to 12 in the control group (hazard ratio 0.31, p=0.06). Asthma related quality of life improved (m-AQLQ difference 0.53, p= 0.04), but FEV1 was unchanged. In study 2, asthma control improved by 0.86 compared to baseline (p=0.007) and quality of life by 0.16 (p=0.64). Participants reported positive attitudes towards the system.

Discussion

Using the myAirCoach support system improves asthma control and quality of life, with a reduction in severe asthma exacerbations. Well validated mHealth technologies should therefore be further studied.

Highlights

1. What is already known about this topic?

   The use of eHealth/mHealth in asthma care is upcoming. Many different apps and systems are currently available, however most systems are not evaluated in a scientific setting.

2. What does this article add to our knowledge?

   This study shows mHealth has the potential to positively influence asthma-related outcomes. Patients are also satisfied using mHealth.

3. How does this study impact current management guidelines?

   mHealth has the potential to transform health care delivery and should therefore be included as an effective option in future guidelines to support self-management.

Key words: asthma, mHealth, app, eHealth, telemedicine, self-management, quality of life, personalized care

List of abbreviations

ACD- Asthma Control Diary

ACQ- Asthma Control Questionnaire

Apps- mobile applications

CI- Confidence Interval

EQ-5D-5L- EuroQol-5 Dimensions-5 Levels questionnaire

FEV1- Forced Expiratory Volume in 1 second

FeNO- Fraction exhaled Nitric Oxide

IQR- Inter Quartile Range

ppb- parts per billion

PM2.5- Particulate Matter 2.5

PM10- Particulate Matter 10

m-AQLQ- mini Asthma-related Quality of Life Questionnaire

MCID- Minimal Clinically Important Difference

MDI- Metered Dose Inhaler

NO2- Nitric dioxide

SD- Standard Deviation

SNOT-22 - Sino-Nasal Outcome Test-22

SO2- Sulphur Dioxide

TAQ- Technology Acceptance Questionnaire

Introduction

Self-management plays an important role in treatment for asthma (1). Effective self-management allows patients to use medication and devices correctly, acknowledge importance of lifestyle and environmental influences, recognize aggravating factors and understand the value of self-monitoring. Additionally, patients need to be able to recognize and treat worsening of symptoms and know when to seek urgent medical attention (2). Therefore, asthma action plans are advised to support patients in evaluating and managing their symptoms (1).

However, patient adherence to self-management programs is low, with only 20% of people reporting the use of an action plan (3). Self-management tasks are often regarded as burdensome and time-consuming while patients indicated that they would prefer different data to be added to their asthma action plan (4). Current action plans based solely on symptoms and/or lung function parameters also lack precision in detecting deteriorations in asthma control and asthma exacerbations (5). Preferably automatically collected data could improve both precision and acceptance.

Mobile health (mHealth) support has the potential to transform health care delivery (6). Home-monitoring applications involving mobile device-based interactive systems are promising tools for overcoming the above mentioned barriers and supporting self-management of asthma (7). mHealth can now integrate physiological, behavioral and environmental information to aid self-management. Therefore, mHealth could encourage patients to be more engaged in self-management activities, given the ease of use of their own mobile phone.

There are over 500 mobile phone applications (apps) for asthma (8), but scientific evidence supporting the majority of these apps is lacking and their quality varies greatly (8, 9). Development and promotion of such apps presently does not appear to require evidence that they indeed improve asthma outcomes (10), which makes it difficult for patients and healthcare to choose the correct and effective apps for their own use (11). Huckvale reported in 2015 that 13% of the available asthma apps made recommendations about self-care procedures that were not based on scientific evidence (12). Importantly, non-evidence-based apps used as medical tools are potentially harmful (13).

Therefore, the objective of the myAirCoach project was to create a validated app, that would contain elements deemed necessary by patients to aid self-management (14). We have previously reported on patients' views on the required content of an asthma-related mHealth system (4) and assessed the feasibility and end-user experience of physiological and behavioral data collection, using already available mHealth and home-monitoring tools (15).

Data from these studies were used by the myAirCoach consortium (www.myaircoach.eu) to develop a mHealth system, which included an app and several portable devices, to integrate support for important self-management aspects and tasks. The system presented data to the participant on factors, including asthma control, inhalation technique and environment exposure, thus providing patients with a wider insight into their condition and how it is affected by their environment and behavior.

In this study we assessed the clinical effectiveness of the mHealth supported myAirCoach self-management system in patients with asthma compared to usual care and present the results of two linked and simultaneously performed studies.

Methods

Setting and participants

The myAirCoach project was EU Horizon2020 funded and conducted by a research consortium of 12 collaborating partners (list of partners available at www.myaircoach.eu). Study 1, a pragmatic randomized controlled trial, registered at www.trialregister.nl (NTR 7200), was originally planned to be performed in the Netherlands and two sites in the United Kingdom (UK). The study was approved by the Medical Ethics Committee of Leiden University Medical Center and North West - Greater Manchester South Research Ethics Committee.

The original sample-size calculated was based on the Asthma Control Questionnaire (ACQ). In order to detect a difference of 0.5 (SD 0.8) points with an alpha error of 0.05 and a power of 80%, the minimum sample-size needed was 41 subjects per group, 82 in total. Due to delays in obtaining ethical and MHRA approval in the UK, the UK part of the study was changed to a before-after study (study 2).

Participants in both studies were eligible if they: had a clinical diagnosis of asthma; were treated with controller medication with a metered dose inhaler (GINA treatment step 2-5 (1)); had a current status of asthma with an Asthma Control Questionnaire (ACQ)-score of ≥ 1.5 (16) and/or ≥ 1 exacerbations or hospital visit due to asthma in the previous year; were 18 years or older; and were able to understand Dutch or English in the respective countries. All participants provided written informed consent.

Design overview

Study 1 was a pragmatic randomized controlled trial in the Netherlands. Participants were included over a period of four months, while we used a fixed end date for all participants, resulting in a varied follow-up duration (3-6 months). Participants were randomized by a computerized algorithm to receive either ‘usual care’ or ‘usual care + self-management support via myAirCoach’. Study 2 was a 3 month before-after study in the UK in which all participants used the myAirCoach system.

All participants attended the research facility twice; once for a 30 minute introductory meeting and again at the end of the study. During these visits participants completed questionnaires and lung function (FEV1), and fraction of exhaled nitric oxide (FeNO) were measured. Participants in the intervention group in study 1 and all participants in study 2 were given instructions on how to use the myAirCoach app and different devices for self-management support, lasting approximately 1 hour. In addition, all participants received periodical questionnaires through email to assess outcome parameters (see online repository). All participants continued care with their usual caregiver.

Intervention

The intervention was developed based on the outcomes of the focus group study and experiences of participants in the observational study (4, 15). During the development phase the research consortium had joint meetings with patient advisory forums in order to obtain feedback and

prototype improvements were made accordingly. The final integrated system consisted of several devices and an app.

Devices

Both an inhaler adapter and indoor air quality monitor were designed and produced by the myAirCoach study consortium. The inhaler adapter was an add-on which fitted different sized Metered Dose Inhalers (MDI's), with or without spacer and it connected to the myAirCoach app through Bluetooth. The inhaler adapter (see online repository figure E8) was developed to improve inhalation technique. It measured correct positioning of the inhaler during inhalation by an accelerometer. Feedback was provided with the use of indicator LED's (red and green) on top of the inhaler adapter. In parallel, the inhaler adapter recorded sound for 24 seconds with the use of a built-in microphone. Sound analysis was performed on the order of actions (inhaling, actuation and exhaling) (17). Based on accelerometer results and sound analyses, an Inhaler Technique Score between 0-100 was calculated and provided to the participant in the myAirCoach app directly after use. If the Inhaler Technique Score was less than 100%, feedback on what could be improved was provided and the participant was redirected to an in-app manual for correct inhalation technique.

The indoor air quality monitor (see online repository figure E10), registering nitrogen dioxide (NO2), Sulphur dioxide (SO2), particulate matter (PM2.5 and PM10), humidity, air pressure and temperature, was placed in the bedroom. Data, recorded every hour, was transmitted by Bluetooth to the smartphone of the participant and results were displayed in the myAirCoach app.

Participants could monitor their FEV1 with a portable spirometer (nSpire Health, PiKO-1 device; available at www.nspirehealth.com) and FeNO with a home sensor (Aerocrine, NIOX VERO device; available at www.niox.com). The results were shown on the displays of the devices and participants were asked to manually enter results in the app.

The Fitbit Charge HR (Fitbit, Inc, Fitbit charge HR; available at http://www.fitbit.com) is a wearable fitness tracker, measuring steps and stairs walked, calories burned and real-time heart rate. Participants were advised to wear the Fitbit continuously. Heart rate and steps data were shown in the myAirCoach app.

myAirCoach app

At the first visit, participants downloaded the myAirCoach app on their smartphone. Since the app was only used in a research setting and required anonymity, the app was not publicly available, but could only be downloaded with the help of the research team. Every participant was also given an anonymous username and password and logging in was required the first time they used the app. In the app, results from all devices were displayed in graphs. Additionally, participants were able to monitor symptoms with questionnaires, including the Asthma Control Diary (ACD) (18), Asthma Control Questionnaire (ACQ) (19) and Sino-Nasal Outcome Test-22 (SNOT-22) (20) (see online repository table E2). Outdoor air quality, measured by the European Copernicus Program (www.regional.atmosphere.copernicus.eu), was also displayed for current location or other favorite locations. A map using color-coding to indicate levels of pollution was provided in addition to an overall statement on air pollution and concentrations of ozone, ultra-fine dust, fine dust, carbon monoxide, NO_2 and SO_2. More detailed information on the app and devices is provided in the online repository (including figure E4-E9).

Outcomes and follow-up

For both studies the primary outcome was asthma control assessed by the Asthma Control Questionnaire (ACQ, range 0-6; Minimal Clinically Important Difference (MCID) = 0.5) at 4-week intervals (19). A lower score represents better asthma control.

Secondary outcomes were severe asthma exacerbation rate, quality of life, FEV1 and technology acceptance. Severe exacerbations were defined as asthma-related hospitalizations, emergency care visits or systemic use of oral corticosteroids for ≥3 days (21). Asthma related quality of life was measured by the mini Asthma Quality of Life Questionnaire (m-AQLQ]; MCID = 0.5 (22)), consisting of four domains: symptoms, activities, emotions and environment, at 12-week intervals. Generic health-related quality of life was assessed by the EQ-5D-5L questionnaire at 12-week intervals (23). FEV1 was measured with the PiKO-1 device throughout the study for the intervention participants and during the visits for the controls. Participant attitudes towards and acceptance of the technology were measured by the Technology Acceptance Questionnaire (TAQ) at 12-weeks (24). The TAQ has eleven domains next to specific questions about the inhaler adapter and the PiKO-1 device (see online repository).

Statistical analysis

In study 1 the outcomes of the ACQ, m-AQLQ, EQ-5D-5L and FEV1 were analyzed using a mixed model analysis, adjusting for repeated measurements within participants, and baseline values of the outcomes. Severe exacerbation rates were compared by the Cox proportional hazard model, allowing analysis of multiple exacerbations per participant. For study 2 paired t-tests were performed for the ACQ, m-AQLQ, EQ-5D-5L and FEV1 comparing baseline measurements with the final results. Boxplots for the TAQ were made, combining results of all participants using the system in both study 1 and 2. All analyses were performed with STATA 14.0 (StataCorp, College Station, TX).

Results

Subjects

Thirty participants were included in study 1 and twelve participants in study 2 (see online repository figure E1). The major reason for declining participation was concern about time. Two participants dropped out of study 1, one in the intervention group due to 'personal circumstances' and one control (no further response to repeated enquiry). Mean follow-up in the intervention group was 166 days and in the control group 154 days. All participants from study 2 finished follow-up with a mean follow-up of 94 days.

Baseline characteristics are shown in table 1. There were no significant differences between control and intervention groups in study 1. Participants in study 2 had a slightly different profile than participants of study 1. They were on average 10 years younger, their age of diagnosis was also lower, FeNO was higher and their baseline ACQ was better.

System use

The app was used for 2345 tasks. These tasks included filling out questionnaires and entering FeNO/FEV1 data (see online repository table E1). In study 1 on average 110 tasks per patient were performed and in study 2 this was on average 67 times.

The number of inhalation registered by the system in study 1 was 219 inhalations/patient and in study 2 this was 81 inhalations/patient. In study 1 the Inhaler Technique Score changed by 1% (from 79% to 80%). In study 2 the Inhaler Technique Score changed from 88% to 76%.

Outcomes

The intervention group had a clinically relevant and statistically significant improvement of asthma control compared to the control group in study 1. In the mixed-model analysis, the difference in ACQ was 0.70 (95%CI -1.21; -0.20, p=0.006) (table 2). A sensitivity analysis additionally adjusting for baseline characteristics age, smoking status, age of diagnosis and gender and a sensitivity analysis for baseline FEV1 and FeNO showed similar results. In study 2 asthma control improved by 0.86 (95%CI 0.29; 1.44, p=0.007) compared to baseline, as shown in figure 1.

The number of severe exacerbations was lower in the intervention group compared to the control group for study 1 (respectively, 6 vs 12 (hazard ratio 0.31, 95%CI 0.09; 1.06, p=0.06), see figure 2). Exacerbation rate for intervention participants was 0.94 per participant per year, compared to 2.04 per participant per year for the participants in the control group. In study 2, three exacerbations occurred. Exacerbation rate was 1.06 per participant per year.

The difference in m-AQLQ assessed by the mixed-model analysis was 0.53 (95%CI -0.22; 1.10, p=0.04) (figure 3). The differences in the subdomains 'symptoms' and 'emotions' both exceeded the MCID of 0.5 and were statistically significant (online repository table E3; figure E11). In study 2, the participants had a baseline m-AQLQ of 5.13 and their score increased by 0.16 (p=0.64). The participants improved in all domains, with the largest improvement in the 'emotions' domain.

The EQ-5D-5L showed an improvement in generic health-related quality of life in the intervention group (coefficient 0.12, p=0.04) in study 1 compared to the controls. In study 2 there was no

314 significant difference in EQ-5D-5L score between baseline and exit (0.04, p=0.23), as shown in figure
315 E2.

316 There was no change in FEV1 measured in both studies. In study 1 the FEV1 was 0.09 liters (p=0.60)
317 lower in the intervention group compared to the control group (see figure E3). In study 2
318 participants had a baseline FEV1 of 2.63L and their exit FEV1 was 2.52L (p=0.42).

319 The TAQ showed favorable attitudes of the participants towards the myAirCoach intervention
320 except for the impact of the system on social influence and attitude towards the inhaler adapter.
321 Participants were most positive on the facilitating conditions and trust in the system. They also
322 reported favorable attitudes on the self-management aspect of the system. The average domain
323 scores are depicted in the figures below (Figure 4).

Discussion

Our study shows that mHealth supported self-management aided by the myAirCoach system was effective in clinically improving asthma control, exacerbation-rates and quality of life. Additionally, end-users of this mHealth platform reported generally positive attitudes towards the system.

In asthma, most research in eHealth has focused on using traditional forms of telemedicine, including remote consultations and SMS reminders (25-27). Even though Huckvale et al. already reported 764 different asthma apps in 2015 (12), the number of trials focusing on mobile app assisted self-management in asthma is limited (28). Moreover, none of the apps assessed in previous studies additionally used such diverse data from wearables, environmental databases and home-monitoring devices (29). As a consequence of our multi-faceted intervention, we opted to assess clinical outcomes, such as asthma control and exacerbation rate. Other studies have focused more on outcomes particularly relevant for medication adherence. For example, the recent ADAPT study by Kosse et al. developed an app with several modules primarily targeting adherence in adolescents and they showed that their app indeed improved this (30).

A Cochrane review in 2012 (updated in 2013) included only two studies regarding asthma self-management with apps compared to paper-based asthma self-management (31). Ryan et al. concluded that monitoring of asthma through mobile phone use does not improve asthma outcomes more than paper based strategies (32). Both groups showed clinically relevant improvements in asthma control and quality of life. It is suggested that monitoring in itself could have a positive effect on asthma related outcomes. However, paper monitoring could be more cumbersome and time-consuming for the participant and it does not allow for collection of other types of data, such as heart rate. mHealth is more user-friendly since a majority of the adults uses a smartphone (33).

A study by Cook was a promising proof of concept study showing the effectiveness of an asthma related mHealth application (34). The asthma related outcomes (asthma control and FEV1) improved and patients were satisfied with the intervention. This study however only consisted of an intervention group without randomization. Our study supports and extends these findings since we have found a beneficial effect on asthma control, severe asthma exacerbations and quality of life and we included a control group in the first study to minimize the effect of confounding factors unrelated to the mHealth. We also reported a high user-satisfaction.

An important aspect of the myAirCoach project was the involvement of participants in different stages of the development of our intervention, including repeated device testing to improve performance. We specifically asked what kind of functionalities they wanted to see in a mHealth system and what they deemed useful information. If no device existed that could measure these parameters, we developed it within our study consortium. Overall, the participants were satisfied with the system and they reported they felt the system aided them in their self-management. We believe that this early involvement of patient users in this project has helped in devising a user-friendly tool for self-management of asthma.

An important strength of our study is that we provided participants with an app which included a wide variety of data on very different aspects of asthma management. The app was used often, with 110 tasks per patients on average in study 1 and 67 tasks per patient in study 2. We were only able to record a task if the participant manually entered data into the app (answering a questionnaire,

entering a measurement). So, the average numbers of tasks indicates the minimal usage, since any other action in the app (e.g. viewing of inhalation score, air quality data or individual graphs on symptoms and measurements) was not recorded.

Although we showed that by providing a comprehensive overview we managed to improve asthma control, exacerbation rate and quality of life, we do not know how much each of the individual components contributed to these improvements. This also relates to the fact that we did not record viewing of results in the app of, for example, the inhalation technique score. We know this improved in some and worsened in others. However, we do not know who actually viewed their inhalation technique results in the app, or who acted upon these results, for example by viewing the in-app inhalation instructions or by going to their healthcare professional. Different components are relevant for different patients. In future studies we recommend to also systematically collect data on page-views and time spent on different components of an app and preferably also on subsequent self-management changes made by patients.

An important limitation of the study is the number of participants included in the study. In the original protocol the intention was to include 90 participants in the study (45 intervention and 45 control). Due to the fixed end date of the study appointed by the EU, combined with strict regulatory laws regarding studies with medical devices in the UK and longer than expected development time of the app and devices, we were only able to include 30 (randomized) participants in the study site in the Netherlands. All UK participants were allocated to the use of the myAirCoach system in order to get as much feedback on the system as possible in a before-after study setting. Even though the amount of participants included in the RCT was limited, the primary outcome parameter improved. One might argue that this might be due to overestimation of the real effect, also known as the winner's curse. However, since most secondary outcomes also showed a consistent improvement and the effect was still statistically significant after correction for multiple tests we are confident that the myAirCoach system had a positive effect on asthma related outcomes.

Another limitation is the lack of long-term data of the system. Participants in the Netherlands used the system for a maximum of 6 months. Even though participants reported in the TAQ that they were willing to continue using the system, it is unknown if the positive effects on asthma control would be sustained after a longer period. Another important aspect is the influence of seasonal factors on the results of our study, since we do not have a year follow-up time. Next, in 74% of the inhalation no inhalation technique score could be calculated due to technical issues, possibly explaining the negative attitudes of the patients towards the inhaler add-on in the TAQ.

Even though the age of participants was highly variable (23 to 77 years old), future studies are called for to further evaluate mHealth systems in larger and more diverse groups. In future projects predictive modelling could be used to make personalized recommendations given by the system to further enhance self-management.

Conclusion

We have shown a clinically significant beneficial effect of the myAirCoach mHealth intervention on asthma related outcomes. Asthma control, quality of life and exacerbation-rate improved during the study. Overall, participants were satisfied with the myAirCoach study app and intervention.

Data availability

Data analyzed in this manuscript are available upon request.

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492

Figure legends

Fig. 1 Asthma Control Questionnaire
Asthma control measured by ACQ. Lower score represents better asthma control (MID=0.5). Note: not all participants finished 6 months follow-up due to a fixed end date ; mean follow-up was 149 days (5 months) in study 1. A questionnaire filled in within 14 days of enrollment is regarded as baseline. In study 1, 28/30 participants finished 12 weeks follow-up and 5 participants (17%) had more than 24 weeks follow-up. Error bars represent 95%CI. Points in the graph have been shifted slightly to the left or the right in order to avoid overlap of error bars.

Fig. 2 Time until first exacerbation per participant
Proportion exacerbation plotted against follow-up time. The numbers depicted in the graph indicate the participants still in follow-up.

Fig. 3 Mini Asthma Quality of Life Questionnaire
Asthma related quality of life measured by the m-AQLQ. Higher score represents better quality of life (MID=0.5). Note: not all participant finished 6 months follow-up in study 1. Error bars represent 95%CI. Points in the graph have been shifted slightly to the left or the right in order to avoid overlap of error bars.

Fig. 4 Boxplots of the Technology Acceptance Questionnaire domains
Thirteen domains of the Technology Acceptance Questionnaire tested in both studies combined. Patients reported how much they agreed with the questionnaire statements on a 7-point Likert scale (ranging from completely disagree =1 to completely agree =7). The higher a score, the more favorable the attitudes of the participants towards the myAirCoach system were. In the figure all 13 domains are plotted and the scores are depicted on the y-axis of every boxplot.

Table 1. Participant demographics

	Study 1 (RCT in the Netherlands)			Study 2 (before-and-after study in the UK)
	Control (n=15)	Intervention (n=15)	*p* value	(n=12)
Age, mean (SD) years*	49.1 (11.0)	51.3 (13.2)	0.65	41.3 (13.8)
Gender, n female*	11	12	0.68	10
Internet experience, n**			0.27	
• None	0	1		
• A little	1	1		
• Quite a lot	2	6		2
• A lot	11	7		10
Smoking, n**			0.14	
• Yes	0	0		1
• No	11	7		10
• Previously	4	8		1
Season enrolled, n**			0.66	
• Winter	2	1		0
• Spring	11	13		0
• Summer	2	1		12
GINA medication step, n**			0.25	
• 2	0	3		1
• 3	8	6		2
• 4	0	1		1
• 5	2	2		
Severe exacerbations previous year ,n **	13	14	0.54	8
Age at diagnosis, mean (SD) years*	26.1 (18.6)	19.5 (21.1)	0.39	16.4 (18.4)
FEV1, median (IQR) L***	2.3 (1.4-2.9)	2.1 (1.5-3.0)	0.85	2.5 (1.9-3.4)
FeNO, median (IQR), parts per billion***	18 (13-28)	14 (12-22)	0.45	17 (11.5-54)
ACQ, mean (SD) score*	2.31 (0.97)	2.33 (0.78)	0.94	1.59 (0.88)
• Controlled (n)	0	0		3
• Partly controlled (n)	3	3		3
• Uncontrolled (n)	11	11		6
SNOT22, mean (SD) score*	35.9 (18.4)	40.4 (17.9)	0.52	27.9 (12.0)

* calculated with t-test

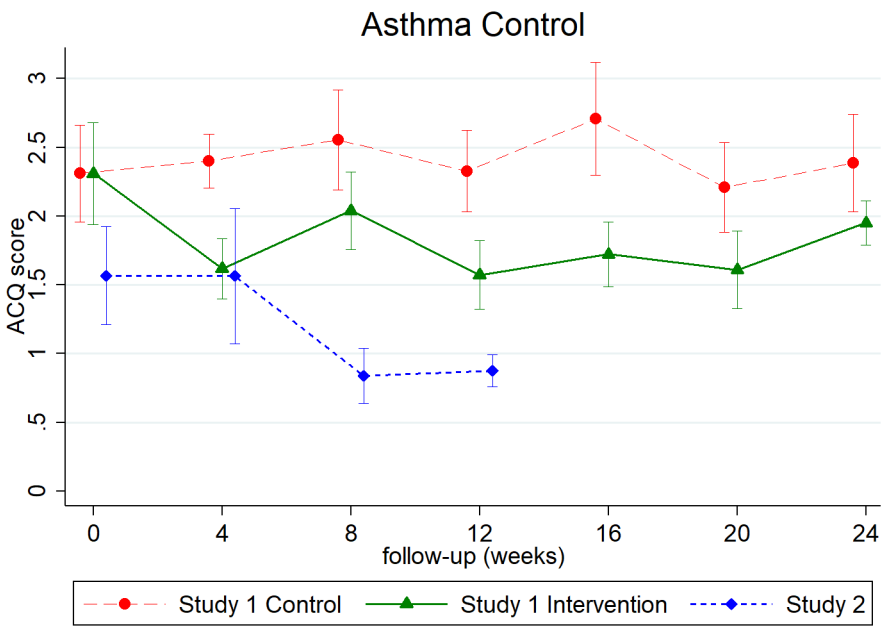
**calculated with chi^2

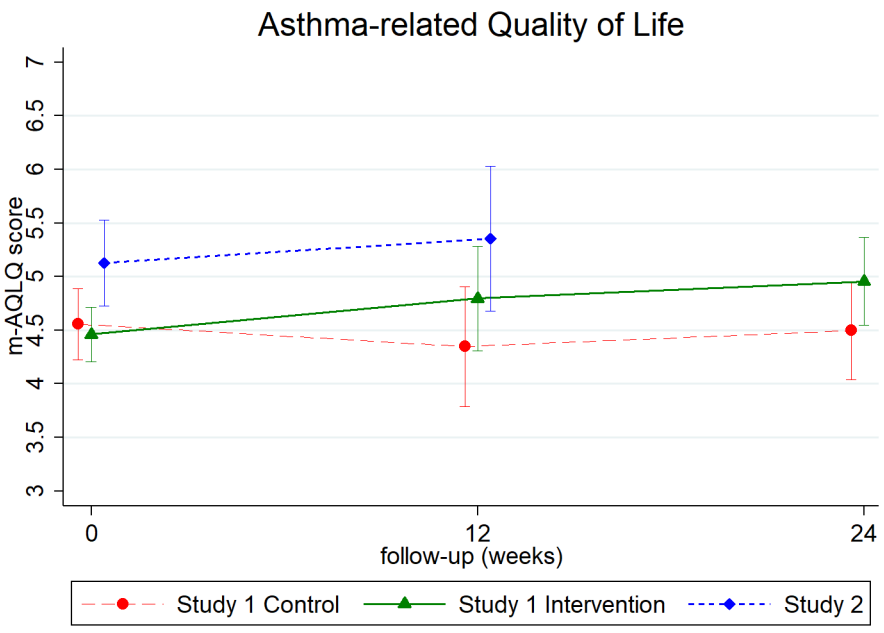
***Mann-Whitney U test

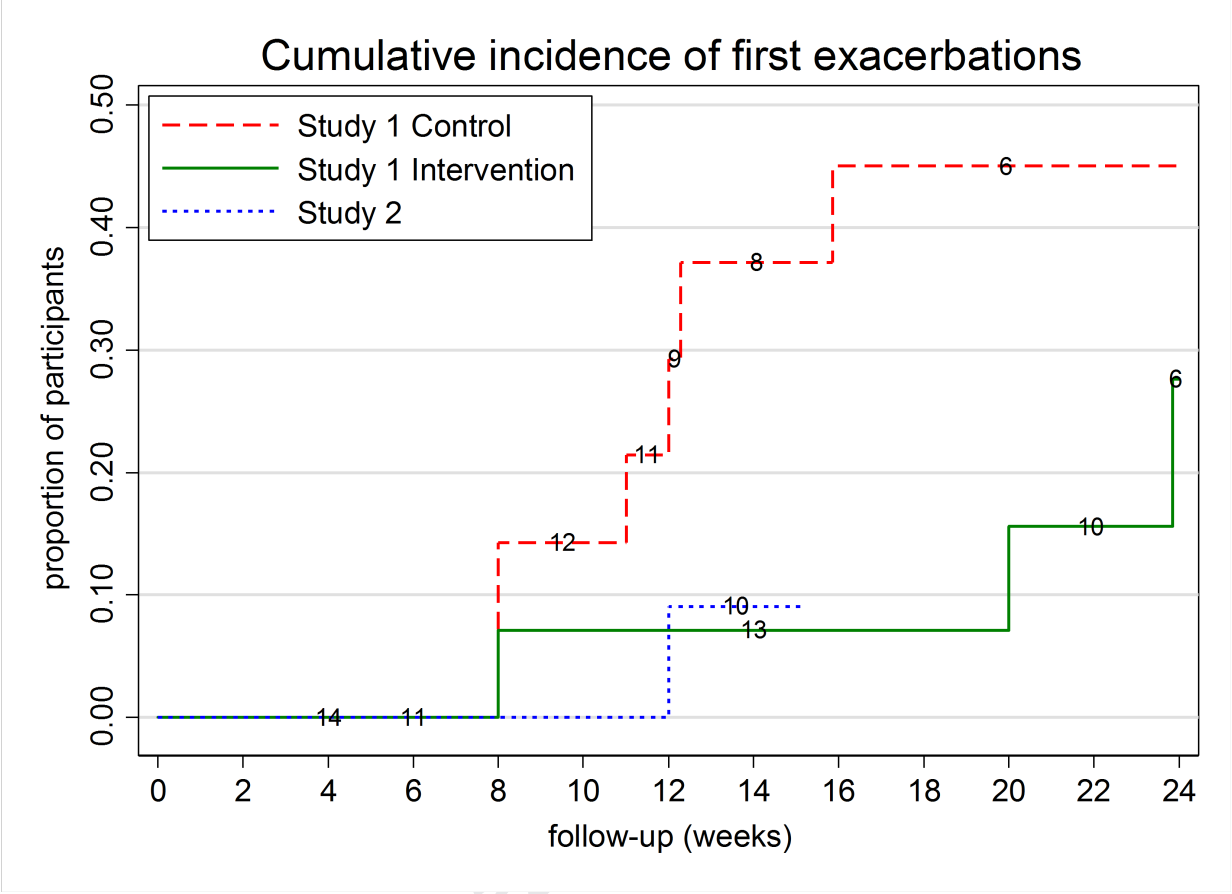
525 **Table 2. Outcome measures.**

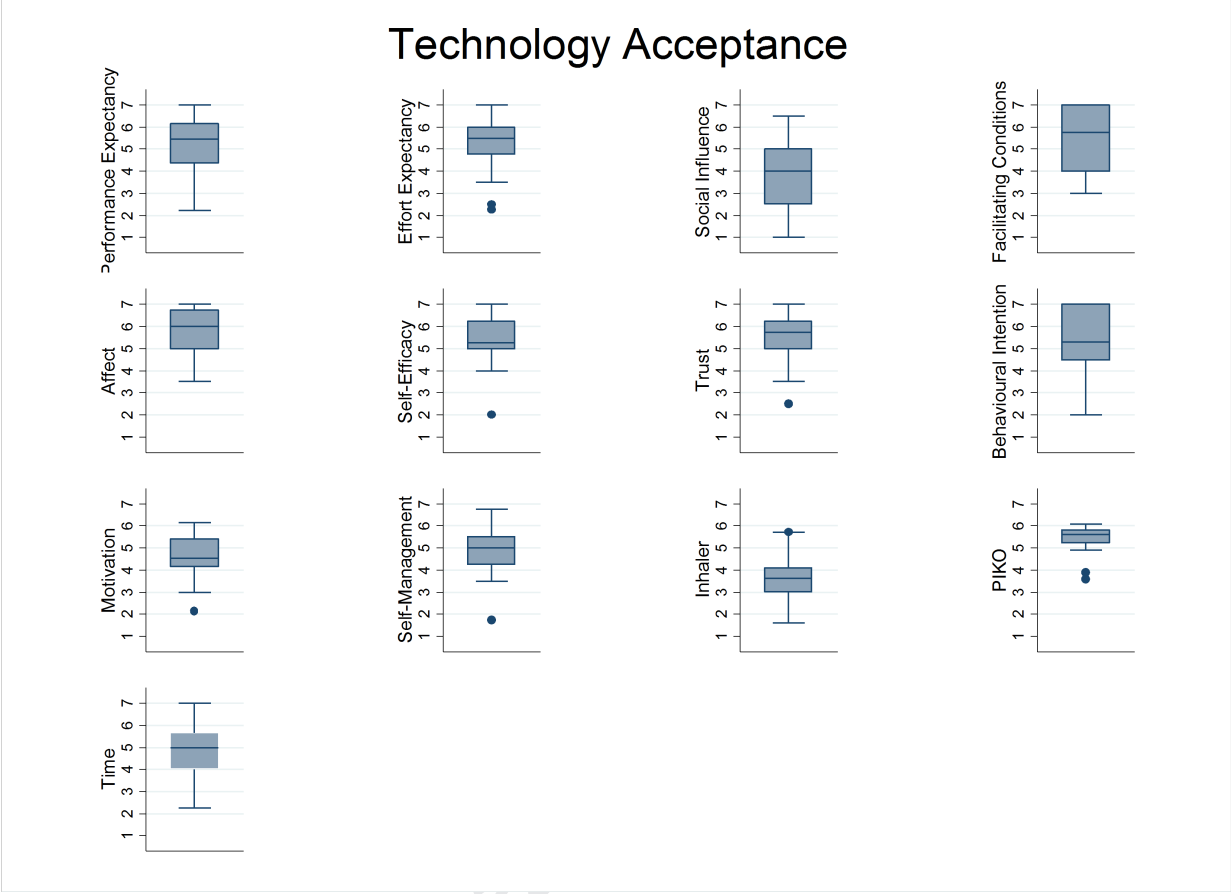
	Study 1		Study 2	
	Difference intervention-control	*p* value	Difference exit-baseline	p value
ACQ , score	-0.70	0.006	-0.86	0.007
m-AQLQ, score	0.53	0.04	0.16	0.64
EQ-5D-5L, score	0.12	0.04	0.04	0.23
FEV1, liters	-0.09	0.60	-0.11	0.42

526 Differences as assessed by mixed model analysis, adjusting for repeated measurements within
527 participants, and baseline values of the outcomes.






Cumulative incidence of first exacerbations
Study 1 Control
Study 1 Intervention
Study 2
proportion of participants
0.00
0.10
0.20
0.30
0.40
0.50
0
2
4
6
8
10
12
14
16
18
20
22
24
follow-up (weeks)
14
11
12
11
9
8
6
10
13
10
6


Technology Acceptance
Performance Expectancy
Effort Expectancy
Social Influence
Facilitating Conditions
Affect
Self-Efficacy
Trust
Behavioural Intention
Motivation
Self-Management
Inhaler
PIKO
Time
1 2 3 4 5 6 7

Online Repository Text

Flowchart participant inclusion

Generic health-related Quality of life

Lung function

Devices and app

The app could be downloaded if the participant had an android phone. If participants used Apple's iPhone, the app could not be installed on their smartphone since every iPhone is linked with a personal Apple account (Apple ID), which prevents anonymous processing of data, because all recorded data is also shared with Apple. Therefore, participants with an iPhone were given an iPod Touch with an anonymous Apple ID specifically created for this study. The iPod Touch was a 6th generation iPod that works in a similar fashion as the iPhone these participants normally used.

When the app was opened, participants could navigate to one of the five menu's: 'Dashboard', 'Measurements', 'Calendar', 'Messages' and 'Me'. The menu 'Dashboard' (figure E4) was divided into five tabs (at the top of the screen) of which 'At a Glance' was the main screen. Here participants could see a quick summary of the most recent measurements in a general overview. In the second screen named 'Action Plan' an asthma action plan was shown to the participants. In the third tab 'Questionnaires' participants could fill out the ACD, ACQ or SNOT22 questionnaires. The following two tabs 'Goals' and 'Notifications' allowed participants and health care providers to set personalized goals (for example: amount of steps a day) and receive (update) notifications. In the screenshots below demo scores are depicted as an illustration.

The second menu at the bottom was 'Measurements' (figure E5), which was divided in three main categories: 'Health', 'Activity' and 'Environmental'. In 'Health' participants could see an overview of their personal scores of Inhaler Use, FeNO, Spirometry and their questionnaires (ACD/ACQ, SNOT22). In 'Activity' participants could see an overview of their Fitbit data. In 'Environmental' participants were able access air quality data for outdoor air quality (www.regional.atmosphere.copernicus.eu) and indoor air quality (measured by the Indoor air quality monitor).

Participants could select every individual measurement to see an overview over time (see figure E6). Mean scores were calculated and displayed in a visual manner. More detailed information about individual measurements was available by pressing the 'all data' button.

In the 'Calendar' participants were shown measurements in a Calendar to more easily identify days with worse (or better) asthma control, as well as to have a complete overview and history of their actions. Participants could also manually enter notes about specific events in order to facilitate in recollecting these details when discussing their asthma with a healthcare professional a few months later (a feature specifically requested by participants) (4).

In the 'Messages' tab participants could chat in real-time with the research team. In possible future projects participants could use this function to chat with their own healthcare provider. The final tab 'Me' was a settings function with guides for the app, inhalation technique instruction material and links to useful websites on asthma. In this tab participants could also enable or disable the virtual support "Airica" (figure E7) which recognized voice commands and text inputs. Airica is based on artificial intelligence, such as machine learning algorithms and natural language processing concepts.

The inhaler add-on shown in the picture below (figure E8) was an add-on to normal MDI's. After activation the device by shaking it, it connected to the app. A screen would pop-up and sound recording would start, which is shown in figure E9 . After sound recording was finished, data was

uploaded, processed and then sent back to the app. A score was calculated varying from 0% to 100% and displayed to the participant.

The indoor air quality monitor (air quality sensor) was a black cube connected through Bluetooth with the smartphone and the app. It was roughly 7cm x 7cm x 7cm (figure E10). Data was recorded every hour, temporarily stored on an internal memory and transmitted to the phone when available. Participants were asked to hold their smartphone at least daily within Bluetooth vicinity of the indoor air quality monitor to allow data transfer.

Table E1. Number of times the app was used to perform tasks.

	Study 1	Study 2	Total
ACD	**130**	**177**	**307**
ACQ	**70**	**27**	**97**
Feno	**570**	**213**	**783**
SNOT22	**67**	**34**	**101**
Spirometry	**700**	**357**	**1,057**
Total	**1,537**	**808**	**2,345**

Activities

Participants were asked to fill out questionnaires and do measurements frequently. Questionnaires not described in this manuscript are: the Food Frequency Questionnaire (GA2LEN FFQ), Hospital Anxiety and Depression Scale (HADS), Health Education Impact Questionnaire (heiQ), Sino-Nasal Outcome Test (SNOT-22) and Cost-Q. The Asthma Control Diary (ACD) is a questionnaire comparable to the ACQ, except it asks questions about the previous day (compared to the previous week).

Table E2. Study procedures

Frequency of tests		**INTERVENTION**		**CONTROL**		
	First visit	**1-2 wk training phase**	**Follow-up**	**1wk test phase**	**Follow-up**	**Final visit**
Patient Questionnaires						
ACD or ACQ	*Once*	*Daily*	*Monthly*	-	*Monthly*	*Once*
Current medication record	*Once*	*Daily*	*Monthly*	-	*Monthly*	*Once*
Exacerbations history	*Once*	*Daily*	*Monthly*	-	*Monthly*	*Once*
m-AQLQ	*Once*	-	*3-monthly*	-	*3-monthly*	*Once*
GA^{2}LEN FFQ	*Once*	-	-	-	-	-
HADS	*Once*	-	-	-	-	-
heiQ	*Once*	-	*3 months*	-	*3 months*	*Once*
SNOT-22	*Once*	-	*Monthly*	-	*Monthly*	*Once*
EQ-5D-5L	*Once*	-	*3-monthly*	-	*3-monthly*	*Once*
Cost-Q	-	-	*3-monthly*	-	*3-monthly*	*Once*
Technology Acceptance Questionnaire		-	*3 months*	-	-	*Once*
Physiological sensors						
Portable spirometry	*Once*	*Daily*	*Weekly*	-	-	-
FeNO	*Once*	*Daily*	*Weekly*	-	-	*Once*
Heart Rate and activity level	*Once*	*Continuous*	*Continuous*	-	-	-
Monitors						
Inhaler usage monitoring	*Once*	*Continuous*	*Continuous*	-	-	-
External environmental monitoring	-	*Continuous*	*Continuous*	-	-	-

m-AQLQ domains

The m-AQLQ can be divided in 4 domains: symptoms, activities, emotions and environment (Table E3; figure E11) . In study 1 improvements in 'symptoms' and 'emotions' were both clinically and statistically significant. Improvements in the 'environments' domain also exceeded the MCID.

Table E3. Quality of life per domain.

	Study 1*		**Study 2[T]**	
	Difference	**P value**	**Change**	**P value**
Domain				
• symptoms	0.69	0.03	0.22	0.51
• activities	0.32	0.41	0.10	0.83
• emotions	0.54	0.04	0.25	0.44
• environment	0.53	0.08	0.03	0.94

*study 1. RCT: intervention compared to controls with mixed-model analysis

[T] study 2. Before-and-after study: baseline compared to end of follow-up with paired t-test

Technology Acceptance Questionnaire (TAQ)
The twelve domains of the TAQ are:

- Performance expectancy: the degree to which participants believe that using the system will help them attain gains or make losses with the performance of their health management
- Effort expectancy: the degree of ease associated with the use of the system
- Social influence: the degree to which participants perceive that important others believe they should use the system
- Facilitating conditions: the degree to which participants believe that there are objective factors available in their environment to support their use of the system
- Affect: participants' overall affective reaction towards using the system
- Self-efficacy: the degree to which participants judge themselves capable of using the system to manage their health
- Trust: the degree to which participants believe that using the system will occur in a safe and reliable manner
- Behavioral intention: the degree to which an individual intends to use of the myAirCoach system for managing their health
- Motivation: the degree to which an individual is motivated to continue the myAirCoach system for managing their health
- Self-management: participants' opinion on conducting self-management through the system
- Inhaler adapter: participants' opinion on the myAirCoach inhaler adapter
- PiKO-1: participants' opinion on the PiKO-1 home spirometer
- Time: the degree to which an individual is satisfied with the amount of time is takes to use the system

Captions

Fig. E1 Flowchart participant enrollment
Study 1 is shown on the upper panel (A) and study 2 on the lower panel (B).

Fig. E2 EQ-5D-5L
Generic health-related quality of life measured by the EQ-5D-5L questionnaire.

Fig. E3 FEV1
Home-measured FEV1 by the intervention patients in study 1 and patients from study 2 with use of the PiKO-1.

Fig. E4 myAirCoach app: Dashboard
Different aspects of the myAirCoach app: 'At a glance', 'Action Plan', 'Questionnaires', 'Goals', and 'Notifications'.

Fig. E5 myAirCoach app: Measurements
Various categories of measurements are presented to the participant: 'Health', 'Activity', and 'Environmental'.

Fig. E6 myAirCoach app: Display of the gathered data
Various visualization capabilities of the collected data via the mobile app.

Fig. E7 myAirCoach app: Airica
Virtual assistant based on artificial intelligence and natural language processing.

Fig. E8 myAirCoach inhaler add-on
The inhaler add-on was capable of measuring several critical parameters, such as correct positioning of the inhaler during inhalation as well as the sound of the inhalation procedure.

Fig. E9 myAirCoach app: Inhalation recording
Audio recording and related feedback to the participant

Fig. E10 myAirCoach air quality monitor
The indoor air quality monitor is capable of measuring several indoor parameters such as nitrogen dioxide (NO2), Sulphur dioxide (SO2), particulate matter (PM2.5 and PM10), humidity, air pressure and temperature.

Fig. E11 m-AQLQ domains
The m-AQLQ divided in the four domain: symptoms, activity, emotions and environment.