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Effect of a mHealth intervention on adherence in adolescents with asthma: A randomized controlled trial

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ABSTRACT

Background: Adherence rates among asthma patients are generally low and decrease during adolescence, resulting in poorly controlled asthma. The aim of our study was to evaluate the effectiveness of the ADolescent Adherence Patient Tool (ADAPT), an interactive mobile health (mHealth) intervention, in supporting self-management and improving inhaled corticosteroid adherence in adolescents with asthma.

Methods: We conducted a cluster randomized controlled trial in 66 Dutch community pharmacies. Asthma patients aged 12–18 years were invited to participate, based on pharmacy medication refill records. The main study outcome was self-reported medication adherence, measured with the Medication Adherence Report Scale (MARS). Secondary outcomes were asthma control and quality of life. Outcomes were measured at start (t = 0 months) and at the end of follow-up (t = 6 months). Mixed-effects models were used to analyze the effect.

Results: In total, 234 adolescents (147 in the control group and 87 in the intervention group) completed the study; mean age 15.1 ± 1.9 years and 52.6% females. Adherence rates of patients with low baseline adherence (MARS scores ≤19; n = 76) increased with 1.42 points in the intervention group (n = 26). Adherence rates of patients in the control group (n = 50) decreased with 0.70 points. Thus there was a positive effect of the intervention on medication adherence (MARS +2.12, p = 0.04). This effect was stronger (MARS +2.52, p = 0.02) in poor adherent adolescents with uncontrolled asthma (n = 74). No effect of the intervention was observed on asthma control or quality of life.

Conclusions: The ADAPT intervention increases medication adherence in adolescents with asthma having poor adherence rates at baseline. Healthcare providers should consider a tailored mHealth approach to improve the asthma treatment.

1. Introduction

Poor inhaled corticosteroid (ICS) adherence is common, i.e., only 22%–63% of the asthma patients is adherent [1]. These poor adherence rates result in poorly controlled asthma and thereby an increased risk of exacerbations, healthcare utilization, rescue medication use, healthcare costs, and decreased quality of life [1–4]. To reach sufficient asthma control, asthma patients should adhere to the prescribed medication regimen. However, previous research has shown that adherence rates decrease during adolescence [2]. It is therefore important to develop an intervention for adolescents with asthma to increase adherence.

Medication intake behavior is affected by multiple intentional (perceptual barriers) and unintentional (practical barriers) factors [5,6]. Adherence is particularly challenging during adolescence, because age-specific issues arise, such as a less parental supervision, social stigma, and risk factors might play a role (e.g., smoking) [5,7]. Moreover, forgetting is one of the main reasons for adolescents to deviate from the prescribed medication regimen [7,8]. To meet the needs of adolescent patients, an adherence intervention should target the multiple aspects of non-adherent behavior, i.e., overcome practical barriers, being educative and informative, motivate the patient, and ensure family or peer support [9,10]. Digital monitoring and feedback from healthcare providers has also shown to be effective in improving pediatric medication adherence [11].

A mobile health (mHealth) intervention seems a feasible and acceptable method to support adherence in young patients, because mHealth can target different aspects of non-adherence behavior and it has the potential to empower patients with different tools [11,12].

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Abbreviations

ADAPT	ADolescent Adherence Patient Tool
AIC	Akaike information criterion
App	Smartphone application
BIC	Bayesian information criterion
CARAT	Control of Allergic Rhinitis and Asthma Test
CI	Confidence intervals
ICS	Inhaled corticosteroids
ICS/LABA	Inhaled corticosteroids in a fixed combination with a long-acting beta-agonist
LABA	Long-acting beta-agonist
logLik	log-likelihood
MARS	Medication Adherence Report Scale
MHealth	Mobile health
OR	Odds ratio
PAQLQ	Pediatric Asthma Quality of Life Questionnaire
SABA	Short-acting beta-agonist
SD	Standard deviation
UPPER	Utrecht Pharmacy Practice network for Education and Research

Moreover, almost all Dutch adolescents own a smartphone [13], and adolescents with asthma also suggested the use of an smartphone application (app) to support their disease management [8,14].

Many mHealth interventions to improve adherence have been developed [15–17]. However most of these were not effective, not intended for adolescents, or targeted just one aspect of non-adherent behavior, e.g., a reminder to prevent forgetting [18–21]. Previous studies showed that solely one element is not effective in improving medication adherence in children and adolescents [22]. Therefore we developed the ADolescent Adherence Patient Tool (ADAPT) [23]. This interactive mHealth intervention has been developed in accordance with adolescents with asthma, is based on the Common Sense Model of Self-Regulation, and has educational, motivational, behavioral, and self-monitoring elements [8,23]. The aim of this study was to evaluate the effectiveness of the ADAPT intervention in improving ICS adherence in adolescents with asthma. In addition, we studied the effect of the intervention on asthma control and asthma related quality of life.

2. Material and methods

We conducted a cluster randomized controlled trial in Dutch community pharmacies affiliated with the Utrecht Pharmacy Practice Network for Education and Research (UPPER) [24]. Detailed rationale and design of the study have been described elsewhere [23].

The participating pharmacies were randomly divided over the control and the intervention group. Interim analyses were performed when 42 pharmacies participated. Thereafter 24 extra pharmacies were included and randomized (1:3) over the control and intervention group, to ensure sufficient power. Patients included in the control group received usual care consisting of inhalation instruction at a first dispensing and automated pharmacy information systems that will detect excessive bronchodilator or insufficient ICS use. Patients and pharmacists in the intervention group had six months access to the ADAPT intervention, in addition to usual care.

Patients fulfilling the following criteria were eligible for inclusion: aged 12–18 years, filling of at least two prescriptions for ICS or a fixed combination of ICS with a long-acting beta-agonist (ICS/LABA) during the previous 12 months, and having a smartphone (iOS or Android). Patients who had insufficient comprehension of the Dutch language or were dependent on (in)formal carers to take their medication were excluded. Due to the nature of the intervention, blinding of group assignments was impossible for both patients and pharmacists [23].

Upon receiving the signed informed consent, the first online questionnaire (baseline measurement) was sent to the patients via e-mail. At the end of follow-up (six months), the second online questionnaire was sent (follow-up measurement) [23].

2.1. The ADAPT intervention

Patients in the intervention group had six months access to the ADAPT intervention. The ADAPT intervention consisted of a smartphone application for patients, which was securely connected to a desktop application of the patient's own community pharmacist. The pharmacist was chosen as healthcare provider to deliver the intervention in this project as in the Netherlands patients generally use one pharmacy to collect all their medication prescriptions. The app contained different elements targeting multiple aspects of non-adherent behavior:

- Weekly Control of Allergic Rhinitis and Asthma Test (CARAT) to monitor disease control over time, both patients and pharmacists had insights in the obtained disease control score [25];
- Short educational and motivational movies on asthma related topics;
- Medication reminder alarm to prevent forgetting;
- Peer chat function to contact peers participating in the study;
- Pharmacist chat function to facilitate contact;
- Two questions once every two weeks to monitor non-adherence; one about forgetting (unintentional) and one about deciding to miss out a dose (intentional).

The intervention was interactive; pharmacists had the possibility to monitor the CARAT scores, to send additional movies, to change app settings, and to contact patients through the chat function. The pharmacists received a half-day training about asthma and medication use by adolescents, additionally they received on the spot instructions on the use of the ADAPT desktop application [23].

2.2. Outcomes

The primary study outcome was self-reported medication adherence, assessed with the Medication Adherence Report Scale (MARS) [26]. This questionnaire consists of five questions on forgetting, changing dosage, stopping, skipping, and taking less. The total score ranges between 5 and 25, where a higher MARS score indicates higher self-reported adherence. Previous studies used a score ≥ 23 to define adherent patients [27,28]. We conducted sensitivity analyses using different cut-offs, varying from MARS ≥ 19 to MARS ≥ 24.

Secondary study outcomes were self-reported disease control and asthma related quality of life. Disease control was assessed with the CARAT [25]. This questionnaire contains ten questions on asthma and allergic rhinitis symptoms, resulting in a score between 0 and 30, where a score > 24 represents good control. For the questions regarding allergic rhinitis (questions 1–4), a score of > 8 is sufficient, and for the asthma related questions (questions 5–10) ≥ 16 is sufficient for control. The CARAT distinguishes the symptoms into lower (asthma) and upper (allergic rhinitis) airway symptoms. This information is important for healthcare providers, to check for appropriate ICS use.

Asthma related quality of life was assessed with the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) [29]. This questionnaire covered three domains: symptoms, activity limitations, and emotional function. All domains were scored between 1 and 7, where seven indicates the highest quality of life. All outcomes were measured at baseline (t = 0 months) and at the end of follow-up (t = 6 months).

2.3. Statistical analysis

The trial was designed with a planned sample size of 352 patients, to detect a relevant difference (1.5 ± 4.0) in MARS scores with a power of 80%, a significance level of 95%, accounting for 35% dropout, and corrected for the cluster randomized design [23]. Based on the interim analyses, we decided to include more pharmacies (clusters) ensuring sufficient power for the final study population.

To compare the groups at baseline we used a mixed-effects model, chi squared test, or fisher's exact test, depending on the type of variable. The effect of the intervention on the primary and secondary outcomes was analyzed using mixed-effects models, which enabled us to correct for the cluster design. In the models, we used the difference between the follow-up measurement and baseline score as an outcome, the intervention as a fixed effect, the pharmacies as a random effect, and we corrected for the score at baseline. As post-hoc analysis, we checked for interactions between intevention and baseline score, performed sensitivity analysis to find the significant cut-off value (based on log-likelihood [logLik], Akaike information criterion [AIC], and Bayesian information criterion [BIC]), and stratified the data by age, gender, adherence, and asthma control. A generalized linear mixed-effects model was used for the binomial variables. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Statistical analyses were performed using R (version 3.4.3) packages 'glmm', 'lme4', and 'nlme'. P values < 0.05 were considered statistically significant.

2.4. Ethics and confidentially

The ADAPT study was approved by the Medical Review Ethics Committee of the University Medical Centre Utrecht (NL50997.041.14) and by the Institutional Review Board of UPPER [24], Department of Pharmaceutical Sciences, Utrecht University. All patients had to complete informed consent before start of the study, and for patients younger than 16 years both parents also had to sign. The trial is registered in the Dutch Trial Register (NTR5061). Personal data was encrypted, using a code consisting of a pharmacy and patient number, to ensure privacy.

3. Results

3.1. Descriptive statistics

A total of 1204 adolescents with asthma were invited from 66 community pharmacies between July 2015 and May 2016. In total, 253 adolescents (21%) agreed to participate (0–13 patients per pharmacy) and 234 adolescents completed the study (Fig. 1). Main reasons for not willing to participate were a lack of interest or not taking daily asthma medication anymore. Data collection was finished in July 2017. Baseline characteristics of the study population are presented in Table 1: half of the patients were female (n = 123; 52.6%), the mean age was 15.1 ± 1.9 years, and most had a Dutch ethnicity (n = 207; 88.5%).

3.2. Primary outcome

No effect of the intervention was observed on the MARS score for the total study population (p = 0.25; Table 2). However there was an interaction between MARS baseline score and the intervention (p = 0.02). Sensitivity analysis showed that adherence rates of patients with low baseline adherence (n = 76; MARS ≤19) increased with 1.42 points in the intervention group (n = 26), whereas it decreased with 0.70 points in the control group (n = 50), Fig. 2a. Thus we observed an intervention effect (MARS +2.12; p = 0.04) in poor adherent patients. This intervention effect was stronger (MARS +2.52, p = 0.02) in poor adherent patients with uncontrolled asthma (n = 74; MARS ≤20 and CARAT ≤24), Fig. 2b. The MARS cut-off scores were based on the best statistical fit.

When using the MARS cut-off (score ≥23) as an indicator for sufficient adherence, there was no effect of the intervention in improving adherence; OR 1.07 [CI 0.54; 2.20]. Sensitivity analysis (varying from MARS ≥19 to ≥24) also showed no effect of the intervention (results not shown). At baseline, 40.1% (n = 59) of the control group and 33.3% (n = 29) of the intervention group were adherent based on the MARS cut-off (score ≥23). This percentage decreased in the control group to 38.8% (n = 57) and increased in the intervention group to 36.8% (n = 32).

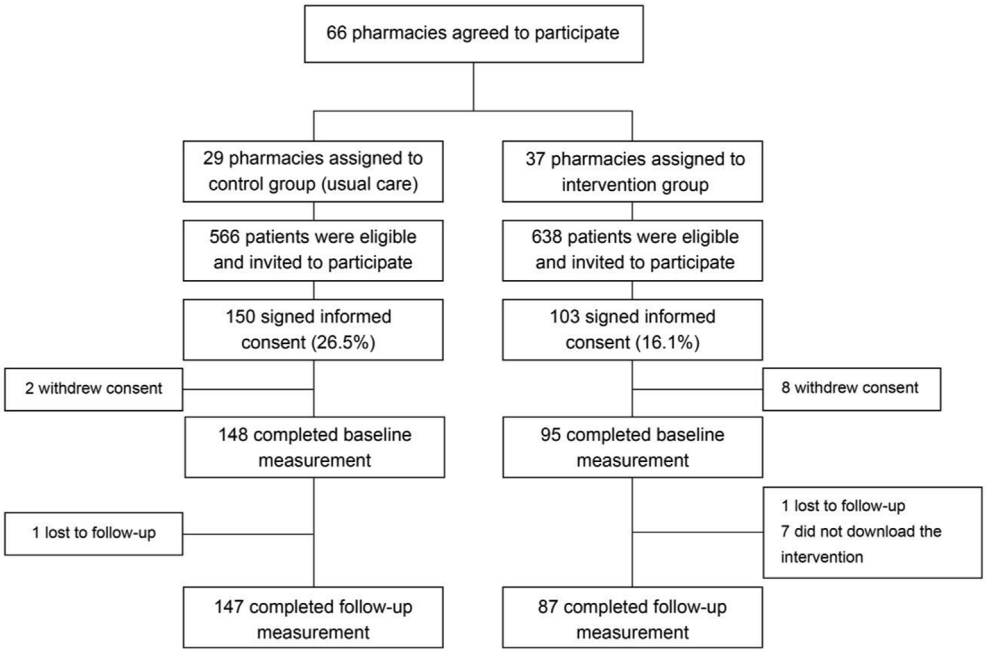

Fig. 1. The ADolescent Adherence Patient Tool (ADAPT) study procedure, including randomization, eligibility, and follow-up.

Table 1
Baseline characteristics of the study participants*.

	Control (N = 147) n (%)	Intervention (N = 87) n (%)
Gender (female)	75 (51.0)	48 (55.2)
Age – years (mean, SD)	15.2 (1.9)	15.0 (2.0)
Native Dutch origin	143 (97.3)	86 (98.9)
Education		
Elementary school	5 (3.4)	4 (4.6)
High school: vocational level	40 (27.3)	18 (20.7)
High school: pre-university level	78 (53.0)	51 (58.6)
Vocational education	14 (9.5)	12 (13.8)
Professional education	9 (6.1)	1 (1.1)
Other	1 (0.7)	1 (1.1)
Living environment		
Urban	63 (42.9)	44 (50.6)
Village	77 (52.4)	42 (48.3)
Other (in between)	7 (4.7)	1 (1.1)
Asthma medication use[a,b]		
SABA	106 (72.1)	67 (77.0)
ICS	82 (55.8)	55 (63.2)
LABA	7 (4.8)	1 (1.1)
ICS/LABA	63 (42.9)	36 (41.4)
Other asthma medication use[b]		
Anti-allergic	9 (6.1)	6 (6.9)
Antibiotics	23 (15.6)	12 (13.8)
Montelukast	10 (6.8)	11 (12.6)
Oral corticosteroids	6 (4.1)	4 (4.6)
Other	2 (1.4)	1 (1.1)
Healthcare use[b]		
Visit asthma related doctor[c]	99 (67.3)	57 (65.5)
Self-reported health status		
Good to excellent	129 (87.8)	73 (83.9)
Bad to moderate	18 (12.2)	14 (16.1)

* No significant differences ($p > 0.05$) between the two groups.
ICS, inhaled corticosteroids; ICS/LABA, inhaled corticosteroids in a fixed combination with a long-acting beta-agonist; LABA, long-acting beta-agonist; SABA, short-acting beta-agonist; SD, standard deviation.

[a] Inclusion criteria were the collection of at least two prescriptions for ICS or ICS/LABA in the preceding year. Patients could use more than one type of medication. Four patients reported no medication use in the previous six months.

[b] Self-reported data on the previous six months.

[c] General practitioner, pediatrician, pulmonologist, pulmonary nurse, physiotherapist, first aid, and/or alternative doctors.

3.3. Secondary outcomes

No intervention effect was observed on asthma control, as measured with the CARAT ($p > 0.05$; Table 2). In total, 26.5% (n = 39) of the control group and 16.1% (n = 14) of the intervention group had control over their symptoms at baseline (CARAT > 24). This proportion remained the same in the control group and increased in the intervention group to 23.0% (n = 20). The effect of the intervention in patients with uncontrolled symptoms (CARAT ≤24) was 1.56, versus 0.71 for controlled patients (CARAT > 24), however this opposite effect was not significant; OR 1.23 [CI 0.56–2.77].

The number of patients with sufficient asthma control (CARAT questions 5–10; score ≥16) differed between the groups at baseline; 26.5% (n = 39) control group and 13.8% (n = 12) intervention group ($p = 0.02$). The percentage of patients with sufficient asthma control increased in both groups, to 29.3% (n = 43) in the control group and 29.9% (n = 26) in the intervention group. However no intervention effect was observed on the CARAT asthma score ($p = 0.51$; Table 2). Additionally, no intervention effects were observed on the Pediatric Quality of Life Questionnaire (PAQLQ) scores ($p > 0.05$; Table 2).

Stratifying the data by age, gender, median MARS score, and median CARAT score did not affect the results (results not shown), thus no intervention effect was found.

3.4. Patient profile

The baseline characteristics of the study population for which the intervention was effective (MARS ≤19; n = 76) are shown in Table 3. These patients were on average 0.7 years older ($p = 0.02$) and had lower disease control ($p = 0.01$) compared to adolescents with high baseline adherence rates. Within the low adherent patients, the CARAT total score and CARAT allergic rhinitis score increased with respectively 1.9 ($p = 0.02$) and 1.1 ($p = 0.01$). Within the high adherent patients (n = 158), the CARAT asthma score and the PAQLQ symptom score increased with respectively 0.8 ($p = 0.04$) and 0.2 ($p = 0.046$). However, within both groups no intervention effect was found on disease control and asthma related quality of life ($p > 0.05$).

More than half of the non-adherent patients (MARS ≤19) had no disease control (CARAT ≤24; n = 65; 85.5%). At the end of follow-up, almost all of these patients (n = 59; 90.7%) remained uncontrolled and six participants improved their control (9.2%). The percentage of uncontrolled patients in the adherent group was 73.4% (n = 116) and 13.8% (n = 16) of those patients improved their control. No differences in the percentage of uncontrolled asthma patients were observed within and between the adherence groups ($p > 0.05$).

4. Discussion

The interactive ADAPT mHealth intervention improved medication adherence of adolescents with asthma having poor adherence rates at baseline. These patients were older and had less control over their symptoms, compared to the patients with high medication adherence

Table 2
Mean outcomes (with standard deviation) and the intervention effect on the validated outcome measurements.

	Control (N = 147)		Intervention (N = 87)		Intervention effect	
	Baseline	Follow-up	Baseline	Follow-up	p value[a]	Effect size (95% CI)
Medication Adherence Report Scale (MARS)						
Total	20.4 (4.0)	19.3 (5.1)	20.4 (3.9)	19.9 (4.0)	**0.25**	+0.60 (−0.43; 1.63)
Control of Allergic Rhinitis and Asthma Test (CARAT)						
Total	19.8 (5.6)	20.9 (5.1)	19.3 (5.3)	20.7 (5.2)	**0.81**	+0.13 (−0.95; 1.22)
Allergic rhinitis	7.1 (3.1)	7.6 (2.7)	7.3 (3.2)	7.6 (2.8)	**0.78**	−0.10 (−0.82; 0.62)
Asthma	12.7 (3.8)	13.3 (3.4)	12.1 (3.2)	13.1 (3.5)	**0.51**	+0.23 (−0.47; 0.93)
Pediatric Asthma Quality of Life Questionnaire (PAQLQ)						
Total	6.0 (1.0)	6.1 (0.9)	5.8 (0.9)	6.0 (0.8)	**0.71**	+0.03 (−0.13; 0.20)
Symptoms	5.7 (1.2)	6.0 (1.0)	5.6 (1.0)	5.9 (1.0)	**0.71**	−0.04 (−0.25; 0.17)
Activity limitation	5.5 (1.1)	5.6 (1.0)	5.2 (1.2)	5.6 (1.1)	**0.34**	+0.11 (−0.12; 0.34)
Emotional function	6.5 (0.8)	6.6 (0.8)	6.4 (0.9)	6.5 (0.8)	**0.55**	+0.05 (−0.11; 0.21)

CI, confidence interval.

[a] Calculated with mixed-effects model.

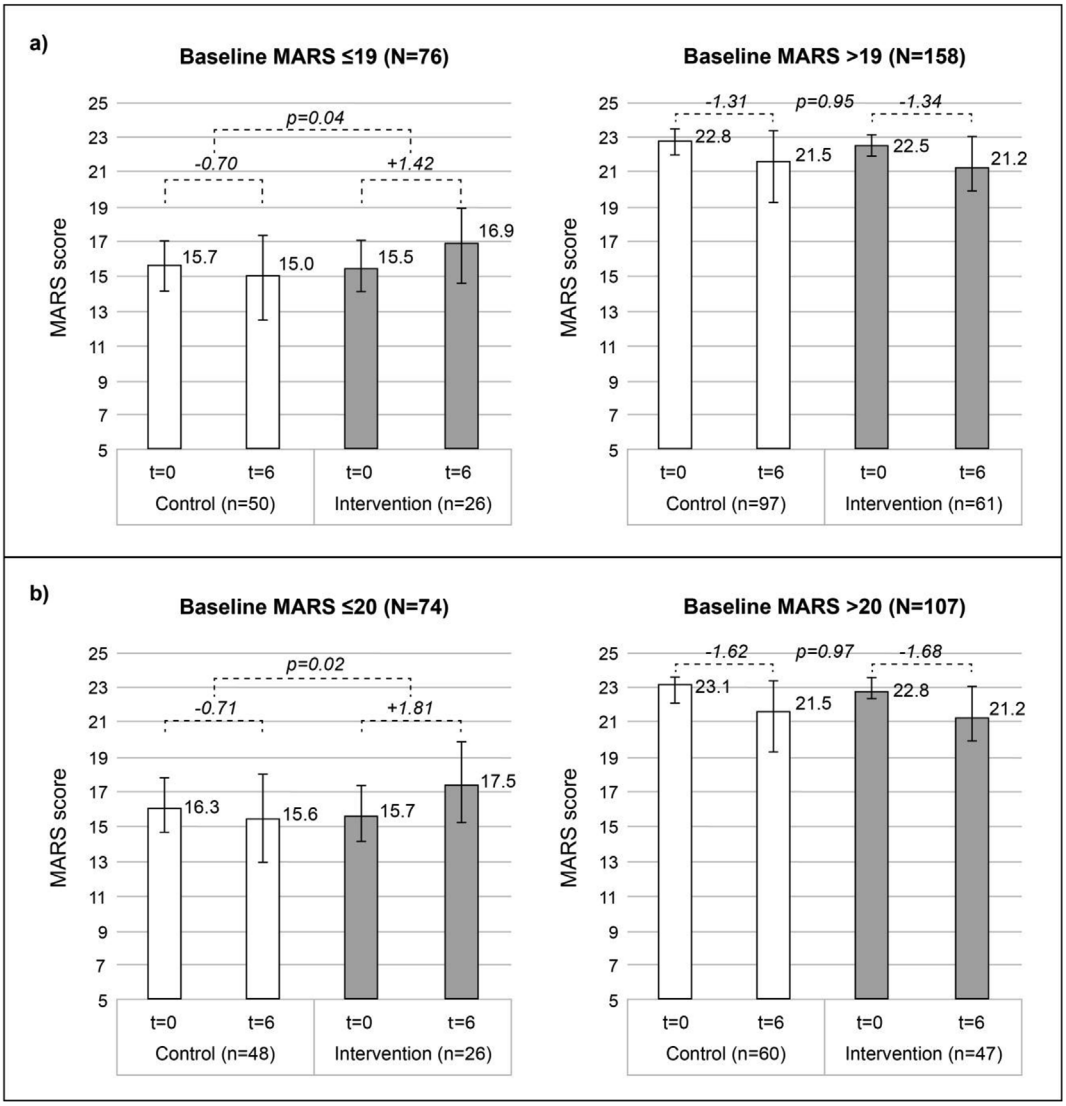

Fig. 2. (a). The mean Medication Adherence Report Scale (MARS) score at start (t = 0) and end of follow-up (t = 6) of 234 patients with low adherence (left) or high adherence rates (right) per group. **(b).** The mean Medication Adherence Report Scale (MARS) score at start (t = 0) and end of follow-up (t = 6) of 181 uncontrolled patients (Control of Allergic Rhinitis and Asthma Test ≤24) with low adherence (left) or high adherence rates (right) per group.

rates. We did not find an intervention effect in the total study population, i.e., only in non-adherent patients. Asthma related quality of life and disease control were also not affected by the ADAPT intervention.

Within patients with high adherence rates (MARS > 19, n = 158) there was no effect of the intervention, although less can be achieved in patients with higher medication adherence rates. These patients also had significant better asthma control, which is in line with previous studies where adherence was related to better asthma control [4,30]. However, still 73.4% of these adherent patients had no control over their disease (CARAT ≤24). This emphasizes the complex relation between adherence and asthma control. Factors such as life style, medication(dosing), and inhaler technique may also affect asthma control, and were not taken into account in the current study [30]. For some patients, there is also a transition of asthma symptoms during adolescence, which might affect the relation between adherence and asthma control [31].

No intervention effects were found on the asthma related quality of life, while one would expect a relation between adherence, asthma control, and quality of life. Previous research showed an association between asthma control and quality of life of adolescents in a five-year period, thus our study period might be too short to find an effect on asthma related quality of life [32]. Additionally, our study population reported high baseline quality of life and the majority had a good to excellent health status, thus there was less to achieve.

We showed the effectiveness of an interactive mHealth intervention in patients with low baseline adherence; there was an increase of 1.5 on the MARS scale (sum scores ranging between 5 and 25). Although it is only a small difference, it was a significant effect, however the clinical relevance is debatable. Therefore, more research is needed towards the effect of mHealth on (self-reported) adherence rates. Based on our findings, the intervention should be tailored to patients who need it most (i.e., poor adherent). A baseline adherence measurement (before using mHealth) might be an useful tool to personalize the treatment, i.e., recommend the use of mHealth, or not.

The current study used pharmacists as the healthcare provider, because pharmacists are increasingly expected to support appropriate use of medication in integrated care settings [33]. Increased collaborations between pharmacists and physicians may facilitate the identification of uncontrolled patients with low adherence rates. Pharmacists can subsequently support these patients with their medication use, by implementing mHealth interventions.

The aim of our study was to increase adherence in adolescents with

Table 3
Patient baseline characteristics per adherent subgroup: low adherent (MARS ≤19) and high adherent (MARS > 19).

	Low adherent (N = 76), n(%)	High adherent (N = 158), n(%)	p value[a]
MARS (mean, SD)	15.6 (3.1); range 7–19	22.7 (1.5); range 20–25	NA
Gender (female)	41 (54.0)	82 (52.0)	0.88
Age – years (mean, SD)	15.6 (2.0)	14.9 (1.8)	0.02
Asthma medication use			
SABA	56 (73.7)	117 (74.1)	1.00
ICS	45 (59.2)	92 (58.2)	1.00
LABA	2 (2.6)	6 (3.8)	0.94
ICS/LABA	30 (39.5)	69 (43.7)	0.51
Other asthma medication use			
Anti-allergic	5 (6.6)	10 (6.3)	0.94
Antibiotics	8 (10.5)	27 (17.1)	0.23
Montelukast	4 (5.3)	17 (10.8)	0.17
Oral corticosteroids	2 (2.6)	8 (5.1)	0.06
Other	1 (1.3)	2 (1.3)	0.98
Healthcare use			
Visit asthma related doctor	47 (61.8)	109 (69.0)	0.28
Self-reported health status			
Good to excellent	65 (85.5)	137 (86.7)	0.18
Bad to moderate	11 (14.5)	21 (13.3)	
Control of Allergic Rhinitis and Asthma Test (CARAT)			
Total (mean, SD)	18.2 (5.7); range 0–28	20.3 (5.3); range 4–30	0.01
Allergic rhinitis (mean, SD)	6.4 (3.4); range 0–12	7.5 (3.0); range 1–12	0.01
Asthma (mean, SD)	11.8 (3.5); range 0–18	12.8 (3.6); range 0–18	0.04
Pediatric Asthma Quality of Life Questionnaire (PAQLQ)			
Total	5.8 (1.0)	5.9 (0.9)	0.20
Symptoms	5.5 (1.2)	5.8 (1.1)	0.10
Activity limitation	5.3 (1.2)	5.4 (1.1)	0.35
Emotional function	6.4 (1.0)	6.5 (0.8)	0.60

ICS, inhaled corticosteroids; ICS/LABA, inhaled corticosteroids in a fixed combination with a long-acting beta-agonist; LABA, long-acting beta-agonist; MARS, Medication Adherence Report Scale; SABA, short-acting beta-agonist; SD, standard deviation.

[a] P value represents the difference between the groups.

asthma. We selected patients based on filling of at least two prescriptions for ICS or ICS/LABA during the previous 12 months. Mulder et al., 2016 showed that this is a reliable proxy for an asthma diagnosis [34]. Moreover, we checked the asthma diagnosis of the participants in the questionnaire.

It was hard to include sufficient adolescents per pharmacy, therefore we recruited extra pharmacies, and we also asked for reasons why patients did not want to participate; a lack of interest and not taking daily asthma medication anymore were mostly mentioned. Previous studies confirmed that it is extra difficult to motivate adolescent patients for healthcare interventions, because adolescents do not want to be different from their healthy peers [5,35]. Moreover, some children with asthma lose their symptoms during adolescence [31]. Thus adolescents require special attention due to their development, and due to the course of their asthma symptoms (which can affect adherence) [5].

Many previous studies focused on mHealth interventions for chronic diseases [12,14,18,19,22], findings of those studies were incorporated in the development of our intervention. For example, the ADAPT intervention was developed in close collaboration with adolescents with asthma and healthcare providers, was based on a theoretical framework, was interactive, and contained multiple elements to target different aspects of non-adherent behavior. This combination made the ADAPT intervention distinctive from previous asthma mHealth interventions [18,22]. Moreover, the elements of the ADAPT intervention contributed to ongoing trends in healthcare, such as shared decision making and blended care, where integrated face-to-face contact is alternated with online information.

A strength of our study was the large number of participants in combination with the low drop-out rate, which is rarely seen in mHealth studies, or studies concerning adolescents [11]. There are also several limitations of the study, such as a response bias, as motivated patients are probably more interested in participating and more willing to use the ADAPT intervention (intervention arm). However, at baseline, 37.6% adolescents (n = 88) were adherent and 22.1% adolescents (n = 51) had control over their symptoms. This finding does not support that only highly motivated or highly adherent patients participated.

Another limitation might be the use of self-reported measurements, resulting in a potential desirability bias. Adherence could also be measured by using pharmacy refill records. However our study period covered only six months, and in the Netherlands patients usually collect chronic medication once every three months. It was therefore not possible to calculate adherence rates during the study period based on refill records. Moreover, quality of life can only be measured by self-report, therefore we used the PAQLQ questionnaire, which is designed for young people with asthma [36]. We used the CARAT to measure disease control, because the CARAT is a validated instrument for Dutch adolescents, which distinguishes between asthma and allergic rhinitis symptoms [37]. Moreover, the CARAT is less invasive than direct measurements and therefore more convenient and accessible for this age-group.

5. Conclusions

An interactive mHealth intervention, such as ADAPT, resulted in significantly higher medication adherence in adolescents with asthma having poor adherence rates. Based on this study, healthcare providers should consider a tailored mHealth approach in the treatment of adolescents with asthma. Future studies should focus on the long-term effects, the intervention use, and the implementation and integration possibilities of a mHealth intervention in clinical practice.

Dutch Trial Register identifier

NTR5061.

Contributions

Bouvy, de Vries, and Koster were responsible for the study concept and design. Kosse managed the trial and was responsible for the data collection. Kosse and Koster had full access to all data and are responsible for the integrity and the accuracy of the data analysis. All authors were involved in the analysis and interpretation of the data. Kosse drafted the manuscript, and all authors critically reviewed and approved the final manuscript.

Conflicts of interest

All authors declare no conflicts of interest.

Statement demonstrating the originality and clinical relevance

Adherence rates are generally low among asthma patients and further decrease during adolescence, resulting in poorly controlled asthma. Mobile health (mHealth) interventions have the potential to support medication adherence, however to date not much attention is paid towards mHealth interventions aiming at adolescent patients. We developed and evaluated an interactive mHealth intervention for adolescents with asthma (ADAPT). This intervention contained an unique combination of different elements targeting several aspects of non-adherent behavior and it increased adherence in adolescent with asthma having poor adherence rates.

Prior postings and presentations

The article has not been published previously, or is currently under consideration for publication elsewhere. Based on this data, oral presentations were held at the conference of the Association for Researchers in Psychology and Health (ARPH) 2018, at the pharmacy practice research in collaboration with pharmacists (PRISMA) symposium 2018, and at the FIP Pharmacy Practice Research conference 2018. Poster presentations based on this data were held at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE) 2018 and at the European Society for Patient Adherence, Compliance and Persistence (ESPACOMP) conference 2018.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2019.02.009.

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