Effect of an mHealth application on clinical outcomes in childhood asthma: Real-world, pragmatic trial in a primary care setting

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Research Article

Keywords: Childhood asthma, Clinical outcomes, mHealth application, Pragmatic trial, Primary Care Setting, Real-world

Posted Date: August 1st, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1637349/v1

Abstract

Medical adherence among children with asthma is a challenging problem. Mobile health applications have been increasingly used to improve adherence and clinical outcomes. Here, we compared clinical outcomes by using a mobile health application (Asmon application) with those receiving usual care, assessed the patient's satisfaction and the usability of this tool.

Methods:

We conveniently allocated children with persistent asthma aged 4–15 years and a guardian to receive the Asmon application or a usual care for 6 months. Assessments were performed at baseline and at the 6-month follow-up. Outcomes were the asthma control test score (ACT), dose of inhaled corticosteroids (ICS), acute exacerbation, and asthma-related quality of life. Participants' satisfaction and reasons for unengaging in long-term use of the application were also analyzed.

Results:

The overall drop-out rate was 24.1% (intervention 13, 16.5%; control 6, 7.6%). The mean ACT scores had increased in both groups from baseline to the 6 months follow-up (intervention, $p < 0.001$; control $p = 0.001$), but did not differ significantly between groups ($p = 0.784$). Among those with poorly controlled asthma at baseline, the intervention group showed possibly higher improvement than the control (37.5% vs 16.7%) even though the value was not significantly different ($p = 0.128$). Acute exacerbation, median dose of ICS usage, and asthma-related quality of life were not significantly different between groups ($p = 0.554$, 0.555, and 0.627, respectively). Approximately one-third of the intervention group never used the application, while 40.5% ever used only 1–7 times during the study period. Perception regarding the application was hard-to-use, self-judged ICS discontinuation, and change in guardians were the main obstacles for regular engagement. Nevertheless, the satisfaction score on the rating scale was high (4.5/5.0).

Conclusion:

The interactive Asmon application potentially improved disease control only in children with poorly controlled asthma at baseline. Acute exacerbation rate, dose of ICS, and asthma-related quality of life were not impacted by the intervention. Healthcare providers should thoroughly consider participants' and guardians' background characteristics before implementing an mHealth application in the real-world daily practices.

1. Introduction

Asthma is the most common chronic disease among children [1]. The incidence and prevalence of asthma both in children and adults have been increasing for decades, in both developed and developing countries [2]. Data from Thailand showed that the prevalence of asthma among children aged 6–7 years

was higher in 2001 than in 1995 [3]. In 2012, the prevalence of asthma in school children aged 6–12 years in Bangkok, Thailand, was 9% [4]. Due to the chronicity of the disease, ensuring adherence to medication, particularly inhaled corticosteroids (ICS) among children with asthma has been challenging. In a study from the Netherlands, inhaled corticosteroid nonadherence among adolescents aged 12–18 years was 62% [5]. This has been the main problem in asthma healthcare [6]. Negative impacts related to asthma medication nonadherence include acute exacerbation that requires emergency management occurs in up to 20% of cases, even though they had been prescribed ICS appropriately [7]. Particularly, in children with severe asthma, suppression of growth and adrenal gland function has been observed [8]. In addition, inevitable burdens related to childhood asthma include increased health expenditures, absenteeism from school, loss of parent's workdays, and decreased quality of life [9–11].

In asthma management, the key medication for continuous symptomatic control is ICS, while inhaled bronchodilators are used for emergency conditions. Persuading pediatric patients to adhere to the appropriate and regular use of ICS remains challenging, and in a real-world situation, this medication is irregularly used, particularly by adolescents. The main reasons for this are the patient's lack of knowledge regarding treatment, an inappropriate attitude, personal preferences related to medication, and reinforcement from a guardian. Moreover, relationships between healthcare providers and patients is also very important in this respect [12].

In order to enhance regular adherence to medication, healthcare providers have to apply health behavior theories in daily clinical practice. From the health belief model, key components of health behaviors are the following predisposing factors: knowledge, attitudes, and beliefs related to disease and its management; the following enabling factors: healthcare providers, patient's skills, and accessory tools, such as mobile applications for medication monitoring; and reinforcing factors: peer, family, and healthcare provider's admiration or rewards [13]. All these factors are key to enhancing perceived self-efficacy and better behavior regarding asthma self-management as per the standard protocol.

In recent years, mobile health applications (mHealth applications) have been invented for continuous monitoring and medical evaluation in asthma patients. Teufel Ii et al. [14] performed a pilot study in children (aged 8–16 years) with asthma, using a smart phone mHealth application for adherence to treatment. The study showed that both patients and caretakers were satisfied with this tool. Davis et al. [15] carried out a pilot study using a smartphone application, Kiss myAsthma, in nine patients. Evaluations were performed before and after 6 weeks' use. They found a high overall satisfaction rate among users and increased quality of life in the emotional function domain. In addition, this application was assessed as having a high likelihood for daily implementation. In a comparative study among asthmatic patients, an intervention group using mobile telephone-based interactive program was compared with a usual care group. The clinical outcomes, peak flow meter values, and quality of life were better in the mHealth application intervention group than in those receiving usual care [16]. Rudin et al. [17] conducted a study regarding perspectives of patients and healthcare providers by using a mixed-method study. Patients considered that using an application on a mobile phone for clinical monitoring was easy, resulted in increased awareness, and made communication with healthcare providers more

convenient. For the healthcare providers' perspective, the tool was very helpful for receiving more detailed information from patients, and required little effort. Nevertheless, numerous studies revealed no additional benefit derived from using smart phone applications than from the usual care [18, 19]. In addition, personal data privacy and cost-effectiveness were concerns in terms of implementing this tool in daily practice [20].

In Thailand, mHealth applications have been used for clinical monitoring in chronic diseases, but their use among children with asthma has been less common. Thus, we here compared the clinical outcomes and quality of life of children with asthma who used an mHealth application with those who received the usual care. Moreover, we evaluated the patients' satisfaction with and the usability of this tool after 6 months.

2. Material And Methods

2.1 Study design

We conducted a prospective, parallel, randomized, controlled, clinical trial at the outpatient department at Thasala hospital, Nakhon Si Thammarat, Thailand (primary care setting). Participants were recruited from June 18, 2020, to October 31, 2021. Simple random sampling was used for recruiting eligible participants into two groups. Patients assigned an odd number in the order of a visit to the doctor were allocated to the intervention group (usual asthma care along with the asthma monitoring application [Asmon application]), while those assigned an even number order were allocated to the control group (usual asthma care). In Thailand, usual asthma care is defined as disease management as according to the GINA Guidelines for Asthma Management [21].

2.2 Population and sample size

Children with asthma who had been treated at Thasala hospital from June 18, 2020, to October 31, 2021, were invited to participate. With α = 0.05, β = 0.20, z α/2 = z 0.05/2 = 1.96 (two-tailed), and z β = z 0.20 = 0.84, the sample size was calculated by using the formula below [22].

$n/group = 2 (z_{\alpha/2} + z_{\beta})^2 Ó^2 / (x_1 - x_2)^2$

From the study of Licskai et al. [23], we used the peak expiratory flow rate % predicted of the control group (73 ± SD 21%). Then, we determined the value of x_1 (mean peak expiratory flow rate % predicted of the control group) as 73% and x_2 (mean peak expiratory flow rate % predicted of the intervention group) as 88%.

We assumed that the peak expiratory flow rate % predicted of the experimental group would increase by approximately 15%, and that the standard deviation of both groups would be equal (SD 21%)

Consequently, with $n /group = 2 (1.96 + 0.84)^2 (21)^2 / (88 - 73)^2$

= (15.68) (441) / 225

= 30.73

and considering a drop-out rate of 15%), 35 participants per group were required.

2.3 Participants

We included patients aged 4–15 years at enrollment, who had been diagnosed with asthma by a physician at least 6 months before enrollment, had been regularly followed-up, and were prescribed ICS for at least 6 months as per the GINA Guidelines for Asthma Management [21]. For inclusion, patients had to be assessed as having controlled, partly controlled, or un-controlled asthma, had to be assessable with a peak flow meter, had to have access to a mobile telephone with an Android operating system either the participant or the guardian), and had to have access to WIFI and be able to make videos at home.

We excluded patients having and infection within 2 weeks prior to the enrollment, having underlying diseases, such as heart disease, renal disease, cancer, AIDs/HIV, or other chronic diseases, not having access to a mobile phone at home, or who refused participation.

2.4 Questionnaires

We modified questionnaires that had been reported previously [24] for use in the initial data gathering, during the follow-up period, and at the second visit 6 months later. Questionnaires included items on sociodemographic data, such as age at enrollment, sex, body mass index, level of education, guardian's education level, monthly household income, religion, onset of asthma, co-morbidities, family allergic diseases, current clinical symptoms, previous medications, etc. Physical examination was performed following the history-taking. Additionally, asthma control was assessed at the first and second visits. In addition, we also included a peak expiratory flow rate value and status of current asthma control. Moreover, we administered the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) at the first and second visits.

To administer the questionnaires at both visits, we assigned well-trained research assistants. The researcher called each participant on the first day and 7 days after an application was uploaded. Clinical outcomes (acute exacerbation during a 6-month period after enrollment, ICS dose), Asthma Control Test (ACT) score, and PAQLQ score were assessed at the end of 6 months' follow-up. In addition, participants' satisfaction with the application was analyzed at the end of the 6-month study period.

2.5 Asthma Control Test (ACT)

We modified the Thai ACT version for use in this study. It consisted of five items that evaluated the clinical outcomes in the previous 4 weeks. Data were submitted by the patient and the guardian. All items were scored from 1 to 5: "1" indicated the least control, "5" indicated the maximal control. Total scores of 20 or higher were defined as good control, whereas scores under 20 were defined as poor control [25].

2.6 Pediatric asthma quality of life questionnaire (PAQLQ)

We modified the Thai version of the PAQLQ to evaluate the quality of life of participants, based on a study in Thai children with asthma. The questionnaires comprised 23 items addressing three domains: limitation in activity, clinical symptoms, and emotions related to asthma. All domains were scored from 1 to 7, with “1” indicating the lowest and “7” indicating the highest quality of life [26].

2.7 The Asmon application (a mobile health application)

A personalized, interactive Android mobile asthma application, the Asmon application, was conceived by two co-authors, and was then constructed by an IT specialist. At the first visit, a researcher informed the participant and guardian of the objectives and benefits of this application. It was then downloaded on the user’s mobile phone. The user signed in with a specific username and password via http://www.wuasmon.com. An identification number, participant’s name, phone number, date of enrollment, type of ICS use, dose/time, frequency/day, emergency visit, hospitalization, missed appointment, etc., were inputted. At the first visit, the researcher trained participants/guardians in the whole process of daily use. An alarm sound was selected by the user for daily ICS reminding according to the physician’s plan. The alarm system would sound for 10 seconds (every 1 minute until the user started ICS use, or persisted for 5 minutes). The participant had to use the ICS (via metered dose inhaler) with or without a spacer every time as prescribed by a physician. While using the ICS, the guardian had to record a video for 3–5 seconds, and uploaded this on the mobile application. After the daily information had been completed and uploaded, a cartoon animated gif provided applause and presented a smile. The daily data were recorded and sent to the research database system (Fig. 1). All participation data files could be accessed by researchers, physicians, and the participants/guardians at any time. We created Asmon application based on Ionic framework. The functions of this application include login, home (welcome page), menus, schedule for using as asthma medication, taking a video, and uploading a video after the patients using an asthma medication (Fig. 2). We implemented the Asmon website with the Yii Framework to collect data from the Asmon application. On the website, we set the initial data for individuals to create usernames and passwords for the Asmon application. In this website or system, we created a login function for a physician to authorize and monitor the videos that the patients uploaded to the system.

2.8 Peak Expiratory Flow Rate Measurement

The mobile peak flow meter was used only at the first visit, but not at the second visit, due to the Covid-19 pandemic. We used a mini Wright peak flow meter (Clement Clarke International, Harlow, Essex, UK). For the measurement, the participant was in a standing position, and held the peak flow meter horizontally. After adjusting the indicator to the zero point, the participant took a deep breath and placed the mouth-piece between upper and lower teeth, and closed the lips around the mouth-piece. The participant then blew out rapidly, in one breath. The process was repeated three times and the highest value was chosen [27].

2.9 Study process

After each patient was seen by the physician, we invited the patient and their guardian to enroll in the study. A well-trained research assistant provided information and explained the objectives of the study. If a participant met the inclusion criteria, informed consent was obtained from the patient and guardian prior to enrollment. Questionnaires were administered by the research assistant in an interview with the subject. The peak flow meter test was performed. The level of asthma control was noted at each visit by using the ACT, with data of the previous 4 weeks. In addition, the PAQLQ questionnaire was conducted with the data of the 7 days before the visit. During the follow-up period, a researcher called participants in the intervention group within the first week to remind them about use of the Asmon application. Both groups were regularly seen, bi-monthly, by their physicians. After the 6 months' study period, a history of acute exacerbation, ICS dose, and ACT and PAQLQ scores were re-evaluated. In addition, in the intervention group, participants/guardians' preference and satisfaction with the application were evaluated using a rating scale, with 1 indicating the least, and 5 indicating the most, for each of five questions: (1) benefit in terms of reminding to use medication; (2) convenience and ease of use; (3) positive reinforcement (a cartoon animated gif and accumulated points) for medication adherence; (4) user-friendly and interesting design; (5) overall satisfaction. Moreover, we also asked what were considered the strengths of the application, and what were the weaknesses that required correction. In addition, participants and guardians were also asked to describe reasons for discontinuing use of this digital tool.

2.10 Statistical analysis

We used mean (SD) or median (interquartile range) for continuous variables, and frequency (percentage) for discrete variables. The Shapiro—Wilk test was utilized to assess the normality of data distribution. To compare participants' characteristics between the intervention and control groups, we compared continuous data using Student's t-test or Wilcoxon's rank-sum test. For within-group comparison of pre-post continuous data, we used the paired t-test (normal distribution) or Wilcoxon's signed-rank tests (non-normal distribution). Pearson's chi-squared test or Fisher's exact test was used to compare discrete variables between the intervention and control groups. Statistical significance was defined at p-values < 0.05. R software version 4.1.1 (https://www.r-project.org) was used for data analysis.

2.11 Ethical issue and confidentiality

The study was approved by the ethics committee of Walailak University (WUEC-20-085-01). The clinical trial was registered at the Thai Clinical Trial identification number is TCTR20220412005 (https://www.thaiclinicaltrials.org/show/TCTR20220412005). Informed consent and assent were provided by the guardians and participants, respectively, before enrollment.

3. Results

3.1 Sociodemographic characteristics of participants

A total of 86 children with asthma and their guardians were invited to evaluate their eligibility. According to inclusion and exclusion criteria, 79 participants were suitable for enrollment between June 18, 2020, and October 31, 2021. All participants were consecutively randomized to the intervention and control groups. Thirteen participants (intervention group) and four (control group) were lost to follow-up, in that they did not respond to telephone calls. At the 6-month follow-up, we used a per protocol analysis with completed data (n = 60) as shown in Fig. 3.

Baseline sociodemographic characteristics of the study participants are presented in Table 1. All sociodemographic characteristics of participants were similar in both groups, without significantly differences ($p > 0.05$). Males accounted for about two-thirds in both groups. The median age at enrollment of the control group was slightly older than that in the intervention group, but this difference was not statistically significant. About two-thirds of guardians had educational levels of secondary school or lower.

Table 1
Baseline sociodemographic characteristics of participants (n = 79)

Parameters	Intervention group (n = 37) n (%)	Control group(n = 42) n (%)	P-value
Gender (female)	11 (29.7)	15 (35.7)	0.745
Age-months (median (IQR))	82 (63,108)	102.5 (64.5,127.5)	0.227
BMI (median (IQR))	16.3 (14,20.7)	17.1 (15,21.3)	0.523
Religious			0.772
Buddhism	25 (67.6)	26 (61.9)	
Muslim	12 (32.4)	16 (38.1)	
Participant's education			0.402
Kindergarten	19 (51.4)	15 (35.7)	
Primary school	17 (45.9)	25 (59.5)	
Secondary School	1 (2.7)	2 (4.8)	
Guardian's education			0.566
Primary school	9 (24.3)	16 (38.1)	
Secondary School	16 (43.2)	13 (31)	
Vocational education	5 (13.5)	5 (11.9)	
Bachelor degree and higher	7 (18.9)	8 (19)	
Tobacco smoke (exposure)	25 (67.6)	30 (71.4)	0.899
Monthly family income (THB)			0.546
<5000	1 (2.7)	2 (4.8)	
5000–9999	6 (16.2)	10 (23.8)	
10000–14999	6 (16.2)	10 (23.8)	
≥15000	24 (64.9)	20 (47.6)	
Family history			
Asthma	19 (51.4)	15 (35.7)	0.241
Allergic rhinitis	13 (35.1)	12 (28.6)	0.701
Allergic conjunctivitis	4 (10.8)	4 (9.5)	1
Anaphylaxis	2 (5.4)	0 (0)	0.216

Parameters	Intervention group (n = 37) n (%)	Control group(n = 42) n (%)	P-value
IQR, Interquartile rang			

Baseline clinical characteristics of participants were also similar in both groups, as shown in Table 2. The median time since onset of asthma in most patients was approximately 2 years. Allergic rhinitis was the most common comorbidity, and was not statistically significantly different between groups. Acute asthmatic exacerbation, asthma control status, ICS usage and median peak expiratory flow rate at enrollment were also comparable between groups.

Table 2
Clinical characteristics of participants (n = 79).

Parameters	Intervention group (n = 37) n (%)	Control group(n = 42) n (%)	P-value
Onset of asthma diagnosis	24 (12,48)	24 (12,36)	0.828
-months (median (IQR))			
Co-morbidity			
Allergic rhinitis	23 (62.2)	16 (38.1)	0.056
Allergic conjunctivitis	8 (21.6)	3 (7.1)	0.126
Atopic dermatitis	8 (21.6)	8 (19)	0.997
Food allergy	7 (18.9)	5 (11.9)	0.581
Anaphylaxis	4 (10.8)	0 (0)	0.044
Other	6 (16.2)	4 (9.5)	0.502
Acute exacerbation	23 (62.2)	24 (57.1)	0.823
(prior 12 months) (yes)			
Asthma control status			0.099
Well controlled	16 (43.2)	14 (33.3)	
Partly controlled	10 (27)	21 (50)	
Uncontrolled	11 (29.7)	7 (16.7)	
Asthma Medications			
ICS	37 (100)	42 (100)	
SABA	19 (51.4)	17 (40.5)	0.458
Antihistamine	6 (16.2)	4 (9.5)	0.502
Peak expiratory flow rate (Lpm) (median (IQR))	145 (118.8,202.5)	180 (110,230)	0.508

ICS, Inhaled corticosteroids; SABA, short-acting beta-agonist; IQR, Interquartile range; Lpm, Litre per min

3.2 Primary outcomes

The mean ACT scores had increased in both groups from baseline to the 6-month follow-up visit (intervention group, $p < 0.001$; control group, $p = 0.001$). Nevertheless, there was no significant difference in this increase between groups ($p = 0.784$). When analyzing base on the data of those with poorly

controlled status at baseline, the intervention group showed a greater trend of improvement than did the control group (37.5% vs 16.7%) even though the value was not significantly different (p = 0.128). The acute asthma exacerbation rate was also not significantly different between the two groups at the 6-month follow-up (p = 0.554). The median dose of ICS used in participants had decreased in both groups from baseline to the 6-month follow-up (intervention group, p < 0.001; control group, p = 0.003). However, this was not significantly different when comparing the dose at the end of the study (p = 0.555), as shown in Table 3.

Table 3
Effect of the mHealth application intervention on clinical outcome measurements (n = 60).

Parameters	Intervention (n = 24) n (%)	Control (n = 36) n (%)	P-value
ACT score (mean, SD)	20.2 (4.6)	21.7 (3.4)	0.135
Visit 1*	24.1 (2.4)	24.2 (2.2)	0.784
Visit 2**	< 0.001	0.001	0.128
P-value (V1 vs V2)	9 (37.5)	6 (16.7)	0.554
Proportion of ACT score improvement†	16 (66.7)	20 (55.6)	
Acute exacerbation			
Dose of ICS‡ (median, IQR)			
Visit 1	125 (100,250)	100(90.6,143.8)	0.072
Visit 2	125 (0,125)	62.5 (50,125)	0.555
P-value (V1 vs V2)	< 0.001	0.003	
*Visit1, baseline; **Visit2, 6-month follow-up.			
†Proportion of ACT score improvement, proportion of patients with poorly controlled level at baseline that got higher score at 6-month follow up compared to total in each group			
‡Dose of ICS (equivalent to flixotide); ICS, Inhaled corticosteroids; ACT, Asthma Control Test; SD, standard deviation. Intervention group VS Control group, using Student's t-test. Within-group Visit 1 VS Visit 2, using paired t-test			

3.3 Secondary outcome

The PAQLQ results are shown in Table 4. Medians of symptoms, activity limitation, and emotional scores had significantly increased from baseline to the 6-month follow-up in both groups. However, by the end of the study, there were no statistically significant differences between intervention and control groups. The median total PAQLQ score yielded similar results.

Table 4
Effect of the mHealth application intervention on Pediatric Asthma Quality of Life Questionnaire scores.

Parameters	Intervention (n = 24) n (%)	Control (n = 36) n (%)	P-value
Symptoms (median, IQR)			
Visit 1	62 (57.8,63)	63 (58,63)	0.690
Visit 2	63 (63,63)	63 (63,63)	0.609
P-value (Visit 1 vs Visit 2)	**0.028**	**0.012**	
Activity limitation (median, IQR)			
Visit 1	34 (32.8,35)	34 (33,35)	0.806
Visit 2	35 (35,35)	35 (35,35)	0.181
P-value (Visit 1 vs Visit 2)	**0.004**	**0.039**	
Emotional (median, IQR)			
Visit 1	62 (60.5,63)	63 (59.5,63)	0.309
Visit 2	63 (63,63)	63 (63,63)	0.937
P-value (Visit 1 vs Visit 2)	**0.009**	**0.082**	
Total (median, IQR)			
Visit 1	157 (152,160.2)	159 (150,161)	0.436
Visit 2	161 (161,161)	161 (161,161)	0.627
P-value (Visit 1 vs Visit 2)	**0.003**	**0.008**	
IQR, Interquartile range; Intervention vs Control group using Wilcoxon's rank-sum test			

Visit 1 vs Visit 2 using Wilcoxon's signed-rank test

3.4 Process evaluation

From 37 allocated patients who received the Asmon application on their mobile phone, only 24 participants completed the 6-month follow-up. Thirteen participants (35.1%) absolutely never used this application, as determined by tracking on our back-up system. Most users (15/37, 40.5%) had used and uploaded a short video between one and seven times. Only four participants (10.8%) had engaged in the Asmon application more than 30 times from baseline to the 6-month follow-up visit, as shown in Table 5.

Table 5
Asmon application used in the Intervention group (n = 37*).

Range of use	Frequency	Percent
Never**	13	35.1
1–7	15	40.5
8–30	5	13.5
> 30	4	10.8
* Participants were provided an uploaded application at baseline (Visit1)		
** No data were detected in back up system & then loss-to-follow-up at 6 months (Visit2)		

3.5 Satisfaction assessment for using the Asmon application

Twenty-four participants/guardians had used the Asmon application at least once from baseline until the 6-month follow-up. The total mean score of satisfaction for the different items was 4.5 (SD = 0.5) out of a total 5.0 points, as shown in Table 6.

Table 6
Satisfaction assessment for using the Asmon application.

Satisfaction items	Mean (SD)
Q1, Benefit for medication reminding	4.4 (0.9)
Q2, Convenient and easy to use	4.4 (1.0)
Q3, Positive reinforcement*	4.4 (1.1)
Q4, User-friendly and interesting design	4.7 (0.5)
Q5, Overall satisfaction	4.8 (0.5)
Total mean score	4.5 (0.5)
*Accumulated points for medical adherence	

3.6 Reasons for a long-term un-engagement

For the intervention group, after we uploaded the Asmon application on their mobile phone and informed them of the details of the processes, a researcher called them back within the first week to determine if they had any question or problem in using the application. Data of participants/guardians' compliance had also been gathered during usual bi-monthly follow-up with their physician. "Not easy to use" was the most common reason discouraging users to continue implementing the application (10/37 participants,

27.0%) followed by ICS discontinuation, change in guardian, insufficient time, financial difficulties, and WIFI not available at home, as shown in Table 7.

Table 7 Main reasons for discontinuation of using Asmon application until the 6 months follow-up (n = 37).

Reason	n	%
Perceived to be hard to use	10	27.0
ICS discontinuation	7	19.0
Change in guardian	6	16.2
Insufficient time	5	13.5
Financial difficulties	4	10.8
WIFI not available	2	5.4
Others	3	8.1

ICS, Inhaled corticosteroids; WIFI, Wireless fidelity

Discussion

To the best of our knowledge, no previous study using an mHealth application among children with asthma in a primary care setting in Thailand has been reported. The interactive Asmon application showed a trend to improve disease control especially in a specific group of children who had poorly controlled asthma at baseline. Acute exacerbation rate and the median dose of ICS used were not significantly different between those who did and those who did not use the application. The PAQLQ also was not impacted by the intervention. Even though the user's satisfaction scores were promising, implementation of the application nevertheless presented a number of challenges, such as the user-friendliness of the application procedure and participants' background factors.

In order to improve clinical outcomes among childhood asthma patients, healthcare providers have various choices in selecting different types of mHealth applications for special functions, characteristics, utility, and quality [28, 29]. Healthcare professionals' perceptions were surveyed regarding creation of innovative electronic monitoring devices. This indicated that attractive features would be new visual evidence to enable clinical discussions with patients and engaging them by means of rewards or motivations. However, data confidentiality and cost-effectiveness need to be considered and addressed before employing these applications in daily practice [30]. From the users' point of view, i.e., for children with asthma, aged 7—12 years, and their guardians, desirable aspects of the application were receiving asthma knowledge in a fun way, including a comic; interactive activity between the child and caregiver; and a user-friendly design, such as the use of colors. Beside knowledge regarding disease management, universal design and enhanced elements, reminding functions, and clinical monitoring of the application

are also needed [31]. The Asmon application had been cooperatively developed by pediatricians and an IT professional to focus on medication adherence through daily reminders, interactive activity with daily uploading of a video by users, which is relayed to the healthcare database, and employment of a reward system (cartoon applause animated gifs).

However, even though we followed behavioral theory and applied an interactive design for creating the Asmon application, there was little effect on the primary outcome regarding disease control. Notably, only children with poorly controlled asthma at enrollment had potentially impacted by using the application. This result was consistent with the study by Cook et al. [32] who followed guidelines and Scripps management pathways to prove the concept of their study. Participants aged 17–82 years with poorly controlled asthma were enrolled to test the usability and effectiveness of their application over a 4-month period. They found that the application improved asthma control, increased FEV1, decreased courses of systemic corticosteroids, and was considered highly satisfactory by users. Another study in youths, aged 12—17 years, with persistent asthma, used a mobile asthma action plan (AAP) application that revealed a promising outcome (disease control). This result was demonstrated only in participants with uncontrolled asthma at baseline [33]. In contrast, a multi-center, randomized controlled trial, performed in primary care setting in the UK, with cost effectiveness analysis, using mobile phone-based interactive management showed that adolescents and adults with poorly controlled asthma did not improve asthma control or increase self-efficacy as compared with paper-based monitoring. This intervention did not show promising cost-effectiveness [34].

Acute asthma exacerbation, dose of ICS used, emergency visits or hospitalization, and quality of life are also important indicators for assessing benefits of intervention. Our study did not show any significant differences between the intervention and control groups. These findings were concordant with many previous studies [35, 36]. In data from the Cochrane Database Systematic Reviews 2014, 12 of 17 randomized controlled trials also showed non-promising results regarding clinical outcomes [37].

In our study, the lack of substantial changes in desirable clinical outcomes may have been due to the status of participants at the initial enrollment. The proportion of participants with well-controlled disease was high in both the intervention group (43.2%) and the control group (33.3%). The mean ACT scores and were also higher than the cut-off point (20) in both the intervention group (20.2) and the control group (21.7). In addition, the median PAQLQ scores at baseline in both groups were also high (intervention group, 157; control group, 159 from 161). These would leave little room for effective changes regarding implementation of an intervention. Lessons learned from our study were in accordance with the study of Kosse et al. [38] and Vasbinder et al. [35]. In addition, due to the Covid-19 pandemic during our research period, most participants/guardians had intentionally adapted their protection behaviors (mask-wearing, physical distancing, hand-washing, etc.), which may have resulted in less exposure to allergens or pollutants.

We were disappointed in participants' adherence to our Asmon application. Based on our backup data, about one-third of the intervention group never used our tool, while 40.5% of those who had ever tried it,

used it between one and seven times during a 6-month period. This was similar to the results of Lau et al. [39], Greenhalgh et al. [40], Christensen & Mackinnon [41], and Kosse et al. [42]. Even though the participants/guardians' mean satisfaction score was promising (4.5/5.0), this may reflect a desire to appease the research team. Data from open-ended questionnaires reported that the application was perceived to be hard to use. Self-judged ICS discontinuation and change in guardians were additional main obstacles for regular engagement with our application. Furthermore, time and financial issues were also challenges. In terms of characteristics of participants who strongly engaged with an mHealth application in other studies were high adherence to mHealth applications at baseline [42], young and middle-aged users [43]. Monetary incentivization and advanced gamification may be needed to promote long-term engagement with applications in chronic diseases such as asthma [44, 45]. Eventually, users' psychosocial—behavioral needs and sociodemographic backgrounds are very significant factors for implementing a novel mHealth application in the real-world daily practices.

The limitations of our study were that this was a non-blinded, conveniently-randomized, small sample-sized, and short-duration (6 months) study. In addition, we did not actively monitor participants/guardians' compliance in the initial weeks or directly track medical adherence, which may have resulted in the less-than-ideal engagement. Moreover, because our participants/guardians were predominantly in the low—middle socioeconomic class, who benefited from a universal health coverage scheme and mostly resided in a rural area, which might limit generalizability to other childhood asthmatic populations. Due to the Covid-19 pandemic, we encountered a variety of challenges, such as a lack of peak flow meter assessment at the end of study, avoidance of pulmonary function test measurement, and a high loss to follow-up.

The strengths of our study included that this clinical trial was conducted in a real-world, primary care setting in a small town, rural area in Thailand, that there was randomization of participants/guardians and comparison with a control group, which is typically burdensome to enroll in an intervention study. We had comparable success in the initial enrollment.

Future research should focus on objective outcome measures and should address patients' background characteristics to allow identification of those in whom it would be more suitable to implement mHealth applications.

Conclusion

The interactive mHealth application possibly improved disease control especially in children with asthma with poorly controlled at baseline. Acute exacerbation rate, dose of ICS and PAQLQ were not impacted by the intervention. Healthcare providers should carefully consider participants and guardians' background factors before implementing an mHealth application in real-world daily practices. Multi-center, well-organized studies with large sample sizes are warranted to clarify the cost-effectiveness of such interventions.

Declarations

Ethics approval and consent to participate: Written informed consent was obtained from all participants and their guardians. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki and was approved by the Walailak University Institutional Review Boards (IRB No. WUEC-20-085-01).

Consent for publication: Not applicable.

Availability of data and material: Only aggregated and anonymized data are available for members of the research group based on agreement with participants/guardians and our ethics committee. It is not possible to share any independent patient level data. If you require any further information, let me know. Please contact Ms.Suppat Rungraungsilp. Her email is suppat.ru@mail.wu.ac.th.

Competing interests: The authors declare that they have no competing interests.

Funding: None

Author contributions: TS designed concept, developed a research protocol, implemented the study, analyzed data, drafted and revised the manuscript. SR designed concept, created and implemented a system and a mobile application, managed data regarding an application adherence. WC and AN performed routine practice for asthma care clinic and regular follow up. All authors read and approved the final manuscript.

Acknowledgements

The authors thank all participants and guardians who participated in this study. In addition, we also thank the Customer Service Team of the Editage for editing the manuscript.

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Figures

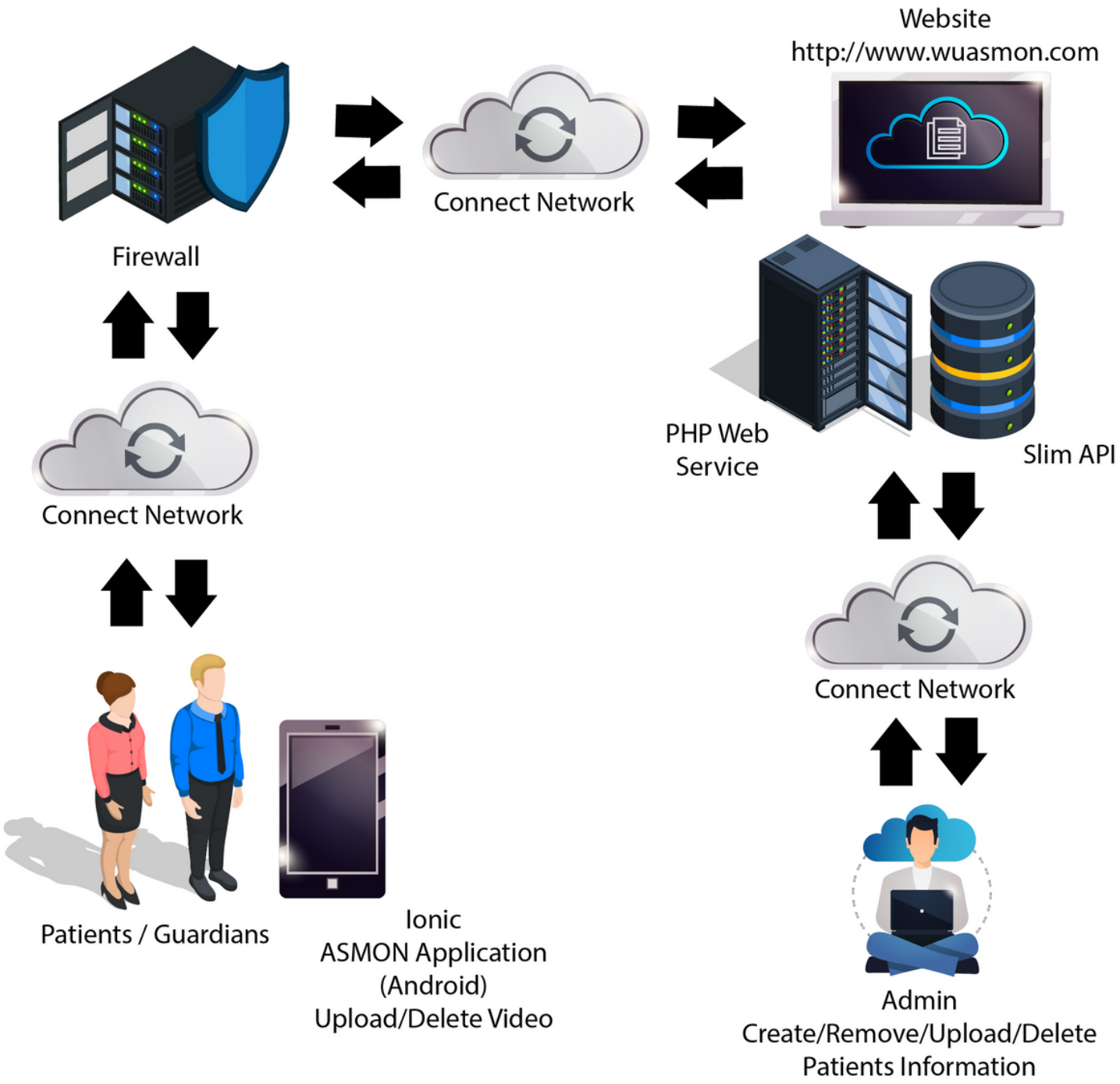

Figure 1

Illustrate the overall both application and website

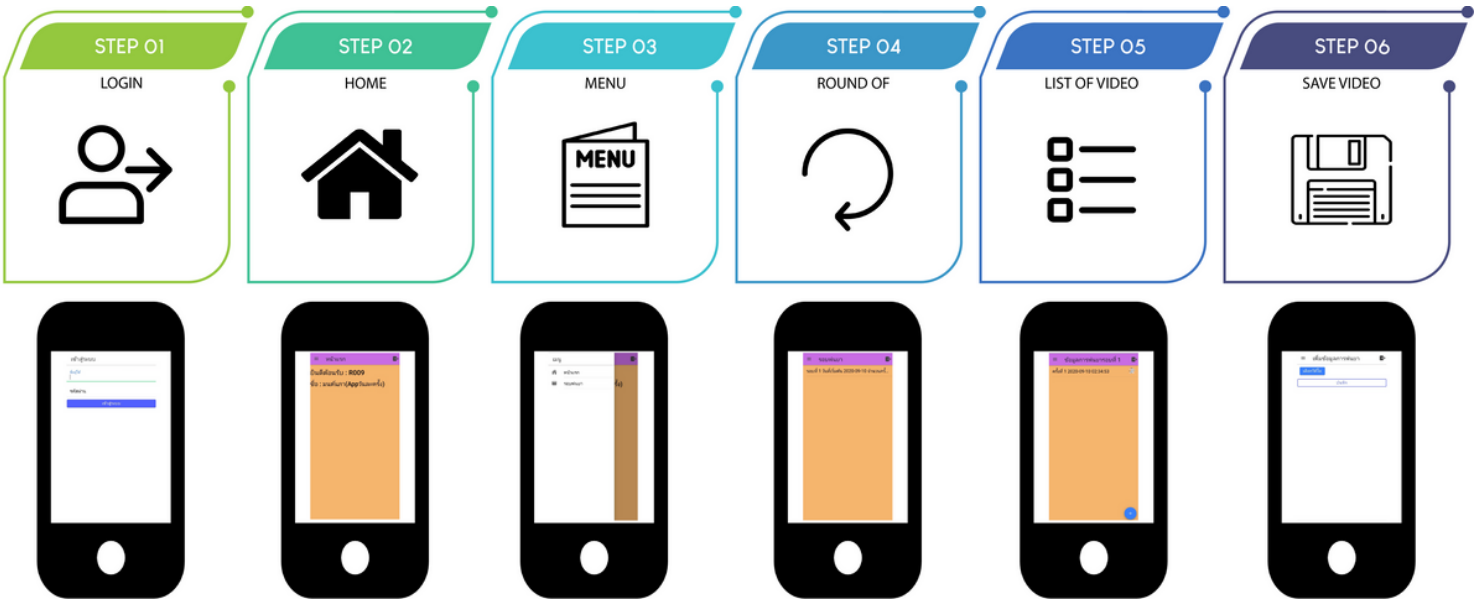

Figure 2

Illustrate user interface for using Asmon application

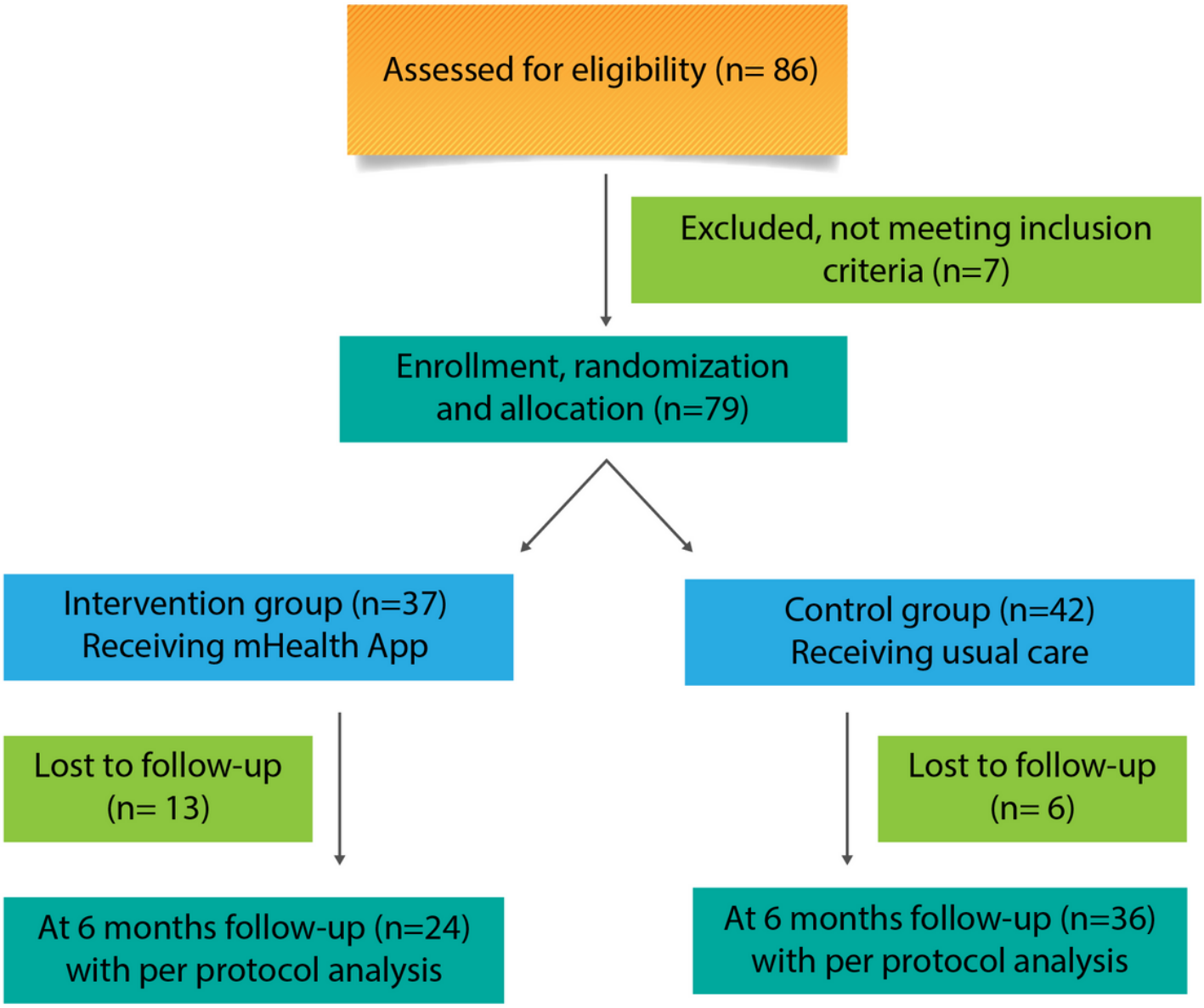

Figure 3

The Asmon application study procedure, including eligibility, randomization and follow-up