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Effect of mHealth Interventions in Improving Medication Adherence among Patients with Asthma: A Systematic Review and Meta-Analysis

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Abstract: ***Objectives: This study aims to systematically review and evaluate the existing evidence on the effectiveness of mobile health technology (mHealth) interventions in addressing medication adherence among people with asthma. The objectives of the study are 1) To evaluate the effectiveness of mHealth interventions on medication adherence among asthma patients. 2) To assess clinical effectiveness of mHealth interventions in asthmatic patients. Methods: Literature searches were conducted in five databases in November 2020. Included studies were randomized controlled trials comparing mHealth interventions versus usual care in improving adherence among patients prescribed asthma medications and control of asthma. Quantitative synthesis was performed using a random effects model. Results: 5 databases are searched systematically and244 records were identified. 9 randomized controlled trails were eligible for qualitative synthesis and 8 RCTs for quantitative synthesis. Adherence of asthma medications and clinical effectiveness of asthma in mHealth intervention and usual care arm are compared. Results show a small but significant overall effect on adherence to asthma medications (SMD = 0.73, 95%CI = 0.59–0.88) across mHealth studies utilizing self-reports, electronic monitoring, and Medication adherence report scale (MARS) to measure adherence. There is significant overall effect on control of asthma (SMD = 0.06, 95%CI = -0.07–0.20) across mHealth studies utilizing Questionnaire, forced expiratory volume (FEV) and Asthma control test (ACT) to measure asthma related quality of life. Conclusion: mHealth interventions are effective and the meta-analysis of data from 8 trials showed improved medication adherence and asthma control.***

Keywords: Asthma, Medication adherence, m-health interventions, Randomized controlled trails, Systematic review and Meta-analysis

1. Introduction

Asthma is a chronic lung disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person. In an individual, they may occur from hour to hour and day to day. It is characterized by reversible airway obstruction due to spasms and secretions in the bronchi usually resulting from an allergic reaction or hypersensitivity and causing difficulty in breathing (1). Asthma was responsible for 21·6 million (95% UI 17·1–27·0) DALYs in 2019, which was 20·8% (17·5–24·7) of total DALYs from chronic respiratory disease. Death rates from asthma were highest in countries of low and middle SDI, while prevalence was highest in high SDI countries (2). Asthma treatment includes daily use of a controller drug and use of short-acting bronchodilators when needed for quick symptom relief (3). Adherence to treatment is essential to optimize the benefits of therapy. The World Health Organization (WHO) defines adherence as ‘‘the extent to which a person’s behavior—taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider’’(4). Non adherence is a condition where the person does not take the prescribed medications properly. According to one study, it was found that medication non-adherence rate is high in asthma i.e., 55% (5).Every year 1,25,000 people die due to failure to take medication or taking medications improperly. Almost 6 out of 10 people are taking a minimum of one prescription drug. More than 1 in 3 medicine-related hospital admissions occur due to people not properly adhering to their medications(6). The statistics of medication non-adherence is shown in fig.1.

Figure 1: Statistics of medication adherence

According to a study there are different reasons for non-adherence why the patients do not take their medications properly. Different reasons for non-adherence along with their percentage are forgetfulness (63), cost (10.1), side effects (5.3), don't understand need for medication (4.8), regimen complexity (2.9) and don't understand how to take medication (2.4). The major factor for non-adherence is forgetfulness and mHealth helps to overcome this. The WHO defined mHealth as the use of mobile devices (mobile phones; patient monitoring devices; personal digital assistants; and other wireless devices) for the support and delivery of medical and public health services(7). mHealth interventions have different features of mobile technologies, including but not limited to short messaging systems (SMS), voice calls, mobile phone applications and Bluetooth(7).A number of strategies have been used to measure patient adherence to therapy. Direct measurements of adherence such as biochemical measures, including monitoring levels of the drug or its metabolites in the blood or urine, are not available for all medications and are generally costly and not practical to perform on large populations (8, 9).Electronic monitoring devices that record the frequency and time of the opening of a pill bottle have also been used to evaluate adherence (10, 11). Many indirect measures, including patient interviews, pill counts, and clinician assessments are also used to estimate medication adherence (11).

2. Methods

This systematic review and meta-analysis were performed in order to characterize the effectiveness of m-health interventions in improving medication adherence among patients with asthma. This review was conducted and written according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (12).

2.1. Data sources & search strategy

A systematic search strategy was developed and advanced literature search was performed using PubMed and Cochrane databases from the time of inception till October 2020. Search strategy for both the databases has been dwelt separately and various effective terms such as "Asthma", "Medication adherence", "Compliance", "SMS", "Mobile health" and "m-health". Clinical Trial and Trials filters were applied for PubMed and Cochrane databases respectively to retrieve the randomized clinical trials of required study. Detailed search strategy is presented in Appendix 1. All study citations were exported to endnote for identification of duplicates and screening according to the PRISMA guidelines.

2.2. Eligibility criteria

The criteria for inclusion of studies are:
1) Studies which are randomized controlled trails
2) Literature published between January 2000 and October 2020
3) Studies which included a mobile device with a wireless connection in the intervention package
4) Trails that had participants that were taking/ prescribed anti-asthmatic medications
5) Trails in which there is medication-adherence-related outcome and clinical outcome

Studies were excluded if
1) Full text was not available
2) The content was not written in English

2.3. Study screening & study selection

Initially two independent reviewers (IS and BM) screened the articles based on title and abstract. And then full text articles were assessed while applying pre-defined inclusion and exclusion criteria. Fig. 2 shows how potential studies were included or excluded from qualitative synthesis. Studies which reported mean adherence to asthma medications as well as the corresponding standard deviation for the intervention and control groups were included in the quantitative synthesis.

2.4 Data extraction

The primary outcome of interest was medication adherence and secondary outcome was clinical outcome (i.e., control of asthma, quality of life). A structured data extraction sheet was developed consisting the following fields: first author, year of publication, country, participant age range, sample size, duration of study, intervention arm, control arm, description of intervention, medication adherence measurement, clinical outcome measurement and results of medication adherence outcome and clinical outcome. Mean,

standard deviation, and number of study participants were also extracted for quantitative analysis.

2.5 Quality assessment

The risk of bias in each study was analyzed using the Cochrane collaborations' risk of bias assessment tool. All the included studies were assessed for risk of bias by two independent reviewers. Final risk of bias assessment summary was shown in Fig. 4.

2.6 Meta-analysis

Meta-analyses were performed using the Review Manager Software 5.4 Copenhagen (The Nordic Cochrane Center, the Cochrane Collaboration, 2014) for comparison of m-Health interventions versus usual care. Standardized mean difference (SMD) was chosen as the summary statistic because of the variation in adherence measures and clinical outcome measures among the studies included in the quantitative synthesis. The SMD was computed by dividing the difference between the post-intervention mean adherence in the treatment and control groups by the pooled standard deviation. The post intervention mean adherence was used rather than change in adherence scores because the latter was not available in majority of the studies. A positive value of SMD indicates a more favorable outcome for the treatment group compared to the control. Due to anticipated heterogeneity based on variability in how adherence was measured, subgroup analyses were performed according to the method of adherence measurement. Separate meta-analyses were also performed for the different types of outcomes, with sub-group analyses based on the type of adherence measurement. In cases of studies utilizing both objective measures and self-report to measure adherence, results from the objective measure were included in the meta-analysis.Effect sizes were weighted using the inverse variance method, while heterogeneity was tested for and quantified using chi-square and I^2 - statistics, respectively.

3. Results

3.1 Study selection & characteristics of included studies

A total of 239 studies were initially identified through PubMed, Cochrane and Google Scholar searching. And 5 additional records were identified from other sources like clinicaltrails.gov. After removing 49 duplicates and the initial screening based on titles, abstracts, 23 studies were excluded. The remaining 140 studies were then screened against the inclusion and exclusion criteria, and another 131 papers were excluded.And hence a total of 9studies were included in the qualitative analysis and 8studies were included in quantitative analysis. The study selection process is outlined in fig.2

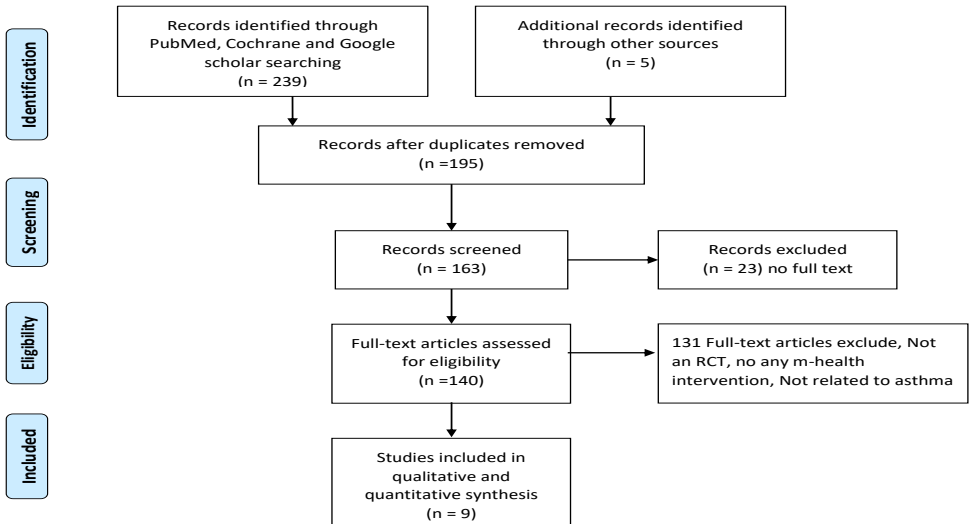

Figure 2: Study selection process

Table 1: Study characteristics of included studies

S. No	Author and year	Country	Age (in years)	Sample size			Completed follow-up			Duration of study	Intervention arm	Control arm
				Total	Intervention	Control	Total	Intervention	Control			
1	Bender et.al. 2010 (14)	USA	18 to 65	50	25	25	50	25	25	10 weeks	Interactive Voice Response (IVR) telephone calls	Usual care
2	Chan et.al. 2015 (15)	New Zealand	6 to 15	220	110	110	213	108	105	6 months	Audio-visual remainders (AVR)	Usual care
3	Charles et.al. 2007 (16)	New Zealand	12 to 65	110	55	55	90	44	46	6 months	Audio-visual remainders (AVR)	Usual care
4	Johnson et.al. 2015 (17)	USA	12 to 17	98	53	45	89	46	43	3 weeks	Personal health application	Usual care
5	Kolmodin et.al. 2016 (18)	USA	18 to 29	49	25	24	49	25	24	3 months	A computerized intervention authoring software	Usual care

											(CIAS) with motivational interviewing	
6	Kosse et.al. 2019 (19)	Netherlands	12 to 18	253	150	103	234	87	147	6 months	ADolescent Adherence Patient Tool (ADAPT)	Usual care
7	Petrie et.al. 2012 (20)	New Zealand	16 to 45	147	73	74	103	57	46	9 months	Text message group	Usual care
8	Strandbygaard et.al. 2010 (21)	Denmark	18 to 45	26	12	14	22	10	12	12 weeks	Text message group	Usual care
9	Yanhua LV et.al. 2012(22)	China	> 18	150	100	50	71	57	14	12 weeks	short text messages reminder	Usual care

The included studies provided 9 m-health treatment vs. control comparisons, with a total of 921 participants. Out of 9 studies, 3 studies were conducted in USA, 3 studies were conducted in New Zealand, 1 study in Denmark, 1 study in Netherlands and 1 study in china. Sample size varied from 22 to 234, while participants ages ranged from 6 to 65 years. Of the 9 studies included in the qualitative synthesis, 8 studies were quantitatively analyzed. One study did not report the mean adherence and standard deviation of the intervention and control groups (22). Regarding studies included in the quantitative synthesis, adherence to asthma medications was measured via electronic monitoring in four of these studies (14-16, 21), Medication adherence report scale (MARS) in one study (19), and self-report in three studies (17, 18, 20). In terms of clinical outcome, three studies utilizedforced expiratory volume (FEV) (15, 16, 18, 21), two used questionnaire (14, 20) and two used asthma control test (17, 19) for measuring asthma related quality of life.

3.2 Risk of bias

Two reviewers (IS and BM) assessed and documented the methodological quality of included studies using the methods detailed in section 8 of the Cochrane Handbook for Systematic Reviews of Interventions, and used Review Manager 5.4 to record and generate a risk of bias graph. The overarching risk of bias was summarized based on the Cochrane risk of bias tool (23).Of the nine studies, five (14, 16, 18, 20, 21) employed appropriate methods of sequence generation. Group assignment was adequately concealed in twoRCTs (14, 15). Risk of bias in blinding of participants and personnel was low in 4 studies(14-16, 22), unclear in 2 studies (20, 21) and high in 3 studies(17-19). Risk of bias in blinding of outcome was low in 2 studies(15, 16), unclear in 6 studies (14, 17, 18, 20-22)and high in 1 study(19). Regarding incomplete outcome data, we evaluated six studies (14-18, 20) as having a low risk of bias and 3 studies with unclear risk of bias (19, 21, 22). For the selective outcome reporting, it was impossible to locate and study the protocols of some of the selected studies(19, 20, 22) and other 6 studies have low ROB (14-18, 21). A summary of the risk of bias in all 9 studies is shown in fig.4.

3.3 m-health interventions

3.3.1. Qualitative synthesis

Studies categorized as using mHealth interventions are those administering clinical interventions that were supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants, and other wireless devices as suggested by WHO's definition of mHealth (24). The nine mHealth studies that were qualitatively evaluated in this review employed text message remainders (20-22), interactive voice response (IVR) telephone calls (14), audiovisual reminders (15, 16), personal

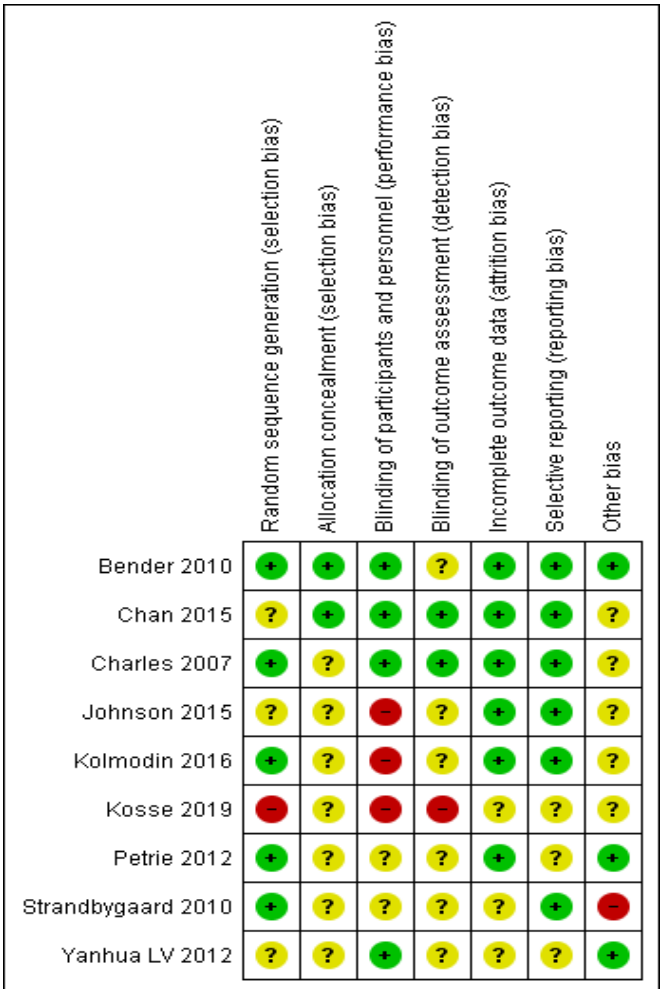

Figure 3: Risk of bias summary: review authors judgments about each risk of bias item for each included study

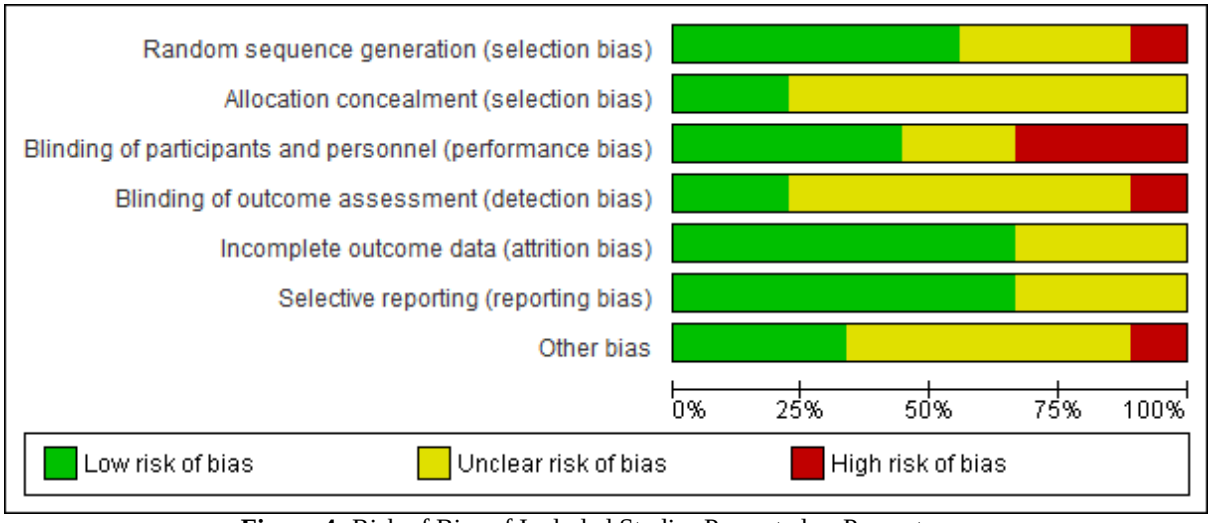

Figure 4: Risk of Bias of Included Studies Presented as Percentages

Table 2: Summary of included studies

S.No	Author and year	Medication adherence measurement	Medication adherence outcome	Clinical outcome measurement	Clinical outcome
1	Bender et.al. 2010 (14)	Electronic monitoring	The IVR intervention improved adherence by 32% during the 10-week study interval. Mean ICS adherence was higher in the group receiving IVR intervention than in the control group by a margin of 64.5% to 49.1% (F 9.66; P .0032)	BMQ (Beliefs about medication questionnaire)	No differences emerged for the Asthma Quality of Life Questionnaire or Asthma Control Test
2	Chan et.al. 2015 (15)	Electronic monitoring (Smart inhaler Tracker, Nexus6)	Median percentage adherence was 84% in the intervention group (10th percentile 54%, 90th percentile 96%), compared with 30% in the control group (8%, 68%; p<0·0001).A higher proportion of participants in the intervention group than in the control group had greater than 70% adherence. The control group had better adherence in the evening than in the morning at all three timepoints (2, 4, and 6 months), whereas in the intervention group, adherence was better in the morning than in the evening (p=0·0003)	FEV (Forced expiratory volume)	The change in asthma morbidity score from baseline to 6 months was significantly greater in the intervention group than in the control group (p=0·008), with a reduction of 2·0 points from a mean baseline score of 9·3 (SD 2·2) to 7·3 (2·1) in the intervention group, compared with a reduction of 1·2 points from a baseline of 9·2 (2·5) to 8·0 (2·2) in the control group
3	Charles et.al. 2007 (16)	Electronic monitoring (Smart inhaler monitoring device)	The proportion of medication taken in the last 12 weeks was greater in the AVRF group (93%) compared with the control group (74%), with a difference of 18% (95% confidence interval [CI] 10-26%; P < .0001). The proportion of subjects taking >50%, >80%, or >90% of their medication was greater in the AVRF group, with a ratio of proportions adherent of 1.33 (95% CI, 1.10-1.61; P 5 .003), 2.27 (95% CI, 1.56-3.3; P < .0001), and 3.25 (95% CI, 1.74-6.1%; P < .0001), respectively.	PEF (Peak expiratory volume)	No significant differences occurred in clinical outcomes between the 2 groups. At the last clinic visit, the mean (SD) PEF was 456 (113) L/min and 454 (129) L/min in the AVRF and control groups, respectively (difference 2 L/ min; P 5 .95). At the last clinic visit, the median (interquartile range) ACQ score was 0.5 (0-1.0) and 0.5 (0.2-1.2) in the AVRF and control groups, respectively (difference 0; P 5 .33).
4	Johnson et.al. 2015 (17)	Self-report	Of 21 (46%) MMH users who set up medication reminders, 17 successfully adopted this feature. Participants received an average of 12 initial reminders (with subsequent SMS dialog as shown in the Appendix) during the 2-week trial period. Based on responses to medication reminders accepted by the system, users took their daily medications an average of 10 times over 2 weeks. MMH was set up by 18 (39%) patients to support rescue medication use. Five users attempted to log their use of a rescue inhaler during the study period, and all succeeded.	ACT (Asthma control test)	Compared with control patients, intervention patients had a significant improvement in selfreported 7-day adherence (Figure 2), with an average gain of 1 day of adherence, and a median change from 4 to 6 days, compared with no median change in the control group (P ¼ .011; median data not shown).

5	Kolmodin et.al. 2016 (18)	Self-report	At 3 months, both groups reported an increase in number of doses missed. This increase was somewhat greater magnitude for the intervention group, t (41) ¼ .97, d ¼ .30, though this was not significant.	FEV (Forced expiratory volume)	The intervention group improved in FEV-1 percent predicted (þ4.41%) and the control group decreased (4.14%),t(41) ¼ 1.89, p .01, d ¼ .59.
6	Kosse et.al. 2019 (19)	Medication adherence report scale (MARS)	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)	CARAT (Control of allergic rhinitis and asthma test)	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].
7	Petrie et.al. 2012 (20)	Self-report	The intervention group also significantly improved adherence over the follow-up period compared to the control group with a relative average increase in adherence over the follow-up period of 10% (p < .001). The percentage taking over 80% of prescribed inhaler doses was 23.9% in the control group compared to 37.7% in the intervention group (p < .05).	BIPQ (Brief illness perception questionnaire)	At 18 weeks, the intervention group had increased their perceived necessity of preventer medication, increased their belief in the long-term nature of their asthma, and their perceived control over their asthma relative to control group (all p's < .05).
8	Strandbygaard et.al. 2010 (21)	Electronic monitoring (Diskus dose recordings)	From week 4 to week 12 the mean adherence rate in the SMS group increased from 77.9% to 81.5%; mean change Z 3.6%, 95% CI (8.5e15.7%), p Z 0.52, whereas the mean adherence rate in the control group decreased from 84.2% to 70.1%; mean change Z 14.2%, 95% CI (24.2e4.1%), p Z 0.01	FEV (Forced expiratory volume)	At the end of the 6-month study period no differences in clinical outcomes (PEF) between the groups were observed.6 In that study the proportion of adherent subjects (80% of their medication taken) after 6 months were 88.6% in the study group compared to 39.1% in the control group

health application (17), A computerized intervention authoring software (CIAS) (18) and Adolescent adherence patient tool (ADAPT) (19). Four mHealth studies assessed adherence via electronic monitoring and three used self-report and one study used medication adherence report scale. In 9 studies, adherence rates improved significantly post-intervention. Two mHealth studies assessed asthma related quality of life via questionnaire, four studies by FEV and two studies used ACT. In four of the nine studies, asthma related quality of life improved significantly post-intervention.

3.3.2. Quantitative synthesis

3.3.2.1 For medication adherence outcome

8 studies using mHealth interventions were included in the quantitative synthesis. The meta-analysis comparing mHealth interventions to control found a significant overall effect on adherence to asthma medications (SMD = 0.73, 95%CI = 0.59–0.88) across mHealth studies utilizing self-reports, electronic monitoring, and Medication adherence report scale (MARS) to measure adherence (Fig. 5). A test for subgroup differences indicated that the overall effect size was not associated with the method of adherence measurement ($\chi 2$ = 88.78, df = 7, p = 0.00001). Indeed, subgroup analysis of mHealth studies found significant improvements in medication adherence in the group of studies utilizing self-reports (SMD = 0.42, 95%CI = 0.16–0.67), studies utilizing electronic monitoring (SMD = 1.46, 95%CI = 1.23–1.69) and those utilizing medication adherence report scale (SMD = 0.13, 95%CI = -0.14–0.39). The self-report sub-group was heterogenous (I2 = 18%), and the electronic monitoring was heterogenous (I2 = 87%), while medication adherence report scales sub-group appeared to be homogenous (I2 = 0%).

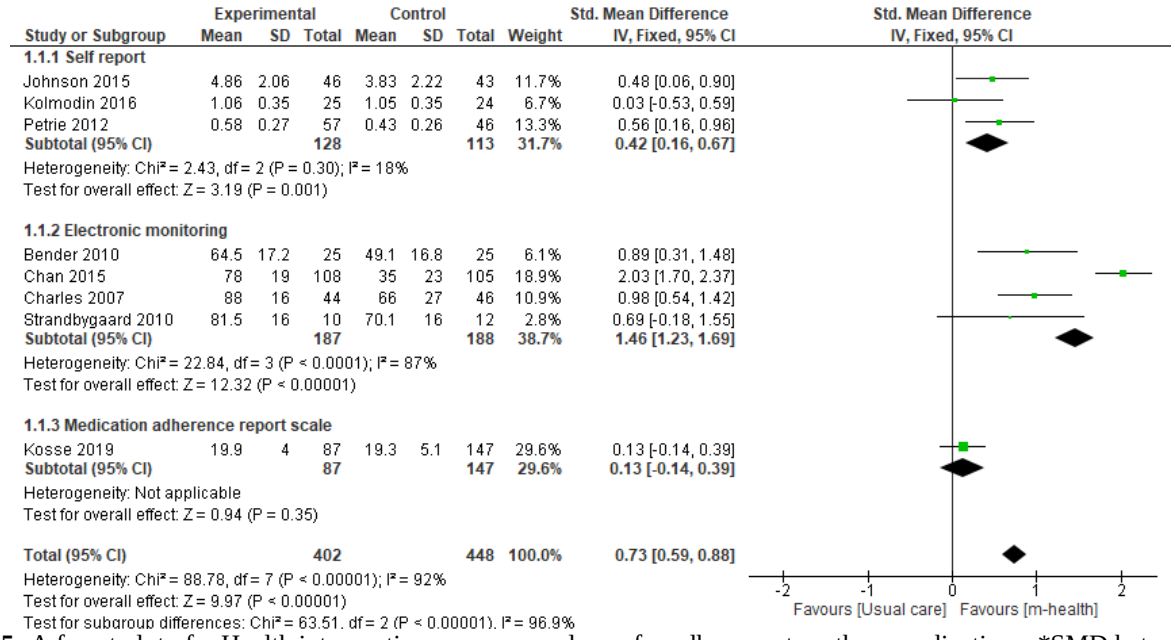

Figure 5: A forest plot of mHealth interventions versus usual care for adherence to asthma medications. *SMD between 0.57 and 0.86 is considered to be a clinically important difference

3.3.2.2 For clinical outcome

8 studies using mHealth interventions were included in the quantitative synthesis. The meta-analysis comparing mHealth interventions to control found a significant overall effect on control of asthma (SMD = 0.06, 95%CI = -0.07–0.20) across mHealth studies utilizing Questionnaire, forced expiratory volume (FEV) and Asthma control test (ACT) to measure asthma related quality of life (Fig. 6). A test for subgroup differences indicated that the overall effect size was not associated with the method of measurement of asthma related quality of life ($\chi 2$ = 6.80, df = 7, p = 0.45). Indeed, subgroup analysis of mHealth studies found significant improvements in asthma related quality of life in the group of studies utilizing Questionnaire (SMD = 0.28, 95%CI = -0.04–0.61), those utilizing forced expiratory volume (FEV)(SMD = 0.07, 95%CI = -0.13–0.27) and those utilizing asthma control test(ACT) (SMD = -0.05, 95%CI = -0.28–0.17). The questionnaire sub-group was heterogenous (I2 = 72%), while FEV and ACT sub-groupsappeared to be homogenous (I2 = 0%).

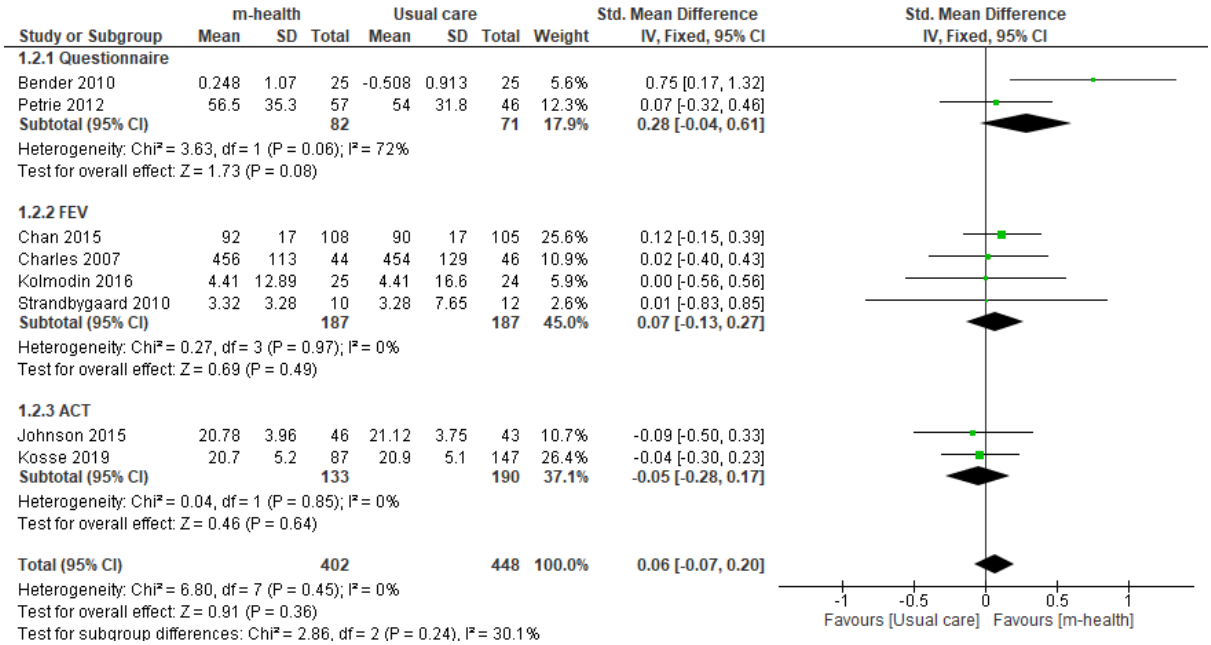

Figure 6: A forest plot of mHealth interventions versus usual care for clinical outcome. *SMD between -0.07 and 0.20 is considered to be a clinically important difference

4. Discussion

To the best of our knowledge, our study is among the first to evaluate effect of m-health intervention in improving medication adherence among patients with asthma. This systematic review included only RCTs with a high level of evidence among interventional studies. The results of our systematic review and meta-analysis provide evidence of the usefulness of m-health interventions as a means of improving the quality of clinical practice as well as guidance

regarding the development of m-health interventions that will be effective in increasing medication adherence. The eight RCTs included in this study were significantly heterogeneous in terms of measurement and data type. Measurement type was divided into objective and subjective medication adherence, and data type continuous data. Therefore, this study had combining all eight studies for a pooled estimate, and sub-analysis was conducted by dividing objective and subjective measurement and continuous data. However, except for the sub-analysis of studies that objectively measured medication adherence and presented the results as continuous data, the statistical heterogeneity was greater than 80%. The meta-analysis demonstrated that the effect size of m-Health interventions for medication adherence was at all significant, with the effects comparable to those reported for the care provided to the control group. Previous systematic reviews considered various interventions and analyzed their effects on improving medication adherence among people with hypertension and most of the studies included in these systematic reviews reported that the interventions were effective (25).

These results should be considered in conjunction with the similar effects of m-Health and conventional interventions in this study, which indicate that m-Health interventions are highly likely to be used in the future. Considering that asthmatic patients need to exercise continuous diligent adherence to medication regimens, as do patients with cardiovascular disease (25). m-Health interventions for improving medication adherence in asthmatic patients are potentially valuable for improving medication adherence in generally. The results of the meta-analysis showed significant differences in the medication adherence of the group provided with m-health interventions and the control group. Based on individual studies included in this meta-analysis, the control group for m-health interventions with a higher effect size was a group that was provided an electronic monitoring, medication adherence report scale intervention and self-report that could occur in usual care. M-health interventions can be used as convenient tools for medication adherence because of their portability and accessibility, which allow for alarms at medication times and make it easy for patients to ascertain to see if they missed a dose. M-health interventions for improving medication adherence in transplant patients are potentially valuable as interventions to improve medication adherence in generally. Further, the likelihood of using m-health interventions is increasing, due to the rapid development of information and communication technology and the increasing use of mobile phone applications. Considering these rapidly advancing technologies, our study results are often seen as timely and relevant. There were eight studies (14-21) in which quantitative or narrative synthesis was conducted to analyze intervention effects for medication adherence. The interventions provided in these studies were mobile based for regarding studies included in the quantitative synthesis, adherence to asthma medications was measured via electronic monitoring in four of these studies (14-16, 21), medication adherence report scale (MARS) in one study (19), and self-report in three studies (17, 18, 20). In terms of clinical outcome, three studies utilized forced expiratory volume (FEV) (15, 16, 18, 21), two used questionnaire (14, 20) and two used asthma control test (17, 19) for measuring asthma related quality of life. The integration of these interventions showed that electronic monitoring, medication adherence report scale and self-reports, forced expiratory volume (FEV), questionnaire, asthma control test and were provided. Electronic monitoring was provided through the intervention group received automated IVR telephone calls, SmartTrack device, Smart inhale. The IVR Calls were used for inquire about asthma symptoms, deliver core educational messages, encourage refilling of inhaled corticosteroid prescriptions, and increase communication with providers and the SmartTrack device records the date, time, and number of actuations used and has 14 different ringtone reminders that ring twice daily, stopping once the proper amount of drug dose is taken or after 15 min. If the proper amount of drug dose is taken within 6 h before the set reminder time, the reminder does not explode. A visual display shows the date and time of the most recent use. The Smart inhaler contained an AVRF. When the alarm was switched on, it generated a single beep, which sounded once every 30 seconds for 60 minutes after the predesignated time, which was programmed into the device. The alarm stopped if the MDI was actuated or after hour if not taken. The device was programmed to emit the alarm at predetermined times twice a day. The AVRF also had a colored light, which was green before MDI use, changing to red once the MDI was taken. This function served to remind patients whether they had taken the MDI as scheduled. Reminders using lights, sounds, and messages were provided in order times wouldn't be missed. One study measured the effect of m-Health interventions on medication adherence report scale (MARS) (19) and in that patients are on 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 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. Three studies measured the effect of m-Health interventions on self-report(17, 18, 20) - in these studies the type of intervention was Personal health application (17), and a computerized intervention authoring software (CIAS) with motivational interviewing (18) and for the other, it was Text message group(20). In personal health application the participants in the intervention group were instructed to create a MMH account. Instructions were sent via email, which included a phone number for 24-h support, a demonstration video, and detailed directions for testing the text message reminder system. And for computerized intervention authoring software the intervention consisted of two CIAS-delivered sessions with personalized, daily text-messaged reminders to take medication delivered between these sessions. EMA via text messaging was conducted before the first intervention session to gather real-time data on participants' medication adherence and asthma symptoms and in text message group participants assigned to the text message group received tailored text messages for 18 weeks. Prior to the study, a bank of 166 text messages was generated with approximately 24 texts for every of the seven target beliefs.

Texts were sent at a frequency of two texts per day during weeks 1–6, one text per day from weeks 7 to 12, and three texts per week from weeks 13 to 18. The type of texts sent was determined by the participant's baseline scores on the BIPQ and the level of medication belief ratings. There were statistically significant differences compared to m-health from usual care. Previous there is no any meta-analysis available on the effect of m-health interventions in improving medication adherence among patient with asthma.

Conventional interventions, such as face-to-face methods, take much time and effort to employ. Therefore, there are limitations in interpreting the results of the meta-analysis, and more research needed be conducted on this issue in the future. The strengths of this study are as follows. First, it is the first study to analyze the effects of m-Health intervention in improving medication adherence among patients with asthma. Second, all possible evidence available up to date were selected for a literature search to reduce the bias of literature selection and the availability of m-Health interventions is likely to increase in the future.

5. Conclusion

Meta-analysis and narrative synthesis showed that m-health interventions for improving medication adherence conducted among patients with asthma had a better effect in improving their medication adherence and knowledge compared to standard care or advanced interventions. Therefore, m-health interventions can be used for medication adherence among patients with asthma. We recommend further development of m-health intervention applications, so they may include more features for medication education, self-recording and monitoring, reminders using signals, and monitoring by medical staff to check participants' health indicators or medication adherence. Further high-quality studies that assess the effects of m-health interventions for improving medication adherence in among patients with asthma should be conducted to provide support for effective interventions. Additionally, there is a requirement for standardized measurements and definitions of medication adherence to enhance the standard of research in this area.

Declaration of interest
None

Conflicts of interest
The authors have no conflict of interest to disclose.

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Supporting information

Appendix 1
PubMed search strategy
(((Asthma[mesh] OR Bronchial Asthma [Title/Abstract] OR airway hyper-responsiveness [Title/Abstract] OR Respiratory hypersensitivity [Title/Abstract] OR airway inflammation [Title/Abstract] OR intermittent airway obstruction [Title/Abstract] OR Asthma-Chronic Obstructive [Title/Abstract] OR Pulmonary Disease Overlap Syndrome Asthma [Title/Abstract] OR Aspirin-Induced Asthma [Title/Abstract] OR Exercise-Induced Asthma [Title/Abstract] OR Status Asthmaticus [Title/Abstract])) AND ((Adherence [Title/Abstract] OR nonadherence [TW] OR compliance [Title/Abstract] OR persistence [Title/Abstract] OR concordance [TW] OR consistency [Title/Abstract] OR consistent [Title/Abstract]))) AND ((m-Health [Title/Abstract] OR "mobile health" [Title/Abstract] OR "cell phone" [Title/Abstract] OR "smart phone" [TW] OR "text message" [Title/Abstract] OR SMS[Title/Abstract] OR "short messaging service" [Title/Abstract] OR "mobile application" [Title/Abstract] OR apps [Title/Abstract] OR application [Title/Abstract]))

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