



Review article

Impact of eHealth on medication adherence among patients with asthma: A systematic review and meta-analysis

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ABSTRACT

Background: Asthma is an important public health issue in the United States. eHealth technology offers a potential solution to asthma treatment adherence, but the relative effect of various types of eHealth interventions has not been systematically studied.

Objectives: To systematically review the effectiveness of eHealth in improving adherence to inhaled corticosteroids (ICS) among patients with persistent asthma, as well as the satisfaction of patients undergoing eHealth interventions.

Methods: Literature searches were conducted in five databases in August 2018. Included studies were randomized controlled trials comparing eHealth interventions versus usual care in improving adherence among patients prescribed ICS for persistent asthma. Quantitative synthesis was performed using a random effects model.

Results: Eighty records were identified after removal of duplicates. Fifteen trials were eligible for qualitative synthesis. Included trials utilized: social media ($n = 1$), electronic health records ($n = 1$), telehealth ($n = 6$), and mHealth ($n = 7$). Twelve trials were eligible for quantitative synthesis. Results show a small but significant overall effect of eHealth interventions on adherence to ICS (Standardized Mean Difference (SMD) = 0.41, 95%CI = 0.02–0.79). Among the different types of eHealth interventions, a significant improvement in adherence was observed for mHealth interventions compared to usual care in a pooled analysis of 4 trials (SMD = 0.96, 95%CI = 0.28–1.64). However, there was considerable heterogeneity among studies. Patient satisfaction was evaluated in 5 trials comparing telehealth ($n = 2$) and mHealth ($n = 3$) with usual care. Participants found the interventions to be helpful and satisfactory.

Conclusion: eHealth interventions, especially mHealth interventions, are effective and acceptable in improving patient adherence to ICS.

1. Introduction

Asthma is a significant public health issue in the United States. As of 2016, asthma was prevalent in almost 8% of the entire population, with over 46% having experienced at least one asthma exacerbation within the past year [1]. In fact, although asthma-related mortality has decreased since the 1990's, the prevalence of asthma has continued to increase since 1980 [2]. The high prevalence of asthma alone leads to a significant burden on the healthcare system, with over \$80 billion in annual healthcare expenditures [3], 1.6 million asthma-related emergency department visits in 2013, and 10.5 million visits to primary care providers in 2012 [4]. The social impact of this disease is significant as well, often leading to missed school and work days [2]. This burden is greater among certain populations who are disproportionately affected

by asthma, including children, women, African Americans, and those with lower household income [2]. Methods to decrease the financial and social burdens of asthma, including improving adherence to asthma medications, thus become vitally important.

Treatment adherence is generally low among patients with asthma [5]. In fact, some studies show that adherence is less than 50% in children [6] and as low as 30% in adults [5,7–9]. This low adherence may be due in part to misinformation or confusion regarding complicated treatment regimens [5,10]. Treatment for persistent asthma generally involves a short-acting inhaled bronchodilator (such as albuterol) to ameliorate symptoms during acute exacerbations, plus a daily maintenance medication including an inhaled corticosteroid (ICS) [5]. The twice-daily dosing of many ICS treatments may pose a burden to some patients who struggle to remember to take their medications

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[5,8]. Additional barriers such as high prescription cost, taste of medication, and uncertainty about the safety of inhaled corticosteroids may contribute to poor adherence to inhaled asthma medications [8,11]. Poor medication adherence is concerning, since it is shown to increase risk of asthma exacerbations [5], leading to higher mortality [12], greater financial burden for the patient and health system [13], as well as decreased quality of life [5,14]. Indeed, non-adherence costs the US approximately \$300 billion in healthcare expenditures each year [13]. Thus, strategies to overcome barriers to inhaled asthma medication adherence are critical.

New eHealth technologies offer potential solutions for improving adherence to inhaled asthma medications. The World Health Organization (WHO) broadly defines eHealth as the use of information and communication technologies (ICT) for health, including patient treatment, research, education of healthcare professionals, and public health monitoring [15]. A variety of technological domains fall under this “eHealth” umbrella, most notably: 1) mHealth, exemplified by clinical interventions supported by mobile devices; 2) telehealth, which often entails the use of telephonic or electronic technology to facilitate long-distance healthcare or education; 3) social media, often incorporating an interactive web-based platform; and 4) use of electronic health records (EHRs) to inform patient care [15–19]. Studies show that eHealth interventions are cost-effective for patients and providers, and improve patient outcomes, medication use, access to care, and quality of life [20–26]. For example, one meta-analysis found that electronic reminders may increase patient adherence to ICS by as much as 19% [27]. Additionally, interventions using interactive voice response (IVR) technology [28] and provider notifications via EHR [29] showed 32% and 35.7% increases in patient adherence to ICS, respectively. However, with such a broad range of eHealth technologies available, it is unclear which type of intervention is most effective in promoting behavior change, specifically medication adherence. Existing reviews focus on subsets of eHealth interventions versus usual care [30,31], while the effectiveness of eHealth in its entirety has not been systematically evaluated. Furthermore, little research exists exploring patient preferences for type of eHealth intervention. Limited evidence suggests that patients prefer “push” reminders and methods that provide personalized feedback [32]. Additional information on the usefulness and acceptability of particular eHealth interventions is needed to aid the translation of ICT and eHealth technologies into clinical practice and potentially improve health outcomes for patients. Therefore, the purpose of this study was to: 1) assess the overall effectiveness of eHealth interventions on patient adherence to ICS; 2) assess and categorize the types of eHealth technology in use; and 3) evaluate the satisfaction of patients using eHealth tools.

2. Materials and methods

We conducted a systematic review and meta-analysis in order to characterize the types of eHealth interventions most commonly found in the literature, as well their relative effectiveness on patient adherence to inhaled corticosteroids. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline was utilized [33].

2.1. Data sources and search strategy

Literature searches were conducted in PubMed, CINAHL, Academic Search Premier, PsycINFO, and the International Pharmaceutical Abstracts (IPA) databases from each database inception until August 28, 2018. Additional articles were identified by hand-searching the reference list of included studies and from clinicaltrials.gov. A comprehensive search strategy was developed with the guidance of a librarian specializing in pharmacy and medicine at the primary author's institution (Table 1). All study citations were exported to reference management software for identification of duplicates and screening

according to the PRISMA guideline.

2.2. Eligibility criteria

Studies were eligible for inclusion if they utilized eHealth interventions such as smartphone applications, text messaging, pagers or web technologies to promote adherence to inhaled corticosteroids among patients with asthma. The World Health Organization (WHO) definition of eHealth, “*The use of information and communication technology for health*” was used in determining whether an intervention utilized eHealth or not [34]. Adherence was defined as the extent to which a person's medication taking behavior corresponds with agreed upon recommendations from a health care provider [35]. Only randomized clinical trials (RCTs) were eligible for inclusion. Unpublished studies reported at clinicaltrials.gov were also eligible for inclusion to prevent publication bias. Studies were excluded if the content was not written in English or medication adherence was not the primary outcome.

2.3. Study selection

Two independent reviewers (RJ and LH) screened study titles, abstracts, and full text while applying pre-defined inclusion and exclusion criteria. Fig. 1 shows how potential studies were added or excluded from qualitative synthesis. Studies that reported mean adherence to ICS as well as the corresponding standard deviation for the treatment and control groups were included in the quantitative synthesis. RJ and LH reviewed all excluded items to determine whether they met the criteria for exclusion. Disagreements were resolved via discourse and consensus.

2.4. Data extraction

A semi-structured form for data extraction was developed consisting of the following fields— authors, year of publication, setting, country, participant age range, sample size, experimental arm versus control arm, study duration, study intervention, medication adherence measurement, and results. For quantitative analysis, the mean adherence, standard deviation, and number of study participants were also extracted. Emails were sent to authors to obtain additional information such as mean adherence and standard deviations whenever needed.

2.5. Quality assessment

The risk of bias in each study was analyzed using the Cochrane collaborations' risk of bias assessment tool [36]. All the included studies were assessed for risk of bias by two independent reviewers. A consensus meeting was then held to resolve discrepancies and to arrive at a final risk of bias assessment summary (Fig. 2). Based on consensus between the two reviewers, studies were rated as “unclear” for other potential sources of bias if self-report was utilized in measuring adherence. Allocation concealment was also rated as “unclear” if there were uncertainties regarding the use of opaque envelopes.

2.6. Meta-analysis

Meta-analyses were performed using the Review Manager Software 5.3 Copenhagen (The Nordic Cochrane Center, the Cochrane Collaboration, 2014) for a comparison of eHealth interventions versus usual care or control. Standardized mean difference (SMD) was chosen as the summary statistic because of the variation in adherence 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 [37]. The post intervention mean adherence was used rather than change in adherence scores because the latter was not

Table 1
Search strategy.

No.	Concept	Strategy
1	eHealth	"telemedicine" [mesh] OR telemedicine [tiab] OR telemonitoring [tiab] OR mhealth [tiab] OR ehealth[tiab] OR "m health" [tiab] OR "mobile health" [tiab] OR smartphone[tiab] OR "smart phone" [tiab] OR "smartphone" [mesh] OR "Cell phones" [tiab] OR "Cell phones" [mesh] OR "phone based" [tiab] OR "mobile based" [tiab] OR "phone app" [tiab] OR "mobile app" [tiab] OR "smartphone app" [tiab] OR "Mobile Applications" [Mesh] OR "Mobile Applications"[tiab]
2	Medication Adherence	"Medication adherence" [mesh] OR "Medication adherence" [tiab] OR ("Patient Compliance" [mesh] AND (Drugs OR medication)) OR "Drug Adherence" [tiab] OR "Drug Persistence" [tiab] OR "Medication Persistence" [tiab] OR "Medication nonadherence" [tiab] OR "Medication Noncompliance" [tiab]
3	Asthma	("Asthma"[Mesh]) OR "Asthma*" [tiab]
4	1, 2 and 3	

available in majority of the studies [38]. A positive value of SMD indicates a more favorable outcome for the treatment group compared to the control. Standard errors were converted to standard deviation by multiplying with the square root of sample size in cases where the authors reported standard errors. In cases where neither standard deviation nor standard error was reported and the authors did not respond to email requests, values were imputed from similar studies as recommended by existing evidence [39]. 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 eHealth intervention, 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. Sensitivity

analyses to detect the effects of targeting physicians versus patients and of including a study conducted in a pediatric setting were performed. A random effects model was used to pull the results from eligible studies. 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 and characteristics

A comprehensive search of the literature yielded 89 records after duplicates were removed. After screening titles and abstracts, 25 records were eligible for full text review. Of these, 15 published articles were eligible for inclusion in the qualitative synthesis (Table 2). The

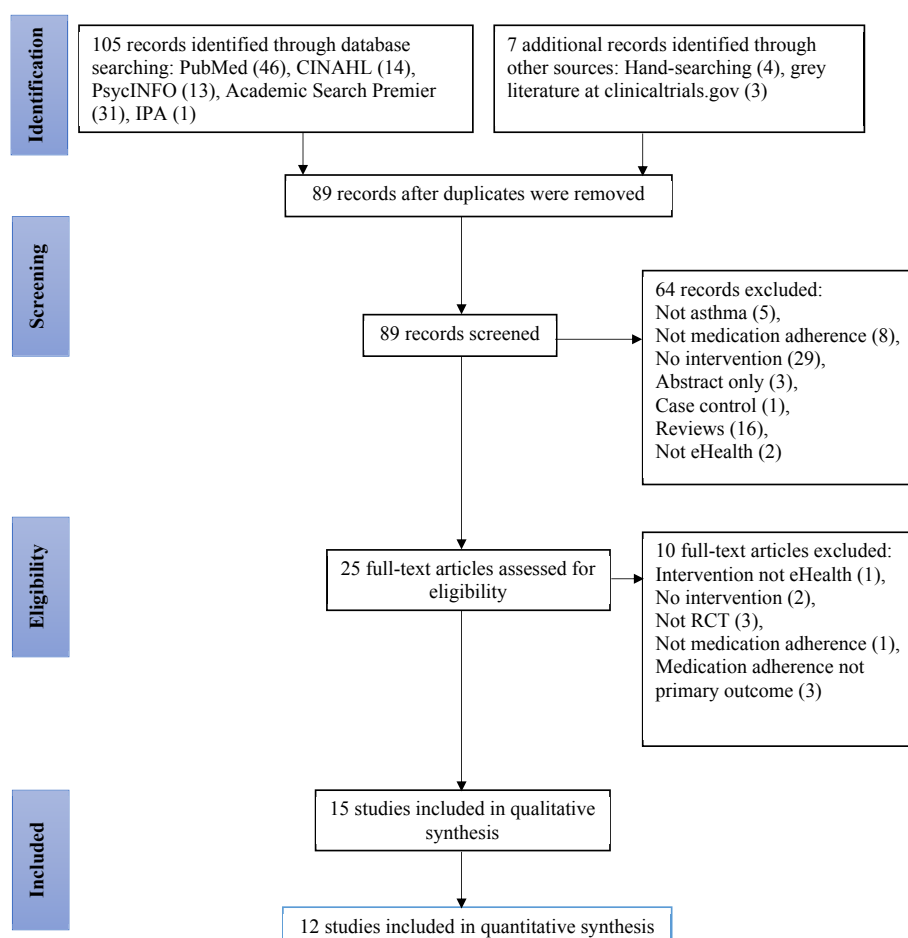


Fig. 1. Study Identification and Selection Process. Flow of information through the different stages of the systematic review and meta-analysis according to PRISMA guidelines.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Bender 2010	+	+	+	?	+	+	+
Bender 2015	?	?	+	?	+	+	+
Chan 2015	?	+	+	+	+	+	?
Charles 2007	+	?	+	+	+	+	?
Chatkin 2006	?	?	?	+	+	+	+
Chen 2010	?	?	+	?	?	+	?
Gustafson 2012	+	?	+	+	+	+	+
Johnson 2016	?	?	+	?	+	+	?
Kolmodin 2016	+	?	+	?	+	+	?
Koufopoulos 2016	+	+	?	?	+	+	?
Petrie 2012	+	?	?	?	+	?	+
Strandbygaard 2010	+	?	?	?	?	+	+
Vollmer 2011	?	?	+	+	+	+	+
Williams 2010	?	?	+	+	+	?	+
Young 2012	?	+	+	?	?	+	?
? Unclear risk, + Low risk, - High risk							

Fig. 2. Risk of Bias of Included Studies. “Other bias” included method of medication adherence measurement. (Print color). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

study selection process is outlined in Fig. 1. The included studies provided 15 e-health treatment vs. control comparisons, with a total of 13,907 participants. One study was conducted in Brazil, an upper middle-income country while the remaining 14 studies were conducted in developed countries including the US, UK, Denmark, New Zealand, and Taiwan. Sample size varied from 26 to 8,517, while participants' ages ranged from 3 to 65 years. Overall, studies utilized four categories of eHealth interventions to promote adherence to ICS: 1) social media (n = 1); 2) electronic health records (n = 1); 3) mHealth (n = 6); and

3) telehealth (n = 7).

Of the 15 studies included in the qualitative synthesis, 12 studies were quantitatively analyzed. Of the three excluded studies, one study did not report the mean adherence and standard deviation of the intervention and control groups post intervention [19]. Another reported only the difference in proportion of adherent individuals as a result of the intervention [18]. The last excluded study utilized both a dichotomous measure of adherence (yes/no) and ecological momentary assessment requested only at baseline and at the endpoint [40]. Regarding studies included in the quantitative synthesis, adherence to ICS was measured via electronic monitoring in four of these studies [16,41–43], pharmacy refill data in three studies [17,29,44], and self-report in four studies [45–48]. One trial used both pharmacy refill data and self-report [49]. In terms of types of eHealth interventions, five studies included in the quantitative analysis utilized mHealth, five used telehealth, one used EHR technology, and one used social media. There was a high level of agreement of 75.5%, between authors evaluating the quality of included studies.

3.2. Risk of bias

A total of seven studies were judged to be at high risk of bias in at least one domain (Fig. 2). Reporting bias, attrition bias, and performance bias were low in more than half of the included studies (Fig. 3). However, it was largely unclear whether selection and detection bias may have impacted the results in more than half of the studies. This was due to insufficient information about allocation concealment and random sequence generation.

3.3. Efficacy of eHealth interventions

The following sections present the efficacy of eHealth interventions both qualitatively and quantitatively, where applicable. First the efficacy of eHealth interventions overall (an aggregate of all intervention types) compared to control is examined. Then, eHealth is broken down into 4 categories or types and the efficacy of mHealth, telehealth, EHR, and social media interventions are analyzed specifically.

3.4. eHealth interventions overall

The comparison of eHealth interventions (all categories) across all measures of adherence versus control yielded a small but significant effect (SMD = 0.41, 95%CI = 0.02–0.79) (Fig. 4). Heterogeneity between the studies was high ($I^2 = 98\%$) and the subgroup difference was significant ($\chi^2 = 8.46$, $df = 2$, $p = 0.01$). The result of the subgroup analysis (based on type of adherence measure) indicated that the overall effect of eHealth was significant in studies utilizing electronic monitoring (SMD = 1.19, 95%CI = 0.49–1.89) in adherence measurement but insignificant in those utilizing pharmacy refill data (SMD = -0.13, 95%CI = -0.70 – 0.44) and self-report (SMD = 0.25, 95%CI = -0.10 – 0.60). Despite having a significant improvement in adherence, heterogeneity was high in the group of studies utilizing electronic monitoring ($\chi^2 = 23.65$, $df = 3$, $p < 0.001$, $I^2 = 87\%$). We conducted a sensitivity analysis by removing a study which was conducted in a pediatric setting [41]. The studies became homogeneous ($\chi^2 = 0.39$, $df = 2$, $p = 0.82$, $I^2 = 0\%$), and the effect size decreased from SMD = 1.19 (95%CI = 0.49–1.89) to SMD = 0.91 (95%CI = 0.58–1.23).

Another sensitivity analysis removing a study with an intervention targeted at physicians rather than patients (Williams 2010) impacted the overall effect of eHealth interventions and heterogeneity. The effect size increased from SMD = 0.41 (95%CI = 0.02–0.79) to SMD = 0.52 (95%CI = 0.22–0.83) while heterogeneity decreased ($I^2 = 98\%$ to $I^2 = 95\%$). The pharmacy refill data subgroup in which this study was categorized was also impacted. Effect size of pharmacy refill interventions increased from SMD = -0.13 (95%CI = -0.70 – 0.44) to

Table 2
Summary of study characteristics.

Author (year)	eHealth Category	Setting, Country	Population	Duration	Trial vs Control Arm	Medication Adherence Measurement	Results
Bender et al. (2010) ^a [16]	Telehealth	Tertiary care center, USA	Ages: 18–65, Sample size: 50.	10 weeks	Interactive voice response (IVR) calls vs usual care	Electronic monitoring (One of Metered-Dose Inhaler Log, Doser-Clinical Trials Version, or Diskus Adherence Monitor) Pharmacy refill	IVR intervention improved adherence by 32%. IVR arm: 64.5%. Control arm: 49.1% ($p = 0.003$). SR intervention improved adherence by 25.4%. SR arm: 44.5%. Control arm: 35.5% ($p < 0.001$). AVR intervention improved adherence. AVR arm: 84%. Control arm: 30%. There was a significant difference between the adherence rate in the treatment group compared to the control ($p < 0.001$).
Bender et al. (2015) ^a [44]	Telehealth	Multiple settings including 18 primary care and 2 specialty care, USA	Ages: 3–12, Sample size: 1,187.	24 months	Computerized speech recognition (SR) vs usual care		
Chan et al. (2015) ^a [41]	mHealth	Emergency care, New Zealand	Ages: 6–15, Sample size: 220.	6 months	Audiovisual reminders (AVR) vs usual care	Electronic monitoring (SmartInhaler Tracker; Nexus6)	
Charkin et al. (2006) ^a [18]	Telehealth	Multiple settings, Brazil	Ages: 12 or older, Sample size: 271.	3 months	Telephone calls vs usual care	Electronic monitoring (Diskus dose recordings)	
Charles et al. (2007) ^a [43]	mHealth	Clinical trial facility, New Zealand.	Ages: 12–65, Sample size: 110.	6 months	Audiovisual reminders (AVR) vs usual care	Electronic monitoring (SmartInhaler monitoring device)	AVR intervention improved adherence by 18%. AVR arm: 88%. Control arm: 66% ($p < 0.0001$). There were significant improvements in adherence between the treatment and control groups ($p = 0.008$).
Chen et al. (2010) ^a [45]	Telehealth	Chest Clinic, Taiwan	Ages: 20 and older, Sample size: 60.	10 months	DVD plus self-efficacy booklet and support group vs usual care	Self-report	
Gustafson et al. (2012) ^a [49]	Telehealth	Asthma clinics, USA	Ages: 4–12, Sample size: 301.	12 months	Phone-based plus web-based health education (eHealth) vs usual care	Pharmacy refill, self-report	There was no significant difference between treatment and control groups.
Johnson et al. (2016) ^a [46]	mHealth	Pediatric outpatient setting, USA	Ages: 12–17, Sample size: 89.	3 weeks	Personal health application vs usual care	Self-report	There were improvements in adherence between the treatment and control groups ($p = 0.016$).
Kolmodin et al. (2016) [40]	mHealth	Outpatient setting, USA	Ages: 18–29, Sample size: 49.	3 months	A computerized intervention authoring software (CIAS) with motivational interviewing vs control	Self-report	There was no significant improvement in adherence between the treatment and control groups ($p = 0.9$).
Koufopoulos et al. (2016) ^a [47]	Social Media	Outpatient care, UK	Ages: 18 and older, Sample size: 103.	9 weeks	Online community vs usual care	Self-report	There was no significant improvement between the treatment and control groups ($p = 0.92$).
Petrie et al. (2012) ^a [48]	mHealth	Outpatient setting, New Zealand	Ages: 16–45, Sample size: 216.	9 months	Text message group vs usual care	Self-report	There was a significant improvement between the treatment (43.2%) and control groups (57.8%) at $p = 0.003$.
Strandbygaard et al. (2010) ^a [42]	mHealth	Outpatient setting, Denmark	Ages: 18–45, Sample size: 26.	12 weeks	Text message vs usual care	Electronic monitoring (Diskus dose recordings)	There was a significant improvement between the treatment (95%) and control groups (17.8%) at $p = 0.019$.
Vollmer et al. (2011) ^a [17]	Telehealth	Health maintenance organization, USA	Ages: 18 and older, Sample size: 8,517.	18 months	Interactive voice recognition (IVR) vs usual care	Pharmacy refill	There was a significant improvement between treatment and control groups (change = 0.02).
Williams et al. (2010) ^a [50]	EHR	Primary care settings, USA	Ages: 5–56, Sample size: 2,698.	12 months	Patient medication adherence feedback vs no feedback	Pharmacy refill	There was no significant improvement between the treatment (21.3%) and control group (23.3%) at $p = 0.553$.
Young et al. (2012) [19]	Telehealth	Outpatient setting, USA	Ages: 19 and older, Sample size: 98.	3 months	Telepharmacy vs usual care	Self-report	There was no significant difference between intervention and control groups ($p = 0.07$).

^a Included in quantitative synthesis.

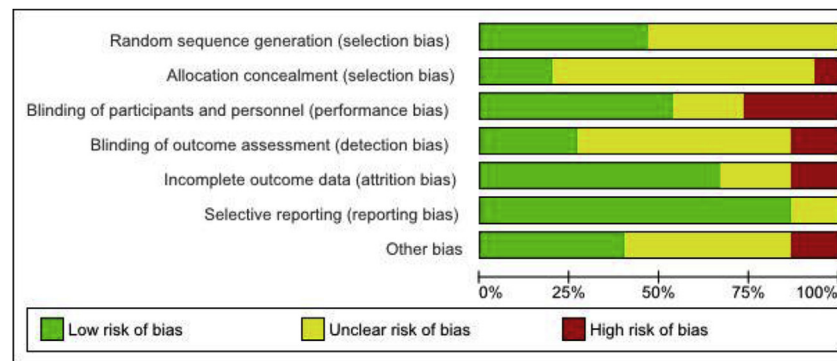


Fig. 3. Risk of Bias of Included Studies Presented as Percentages. “Other bias” included method of medication adherence measurement. (Print color). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

SMD = 0.13 (95%CI = -0.11 – 0.36) but remained statistically insignificant. Heterogeneity among studies decreased by 9% but still remained high ($I^2 = 90\%$).

3.5. mHealth interventions

3.5.1. Qualitative synthesis

Studies categorized as using mHealth interventions were 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 [15]. The six mHealth studies that were qualitatively evaluated in this review employed text messages, either primarily [42,48] or as an adjunct reminder [40,46], and audiovisual reminders [41,43]. Of the two studies primarily assessing the effect of text messages on adherence to ICS, one delivered tailored text messages based on individuals' illness and medication beliefs while the other delivered untailored messages. The frequencies of texting were daily

versus three text messages per week, respectively. Among the studies utilizing text messages as an adjunct reminder, one employed a personal health application that enabled users to set up text message reminders while the other utilized motivational interviewing strategies via two computer sessions before following up with text message reminders. Three mHealth studies assessed adherence via electronic monitoring while the other three used self-report. In five of the six studies, adherence rates improved significantly post-intervention.

3.5.2. Quantitative synthesis

Five 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 ICS (SMD = 0.96, 95%CI = 0.28–1.64) across mHealth studies utilizing electronic monitoring and self-reports 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 ($\chi^2 = 2.61$, $df = 1$, $p = 0.11$). Indeed, subgroup analysis of mHealth studies found

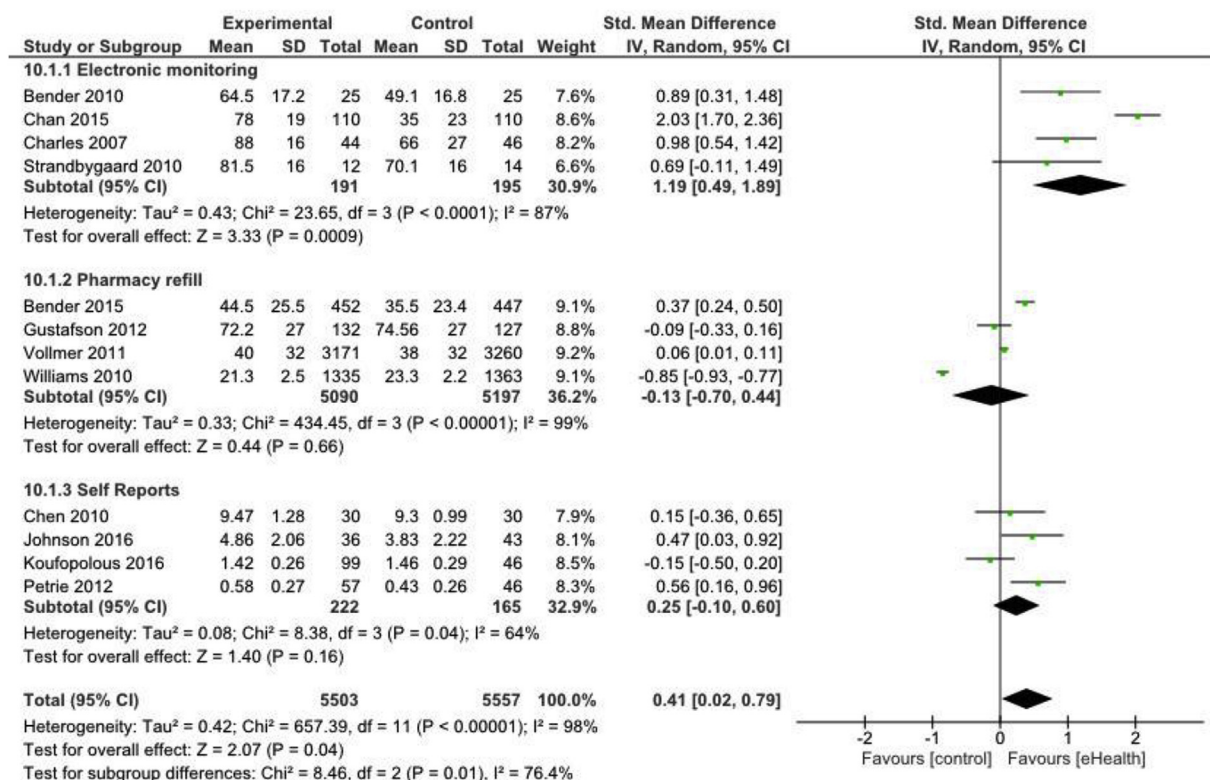


Fig. 4. eHealth Interventions Overall. A forest plot of eHealth interventions versus control for adherence to ICS.*.

*SMD between 0.3 and 0.5 is considered to be a clinically important difference.

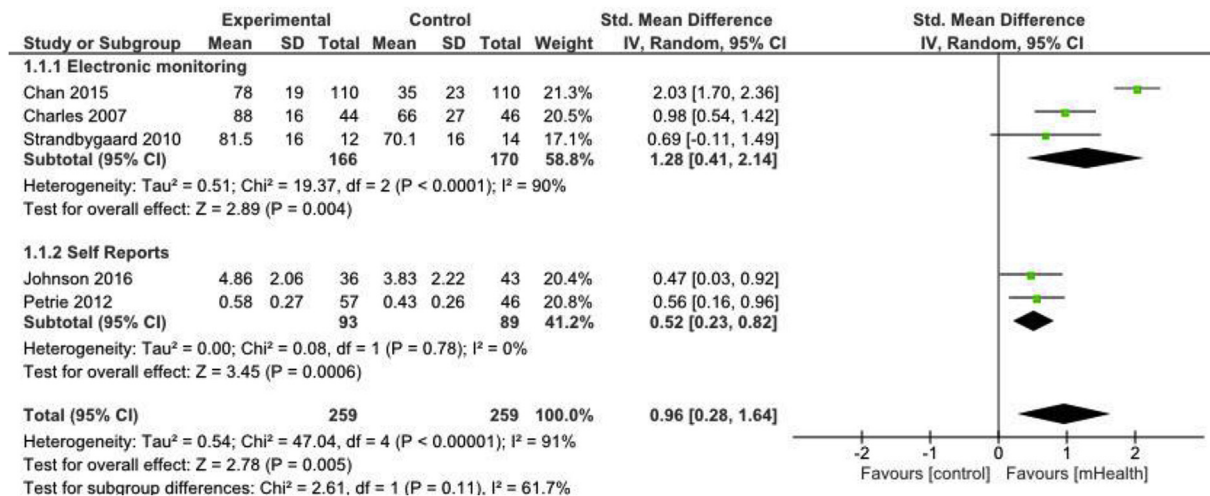


Fig. 5. mHealth Interventions. A forest plot of mHealth interventions versus control for adherence to ICS.*.

*SMD between 0.3 and 0.5 is considered to be a clinically important difference.

significant improvements in adherence both in the group of studies utilizing electronic monitoring (SMD = 1.28, 95%CI = 0.41–2.14) and those utilizing self-reports (SMD = 0.52, 95%CI = 0.23–0.82). No mHealth study utilized pharmacy refill data as a measure of adherence. The electronic monitoring sub-group was heterogenous ($I^2 = 90\%$), while the self-report sub-group appeared to be homogenous ($I^2 = 0\%$).

3.6. Telehealth interventions

3.6.1. Qualitative synthesis

Telehealth interventions were those utilizing technology to support long-distance clinical healthcare, patient and professional health education, public health, or health administration [15]. Of the seven studies included in the qualitative analysis for this category, interactive voice response (IVR) calls were employed as refill reminders in two studies [16,17] while speech recognition was used for the same purpose in another study [44]. Two studies utilized telephone calls by health professionals as parts of their intervention – a trained nurse made bi-weekly telephone calls to provide asthma education with emphasis on treatment adherence in one study while monthly telephone consultations were made by trained pharmacists in another study [18,19]. Furthermore, one study exposed participants in the treatment group to a multimedia intervention involving self-efficacy promotion followed by individual follow up via telephone calls [45]. Gustafson et al. used an online interactive information program for caregivers combined with monthly case management phone calls by nurses [49]. Of the seven telehealth studies, two studies did not find any significant difference in the medication adherence level between the treatment and usual care groups post-intervention.

3.6.2. Quantitative synthesis

Five studies employing telehealth interventions were included in the quantitative synthesis. Three out of the five studies measured adherence to ICS using pharmacy refill data, one utilized self-report while one used electronic monitoring. A pooled analysis of these studies found a small and insignificant effect on adherence to ICS (SMD = 0.20, 95%CI = -0.02 – 0.43) when compared to control (Fig. 6).

3.7. EHR interventions

One study was categorized as an EHR intervention based on the use of EHR technology to provide real-time, patient adherence information to physicians in the treatment group [50]. The feedback was intended to enable discussions with patients by physicians during visits. There

was no difference in adherence rate between the treatment and usual care groups. A separate meta-analysis was not conducted for the EHR intervention due to the availability of only one study eligible for inclusion in the review.

3.8. Social media interventions

One study was categorized as a social media intervention and employed web technology to create an interactive platform through which individuals could share or discuss user-generated content [47]. Joining this online community did not improve adherence to ICS. A separate meta-analysis could not be conducted as a result of having only one study in the social media category.

3.9. Patient satisfaction

Patient satisfaction was measured in only five of fifteen reviewed studies. Of those five studies, two utilized mHealth interventions. One of the mHealth studies assessed the effect of daily text reminders on adherence [42]. Participants were satisfied with the daily text reminders but found the timing (10am) unsuitable. In another mHealth study, real-time data on adherence and asthma symptoms was used in personalizing an intervention that included daily text message reminders [40]. Participants rated the program highly in overall satisfaction (mean rating = 3.6 out of 4 possible points, from 1 = poor to 4 = excellent) and helpfulness (3.7 out of 4 possible points).

The remaining three studies assessed patients' satisfaction with different kinds of telehealth interventions. In the study conducted by Young et al., 80% of the participants were satisfied with the program and did not have a desire to modify the telepharmacy intervention [19]. Of the 56% participants providing feedback on the interactive voice response (IVR) call intervention by Vollmer et al., half indicated that the program was helpful and should be continued while one-third believed that their asthma was better controlled as a result of the intervention [17]. Bender et al. compared IVR with usual care and more than 90% of participants found the intervention helpful [17]. In all, participants were satisfied with eHealth interventions.

4. Discussion

This study is the first to report the effect of various types of eHealth interventions on adherence to inhaled corticosteroids among patients. Our findings indicate that eHealth interventions in general are effective in improving adherence to ICS. A recent Cochrane review of electronic

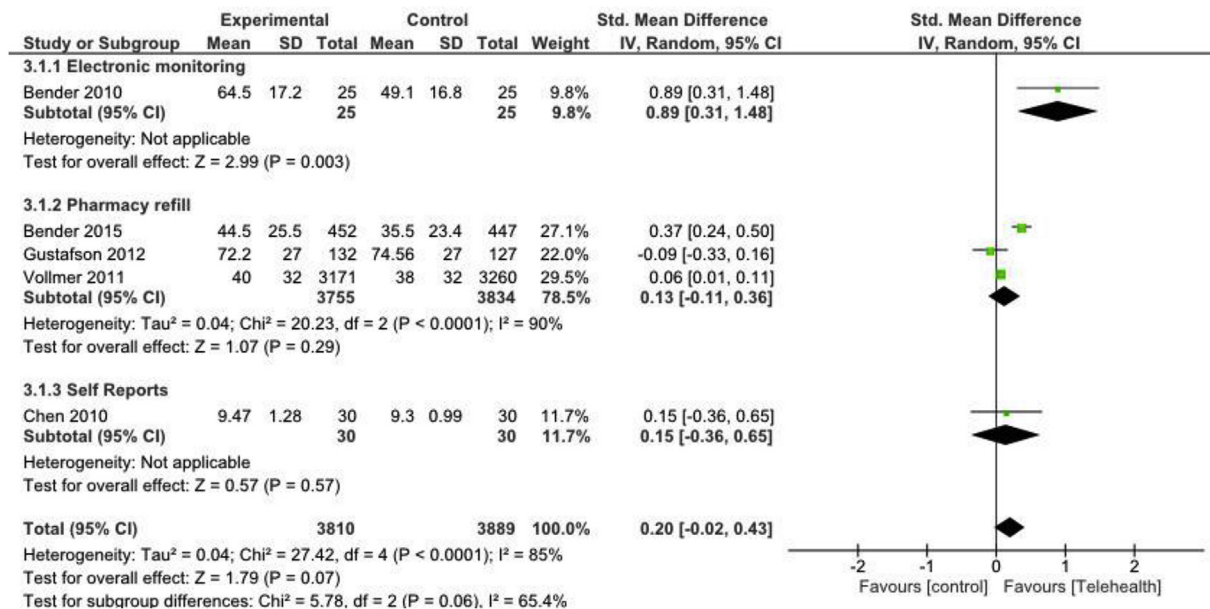


Fig. 6. Telehealth Interventions. A forest plot of telehealth interventions versus control for ICS adherence.*.

*SMD between 0.3 and 0.5 is considered to be a clinically important difference.

reminders, a type of eHealth-based intervention also found positive results in terms of improvement in adherence [51]. Similarly, a previous systematic review on reminder systems, of which all were information technology-based, suggested that reminders are effective in improving adherence to inhaled corticosteroids [31]. The moderate effect that was found for eHealth interventions in the current study is similar to the findings by a recent meta-analysis of mobile technology interventions for asthma self-management [30]. Furthermore, our findings showed that the approach employed in measuring adherence impacted the effect obtained by the intervention. For instance, studies utilizing electronic monitoring devices had an overall effect size of 1.19 while self-reports had an overall effect size of 0.25. Evidence suggests that a standardized mean difference, of 0.3–0.5 is a minimal clinically important difference [52]. Interestingly, the overall effect obtained when electronic adherence monitoring was used was more than two-fold the overall effect obtained from pooling studies of all the different categories of adherence measures. The effect size in the eHealth self-report subgroup indicated a minor effect of the intervention but was not statistically significant. This may have been due to the different types of self-report measures employed by studies in this report, which ranged from established validated instruments like the simplified adherence medication questionnaire to single items in a questionnaire and phone calls. Unlike the electronic monitoring and self-report subgroups, the pooled estimate for the pharmacy refill data subgroup was in favor of control rather than eHealth interventions. A potential reason for this observation is the inclusion of an intervention aimed at the physician rather than the patients. A sensitivity analysis that involved removal of this study caused the overall point estimate of the pharmacy refill subgroup to lie in favor of the treatment group.

Among the different types of eHealth interventions, our results indicate that mHealth interventions are effective in improving adherence to ICS compared to usual care. Contrary to findings by Miller et al., mHealth interventions exhibited a large overall effect on adherence [30]. In their study, mHealth interventions had a moderate positive effect on medication adherence compared to standard treatment. Looking at the different methods of adherence measurement, studies utilizing self-report had a moderate effect on adherence while those utilizing electronic monitoring obtained a large effect. A possible explanation for the difference in effect sizes is the fact that electronic monitoring is a more objective measure of adherence. Slight disparities

in effect sizes based on method of adherence measurement is not new and have been previously reported by a meta-analysis investigating the effect of self-monitoring of blood pressure on adherence to anti-hypertensives [53]. Regarding studies using telehealth interventions, the effect size indicated a treatment effect compared to control, but was not statistically significant. However, our narrative review of telehealth interventions found five reports of significant effects of telehealth intervention over control. Furthermore, a previous meta-analysis on telemedicine delivered by pharmacists found significant effects on adherence [54]. It is possible that the analysis in our study was not sufficiently powered to detect a significant effect of telehealth interventions, suggesting a need for more telehealth interventions to be conducted. Other subsets of eHealth such as EHR and social media had insufficient studies to be included in the meta-analysis.

Heterogeneity among studies found in this review are likely due to population and methodological differences such as differences in age of the target population, method of adherence measurement, and other sociodemographic differences in intervention recipients. For example, a sensitivity analysis that involved removal of a study conducted in a pediatric setting [41] caused included mHealth studies to become more homogeneous ($I^2 = 0\%$). Similarly, removal of a study utilizing an intervention directed at physicians [29] rather than patients reduced the heterogeneity among the pharmacy refill data subgroup in the analysis of eHealth versus control by 9%. Furthermore, variation of adherence measurement in this review may have contributed greatly to heterogeneity. For example, only one study utilizing self-report in adherence measurement used a validated instrument. Even at that, the validated tool was modified for the study. Also, others used un-validated items within a questionnaire or telephone calls to assess adherence.

We found that few of the studies included in this review examined patient satisfaction and preference for particular types of eHealth interventions. Among included studies, participants found mHealth interventions such as text message reminders acceptable; however, timing may need to be modified to suit the population at hand. Additionally, telehealth interventions such as phone calls by trained health professionals and interactive voice response calls are also acceptable and helpful to users. There is need for more studies to evaluate user satisfaction with eHealth interventions targeted at improving adherence to ICS.

This study is not without limitations. As discussed above, there was

considerable heterogeneity among studies that were quantitatively synthesized. Also, the adherence measurement scales contributing to the standardized mean difference (SMD) calculations may have introduced variation that could not be fully addressed in the meta-analysis. There were less than three studies in some of the subgroups in the analyses involving mHealth and telehealth studies versus control. Furthermore, there were insufficient studies in certain eHealth categories, such as social media and EHR, limiting generalizability. Additionally, free computers were provided to participants in one study, and free medications in two other studies – this may have motivated participants, introducing an element of selection bias. Lastly, a total of seven studies were judged to be of high risk of bias in at least one domain. Future studies should employ either objective methods of adherence measurement or validated self-report instruments.

5. Conclusion

The evidence from this review suggests that eHealth-based interventions are effective in improving adherence to ICS. This is especially true for mHealth studies, including audiovisual and text message reminders. Patients perceive telephone consultations by health professionals, interactive voice response calls, and text message reminders as acceptable and helpful. However, the timing of messages may need to be modified to suit the population at hand. These findings can be translated into future practice-based interventions in order to optimally improve patient adherence to ICS and ultimately improve health outcomes for patients with persistent asthma.

Declarations of interest

None.

Conflicts of interest

The authors have no conflict of interest to disclose.

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