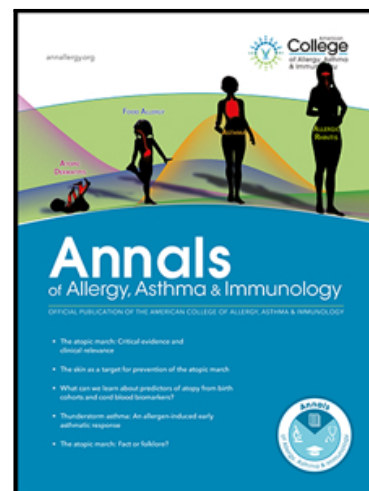


Accepted Manuscript

A Review of the Use and Effectiveness of Digital Health Technologies in Asthma Patients

Elizabeth Unni BSP Pharm, MBA, PhD , Susan Gabriel PhD ,
Rinat Ariely PhD

PII: S1081-1206(18)31314-0
DOI: <https://doi.org/10.1016/j.anai.2018.10.016>
Reference: ANAI 2727



To appear in: *Annals of Allergy, Asthma Immunology*

Received date: 17 August 2018
Revised date: 12 October 2018
Accepted date: 16 October 2018

Please cite this article as: Elizabeth Unni BSP Pharm, MBA, PhD , Susan Gabriel PhD ,
Rinat Ariely PhD , A Review of the Use and Effectiveness of Digital Health Technologies in Asthma
Patients, *Annals of Allergy, Asthma Immunology* (2018), doi: <https://doi.org/10.1016/j.anai.2018.10.016>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

A Review of the Use and Effectiveness of Digital Health Technologies in Asthma Patients**Short title/running head: Digital Health Technologies in Asthma Patients**

Elizabeth Unni, BSPHarm, MBA, PhD¹; Susan Gabriel, PhD^{2,a}; Rinat Ariely, PhD²

¹Roseman University of Health Sciences, South Jordan, UT; ²Global Health Economics and Outcomes Research, Teva Pharmaceuticals, Frazer, Pennsylvania, USA

^aCurrent affiliation: CSL Behring, King of Prussia, Pennsylvania, USA

Corresponding author: Rinat Ariely

Senior Director, Global HEOR, Respiratory

Teva Pharmaceuticals

41 Moores Rd

Frazer, PA, USA 19335

Tel: +1-610-727-6358

Fax: +1-610-727-6150

Rinat.Ariely@tevapharm.com

Conflict of Interest: None

Funding Source: Teva Pharmaceuticals

Clinical Trial Registration: Not applicable

Keywords (max 12): mHealth; eHealth; telemedicine; adherence; digital health technology

Abbreviations/Acronyms: AAP, asthma action plan; ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; C-ACT, Childhood Asthma Control Test; ED, emergency department; EMD, electronic monitoring device; DHT, digital health technologies; FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume exhaled in the first second; HRQoL, health-related quality of life; ICS, inhaled corticosteroids; NA, not available; NR, not recorded; PEF, peak expiratory flow; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta Analyses; QoL, quality of life; RCT, randomized controlled trial; SABA, short-acting beta-agonist; SD, standard deviation; SMAQ, self-reported preventer adherence; SPA, smart phone application; UK, United Kingdom; USA, United States of America.

Word count (max 4000 excluding acknowledgements): 3998

Figures: 1

Tables: 4

References (max 60): 60

Key Messages

- Despite the availability of proven treatment guidelines and effective therapies for asthma, poor adherence and the lack of guideline implementation remain barriers to asthma control
- Use of digital health technologies (DHT) is growing rapidly worldwide and is well-suited to improving medication adherence and symptom control for patients with asthma
- A wide range of DHT were evaluated and the majority were reported to have had at least some patient benefit

- DHT that included more interactive features or real-time feedback were associated with better outcomes, including increased asthma control

Introduction

Despite the availability of evidence-based treatment guidelines and effective therapies for asthma, poor adherence to treatment¹⁻⁵ and lack of guideline implementation into daily practice⁶ remain significant barriers to asthma control. Asthma management can be improved by providing information to the patient or caregiver to support adherence and verify correct dose intake, by relaying information to the clinician to facilitate timely therapeutic adjustment, and by allowing patient self-quantification. A new generation of multidimensional digital communication technologies that combine complementary features can be applied to clinical practice to improve these various aspects of patient care.

Telehealth or telemedicine, also referred to as eHealth, is defined as any medical activity involving an element of distance and the use of a telecommunications strategy.⁷ Digital health technologies (DHT) is a subcomponent of eHealth and refers to the use of mobile communication technologies to promote health by supporting healthcare practices, such as data collection, delivery of healthcare information, or patient observation and provision of care.⁸ Text messaging, or short message service, has been predominately used as a method to remind patients to take their medications and secondarily as a means to provide disease-related information,⁹ and is the most common technology tool used to increase medication adherence.¹⁰

Mobile applications or “apps” are software programs that run on personal mobile devices and offer functions such as disease tracking, access to clinical and peer support, health information, and reminders.¹¹ Mobile apps are currently the fastest growing form of DHT. The number of asthma-specific apps has more than doubled between 2011 and 2013 from 93 to 191; however, most apps provide patients with either basic information about asthma or simple diary functions. The proportion of apps that contain information consistent with national treatment guidelines and correct inhaler instructions is small.¹² For better asthma management and improved adherence to the therapy, personalized interventions and messages need to be delivered to patients. Interventions increasingly use more than 1 functionality, such as mobile apps that incorporate text messaging and social media and may fit well with the movement toward personalized and participatory respiratory medicine.¹³ Electronic monitoring devices (EMDs) were originally developed as an objective alternative to subjective patient reports of medication adherence. In asthma therapy, when EMDs are used in conjunction with inhalers, EMDs can capture a granular level of detail by recording usage and providing precise, personalized data to support medication adherence strategies.¹⁴ EMDs can also be connected to mobile devices and apps to provide adherence reminders and feedback and to transmit data to healthcare professionals.

A previous targeted literature review of DHT applied to the management of patients with different chronic diseases between 2003 and 2014 found that 40% used text messaging, 18% used mobile apps, 18% used a wireless device connected to a phone, and 13% used a specific instrument (such as a glucose monitor) connected to a phone.¹⁰ Early studies that examined the effectiveness of asthma-specific DHT have reported a positive effect of text messages sent directly to the patient at predetermined times.¹⁵⁻²⁰ A Cochrane review assessing the effect of mobile app-based asthma self-management interventions on asthma control was limited to

2 studies and reported mixed findings.²¹ An early randomized controlled trial (RCT) that investigated EMD-based reminder interventions in patients with asthma found that medication adherence was significantly improved in the reminder group compared with controls.²² The objective of this study was to conduct a targeted review of the recent literature to summarize the use of DHT and evaluate their impact on health outcomes in patients with asthma. For the purposes of this review, DHT was defined broadly to also include technologies that did not necessarily require a mobile device, such as web-based tools (eg, diaries, monitoring, patient portals, and educational resources), as well as reminders linked to medical and demographic information from patients' electronic health records.

Methods

This targeted review followed the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement for transparent and comprehensive reporting of methodology and results.²³ PubMed and Embase[®] were searched to identify articles published over the past 5 years (July 12, 2013, to July 12, 2017) using the following terms, as well as all associated Medical Subject Headings terms: (1) telemedicine, (2) mHealth, (3) mobile application, (4) smartphone, (5) mobile phone, (6) reminder system, (7) electronic monitoring, (8) internet, and (9) asthma. The complete search strategy for PubMed and Embase is provided in Appendix A.

Articles were included if they reported results from any DHT intervention, including RCTs and uncontrolled observational studies, were used in patients with asthma, and reported selected patient outcomes associated with the intervention (eg, medication

adherence, asthma control). Review articles, editorials, research commentaries, and letters to the editor were excluded a priori within the search criteria. Articles were excluded if they (a) were not written in English, (b) did not report quantitative results, or (c) did not focus primarily on patients with asthma.

Records identified through the PubMed and Embase searches were reviewed and judged for eligibility through 2 phases. In the first phase, the title and the abstract of each article were reviewed by 2 independent reviewers and any disagreements were resolved through discussion. Articles that clearly did not meet the inclusion criteria were excluded and full-text copies of the remaining articles were obtained. In the second phase, the same 2 independent reviewers reviewed each full-text version to determine if the content of the article met the inclusion criteria; those articles that did were retained and the data from each were extracted.

For each included study, data were extracted using a systematic extraction form. Data extracted included: (a) study location (country); (b) patient population (pediatrics and/or adult); (c) study design; (d) DHT used; and (e) key components of the DHT used. Data on several potential outcomes were also extracted and included: (a) medication adherence; (b) asthma control; (c) clinical lung function; (d) exacerbations; (e) healthcare utilization; (f) healthcare costs; and (g) adherence/compliance to intervention protocol.

Results

Literature Search Results

A total of 627 records were reviewed after removal of duplicates (**Figure 1**). Full-text copies for 43 articles were obtained and reviewed, of which 15 were excluded. The reasons for exclusion were no data reported for selected patient outcomes (n = 6), [did not include a](#) patient-based DHT intervention (n = 4), protocol only (n = 3), duplicate publication (n = 1), and lack of detail on the intervention (n = 1). The final analysis included extracted data from a total of 28 articles.

Details of the extracted studies are provided in **Table 1**. Of the 28 studies, 16 (57%) were conducted with pediatric patients with asthma (primarily younger than 18 years of age) and 12 (43%) with adult patient cohorts. Among the pediatric studies, 11 (69%) were RCTs and the remaining 5 (31%) were prospective observational studies. With regard to the DHT in the pediatric studies, 8 used interactive websites, 4 used EMDs, 3 used mobile apps, 2 used phone calls, 2 used text messaging, and a single study used prerecorded messages via MP3 players. Of the 12 studies that used adult samples, 9 (75%) were RCTs and 3 (25%) were prospective observational studies; 6 studies used interactive websites, 6 used mobile apps, 2 used EMDs, and a single study used text messaging. Of the 28 studies reviewed, 14 were conducted in the United States, 3 in the Netherlands, 3 in the United Kingdom (UK), 2 in Australia, 2 in Canada, and 1 study each in Ireland, New Zealand, South Korea, and Turkey.

There were 3 main technology platforms reported in these studies: EMDs, mobile apps, and websites. EMDs commonly included alarms or reminders to take medication and adherence monitoring. Features of mobile apps included personalized action plans, reminders, educational materials, and adherence tracking functions. Websites had diverse functionality, but most included an educational component (**Tables 2 and 3**).

Effectiveness of DHT

Pediatric Patients. Among the 16 studies that focused on children, the majority of interventions that utilized interactive websites reported at least some benefit (Table 2), although results varied based on the specific outcome and method of assessment.²⁴⁻³⁰ For example, a 1-year RCT of the website-based Puff City intervention was associated with significant reductions in asthma symptom days (≥ 2 days/week/30 days; adjusted odds ratios [aOR] = 0.5 [95% CI: 0.2 to 0.8]; $P = .006$), asthma symptom nights (≥ 3 nights; aOR = 0.6 [95% CI: 0.4 to 1.0]; $P = .074$), and restricted activity days (> 4 days; aOR = 0.5 [95% CI: 0.3 to 0.9]; $P = .010$) versus no intervention among 422 urban (Detroit) high school students aged 15–19 years.²⁷ In a 1-year RCT in 237 children aged 6–12 years from 20 medical practices in the United States, increases in medication changes/refills (14% [95% CI: 2% to 27%]) and asthma-related primary care visits (16% [95% CI: 3% to 28%]) were observed in the subset of 76 patients with uncontrolled asthma after parents used the portal compared with the same period the year prior.²⁵ In a 2-week RCT involving 98 children aged 12–17 years from academic outpatient settings in the United States, use of the MyMediHealth website versus usual care was associated with significant improvements in self-reported medication adherence (median data not shown; $P = .011$), quality of life (increase by a median of 5.7–6.3 on a 7-point scale; $P = .037$), and self-efficacy (perceived ability to prevent and manage asthma attacks³¹; increase by a median of 4.1–4.4, between “quite sure” and “completely sure” of self-efficacy in asthma management; $P = .016$).²⁶ In a 6-month RCT conducted at an inner-city (Boston) hospital, use of a website (BostonBreathes), versus usual care, by 58 children aged 7–17 years and

their parents was associated with improved adherence in the subgroup of 23 patients with low controller medication adherence (<75% adherence) at baseline (mean change in primary controller compliance: +29.8%; $P = .01$).³² Among 228 Dutch children aged 4–18 years in a 1-year RCT, use of a web-based diary was found to be valid for recording asthma symptoms given that the diary scores correlated strongly with Childhood Asthma Control Test (C-ACT) and Asthma Control Test (ACT) scores ($r = -0.73$; $P < .01$; and $r = -0.64$; $P < .01$, respectively).²⁸ Pre- and posttests showed increased asthma knowledge among 50 students aged 15–16 years in a secondary school in Ireland after completing 4 e-learning modules.³⁰ However, an economic analysis alongside another RCT found no effect on costs or quality-adjusted life years after web-based monitoring, versus standard care, in 272 children aged 4–18 years with allergic asthma in the Netherlands.²⁴

Interventions that incorporated EMDs reported mixed results with regard to medication adherence and asthma control.³³⁻³⁵ One RCT of EMD, comparing care with a feedback/alarm function versus usual care, showed decreased oral steroid use among 70 children aged 6–16 years in hospital clinics in Sheffield or Rotherham, UK, compared with an EMD with no feedback, over a 12-month period (average medication adherence was 70% for the intervention group vs 49% for the control group; $P \leq .001$).³³ In that UK study and another study in the regional emergency department (ED) in Auckland, New Zealand, among 220 children aged 6–15 years, EMDs did not demonstrate an improvement in forced expiratory volume exhaled in the first second (FEV₁).³⁴ In a 3-month observational prospective study among 14 children aged 3–16 years at an inner-city (Philadelphia) medical center, EMD use was found to be feasible and ACT scores significantly improved by a mean of 2.7 points ($P = .05$).³⁵

Of the 3 studies that used mobile apps,³⁶⁻³⁸ 2 reported a benefit in asthma control^{36,38} and this effect was particularly salient in children with uncontrolled asthma, whose median ACT scores significantly improved from 16 to 18 ($P = .03$).³⁶ However, another study using an app found no improvement in asthma control, measured by ACT and self-efficacy scores.³⁷ Improvements in inhaled corticosteroid (ICS) adherence from 19% to 50% (intent-to-treat)/67% (observed) and a reduction in the use of reliever short-acting beta-agonist (SABA) medications from a median of 13 to 0 puffs per week were observed in an 8-week observational study with 12 children aged 11–16 years diagnosed with persistent asthma and treated at a large US (Chicago) medical center.³⁸

The few studies that included phone calls and text messaging tended to combine these components with other technology.^{29,39,40} Phone calls alone were associated with an increase in medication adherence in a Health Maintenance Organization RCT study among children aged 3–12 years (ICS adherence 24-month mean: 44.5% for intervention vs 35.5% for usual care; $P < .001$).⁴⁰ ~~Whereas the use of recorded messages via MP3 players was not associated with medication adherence in an observational study at an urban (Chicago) medical center among children aged 11–16 years.³⁸~~ Text messages significantly improved medication adherence among adolescents in an RCT (an average gain of 1 day of adherence; median change from 4 to 6 days with intervention versus no median change in the control group [$P < .011$]); but, no effect on asthma control was observed.²⁶

Adult Patients. Among the studies that focused on adults, most interventions using interactive websites also reported some benefit (**Table 3**)⁴⁰⁻⁴⁵; although the results were generally less consistent compared with the pediatric studies. Website-based DHT for adults was associated with mixed results regarding medication adherence, with 1 study⁴⁰ showing improvement and 3 studies showing

no effect.⁴¹⁻⁴³ In a 6-month RCT in 143 adults with moderate-to-severe asthma, medication adherence was significantly higher in the intervention group using an EMD combined with a website than in the control group (73% vs 46% of prescribed daily doses; $P < .0001$).⁴⁰ The multidisciplinary intervention in that study was also associated with diminished asthma exacerbations (11% vs 28% of patients; $P = .013$).⁴⁰ Three studies found no effect of an interactive website on asthma control,^{40,41,42} whereas a single study found improved asthma control (ACQ adjusted between-group difference: -0.33 [95% CI: -0.61 to -0.05]).⁴⁴ Health-related quality of life (HRQoL) improved in 1 study (AQLQ adjusted between-group difference: 0.29 [95% CI: 0.01 to 0.57])⁴⁴; but no effect was found in another.⁴³ Improvements in clinical measures, such as FEV_1 ⁴⁴ and fractional exhaled nitric oxide,⁴³ were not found. A single study, which enrolled 34 adults from tertiary care asthma clinics in Toronto, Canada, reported an increase in asthma knowledge (significant improvement in scores on a brief work-related asthma questionnaire) following interaction with a web-based educational tool.⁴⁵ The inconsistent results among these studies may be attributed to differences in study methodology and design (eg, RCT vs observational study), as well as differences in enrolled patient populations.

The 5 studies that evaluated mobile apps⁴⁶⁻⁵⁰ in adult patients reported more consistent benefits in a range of outcomes. The outcomes most commonly found to improve were asthma control,^{46,48,50} HRQoL,^{47,48,50} and adherence.⁴⁷ Two of the 3 studies found no effect on clinical assessments of lung function.^{47,48}

The few adult interventions that included EMDs combined this technology with either an app⁵¹ or an interactive website.⁴⁰ One RCT that enrolled 495 adults in the United States and focused on a robust EMD reported a significant decrease in short-acting

medication use (change from baseline in mean daily SABA use per person: -0.51 for routine care vs -0.62 for intervention; $P = .004$) and improved asthma control in previously uncontrolled patients (change from baseline in percentage of patients with controlled asthma: $+49\%$ for routine care vs $+63\%$ for intervention; $P = .02$).⁵¹

Patient Adherence to and Perceptions of DHT

Data on patient adherence to the intervention protocol (measured via the EMD or logging into the websites) were reported in 14 of the 28 studies reviewed. Most of the studies in pediatric patients reported intervention completion rates above 80% (**Table 4**).^{26-29,38} Daily usage rates were also high in pediatric samples, with a median usage rate of 4.3 days per week³⁶ and response to 5.5 of 7 texts per day.²⁹ However, in adult patients, adherence rates were mixed, from only 37.8% of patients completing the intervention in 1 study⁴² to approximately 80% completion in 2 other studies.^{41,43} [In a year-long study,⁴¹ adherence to a web-based intervention dropped by approximately 20% after the first month and declined further in subsequent months to a low point of approximately 55% of participants using the intervention. E-mail and phone reminders appeared to boost intervention adherence to ~80% in the months they were used.⁴¹](#)

Table 4 also contains information pertaining to patients' and parents' (where applicable) attitudes toward or perception of the DHT intervention. Less than half (12/28) of the studies provided any data pertaining to the perceptions of, or attitudes toward, the

DHT intervention being used. Seven of the 16 pediatric studies reported patients' perceptions^{26,29,30,35,36,37,52} and 2 of those studies also reported parents' perceptions.^{35,52} Across all of these studies, satisfaction with the intervention and perceptions of effectiveness were high. Five studies in adults^{46,47,49-51} reported data pertaining to patients' perceptions of the DHT intervention. Like the pediatric studies, satisfaction with the intervention among adult patients was high and most patients indicated they would recommend the technology to a friend or family member.

Ninety percent of the parents believed a speech recognition technology to remind parents of medication refills and to provide treatment education would be efficacious and 84% believed the technology contributed to better asthma control in their children.⁵²

Discussion

The use of DHT technologies designed to improve healthcare behaviors by patients has increased rapidly in recent years. Additionally, there have been changes in the specific technology used, from an initial focus on simple text messaging to the more recent utilization of mobile apps for smartphones and other multidimensional web-based tools and biosensors (eg, EMDs). These DHT are well suited for asthma, a chronic disease where poor adherence to effective treatment and infrequent assessments may limit the effectiveness of treatment. In addition, novel DHT can help patients minimize errors of inhaler use by alerting them to the quality of their technique.⁵³

The majority of the asthma-focused DHT research in the past 5 years has been conducted with children and adolescents. The current review found differences in the type of DHT used with children compared with adults. Half of all studies used interactive websites and fewer than 1 in 5 pediatric studies and approximately half (5 out of 12) of adult studies used mobile apps. In addition, the majority of the pediatric studies took place in the United States; whereas, only one-quarter of the adult studies occurred in the United States, with 6 other countries represented. There did not seem to be any pattern between the type of DHT used and the study location.

In children and adolescents, the effectiveness of interventions that used websites varied based on the specific features of the websites and the outcomes assessed. More interactive features, such as daily diary entries, were generally associated with better outcomes, including improved asthma control; whereas, combining the use of website technology with text messaging capabilities also resulted in improvements in asthma symptoms, medication adherence, and clinical outcomes. Although few asthma-specific apps were evaluated within pediatric cohorts, 1 study, an observational feasibility study, reported that study participants experienced a significant decrease from baseline in controller medication dose while using an interactive app with gamification features that provided adolescents with immediate and long-term rewards each time they used their controller medication.⁵⁴ This approach is particularly noteworthy given that the patients were African-American adolescents scoring low in literacy who represent a highly vulnerable cohort.⁵⁴ [An important factor for DHT aimed at younger pediatric patients is that utilization or access to the technology may typically be mediated by a parent or other caregiver. For adolescents, who are increasingly users of smartphones and social media, smartphone-based technologies and gamification seem especially promising ways to encourage these patients to be motivated and empowered to self-manage their asthma.](#)

For adult patients, interventions that included patient access to websites reported less consistent benefits than for the pediatric studies; although these also varied based on the features of the websites and outcomes assessed. More interactive self-management features, such as asthma control monitoring and treatment advice, online and group education, or communication with providers, resulted in significant improvements in asthma control and patient-reported HRQoL; whereas, websites that focused on 1 specific goal (eg, online communities without provider feedback, asthma knowledge) tended to report less benefit on measures of medication adherence and asthma control. Interactive self-management tools improved asthma control in adults in 1 study.⁴⁴ Multidimensional approaches that combined a website with an EMD demonstrate improved medication adherence and decreased asthma exacerbations in 1 study⁴⁰ and decreased rescue medication use and improved asthma control in another study.⁵¹ Interventions that included mobile apps reported more consistent benefits across a range of outcomes than website-based interventions, likely due to the more interactive nature of the apps, which included prompts for patients to record their asthma symptoms, asthma medication adherence, individualized coaching, and real-time feedback based on their previous inputs. As new technologies are developed, interventions that record data automatically may further improve or sustain these benefits.

Only a single study reported data pertaining to the cost-effectiveness of an intervention, consistent with previous meta-analytic reviews.^{10,12,55-57} Most of the studies have had fairly small sample sizes, and the primary goal of most studies was to determine if the technology actually improved medication adherence. Cost-effectiveness studies may be facilitated by larger patient populations once the DHT has been adopted into clinical practice. Most of the reviewed studies included patients with persistent asthma or who were poorly controlled, so the benefits provided by DHT were clinically significant given the severity of their illness.

Fewer than half of the studies reported data pertaining to patient and caregiver perceptions of and beliefs in the efficacy of DHT. Where reported, patient and parent/caregiver satisfaction with and acceptance of DHT for asthma were generally found to be positive. Previous reviews and meta-analyses have found considerable evidence that patients have significantly positive experiences with technology designed to aid medication adherence.^{9,10,55,56}

Limitations With the Current Studies and Recommendations for Future Research

Several of the DHT approaches reviewed here incorporated these characteristics such being interactive, adaptive, and/or engaging, were age-appropriate, and were beneficial in pediatric populations. ~~DHT may be best suited for patients with more severe symptoms because these patients could potentially derive the greatest degree of benefit (versus patients with mild disease who may not notice significant changes in their disease status).~~ Although very few asthma-specific mobile apps were evaluated within pediatric cohorts, due to the interactive nature of the apps (eg, earning rewards), this technology deserves additional attention with adolescent patients.

The majority of the studies reviewed were RCTs (20 of 28 studies), which is a strength of this analysis. RCTs are effective in evaluating the benefits of DHT because these studies typically compare an intervention group (patients using DHT) with a control group (patients receiving usual care). In this review, the benefits of DHT approaches were observed in both RCTs (17 of 20 studies) and observational studies (8 of 8 studies). Future DHT should continue to use strong methodological approaches to minimize bias. For

example, cluster randomization trials, which randomize patient groups rather than individual patients, may be ~~the ideal study methodology~~ advantageous for evaluating healthcare improvement interventions; ~~although~~ Although these studies have certain limitations, such as decreased statistical power, they more closely approximate real-world implementation of such interventions and facilitate assessment of group-level outcomes.⁵⁸

The amount of follow-up time varied across studies from as little as 3 weeks to as much as 2 years; ideally, longer follow-up may help to assess the medium- to long-term benefits of the use of DHT and determine whether adherence to DHT is durable over time. When assessing children and adolescents, studies should also collect data from caregivers because they are typically involved with the administration of asthma medication.

Future studies should also include the use of objective assessments of medication adherence via EMDs, reliable and valid (though subjective) patient-reported outcomes, such as the ACT,^{59,60} and objective measures, such as rescue medication use and FEV₁, where possible. Few studies reviewed reported on healthcare utilization of patients during the follow-up period; these data would be helpful in linking technology directly with economic outcomes because only a single study examined the cost-effectiveness of DHT compared with standard of care. The cost-effectiveness of DHT can be evaluated in large patient populations once these approaches have been adopted into clinical practice.

Conclusions

The use of DHT is growing rapidly worldwide and is well-suited to improving medication adherence and symptom control for patients with asthma. This review of recent literature found that interactive websites and mobile apps have been the most frequently evaluated types of DHT in adult patient cohorts. The studies reviewed were heterogeneous; the majority of interventions reported at least some benefit, although results varied based on the specific outcome. Overall, technology that included more interactive features or real-time feedback were associated with better outcomes, including increased asthma control, as was the case for multidimensional interventions that combined the use of several complementary types of DHT.

Acknowledgments

The authors thank Jason Allaire of Generativity Solutions Group for conducting the literature search. This study was sponsored by Teva Pharmaceutical Industries Ltd. Medical writing and editorial support were provided by Mark Palangio and Michele Salernitano, respectively, of StemScientific (an Ashfield Company, part of UDG Healthcare plc), and was funded by Teva Pharmaceuticals Industries Ltd (Frazer, PA) for the preparation of this manuscript. Teva provided a full review of the article. The authors were fully responsible for all content and editorial decisions, and were involved at all stages of manuscript development.

Appendix A

The search strategy is as follows:

((((((("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "mhealth"[All Fields]) OR ("mobile applications"[MeSH Terms] OR ("mobile"[All Fields] AND "applications"[All Fields]) OR "mobile applications"[All Fields])) OR ("telemedicine"[MeSH Terms] OR "telemedicine"[All Fields] OR "telehealth"[All Fields])) OR ("smartphone"[MeSH Terms] OR "smartphone"[All Fields])) OR ("cell phones"[MeSH Terms] OR ("cell"[All Fields] AND "phones"[All Fields]) OR "cell phones"[All Fields] OR ("cell"[All Fields] AND "phone"[All Fields]) OR "cell phone"[All Fields])) OR ("reminder systems"[MeSH Terms] OR ("reminder"[All Fields] AND "systems"[All Fields]) OR "reminder systems"[All Fields])) OR (("electronics"[MeSH Terms] OR "electronics"[All Fields] OR "electronic"[All Fields]) AND monitoring[All Fields])) OR ("internet"[MeSH Terms] OR "internet"[All Fields])) AND ("asthma"[MeSH Terms] OR "asthma"[All Fields]) NOT (letter[pt] OR editorial[pt] OR comment[pt] OR Duplicate Publication[pt] OR Guideline[pt] OR Technical Report[pt] OR Review[pt]) AND ("2013/07/11"[PDAT] : "2017/07/12"[PDAT]))

References

1. Eakin MN, Rand CS. Improving patient adherence with asthma self-management practices: what works? *Ann Allergy Asthma Immunol.* 2012;109(2):90-92.
2. Morton RW, Everard ML, Elphick HE. Adherence in childhood asthma: the elephant in the room. *Arch Dis Child.* 2014;99(10):949-953.

3. Horne R. Compliance, adherence, and concordance: implications for asthma treatment. *Chest*. 2006;130(1 suppl):65s-72s.
4. Corsico AG, Cazzoletti L, de Marco R, et al. Factors affecting adherence to asthma treatment in an international cohort of young and middle-aged adults. *Respir Med*. 2007;101(6):1363-1367.
5. Rand CS, Wise RA. Measuring adherence to asthma medication regimens. *Am J Respir Crit Care Med*. 1994;149(2 Pt 2):S69-S76; discussion S77-S78.
6. Chapman KR, Hinds D, Piazza P, et al. Physician perspectives on the burden and management of asthma in six countries: The Global Asthma Physician Survey (GAPS). *BMC Pulm Med*. 2017;17(1):153.
7. Wootton R. Recent advances: Telemedicine. *BMJ*. 2001;323(7312):557-560.
8. World Health Organization (WHO). mHealth: New horizons for health through mobile technologies: Global Observatory for eHealth series—Volume 3. 2011: Geneva. http://www.who.int/goe/publications/goe_mhealth_web.pdf?Cached. Accessed June 6, 2018.
9. Anglada-Martinez H, Riu-Viadoms G, Martin-Conde M, Rovira-Illamola M, Sotoca-Momblona JM, Codina-Jane C. Does mHealth increase adherence to medication? Results of a systematic review. *Int J Clin Pract*. 2015;69(1):39-32.

10. Hamine S, Gerth-Guyette E, Faulx D, Green BB, Ginsburg AS. Impact of mHealth chronic disease management on treatment adherence and patient outcomes: a systematic review. *J Med Internet Res*. 2015;17(2): e52.
11. Klasnja P, Pratt W. Healthcare in the pocket: mapping the space of mobile-phone health interventions. *J Biomed Inform*. 2012;45(1):184-198.
12. Huckvale K, Morrison C, Ouyang J, Ghaghda A, Car J. The evolution of mobile apps for asthma: an updated systematic assessment of content and tools. *BMC Med*. 2015;13:58.
13. Agustí A, Antó JM, Auffray C, et al. Personalized respiratory medicine: exploring the horizon, addressing the issues. Summary of a BRN-AJRCCM workshop held in Barcelona on June 12, 2014. *Am J Respir Crit Care Med*. 2015;191(4):391-401.
14. Chan AH, Reddel HK, Apter A, Eakin M, Riekert K, Foster JM. Adherence monitoring and e-health: how clinicians and researchers can use technology to promote inhaler adherence for asthma. *J Allergy Clin Immunol Pract*. 2013;1(5):446-454.
15. Ostojic V, Cvoriscec B, Ostojic SB, Reznikoff D, Stipic-Markovic A, Tudjman Z. Improving asthma control through telemedicine: a study of short-message service. *Telemed J E Health*. 2005;11(1):28-35.
16. Strandbygaard U, Thomsen SE, V. Backer V. A daily SMS reminder increases adherence to asthma treatment: a three-month follow-up study. *Respir Med*. 2010;104(2):166-171.

17. Strandbygaard U, Thomsen SF, Backer V. Daily SMS reminders for asthma treatment adherence: A comment on Strandbygaard et al. *Respir Med*. 2010;104(8):1236.
18. Petrie KJ, Perry K, Broadbent E, Weinman J. A text message programme designed to modify patients' illness and treatment beliefs improves self-reported adherence to asthma preventer medication. *Br J Health Psychol*. 2012;17(1):74-84.
19. Lv Y, Zhao H, Liang Z, et al. A mobile phone short message service improves perceived control of asthma: a randomized controlled trial. *Telemed J E Health*. 2012;18(6):420-426.
20. Tran N, Coffman JM, Sumino K, Cabana MD. Patient reminder systems and asthma medication adherence: a systematic review. *J Asthma*. 2014;51(5):536-543.
21. Marcano Belisario JS, Huckvale K, Greenfield G, Car J, Gunn LH. Smartphone and tablet self-management apps for asthma. *Cochrane Database Syst Rev*. 2013;(11):CD010013.
22. Charles T, Quinn D, Weatherall M, Aldington S, Beasley R, Holt S. An audiovisual reminder function improves adherence with inhaled corticosteroid therapy in asthma. *J Allergy Clin Immunol*. 2007;119(4):811-816.
23. Moher D, Liberati A, Tetzlaff J, Altman DG; for the PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.

24. Beerthuisen T, Voorend-van Bergen S, van den Hout WB, et al. Cost-effectiveness of FENO-based and web-based monitoring in paediatric asthma management: a randomised controlled trial. *Thorax*. 2016;71(7):607-613.
25. Fiks AG, DuRivage N, Mayne SL, et al. Adoption of a portal for the primary care management of pediatric asthma: a mixed-methods implementation study. *J Med Internet Res*. 2016;18(6):e172.
26. Johnson KB, Patterson BL, Ho YX, et al. The feasibility of text reminders to improve medication adherence in adolescents with asthma. *J Am Med Inform Assoc*. 2016;23(3):449-455.
27. Joseph CL, Ownby DR, Havstad SL, et al. Evaluation of a web-based asthma management intervention program for urban teenagers: reaching the hard to reach. *J Adolesc Health*. 2013;52(4):419-426.
28. Voorend-van Bergen S, Vaessen-Verberne AA, Landstra AM, et al. Monitoring childhood asthma: web-based diaries and the asthma control test. *J Allergy Clin Immunol*. 2014;133(6):1599.e2-1605.e2.
29. Kolmodin MacDonell K, Naar S, Gibson-Scipio W, Lam P, Secord E. The Detroit Young Adult Asthma Project: pilot of a technology-based medication adherence intervention for African-American emerging adults. *J Adolesc Health*. 2016;59(4):465-471.
30. Hughes M, Murphy M. Evaluation of a pilot national online asthma e-learning program for secondary school students. *Issues Compr Pediatr Nurs*. 2014;37(2):136-146.

31. Bursch B, Schwankovsky L, Gilbert J, Zeiger R. Construction and validation of four childhood asthma self-management scales: parent barriers, child and parent self-efficacy, and parent belief in treatment efficacy. *J Asthma*. 1999;36(1):115-128.
32. Wiecha JM, Adams WG, Rybin D, Rizzodepaoli M, Keller J, Clay JM. Evaluation of a web-based asthma self-management system: a randomised controlled pilot trial. *BMC Pulm Med*. 2015;15:17.
33. Morton RW, Elphick HE, Rigby AS, et al. STAAR: a randomised controlled trial of electronic adherence monitoring with reminder alarms and feedback to improve clinical outcomes for children with asthma. *Thorax*. 2017;72(4):347-354.
34. Chan AH, Stewart AW, Harrison J, Camargo CA Jr, Black PN, Mitchell EA. The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: a randomised controlled trial. *Lancet Respir Med*. 2015;3(3):210-219.
35. Kenyon CC, Chang J, Wynter SA, Fowler JC, Long J, Bryant-Stephens TC. Electronic adherence monitoring in a high-utilizing pediatric asthma cohort: a feasibility study. *JMIR Res Protoc*. 2016;5(2):e132.
36. Burbank AJ, Lewis SD, Hewes M, et al. Mobile-based asthma action plans for adolescents. *J Asthma*. 2015;52(6):583-586.
37. Perry TT, Marshall A, Berlinski A, et al. Smartphone-based vs paper-based asthma action plans for adolescents. *Ann Allergy Asthma Immunol*. 2017;118(3):298-303.

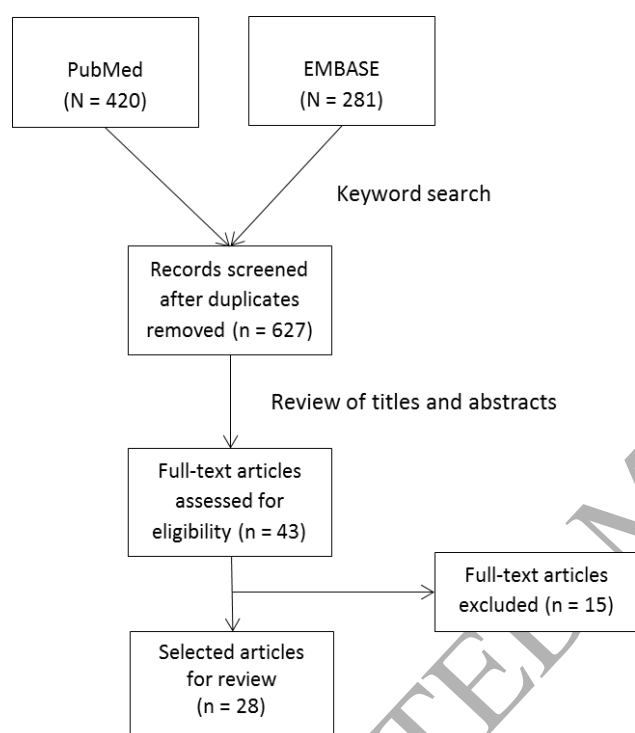
38. Mosnaim G, Li H, Martin M, et al. A tailored mobile health intervention to improve adherence and asthma control in minority adolescents. *J Allergy Clin Immunol Pract*. 2015;3(2):288.e1-290.e1.
39. Johnson KB, Patterson BL, Ho YX, et al. The feasibility of text reminders to improve medication adherence in adolescents with asthma. *J Am Med Inform Assoc*. 2016;23(3):449-455.
40. Foster JM, Usherwood T, Smith L, et al. Inhaler reminders improve adherence with controller treatment in primary care patients with asthma. *J Allergy Clin Immunol*. 2014;134(6):1260.e3-1268.e3.
41. Pool AC, Kraschnewski JL, Poger JM, et al. Impact of online patient reminders to improve asthma care: A randomized controlled trial. *PLoS One*. 2017;12(2):e0170447.
42. Koufopoulos JT, Conner MT, Gardner PH, Kellar I. A web-based and mobile health social support intervention to promote adherence to inhaled asthma medications: randomized controlled trial. *J Med Internet Res*. 2016;18(6):e122.
43. Morrison D, Wyke S, Saunderson K, et al. Findings from a pilot randomised trial of an Asthma Internet Self-management Intervention (RAISIN). *BMJ Open*. 2016;6(5):e009254.
44. van Gaalen JL, Beerthuizen T, van der Meer V, et al; for the SMASHING Study Group. Long-term outcomes of internet-based self-management support in adults with asthma: randomized controlled trial. *J Med Internet Res*. 2013;15(9):e188.

45. Lipszyc JC, Gotzev S, Scarborough J, Liss GM, Gupta S, Tarlo SM. Evaluation of the efficacy of a web-based work-related asthma educational tool. *J Asthma*. 2016;53(10):1071-1075.
46. Cingi C, Yorgancioglu A, Cingi CC, et al. The "physician on call patient engagement trial" (POPET): measuring the impact of a mobile patient engagement application on health outcomes and quality of life in allergic rhinitis and asthma patients. *Int Forum Allergy Rhinol*. 2015;5(6):487-497.
47. Kim MY, Lee SY, Jo EJ, et al. Feasibility of a smartphone application based action plan and monitoring in asthma. *Asia Pac Allergy*. 2016;6(3):174-180.
48. Zairina E, Abramson MJ, McDonald CF, et al. Telehealth to improve asthma control in pregnancy: a randomized controlled trial. *Respirology*. 2016;21(5):867-874.
49. Cook KA, Modena BD, Simon RA. Improvement in asthma control using a minimally burdensome and proactive smartphone application. *J Allergy Clin Immunol Pract*. 2016;4(4):730.e1-737.e1.
50. Licskai C, Sands TW, Ferrone M. Development and pilot testing of a mobile health solution for asthma self-management: asthma action plan smartphone application pilot study. *Can Respir J*. 2013;20(4):301-306.
51. Merchant RK, Inamdar R, Quade RC. Effectiveness of population health management using the propeller health asthma platform: a randomized clinical trial. *J Allergy Clin Immunol Pract*. 2016;4(3):455-463.

52. Bender BG, Cvietusa PJ, Goodrich GK, et al. Pragmatic trial of health care technologies to improve adherence to pediatric asthma treatment: a randomized clinical trial. *JAMA Pediatr.* 2015;169(4):317-323.
53. Sulaiman I, Greene G, MacHale E, et al. A randomised clinical trial of feedback on inhaler adherence and technique in patients with severe uncontrolled asthma. *Eur Respir J.* 2018;51(1). doi: 10.1183/13993003.01126-2017.
54. Mosnaim G, Li H, Martin M, et al. The impact of peer support and MP3 messaging on adherence to inhaled corticosteroids in minority adolescents with asthma: a randomized, controlled trial. *J Allergy Clin Immunol Pract.* 2013;1(5):485-493.
55. Park LG, Howie-Esquivel J, Dracup K. A quantitative systematic review of the efficacy of mobile phone interventions to improve medication adherence. *J Adv Nurs.* 2014;70(9):1932-1953.
56. Sarkar S, Sivashankar P, Seshadri H. Mobile SMS reminders for increasing medication adherence. *Int J Pharm Sci Rev Research.* 2015;32(1):228-237.
57. Wald DS, Butt S, Bestwick JP. One-way versus two-way text messaging on improving medication adherence: meta-analysis of randomized trials. *Am J Med.* 2015;128(10):1139.e1-5.
58. Garrison MM, Mangione-Smith R. Cluster randomized trials for health care quality improvement research. *Academic Pediatr.* 2013;13(6 suppl):S31-S37.

59. Schatz M, Zeiger RS, Drane A, et al. Reliability and predictive validity of the Asthma Control Test administered by telephone calls using speech recognition technology. *J Allergy Clin Immunol*. 2007;119(2):336-343.
60. Schatz M, Zeiger RS, Vollmer WM, et al. Validation of a beta-agonist long-term asthma control scale derived from computerized pharmacy data. *J Allergy Clin Immunol*. 2006;117(5):995-1000.

Figure 1. PRISMA Flow Chart of Study Selection



Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1. Study Characteristics of Reviewed Studies (n = 28)

Study	Site/Location	Age Group	Number of Subjects	Study Group Characteristics	Study Design	Key Outcomes	Observation Time	DHT Used
Morton et al, 2017 ³³	Hospital clinics, Sheffield and Rotherham, UK	Pediatric (aged 6–16 years)	77	Asthma diagnosis	RCT	ACQ scores	1 year	EMD
Chan et al, 2015 ³⁴	Regional ED, Auckland, New Zealand	Pediatric (aged 6–15 years)	220	ED visit; ICS use	RCT	Preventive ICS adherence, number of days absent from school for any reason	6 months	EMD
Kenyon et al, 2016 ³⁵	Inner-city medical center, Philadelphia, Pennsylvania, USA	Pediatric (aged 3–16 years)	14	Hospital and ED “high utilizer”; non-Hispanic African-American	Observational (prospective)	EMD acceptability and feasibility	3 months	EMD and phone calls
Perry et al, 2017 ³⁷	University medical center, Little Rock, Arkansas, USA	Pediatric (aged 12–17 years)	34	Persistent asthma; 62% African-American	RCT	AAP use rates, asthma outcomes	6 months	Mobile app
Burbank et al, 2015 ³⁶	University medical center, Little Rock, Arkansas, USA	Pediatric (aged 12–17 years)	12	Persistent asthma; 60% minority	Observational (prospective)	ACT scores, child asthma self-efficacy scores	8 weeks	Mobile app
Mosnaim et al, 2015 ³⁸	University medical center, Chicago, Illinois, USA	Pediatric (aged 11–16 years)	12	Persistent asthma; African-American	Observational (prospective)	ICS adherence, ACT scores	8 weeks	EMD and mobile app
Beerthuis et al, 2016 ²⁴	University medical center, Rotterdam, Netherlands	Pediatric (aged 4–18 years)	272	Allergic asthma	RCT	ACT scores	1 year	Website
Voorend-Van Bergen et al, 2014 ²⁸	Multiple centers in the Netherlands	Pediatric (aged 4–18 years)	228	Atopic asthma; ICS use	RCT	Web-based diary, C-ACT, ACT, asthma-	1 year	Website

						related QoL		
Joseph et al, 2013 ²⁷	Public high schools, Detroit, Michigan, USA	Pediatric (aged 15–19 years)	422	Asthma diagnosis; 98% African-American	RCT	Asthma questionnaires	1 year	Website
Fiks et al, 2016 ²⁵	20 medical practices in the USA (in 11 states)	Pediatric (aged 6–12 years)	237	Asthma diagnosis; ≥ 1 office visit in the last 12 mo	Observational (prospective)	Adoption of the portal	1 year	Website
Hughes and Murphy, 2014 ³⁰	Secondary school in South Ireland	Pediatric (aged 15–16 years)	50	22% had asthma; 44% had a family member with asthma; 86% had a friend with asthma	Observational (prospective)	Knowledge of Asthma survey	5 days	Website
Johnson et al, 2016 ²⁶	Academic outpatient settings, USA	Pediatric (aged 12–17 years)	98	Asthma diagnosis; 47% African American	RCT	Medication adherence, perceived self-efficacy	2 weeks	Website and text messaging
Kolmodin MacDonell et al, 2016 ²⁹	Urban university and affiliated medical center, Detroit, Michigan, USA	Pediatric/young adult (aged 18–29 years)	48	Persistent asthma; controller medication use; African American	RCT	Adherence to medication, asthma control	3 months	Website and text messaging
Bender et al, 2015 ⁵²	Health maintenance organization, Colorado, USA	Pediatric (aged 3–12 years)	1,187	Persistent asthma; ICS use	RCT	Adherence to medication	2 years	Phone calls
Mosnaim et al, 2013 ⁵⁴	Inner-city medical center Chicago, Illinois, USA	Pediatric (aged 11–16 years)	34	Persistent asthma; poor adherence; low-income African American and/or Hispanic	RCT	Adherence to medication	10 weeks	MP3
Wiecha et al, 2015 ³²	Inner city, Boston, Massachusetts, USA	Pediatric (aged 7–17 years)	58	Persistent asthma	RCT	Self-reported symptoms and medication	6 months	Website

						use		
Merchant et al, 2016 ⁵¹	Two medical groups, Sacramento, California, USA	Adult	199	Controlled and uncontrolled asthma	RCT	Reduction in SABA use	1 year	EMD and mobile app
Cingi et al, 2015 ⁴⁶	Multiple centers in Turkey	Adult	327	Persistent allergic rhinitis or mild-to-severe persistent asthma	RCT	ACT	3 months	Mobile app
Kim et al, 2016 ⁴⁷	University medical center, Seoul, South Korea	Adult	44	Asthma diagnosis	RCT	User-satisfaction, clinical parameters	8 weeks	Mobile app and text messaging
Zarina et al, 2016 ⁴⁸	Two antenatal clinics, Melbourne, Australia	Adult	72	Pregnant women with asthma	RCT	Asthma control	6 months	Mobile app
Cook et al, 2016 ⁴⁹	Multispecialty clinic network, San Diego, California, USA	Adult	60	Poorly controlled asthma	Observational (prospective)	ACT	4 months	Mobile app
Licskai et al, 2013 ⁵⁰	Single hospital, Canada	Adult	22	Asthma diagnosis	Observational (prospective)	SPA use, asthma control	3 months	Mobile app
Foster et al, 2014 ⁴⁰	Primary care centers in Sydney, Australia	Adult	143	Moderate-to-severe asthma	RCT	Medication adherence, asthma control	6 months	EMD and website
Pool et al, 2017 ⁴¹	Insurance plan enrollment, USA	Adult	408	Persistent asthma	RCT	ACT	1 year	Website
Koufopoulos et al, 2016 ⁴²	40 large universities, UK	Adult	103	Asthma diagnosis; ICS use	RCT	SMAQ scores	9 weeks	Website
Morrison et al, 2016 ⁴³	20 general practices, Glasgow, UK	Adult	51	Symptomatic asthma	RCT	Recruitment/retention, website use, ACQ, mini-AQLQ	12 weeks	Website

van Gaalen et al, 2013 ⁴⁴	37 general practices and 1 academic outpatient department in the Netherlands	Adult	200	Asthma diagnosis; ICS use	RCT	Asthma-related QoL; asthma control	1.5 year	Website
Lipszyc et al, 2016 ⁴⁵	Tertiary care asthma clinic, Toronto, Canada	Adult	34	Asthma diagnosis; 68% female	Observational (prospective)	Work-related asthma questionnaire	1 year	Website

Abbreviations: ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AAP, asthma action plan; AQLQ, Asthma Quality of Life Questionnaire; C-ACT, Childhood Asthma Control Test; ED, emergency department; EMD, electronic monitoring device; ICS, inhaled corticosteroid; QoL, quality of life; RCT, randomized controlled trial; SABA, short-acting beta-agonist; SMAQ, self-reported preventer adherence; SPA, smart phone application; UK, United Kingdom; USA, United States of America.

Table 2. DHT Components and Outcomes Used in Studies With Pediatric Patients (n = 16)

Study	Technology Used	Technology Components	Key Asthma Outcomes	Parent Involvement	Observation Time
Morton et al, 2017 ³³	EMD (SmartInhaler, SmartTurbo)	- Daily reminder alarms 3-month medication adherence data uploaded at clinic - Feedback given at clinic	- Medication adherence – increased (70% [intervention] vs 49% [control], $p \leq 0.001$) - Asthma control – no difference - Oral steroid use – fewer (0.411 vs 0.676 courses per 100 child days, $p=0.008$) - Hospital admissions – fewer (0.0254 vs 0.129 per 100 child days, $p<0.001$) - FEV₁ – no difference	Parent-reported events	1 year

Chan et al, 2015 ³⁴	EMD (SmartTrack)	• Ringtone reminder if dose was missed or incorrect dose taken	• Medication adherence – increased (84% [intervention] vs 30% [control], $p<0.0001$) • Morbidity – decreased (change in asthma morbidity score: -2.0 vs -1.2, $p=0.008$) • Asthma control – no difference • Reliever medication use – decreased (median percentage of days: 9.5% vs 17.4%, $p=0.002$) • FEV₁ – no difference	Parent-reported events	6 months
Kenyon et al, 2016 ³⁵	EMD (SmartTouch) and phone calls	• Inhaler usage information uploaded to website in real time • Website monitored daily by clinicians • Patients contacted by phone for inhaler underuse	• Asthma control – increased (mean ACT score improvement: 2.7 points, $p=0.05$)	Parental perception of asthma control	3 months
Perry et al, 2017 ³⁷	Mobile app	• Personalized action plan for routine and worsening asthma symptoms • Daily medication reminders • Monthly prescription refill reminders • Self-management tips • Asthma symptoms and/or peak flow diary	• Asthma control – no difference	Parental confirmation of medications	6 months
Burbank et al, 2015 ³⁶	Mobile app	• Personalized asthma action plan • Asthma symptoms and/or peak flow diary • Immediate feedback • Weekly asthma education tips	• Asthma control – increased in patients with uncontrolled asthma (median ACT scores improved from 16 to 18, $p=0.03$)	–	8 weeks

Mosnaim et al, 2015 ³⁸	EMD (MAdept) and mobile app	- Twice-daily visual medication reminders - Immediate reinforcement for taking medication - Positive text message for inhaler use - Immediate and long-term rewards for completion of correct dose	- Medication adherence – increased (19% to 50%) - Asthma control – increased (median ACT scores improved from 18 to 23) - Reliever medication use – decreased (median puffs per week improved from 3 to 0)	–	8 weeks
Beerthuisen et al, 2016 ²⁴	Website	- Daily ACT score entered on website - Treatment adapted monthly according to the web-based ACT score	- Asthma symptom-free days – no difference - Controller dose – decreased ($p<0.01$) - HRQoL – no difference - Economic costs – no difference	Parents completed questionnaires	1 year
Voorend-Van Bergen et al, 2014 ²⁸	Website	Web-based diary recorded daytime and nighttime symptoms (coughing, wheezing, shortness of breath), limitations in activity, and use of reliever medication	Web-based diary was found to be valid for recording asthma symptoms (diary scores correlated with C-ACT [$r=-0.73$, $p<0.01$] and ACT scores [$r=-0.64$, $p<0.01$])	Parents completed questionnaires	1 year
Joseph et al, 2013 ²⁷	Website	Provided health messages and information based on empirical approaches to behavior change relevant to asthma control	- Asthma symptom-free days – decreased (aOR=0.5 [95% CI: 0.2–0.8], $p=0.006$) - Asthma symptom-free nights – decreased (aOR=0.6 [95% CI: 0.4–1.0], $p=0.074$) - School absences – decreased (aOR=0.7 [95% CI: 0.4–1.1], $p=0.090$) - Restricted activity days – decreased (aOR=0.5 [95% CI: 0.3–0.9], $p=0.010$)	–	1 year

Fiks et al, 2016 ²⁵	Website	• Provided educational material • Enabled sharing of families' treatment concerns, goals, asthma symptoms, medication adherence, and side effects with the clinical team • Tracked asthma control over time for families and clinicians	• Medication changes or refills – increased (14% [95% CI: 2–27]) • Asthma-related provider visits – increased (16% [95% CI: 3–28])	Parents completed surveys	1 year
Hughes and Murphy, 2014 ³⁰	Website	• Online asthma e-learning program	• Asthma knowledge – increased (mean Knowledge of Asthma survey scores: 8.6 [pre-intervention] vs 11.5 [post-intervention])	–	5 days
Johnson et al, 2016 ²⁶	Website and text messaging	• Provided a create-and-print structured medication list • Dosing schedule attached to each medication • Text message reminder for each dose • Visualize medication adherence performance	• Medication adherence – increased (median change in self-reported 7-day adherence: 4–6 days [intervention] vs 0 days [control], $p<0.011$) • Asthma control – no difference • HRQoL – increased (5.7–6.3 on the 7-point mini PAQLQ scale, $p=0.037$)	Parent responses	2 weeks
Kolmodin MacDonell et al, 2016 ²⁹	Website and text messaging	• Personalized daily text messages to take medications • Educational software program regarding medication adherence	• Total asthma symptoms – decreased (intervention vs control, $p<0.05$, Cohen's $d=0.071$) • Average asthma symptoms per day – decreased ($p<0.05$, Cohen's $d=0.071$) • FEV₁ – increased (+4.41% vs -4.14%, $p\leq 0.01$, Cohen's $d=0.59$)	–	3 months

Bender et al, 2015 ⁵²	Phone calls	• Phone call reminders to refill controller medication • Option to speak with clinician	• Medication adherence – increased (44.5% [intervention] vs 35.5% [control], $p<0.001$) • Health care utilization – no difference • Reliever medication use – no difference	Parents completed questionnaires	2 years
Mosnaim et al, 2013 ⁵⁴	MP3	• Patients developed and recorded messages for peers that focused on encouragement to take controller medication • Messages were placed as selections on patients' MP3 players to be played at random between the music tracks	• Medication adherence – no difference	–	10 weeks
Wiecha et al, 2015 ³²	Website	• A web-based interactive asthma education, monitoring, and communication system. Subjects completed asthma education activities and earned points that were redeemable for gift cards • A separate web interface allowed tracking by the clinician	• Medication adherence – increased in patients with low controller medication adherence at baseline (mean change for intervention vs control: +29.8%, $p=0.01$) • Reported wheezing – no difference • Nighttime awakening and parental loss of sleep – decreased (change over 2 weeks: -0.8 days, $p=0.04$; and -0.6 days, $p=0.01$, respectively)	Parents were encouraged to participate in the website	6 months

Abbreviations: ACT, Asthma Control Test; aOR, adjusted odds ratios; C-ACT, Childhood Asthma Control Test; CI, confidence interval; EMD, electronic monitoring device; FEV₁, forced expiratory volume exhaled in the first second; HRQoL, quality of life; PAQLQ, Pediatric Asthma Quality of Life Questionnaire.

Table 3. DHT Components and Outcomes Utilized with Adult Patients (n = 12)

Study	Technology Used	Technology Components	Key Asthma Outcomes	Observation Time
Merchant et al, 2016 ⁵¹	EMD (Propeller Health) and mobile app	• Sensor monitored the use of inhaled medication and transmitted the information to remote servers • Platform facilitated appropriate patient self-management by providing a data-driven assessment of asthma control • Personalized educational guidance based on observed morbidity and national guidelines	• Reliever medication use – decreased^a • Reliever medication-free days – increased^a • Asthma control – increased^a in uncontrolled patients	12 months
Cingi et al, 2015 ⁴⁶	Mobile app	• Provided educational material • Enabled sharing of families' treatment concerns, goals, asthma symptoms, medication adherence, and side effects with the clinical team • Tracked asthma control over time and provided decision support regarding asthma control and side effects	• Asthma control – increased^a • Unplanned provider visits – decreased^a • Emergency department visits – decreased^a	3 months
Kim et al, 2016 ⁴⁷	Mobile app and text messaging	• Self-reported asthma symptoms and PEF information sent to an online server • Patients contacted via text regarding risky signals, such as medical alert	• Medication adherence – increased^a • HRQoL – increased^a • Asthma control – no difference • FEV₁ – no difference	8 weeks

Zarina et al, 2016 ⁴⁸	Mobile app	• Patients recorded asthma symptoms and asthma medication usage weekly with information transmitted to a central server • Automated feedback message regarding asthma status was sent weekly, based on inputs	• Asthma control – increased^a • FEV₁ and PEF – no difference • HRQoL – increased^a	6 months
Cook et al, 2016 ⁴⁹	Mobile app	• Patients recorded the following when prompted: self-assessment of asthma control and assessment of knowledge regarding asthma self-care • Received individualized coaching based on their previous entries • Provided evidence-based educational materials	• Asthma control – improved^a • FEV₁ – improved^a • Controller medication use – decreased^a	4 months
Licskai et al, 2013 ⁵⁰	Mobile app	• Current and future health-related air quality information provided • Patients recorded PEF, symptoms, and adherence information • Viewable action plan	• Air quality knowledge – increased^a • HRQoL – increased^a • Asthma symptoms – decreased^a	3 months
Foster et al, 2014 ⁴⁰	EMD and website	• Recording of dosage with reminders for missed doses, included customizable ring tones • Web portal for clinicians and patients to monitor medication adherence • Clinician gave direct feedback	• Medication adherence – increased^a • Asthma control – no difference • Asthma exacerbations – decreased^a	6 months

		to patients		
Pool et al, 2017 ⁴¹	Website	Tailored feedback reminded patients to ask providers specific questions that may improve asthma control and to consistently perform specific self-care behaviors, such as proper inhaler techniques	- Asthma control – increased^a - Medication adherence – no difference - Number of controller medications used – no difference - Healthcare utilization – no difference	12 months
Koufopoulos et al, 2016 ⁴²	Website	- Online community where patients could report their preventer medication use, write posts, make comments, or ask questions - Patients only received feedback from other patients	Medication adherence – no difference	9 weeks
Morrison et al, 2016 ⁴³	Website	No clear description provided	- Medication adherence – no difference - Reliever medication use – decreased^a - Asthma control – no difference - FeNO – no difference - HRQoL – no difference	12 weeks
van Gaalen et al, 2013 ⁴⁴	Website	- Internet-based self-management tool - Weekly asthma control monitoring and treatment advice, included online and group education and	- Asthma control – increased^a - HRQoL – increased^a - Controller dose – no difference - FEV₁ – no difference	30 months

		communication with a respiratory nurse		
Lipszyc et al, 2016 ⁴⁵	Website	Web-based educational tool provided information on work-related asthma	Work-related asthma knowledge – increased^a	1 year

^aDenotes a statistically significant difference ($P < 0.05$).

Abbreviations: EMD, electronic monitoring device; FeNO, fractional exhaled nitric oxide; FEV₁, forced expiratory volume in the first second; HRQoL, health-related quality of life; PEF, peak expiratory flow.

Table 4. Completion of and/or Compliance to and Attitude Toward and/or Perception of mHealth Interventions

Study	DHT Used	Intervention Completion/Compliance	Attitude Toward/Perception of Intervention
Morton et al, 2017 ³³	EMD	- The mean number of days in study (SD) was 351 (117) for the intervention group and 358 (101) for the control group – not significant - Only 41% of participants in the intervention group received feedback at all 3 time points (3, 6, and 9 months)	NR
Chan et al, 2015 ³⁴	EMD	NR	NA
Kenyon et al, 2016 ³⁵	EMD and phone calls	NA	- Of the 9 (64% of total) caregivers who completed the final study visit, all viewed the EMD favorably and would recommend to friends 5 (56%) believed that the device helped to improve asthma control
Perry et al, 2017 ³⁷	Mobile app	NR	75% thought app helped them better control asthma

			• 83% thought app helped them remember to take their medications • 83% liked receiving the asthma tips and education • 33% thought app had too many reminders
Burbank et al, 2015 ³⁶	Mobile app	• Adolescents used the mobile app a median of 4.3 days per week	• 93% stated that they were better able to control asthma by using app
Mosnaim et al, 2015 ³⁸	EMD and mobile app	• 83% of the adolescents completed the 8-week treatment	NR
Beerthuis et al, 2016 ²⁴	Website	NR	NR
Voorend-Van Bergen et al, 2014 ²⁸	Website	• The completion rate of the web-based diaries was 89%	NR
Joseph et al, 2013 ²⁷	Website	• 88.4% of students completed all 4 computer sessions	NR
Fiks et al, 2016 ²⁵	Website	NA	NR
Hughes, Murphy, 2014 ³⁰	Website	NR	• Teenagers who had asthma found the e-learning program to be informative and relevant to them
Johnson et al, 2016 ²⁶	Website and text messaging	• 87% of participants signed into the website at least once • 21 (46%) patients set up medication reminders, 17 successfully adopted this feature	• Teenagers who had asthma found the e-learning program to be informative and relevant to them
Kolmodin MacDonell et al, 2016 ²⁹	Website and text messaging	• Participants responded to mean = 5.5 (SD = 1.1) and mean = 5.3 (SD = 1.3) out of 7 texts per day at baseline and 3 months, respectively	• Both intervention and control groups rated the program favorably • No intervention group participants chose to opt out of text messages between sessions
Bender et al, 2015 ⁵²	Phone calls	NR	• Parents were highly satisfied with the intervention program • More than 90% of parents agreed regarding

			improved outcomes
Mosnaim et al, 2013 ⁵⁴	MP3	83% of the adolescents completed the 8-week treatment	NR
Wiecha et al, 2015 ³²	Website	NR	NR
Merchant et al, 2016 ⁵¹	EMD and mobile app	NR	86% of adults and 84% of children in the study found Propeller reports useful in learning more about their asthma
Cingi et al, 2015 ⁴⁶	Mobile app	- Patients shared 28.5 status updates - More intervention users completed the study compared with the control group	The patient satisfaction score was 4.0 (median; range, 3.0 to 5.0) on a 6-point scale (5 = very good, 0 = extremely bad)
Kim et al, 2016 ⁴⁷	Mobile app and text messaging	A total of 2226 signals were generated by 22 patients during the 8-week trials (average 1.8 signals generated per day from each patient)	73% answered that the application was very useful for asthma care
Zairina et al, 2016 ⁴⁸	Mobile app	NR	NR
Cook et al, 2016 ⁴⁹	Mobile app	58 of 60 patients completed the final survey	- In response to the statement "Using the app was easy," patients scored the app a mean of 9.3 (10 indicated strong agreement) - In response to the statements "The overall app experience felt relevant/personalized to my asthma" and "The app helped me manage my asthma more effectively," mean scores were 7.9 and 7.4, respectively
Licskai et al, 2013 ⁵⁰	Mobile app	NR	82% agreed or strongly agreed that the system "improved my ability to control my asthma" 95% agreed or strongly agreed that the system "is ready for use by people with asthma"

			Almost all subjects indicated that they would continue to use the app if it was available after the study
Foster et al, 2014 ⁴⁰	EMD and website	NR	NR
Pool et al, 2017 ⁴¹	Website	Over the course of the 12-month study, participants used the intervention in 76.7% of months	NR
Koufopoulos et al, 2016 ⁴²	Website	103 participants completed the study (intervention: 37.8%, 39/99; control: 62.2%, 64/117)	NR
Morrison et al, 2016 ⁴³	Website	- The attrition rate was 12%: 20% in the intervention group, 4% in the comparison group ($P = 0.10$) 19 (76% of the intervention group) used the website	NR
van Gaalen et al, 2013 ⁴⁴	Website	NR	NR
Lipszyc et al, 2016 ⁴⁵	Website	NR	NR

Abbreviations: EMD, electronic monitoring device; NA, not available; NR, not recorded; SD, standard deviation.

ACCEPTED MANUSCRIPT