



## Early View

### Review

# Digital Technologies and Adherence in Respiratory Diseases: The Road Ahead

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# Digital Technologies and Adherence in Respiratory Diseases: The Road Ahead

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**Running Title:** Digital Technologies in Respiratory Diseases

**Take-home Message:**

Digital technologies hold promise to improve adherence and personalize care in patients with respiratory diseases

**Plain Language Summary:**

Ensuring that patients with respiratory diseases take their medication as agreed with their healthcare professionals is an important part of improving the chances that patients get the best care and are able to manage their disease. Digital technologies, such as smart phone apps, are increasingly accessible to help patients with asthma, COPD, and cystic fibrosis manage their treatment. They offer patients increasing options to customize the digital content based on their personal preferences and individual needs. For physicians, collecting large amounts of data on individual patients can provide a better understanding of each

patient's unique situation. This information can be used to help personalize care, which may improve symptoms and prevent worsening disease. To be successful, digital technologies need to be developed with the needs of the patient and their healthcare team in mind, including measures to ensure easy access, effective incorporation into existing treatment plans, and appropriate data security measures.

### **Abstract**

Outcomes for patients with chronic respiratory diseases remain poor despite the development of novel therapies. In part, this reflects the fact that adherence to therapy is low, and clinicians lack accurate methods to assess this issue. Digital technologies hold promise to overcome these barriers to care. For example, algorithmic analysis of large amounts of information collected on health status and treatment use, along with other disease relevant information such as environmental data, can be used to help guide personalized interventions that may have a positive health impact, such as establishing habitual and correct inhaler use. Novel approaches to data analysis also offer the possibility of statistical algorithms that are better able to predict exacerbations, thereby creating opportunities for preventive interventions that may adapt therapy as disease activity changes. To realize these possibilities, digital approaches to disease management should be supported by strong evidence, have a solid infrastructure, be designed collaboratively as clinically effective and cost-effective systems, and reflect the needs of patients and health care providers. Regulatory standards for digital interventions and strategies to handle the large amounts of data generated are also needed. This review highlights the opportunities provided by digital technologies for managing patients with respiratory diseases.

**Keywords:** personalized care, asthma, chronic obstructive pulmonary disease (COPD), digital medicine, health care systems.

## 1. Current and emerging digital technologies in respiratory medicine

In the context of respiratory disease, poor adherence to medication is a significant concern associated with poor patient outcomes, unnecessary escalation of medication, and increased health care costs [1]. Complex treatment regimens for patients with asthma and chronic obstructive pulmonary disease (COPD), including both “as needed” medications for acute symptoms and long-term maintenance medications in a mixture of device types, are among the barriers to adherence [2-4]. Further, optimal self-management often requires multiple components in addition to adherence, such as measuring lung function and recording symptoms, which are not easy for patients to maintain. To address the need for optimized adherence to maintenance medication in patients with respiratory diseases, a number of digital technologies have been developed. Strategies used to date include approaches to monitor and improve adherence such as electronic inhalers, text messaging and reminders, and self-management tools such as web-based and mobile applications to record symptoms and monitor lung function [5-8]. Examples of digital interventions targeting adherence (including electronic monitoring devices, text messaging, and web and mobile applications) in patients with asthma and COPD published between 2007 and 2017 are summarized in Table 1. However, technology is rapidly advancing and additional features and enhancements are continually being developed.

These advancements include strategies to better monitor adherence. In patients with cystic fibrosis, chipped-nebulizers are available that provide objective date- and time-stamped adherence data [36]. Inhalers and inhaler add-ons (digital devices attached to an existing inhaler) designed to measure and assess inhaler technique/quality of inhalation are also available, which can help identify and overcome unintentional poor adherence [1, 37, 38]. Smart inhalers have also been developed that wirelessly send data on inhaler usage directly to a mobile health platform or website [1, 3]. Such platforms offer several advantages including visualization of measurements and integration into a wider dataset; for example, those contained in a patient’s electronic medical records [25, 39].

Technologies are also available that remotely monitor physiological parameters including Bluetooth-connected devices and mobile applications that measure peak flow, fractional exhaled nitric oxide, physical activity, and ambient pollution. These data can link adherence management with other aspects of patient self-management [40, 41]. These may be used to provide appropriate information to promote healthy behaviors such as warning individuals of changes in ambient pollution that may require them to use their preventer treatment and carry their reliever treatment. Such connected information may also provide mechanistic insights into the effect of treatment adherence on health outcomes [42]. New and detailed information can also be obtained from wearable biosensors that continuously monitor respiratory and cardiac parameters using acoustic signals [43]. Together, digital approaches targeting adherence and advances in physiological monitoring of disease open a range of possibilities for understanding the causes and consequences of poor adherence and, hence, a rational way to deliver effective adherence management.

## 2. Potential opportunities provided by digital technologies in respiratory medicine

Several attributes of digital technologies, which could be summarized under the headings of precision, penetration, prediction, and personalization, suggest how current and future technologies may be incorporated into the multidimensional nature of health care.

### 2.1. Precision

Longitudinal data collected via digital applications on patients’ adherence, particularly when supported by digitally collected information on symptoms and physiological and environmental parameters, can provide a detailed and precise basis for understanding an individual’s disease [44, 45]. For example, digitally collected real-time data on patients’ adherence and symptoms can help health care professionals (HCPs) differentiate between symptoms or changes in lung function due to low adherence versus those indicating refractory disease or disease progression in patients with asthma [46]. This is illustrated in Figure 1, which shows patterns of change in lung function based on digitally collected data on inhaler technique and inhaler use coinciding with peak expiratory flow (PEF). Based on such data, HCPs can identify patients for whom additional training on

inhaler technique or interventions to optimize inhaler use may be beneficial. Additionally, identifying inconsistencies between recorded data on symptom severity and measures of lung function may lead HCPs to assess and adjust both reliever and controller medication. Such data can help HCPs differentiate between low implementation (short periods with no medication use) and nonpersistence (medication discontinuation) followed by re-initiation. Digital solutions that effectively link symptoms, data recorded by electronic peak flow meters (as a substitute for measures of lung function), and adherence (measured by digital records of medication use) can be helpful both in terms of accurately assessing medication use, as well as helping patients understand and self-manage their disease. Such an approach is analogous to how a patient with diabetes alters insulin therapy in response to glucose levels based on day-to-day circumstances. Incorporating information on other aspects important to patients' health, such as environmental exposures and physical activity, can further support optimal patient self-management.

## 2.2. Penetration

Many people in remote or low-income settings are not well supported by conventional health care [47, 48]. These individuals often have the poorest disease understanding, low use of maintenance medications, and the worst health outcomes [49]. The reach of wireless networks coupled with the relative reduction in cost and increased capability of mobile communications has led to its greater penetration into traditionally difficult-to-reach communities than robust conventional health care [47]. For example, individuals with cystic fibrosis living in rural or remote areas may face challenges (ie, long-travel time) accessing specialist care [50, 51]. However, offering telehealth clinics via videoconferencing for patients with cystic fibrosis in remote areas of Western Australia increased clinic visits, and increased detection and treatment of exacerbations [51]. Although little research has been done to date regarding the use of digital technologies to support respiratory medicine in these settings, smartphones are increasingly being used to collect data in research studies [52-54]. A recent report highlighted the speed of deployment and value of tele-monitoring in intensive care units in Syria, indicating the potential for technologies in this sphere [55]. Another area where digital technologies could increase the penetration of health care expertise is in community pharmacies where instruction from pharmacists supported by digitally enabled inhalers could establish habitual and correct inhaler use in people starting medication [56].

## 2.3. Prediction

A major strategy for improving health outcomes in respiratory patients is through decreasing the likelihood and magnitude of clinical deterioration and exacerbations and disease complications. Digitally collected patient data on physiology, patterns of medication adherence, trends in reliever usage, and exposure to environmental pollution may identify "digital biomarkers" that help predict future exacerbations [41, 45, 57]. The use of newer data mining and analysis techniques leveraging growing mobile computing power holds particular promise to extract useful information from large datasets, as does the use of existing large and comprehensive databases as "training sets" for the development of prediction tools [58, 59]. Thus, as technology advances, data analysis and risk stratification tools could be incorporated into smart inhalers that suggest measures to prevent severe exacerbations before they occur [44, 45]. A recent study monitoring lung function in patients with idiopathic pulmonary fibrosis showed the value of serial measures of lung function as a way to identify different disease trajectories [60]. Additionally, *in many countries, patients with respiratory conditions can also receive daily air quality alert emails or text messages intended to help them manage triggers by carrying inhalers and avoiding high pollution areas. However, adherence to behavioral recommendations following air quality alerts is poor, and is an area where additional research is needed* [61].

## 2.4. Personalization

As described above, digital technologies are being used to gather physiological parameters over time that can help define the subtype of airway or parenchymal disease present [44, 62]. They also provide unique objective insights into the behavioral aspects of a patient's life such as his or her activity, environmental exposures, and medication adherence. The latter feature may be the most important value of these technologies, particularly if patient-related factors influencing adherence are effectively matched to digital interventions that are tailored to address individual patient determinants of adherence.

Many factors impact adherence in patients with respiratory disease, highlighting the need for different approaches to address nonadherence depending on the root(s) of the issue. For example, electronic reminders and digital versions of COPD or asthma action plans could benefit patients with unintentional nonadherence due

to forgetfulness or difficulty managing complex treatment regimens [42]. Forming stronger habits has been linked to better adherence in patients with cystic fibrosis, suggesting that strategies linking medication use to daily habits could be beneficial in patients with respiratory diseases [63]. Interventions that include a disease education component have the potential to improve adherence, which may in turn lead an individual to engage in other beneficial health behaviors. Digital technologies that collect patient information and provide insights into the specific barriers that drive patients' self-management behaviors can lead to meaningful communication between patients and HCPs, based on objective information [64]. Some factors cannot be changed or are difficult to modify (ie, age, sex, socioeconomic status); however, barriers specific to each population can be identified and patient care tailored accordingly [65, 66].

To be successful, digital interventions targeting patient adherence should incorporate behavioral theory and focus on modifiable determinants relevant for the specific behaviors targeted [65]. Program development tools such as the Intervention Mapping protocol, the Capability, Opportunity, Motivation, and Behavior (COM-B) model, or the Theoretical Domains Framework (TDF), as well as measurement tools such as the Beliefs about Medicines Questionnaire (BMQ), and the Brief Illness Perception Questionnaire (Brief IPQ) can help match interventions to patient determinants [67, 68]. Recently, factors influencing nebulizer use in patients with cystic fibrosis were identified using the TDF and were used to inform development of the CFHealthHub, a digital behavioral intervention tool currently being evaluated in a large randomized trial [69, 70].

Further, profiling tools that assign patients to an appropriate attitudinal cluster are promising approaches for grouping patients based on their beliefs and attitudes [71]. Personalizing interventions to identify and target specific patient behaviors requires a baseline assessment of patient beliefs (ie, using BMQ or Brief IPQ), which can then be automatically processed to ensure that the choice of patient messages, channels of communication, and digital interventions are matched to the specific drivers of suboptimal adherence that are relevant to a patient [17].

In addition to timing of medication intake, optimal adherence to inhaled medications requires effective inhaler technique to ensure appropriate medication deposition in the lungs [72]. The estimated prevalence of poor inhaler technique ranges from 14% to 90% depending on the device and context [73], and is caused by a lack of knowledge on how to use the inhaler, lack of motivation to learn or implement proper technique, and the need for repeated training. The use of multiple types of inhaler devices is associated with a higher prevalence of errors. Many inhaler errors, including general (ie, not exhaling, not holding breath, inappropriate inhalation speed) and device-specific errors (ie, dose preparation for dry powder inhalers and coordination problems for metered dose inhalers) are associated with reduced asthma symptom control and increased rates of exacerbations [74, 75]. Despite efforts invested in education, training, and device development, little progress has been made to improve inhaler use over the past 40 years [76]. Recently, devices have been developed that can detect inadequate inhaler technique, helping to identify patients requiring additional training [1, 77, 78]. Some inhalers can also provide feedback directly to patients, helping them optimize their technique and, when used in newly diagnosed patients, could help them develop good habits from the outset. When lack of motivation is at the root of a patient's poor inhaler use, combining digital monitoring and feedback on inhaler technique with other strategies (eg, education on the importance of proper medication uptake) could prove beneficial.

Other critical factors for a successful tailored approach will involve delivering digital patient-related information to a patient's clinical team to allow for meaningful conversations during medical visits. Ensuring that tailoring is dynamic may also be important since factors that influence patients' adherence can change over time. For example, a patient's initial beliefs about treatment may change after experiencing side effects, and effective digital interventions should have the capacity to detect and respond to these changes over time in a flexible way (See Figure 1C and D).

The flexible nature of digital technologies provides an opportunity to develop generalizable core features and customizable elements according to patient preferences or clinician requirements to meet the individual patient's needs. The aim would be interactive and adaptable digital versions of individual treatment action plans that use personal, not population, thresholds for changes in treatment, examples of which are already available [35]. Key features such as educational content could be customized based on a patient's health literacy, treatment perceptions, and disease experience to facilitate engagement.

### 3. Key considerations toward successful implementation and uptake of digital applications

Digital technologies have the ability to improve the precision, penetration, prediction, and personalization of respiratory care. However, for this potential to be realized, several conditions need to be in place: a strong evidence base that represents the users, strategies for how technologies will be integrated into health systems, as well as the appropriate regulatory standards.

#### 3.1. *How strong is the evidence base underpinning new technologies?*

Research on critical factors that could impact the use of digital technologies to manage adherence in the clinical setting has not kept pace with the rapid advances in the technologies themselves, in part because the pace at which research is funded, completed, and published cannot keep up with the rapid evolution of available technologies [79, 80]. Frameworks have been published that describe key elements to be included in studies describing and evaluating new digital applications [12, 80-83]. However, most published studies to date have not measured up to these standards, with the majority being of short duration and not describing in sufficient detail the features of the technologies or how they were evaluated [81, 82, 84]. To proceed with widespread implementation of newer technologies, we need a more complete and detailed understanding of factors related to the use of digital interventions by patients and clinicians, the impact of these interventions on HCP workload and their integration with existing services, as well as their economic impact.

#### 3.2. *Considering the intended users of the interventions*

To avoid restricted entry criteria and rigid ecology of care issues that characterize traditional trials of medications, studies of digital interventions must reflect the user base and the usual clinical environment, not simply study early technology adopters using teaching hospitals.

This is especially important since patient engagement and sustained use in the real-world setting are critical factors for the success of digital technologies. Unfortunately, high rates of discontinuation are common with digital tools [13, 52]. Therefore, research is needed to understand the reasons for initiation, persistence, and discontinuation of use. Many authors have provided useful overviews of this problem along with guidelines for promoting more effective engagement [85, 86]. Recording and monitoring events, with reminders and feedback on performance, are often desirable features [87, 88]. However, the intrusive nature of this monitoring and subsequent judgment may lead some patients to disengage. For example, a study of smart inhaler use in children with asthma showed a greater rate of lost or damaged inhalers than what might reasonably be expected in usual practice or in the control



group [13]. Continuous improvement and customization is also possible, starting from a basic user experience and incorporating user feedback features [17, 89-91].

### *3.3. Integrating digital technologies into existing health care systems*

Huge amounts of data will be generated by new connected devices and mobile applications. For example, an asthma specialist with a moderate caseload would receive data on many thousands of actuations per year if all inhalers were digitally equipped. Despite offering great promise in improving clinical outcomes, handling this volume of data is somewhat daunting. At a basic level, information from connected devices should integrate with patients' electronic medical records to facilitate decision making in the same way clinicians view blood test results. Devices or mobile software that demand a stand-alone interface are less practical and will be short-lived. Progress is being achieved by consortia such as INTEROPen ([www.interopen.org](http://www.interopen.org)) by improving standardization and facilitating transfer of information between devices and different health care settings, and by secure communication formats such as Blockchain ([www.blockchain.com](http://www.blockchain.com)).

Integrating digital technology into usual care may also involve substantial changes in routine clinician practices. These changes need to be approached using the same behavioral principles applied to patients: clearly define the behaviors requiring change, identify relevant determinants, and incorporate behavior change techniques that effectively target these behaviors and determinants [92]. Additionally, evidence-based data from clinical trials are needed so that clinicians can be confident in the effectiveness and cost-effectiveness of proposed digital interventions. Further, preparing organizations for technology-supported care of chronic conditions is likely to represent a financial burden with a significant scope of costly challenges, with many institutions currently lacking the appropriate infrastructure to support digital innovation (**Figure 2**) [93]. Additionally, the handling of large volumes of data collected from different digital devices and at different medical institutions is a necessary step to allow meaningful aggregation of information [94].

### *3.4. Developing appropriate regulatory standards for digital technologies*

Meeting the regulatory standards for medicines is costly and time consuming, and is possible only with robust intellectual property protection to secure future income. It is clear that the situation in terms of regulatory needs for new technologies is very different than for standard medications [95]. As devices and software can be readily mimicked, there is a race to market

to secure an initial income. Offerings are therefore marketed as lifestyle rather than health products, and are of myriad and usually low quality [84]. As such, regulatory standards for digital technologies may need to be appropriately tailored to encourage development of medically focused digital applications.

Finally, the challenges in maintaining anonymity and data security for both data in transit and stored data are a concern across all medical specialties [96]. A full discussion of this complex topic is beyond this article, but it appears we could well see a transition from large commercial institutions storing data on many patients to individuals holding their own data (eg, the personal data management system described by Mortier et al.) [97]. This scenario provides the strongest protection to end-users in terms of deciding who will use their data, but could compromise the potential for using aggregated de-identified information for research purposes.

#### **4. Conclusions**

For patients, clinicians, and researchers, digital technologies such as those addressing adherence and inhaler technique offer the opportunity to advance personalized care for patients with respiratory diseases. Longitudinal, real-time data collected through digital platforms can provide a precise understanding of the interaction of a patient's adherence, symptoms, and disease course, which can be used to develop and support adherence management strategies. Digital technologies also offer the possibility of extending the reach of health care into underserved communities, where adherence is often the poorest, or empowering HCPs who are not specialists. Digital biomarkers may be developed that link adherence with physiological parameters and environmental exposures to help predict events such as loss of symptom control or exacerbations. Finally, digital interventions can be tailored to address individual patient determinants of adherence.

For such approaches to be successful, strategies to promote uptake and implementation of new technologies need to be developed in parallel. These include guideline-based design and evaluation of new technologies to develop a strong evidence base underpinning digital interventions. The features and capabilities of digital interventions should also be designed with the end user in mind to promote long-term use. Strategies to facilitate uptake by HCPs also need to be implemented to allow for their successful integration into existing health care systems. Finally, the appropriate regulatory processes for digital interventions remain to be identified, and appropriate tools and security measures are needed to manage the large amounts of data generated. Ongoing investigation of digital solutions will establish their place in the management of asthma and COPD.

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**Table 1. Current Digital Strategies to Improve Adherence in Asthma and COPD**

Electronic Monitoring Devices			
Study Description	Features	Effect on Adherence	Other Outcomes
<i>Charles et al. 2007</i> [6] • 24-week RCT • 110 patients (aged 12 to 65 years) with asthma	• EMD recorded date/time and number of actuations • Intervention group also utilized an audiovisual reminder function	• Significantly higher adherence in patients who received an audiovisual reminder compared with the control group (93% vs 74% median percentage taken in last 12 weeks of trial, $P < .001$ )	• No significant differences occurred in clinical outcomes between the 2 groups
<i>Burgess et al. 2010</i> [9] • 4-month RCT • 26 patients (aged 6 to 14 years) with suboptimal asthma control	• EMD recorded date and time of actuation • Intervention group also received feedback based on EMD measured adherence	• Significantly higher adherence in patients who received feedback compared with the control group (79% vs 58%, $P < .01$ ) • Adherence in the control group declined slightly over the study, whereas in the intervention group mean adherence was maintained ( $P < .01$ )	• Change in forced FEV was greater in the intervention group (13.8%) than in the control group (9.8%), but did not reach statistical significance
<i>Foster et al. 2014</i> [10] • 6-month RCT • 143 patients (aged 14 to 65 years) with suboptimal asthma control	• EMD recorded date/time of all actuations and uploaded data monthly to a secure Web site • Intervention group also received IRF and/or personalized adherence discussions	• Significantly higher adherence in the IRF groups than in the non-IRF groups (73% vs 46% of prescribed daily doses; $P < .0001$ ) • Adherence decreased over time in all groups, but remained twice as high in the IRF groups vs the non-IRF groups ( $60\% \pm 38\%$ vs $29\% \pm 33\%$ )	• 11% of patients in the IRF groups had exacerbations compared with 28% in the non-IRF groups ( $P = .013$ ); this difference was not significant ( $P = .06$ ) after adjustment for clustering and past self-reported prednisone use
<i>Chan et al. 2015</i> [5] • 6-month RCT • 220 children (aged 6 to 15 years) with prior history of asthma exacerbation	• EMD recorded date/time and number of actuations • Intervention group also utilized an audiovisual reminder function	• Significantly higher adherence in the intervention group compared with the control group (median 84% vs 30%, $P < .001$ ) • Overall adherence fell in both groups over time, with no difference in the rate of decline ( $P = .10$ )	• Reduction in asthma morbidity score from baseline to 6 months was significantly greater ( $P = .008$ ) in the intervention group (9.30 to 7.3) than in the control group (9.20 to 8.0)
<i>Vasbinder et al. 2016</i> [11] • 12-month RCT • 209 children (aged 4 to 11 years) with asthma	• EMD recorded date and time of actuation • Intervention group also received tailored SMS reminders when a dose was at risk of omission	• Higher mean adherence in the intervention group compared with the control group (69.3% vs 57.3%; difference 12.0%, 95% CI 6.7%–17.7%)	• No differences were found between groups for asthma control, quality of life, or asthma exacerbations
<i>Merchant et al. 2016</i> [12] • 12-month parallel arm study • 495 patients	• Intervention included a sensor to monitor inhaler use, an education component, reminders and alerts, data visualization and trends, and predictive analytics and feedback	• Greater decrease in mean daily SABA uses per person in the intervention group (-0.41) vs routine care (-0.31), $P < .001$ • Greater increase in the proportion of SABA-free	• Improved ACT scores among adults initially lacking asthma control

(aged >5 years) with asthma	<ul style="list-style-type: none"> <li>Control group utilized sensors to monitor inhaler use along with usual care</li> </ul>	days increased in the intervention group (21% vs routine care (17%), $P < .01$ )	
<i>Morton et al. 2017</i> [13] <ul style="list-style-type: none"> <li>1-year RCT</li> <li>90 children with asthma (aged 6 to 16 years)</li> </ul>	<ul style="list-style-type: none"> <li>EMD recorded date and time of actuation</li> <li>Adherence data also reviewed by patient and caregiver every 3 months and reminders utilized in the intervention group</li> </ul>	<ul style="list-style-type: none"> <li>Significantly higher adherence in the intervention group compared with the control group (70% vs 49%; <math>P \leq .001</math>) was maintained in the intervention group, but declined in the control group over 1 year</li> </ul>	<ul style="list-style-type: none"> <li>Significant decrease in exacerbations requiring oral steroids or hospitalization in the intervention group</li> <li>Decrease in ACQ in both groups (1.0 in control group and 0.9 in intervention group) but no significant difference between groups</li> </ul>
<b>Text messaging</b>			
<b>Study Description</b>	<b>Features</b>	<b>Effect on Adherence</b>	<b>Other Outcomes</b>
<i>Strandbygaard et al. 2010</i> [14] <ul style="list-style-type: none"> <li>12-week RCT</li> <li>26 patients (aged 18 to 45 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group received daily SMS reminder to take asthma medication</li> </ul>	<ul style="list-style-type: none"> <li>Mean medication adherence increased in the SMS group (77.9% to 81.5%) and decreased in the control group (84.2% to 70.1%)</li> <li>The absolute difference in mean medication adherence between the 2 groups was 17.8%, <math>P = .019</math></li> </ul>	<ul style="list-style-type: none"> <li>No between-group differences in change in exhaled nitric oxide levels, FEV1 (% of predicted), ACQ, or mini AQLQ</li> </ul>
<i>Prabhakaran et al. 2010</i> [15] <ul style="list-style-type: none"> <li>12-week RCT</li> <li>120 patients (aged &gt;21 years) hospitalized for asthma</li> </ul>	<ul style="list-style-type: none"> <li>All patients received inpatient individualized asthma education at the beginning of the study</li> <li>Intervention group received SMS messages to assist with asthma management, including medication use, according to a structured workflow</li> </ul>	<ul style="list-style-type: none"> <li>Not measured</li> </ul>	<ul style="list-style-type: none"> <li>No significant difference in ACT scores, number of nebulizations, or ED visits between groups</li> </ul>
<i>Lv et al. 2012</i> [16] <ul style="list-style-type: none"> <li>12-week RCT</li> <li>150 patients (aged &gt;18 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Verbal asthma education (all groups)</li> <li>Individualized asthma action plan with peak expiratory flow monitoring and asthma diary (traditional and SMS groups)</li> <li>Daily SMS reminders on how to manage asthma and option to ask questions via text message (SMS group)</li> </ul>	<ul style="list-style-type: none"> <li>Medication adherence was higher in the SMS (80.0%) and traditional (74.1%) groups than in the control group (50.0%), but changes were not significant.</li> <li>Follow-up appointment rates were significantly higher in the SMS (60%) and traditional (54%) groups compared with the control group (28%)</li> </ul>	<ul style="list-style-type: none"> <li>Significant increase in perceived asthma control and AQLQ in the SMS and traditional groups relative to control</li> <li>Improved FEV1 (% predicted) in all groups, but no significant between-groups difference.</li> </ul>
<i>Petrie et al. 2012</i> [17] <ul style="list-style-type: none"> <li>9-month RCT</li> <li>147 patients (aged 16 to 45 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Treatment group received individually tailored text messages for 18 weeks based on their illness and medication beliefs</li> </ul>	<ul style="list-style-type: none"> <li>Average self-reported adherence was higher (57.8%) in the intervention group than the control group (43.2%) (<math>P &lt; .05</math>)</li> <li>Percentage taking over 80% of prescribed inhaler doses was 25.9% in the intervention group and 10.6% in the control group (<math>P &lt; .05</math>)</li> </ul>	<ul style="list-style-type: none"> <li>At 18 weeks, the text-message group was significantly higher than control on perceived necessity of preventer medication, belief in the long-term nature of their asthma, and perceived control over their asthma</li> </ul>

<p><i>Kolmodin MacDonell et al. 2016 [18]</i></p> <ul style="list-style-type: none"> <li>• 3-month RCT</li> <li>• 48 African American adults (aged 18 to 29 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group received 2 computer-delivered motivational interviewing (MI) sessions with text reminders between sessions</li> <li>• Control group completed asthma education matched for length, location, and method of delivery of the intervention MI sessions</li> </ul>	<ul style="list-style-type: none"> <li>• Both groups missed fewer doses of controller medication at 3 months than at baseline</li> <li>• The magnitude of the trend was greater for the intervention group for total doses missed, average doses missed per day, and number of days medication was missed, but did not reach statistical significance</li> </ul>	<ul style="list-style-type: none"> <li>• There was a larger magnitude decrease in symptoms in the intervention vs control group in total symptoms, <math>P &lt; .05</math> and average symptoms per day, <math>P &lt; .05</math></li> <li>• Intervention group improved in FEV-1 percent predicted (+4.41%) and control group decreased (-4.14%), <math>P \leq .01</math></li> </ul>
<p><i>Britto et al. 2017 [19]</i></p> <ul style="list-style-type: none"> <li>• 6-month RCT</li> <li>• 64 patients (aged 12 to 22 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group received text message reminders personalized by the patient</li> <li>• Ability to change, add, or delete reminders as desired</li> <li>• Participants divided into intervention from baseline to month 3 or intervention from month 3 to month 6</li> </ul>	<ul style="list-style-type: none"> <li>• Increased adherence to ICSs by 2.75% per month with the intervention vs without (<math>P &lt; .01</math>).</li> <li>• For the group that received text messages first, adherence subsequently declined, suggesting no long-term effect</li> </ul>	<ul style="list-style-type: none"> <li>• Improved ACT score after 1 month that was maintained for the 6-month duration of the study in both groups</li> <li>• Asthma symptoms improved and asthma worry decreased in both groups</li> </ul>
<p><i>Akrom et al. 2015 [20]</i></p> <ul style="list-style-type: none"> <li>• Controlled pre- and post-intervention study</li> <li>• 66 patients (aged 18 to 80 years) with COPD</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group received daily text messages with motivational messages and reminders to take medication, and brief counseling</li> <li>• Control group received hospital standard of care</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group experienced significant improvement in MMAS score (from 46% to 88% high compliance) from pretest to posttest; control group did not (55% to 61% high compliance).</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>

### Web-based and Mobile Applications

Study Description	Features	Effect on Adherence	Other Outcomes
<p><i>Van der Meer et al. 2009 [21]</i></p> <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 200 patients (aged 18 to 50 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Internet-based self-management program included weekly asthma control monitoring, treatment advice, online and group education, and remote communication with an asthma nurse</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Inhalation technique improved in both groups but improvements did not differ between groups (<math>P = .143</math>)</li> <li>• Self-reported medication adherence did not differ between groups</li> </ul>	<ul style="list-style-type: none"> <li>• Internet-based self-management was associated with improved asthma control and lung function</li> <li>• Asthma-related quality of life improved, but was not statistically significant in the intervention group vs control and exacerbations did not differ between groups</li> </ul>
<p><i>Liu et al. 2011 [22]</i></p> <ul style="list-style-type: none"> <li>• 6-month prospective, controlled study</li> <li>• 120 patients with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Mobile phone-based interactive asthma self-care system including electronic symptoms diary and record of reliever use and PEFR</li> <li>• Control group received a written symptoms booklet and asked to record PEFR regularly</li> </ul>	<ul style="list-style-type: none"> <li>• Significant increase in mean daily dose of either systemic or ICSs in intervention group compared with control group</li> </ul>	<ul style="list-style-type: none"> <li>• Significant increase in PEFR in intervention group compared with control group at 4 and 6 months</li> <li>• Improved quality of life and fewer exacerbations in the intervention group</li> </ul>

<p><i>Ryan et al. 2012</i> [23]</p> <ul style="list-style-type: none"> <li>• 6-month RCT (aged &gt;12 years)</li> <li>• 288 patients with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Mobile phone-based system with twice-daily recording and transmission of symptoms, drug use, and peak flow, with immediate feedback</li> <li>• Control group recorded the same data using a paper diary</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in change in asthma control or self-efficacy between groups</li> <li>• No significant difference in number of acute exacerbations, prescribed steroid courses, and unscheduled HCP consultations or ED visits between groups</li> </ul>
<p><i>Farooqui et al. 2015</i> [24]</p> <ul style="list-style-type: none"> <li>• 30-day single-arm study</li> <li>• 24 patients (aged 9 to 16 years) with asthma</li> </ul>	<p>Intervention included:</p> <ul style="list-style-type: none"> <li>• Daily reminders for medication use</li> <li>• Personalized trigger avoidance measures</li> <li>• Algorithm-based, interactive asthma treatment plan</li> <li>• Gamification features and reward points based on medication use and interaction with the app</li> </ul>	<ul style="list-style-type: none"> <li>• Increased adherence to controller medication in 18 of 21 subjects (85%) during the intervention period compared with the 30 days immediately preceding enrollment</li> </ul>	<ul style="list-style-type: none"> <li>• Increase in measures to avoid asthma triggers after intervention period</li> </ul>
<p><i>Mosnaim et al. 2015</i> [25]</p> <ul style="list-style-type: none"> <li>• 8-week single-arm study</li> <li>• 12 African American patients (aged 11 to 16 years) with persistent asthma</li> </ul>	<p>Intervention included:</p> <ul style="list-style-type: none"> <li>• Daily visual reminders to take their ICS</li> <li>• Positive reinforcement (texts and gaming) for taking ICS</li> <li>• Immediate (ability to customize avatar) and long-term (\$1.00/dose-to purchase music, movies, applications, and games) rewards</li> </ul>	<ul style="list-style-type: none"> <li>• Median ICS adherence increased from 19% at baseline to 67% at 8 weeks</li> <li>• At baseline 8% of patients met target ICS adherence (&gt;50%); at week 8, 58% of patients met target ICS adherence</li> </ul>	<ul style="list-style-type: none"> <li>• ACT scores increased from baseline to week 8 (18 vs 23) with 58% of participants achieving the minimal clinically important difference (3 points) in ACT score</li> <li>• SABA use decreased from a median of 3 puffs per week at baseline to 0 puffs per week at 8 weeks</li> </ul>
<p><i>Cingi et al. 2015</i> [26]</p> <ul style="list-style-type: none"> <li>• 3-month RCT</li> <li>• 136 patients with asthma (aged 25 to 41 years)</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention included physician/patient communication; health status and medication compliance tracking; sharing of motivational and educational content; and medication reminders</li> <li>• Control group received standard care</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• In the intervention group, more patients (49%) achieved a well-controlled asthma score (ACT &gt;19) compared with the control group (27%, (<math>P &lt; .05</math>))</li> </ul>
<p><i>Johnson et al. 2016</i> [27]</p> <ul style="list-style-type: none"> <li>• 3-week RCT</li> <li>• 98 patients with asthma (aged 12 to 17 years)</li> </ul>	<ul style="list-style-type: none"> <li>• Personalized health application (MyMediHealth) to help patients manage medications and receive dosing reminders</li> <li>• Control group received action lists as part of usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Significant improvement in self-reported 7-day adherence (<math>P = .011</math>) in the intervention group vs control group</li> </ul>	<ul style="list-style-type: none"> <li>• Increased quality of life (<math>P = .037</math>) and perception of self-efficacy (<math>P = .016</math>) in the intervention group compared with the control group</li> </ul>
<p><i>Ahmed et al. 2016</i> [28]</p> <ul style="list-style-type: none"> <li>• 6-month, RCT</li> <li>• 100 patients (aged 18 to 69 years) with</li> </ul>	<ul style="list-style-type: none"> <li>• My Asthma Portal mobile application, which allowed participants to view personal health information, receive information tailored to</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• No significant between-group effects on asthma-related quality of life</li> <li>• No significant effect on asthma control</li> </ul>

asthma	<p>identified knowledge gaps, and monitor and receive feedback on current self-management practices</p> <ul style="list-style-type: none"> <li>• Control group received usual care</li> </ul>		
<p><i>Cook et al. 2016</i> [29]</p> <ul style="list-style-type: none"> <li>• Prospective single-arm, treatment-only, 4-month study</li> <li>• 60 adults (aged 17 to 82 years) with asthma</li> </ul>	<p>Intervention included:</p> <ul style="list-style-type: none"> <li>• Continuous patient data collection including self-assessment of asthma control and assessment of patient knowledge regarding asthma control</li> <li>• Individualized alerts, coaching, and educational materials</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• Statistically significant improvement in ACT scores and FEV<sub>1</sub> (in subset of patients with available before-and-after spirometry data)</li> <li>• Nonsignificant decrease in total number of systemic corticosteroids prescribed</li> </ul>
<p><i>Koufopoulos et al. 2016</i> [30]</p> <ul style="list-style-type: none"> <li>• 9-week RCT</li> <li>• 216 patients (aged 18 to 64 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group included access to “AsthmaVillage,” an online community for patients with asthma</li> <li>• Control group did not have access to the online community, but utilized the “AsthmaDiary,” an online diary for recording ICS preventer use</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in self-reported medication adherence in the intervention group vs control</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>
<p><i>Kim et al. 2016</i> [31]</p> <ul style="list-style-type: none"> <li>• 8-week study</li> <li>• 44 patients (aged &gt;19 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group utilized an application that included: <ul style="list-style-type: none"> <li>○ Asthma monitoring application and peak flow meter</li> <li>○ Questionnaires and daily patient symptom score</li> <li>○ Daily alerts and action plans based on asthma control status</li> </ul> </li> <li>• The control group did not use the application</li> </ul>	<ul style="list-style-type: none"> <li>• Adherence improved in the intervention group (<math>P = .017</math>) but not in the control group (<math>P = .674</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Lung function parameters did not significantly differ between visits or between the intervention and control groups at each visit</li> </ul>
<p><i>Morrison et al. 2016</i> [32]</p> <ul style="list-style-type: none"> <li>• 12-week RCT</li> <li>• 51 patients (aged ≥16 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• “Living Well with Asthma” Web site designed to assess current level of asthma control and support optimal medication management; challenge attitudes and concerns around medication; and prompt use of personal action plan</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• No significant between-group difference in the percentage of recommended ICS doses self-reportedly taken, nor the equivalent beclometasone doses prescribed</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in ACQ scores and mini-AQLQ scores</li> <li>• Significant improvement in PAM scores in the intervention group compared with the control group</li> </ul>
<p><i>Pool et al. 2017</i> [33]</p> <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 408 adults (aged</li> </ul>	<ul style="list-style-type: none"> <li>• Tailored feedback and reminders based on answers to questions (at least once per month)</li> </ul>	<ul style="list-style-type: none"> <li>• No differences were observed in medication adherence between the intervention group and control</li> </ul>	<ul style="list-style-type: none"> <li>• Greater mean improvement in ACT score in the intervention group (2.3 vs 1.2; <math>P = .02</math>)</li> <li>• No differences in asthma-</li> </ul>

21 to 60 years) with asthma	<p>related to asthma symptoms, medications, provider care, and asthma management plan</p> <ul style="list-style-type: none"> <li>• Control group received similar questions and feedback, but focused on preventive services unrelated to asthma control (eg, cancer screening)</li> </ul>		related health care utilization
<p><i>Pinnock et al. 2013</i> [34]</p> <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 256 adults with COPD</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group recorded symptoms and medication use and monitored oxygen saturation daily</li> <li>• Intervention included algorithm-generated alerts to clinical team based on patient input</li> <li>• Control group utilized standard self-monitoring</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• Number and mean duration of hospital admissions for COPD did not differ significantly between groups</li> <li>• No significant effect on health-related quality of life between groups</li> </ul>
<p><i>Farmer et al. 2017</i> [35]</p> <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 166 patients (aged <math>\geq 40</math> years) with COPD</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention included daily symptom diary including medication use; Bluetooth-enabled pulse oximeter with finger probe; monthly mood screening questionnaires; and tailored videos and education based on patient entries</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• No difference on MARS in self-reported medication adherence</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in number of exacerbations, relative risk of hospital admission, quality of life, self-reported smoking cessation, depression, or anxiety</li> <li>• Better overall health status (measured with 5-Level EuroQol 5-Dimension Questionnaire) in the intervention group (<math>P = .03</math>)</li> </ul>

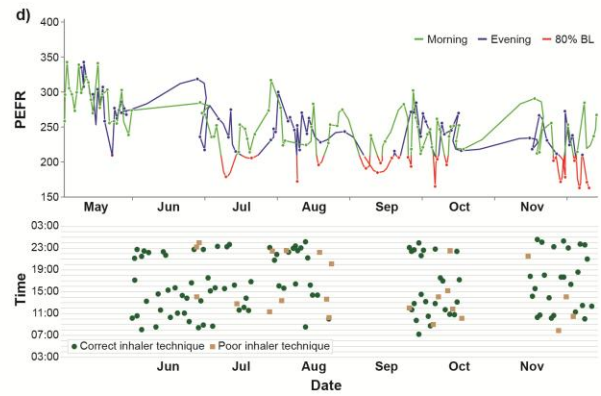
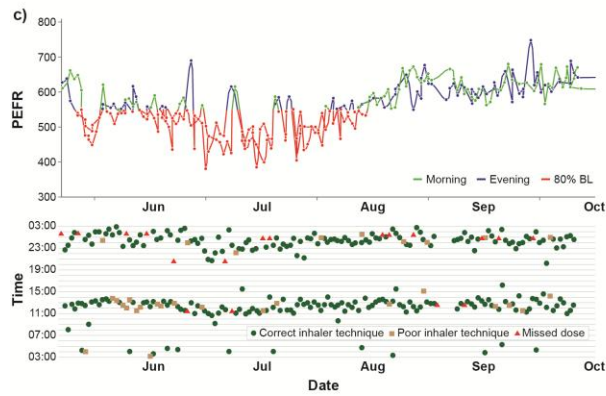
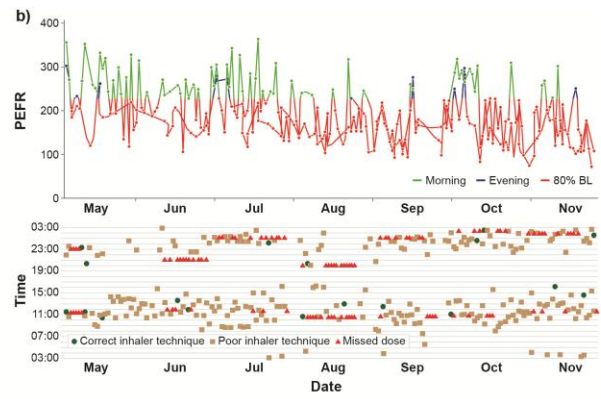
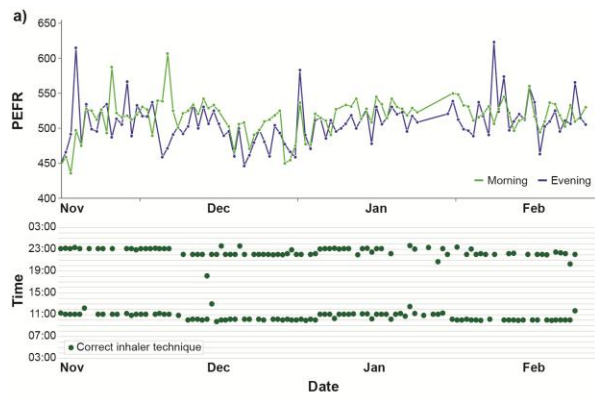
ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ED, emergency department; EMD, electronic monitoring device; FEV1, forced expiratory volume in one second; HCP, health care provider; ICS, inhaled corticosteroid; IRF, inhaler reminders and feedback; MARS, Medication Adherence Report Scale; MI, motivational interviewing; MMAS, Morisky Medication Adherence Scale; PAM, patient activation measure; PEF, peak expiratory flow rate; RCT, randomized controlled trial; SABA, short-acting beta agonist; SMS, short message service.

## Figure Legends

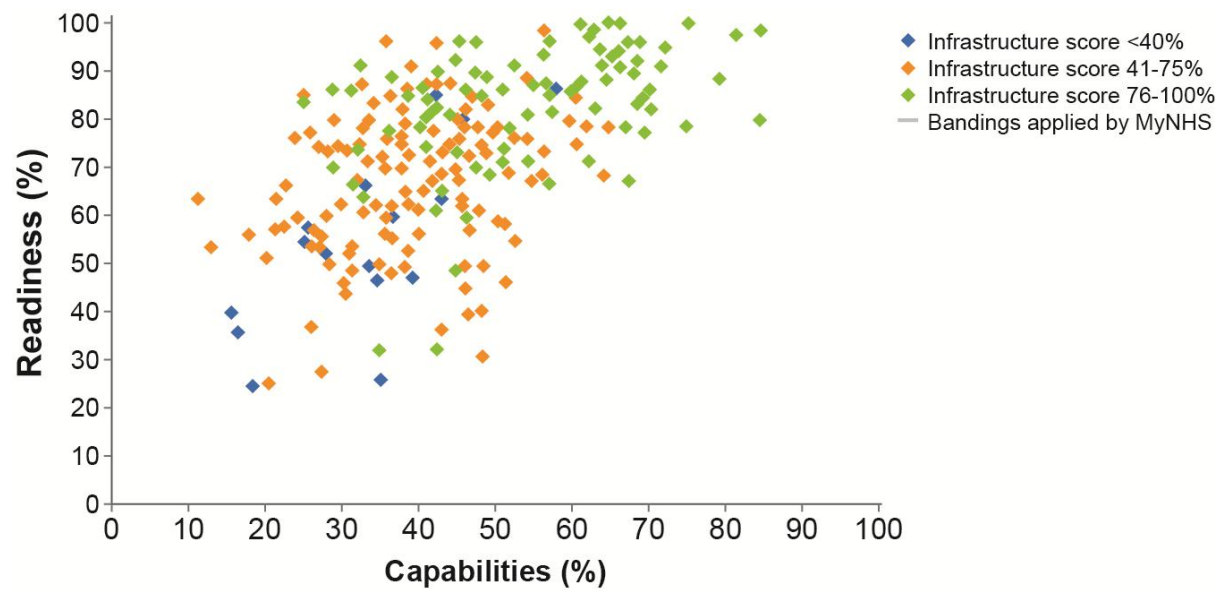
**Figure 1.** Four patterns of digitally monitored lung function, adherence, and inhaler technique, as assessed by a digital audio recording device attached to the inhaler. A, A well-controlled asthma patient with stable PEF and regular use of a twice daily preventer inhaler. Normal lung function (peak expiratory flow rate [PEFR]) is maintained by proficiently and regularly taken treatment (green dots on the lower graph in each panel indicate correct inhaler technique). B, Patient with poor lung function (PEFR recordings in red indicate lung function at 80% of baseline) due to poor inhaler technique, shown by orange squares, and missed doses, shown as red triangles. C, Patient with initial poor lung function who subsequently improves. Improved lung function is associated with regular and correct inhaler use. D, Patient with periods of intermittent inhaler use and poor lung function followed by periods of improved adherence and lung function. Drops in lung function are associated with intermittent inhaler use and appear to prompt the patient to restart inhaler use. The absence of dots on the time graph indicates that no doses were taken. BL, baseline; PEFR, peak expiratory flow rate.

**Figure 2.** Results of the Digital Maturity Self-Assessment survey in 2016 measuring how well secondary care providers in England are making use of digital technology to achieve a health and care system that is paper-free at the point of care. Readiness indicates how well providers are able to plan and deploy digital services, while capabilities indicate whether providers have staff with the digital skills needed. The infrastructure score is based on whether providers have the right technology in place. Data from the National Health Service, England.









## Supplementary Material

**Table E1. Current Digital Strategies to Improve Adherence in Asthma and COPD**

Electronic Monitoring Devices			
Study Description	Features	Effect on Adherence	Other Outcomes
<i>Charles et al. 2007</i> [1] <ul style="list-style-type: none"> <li>• 24-week RCT</li> <li>• 110 patients (aged 12 to 65 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• EMD recorded date/time and number of actuations</li> <li>• Intervention group also utilized an audiovisual reminder function</li> </ul>	<ul style="list-style-type: none"> <li>• Significantly higher adherence in patients who received an audiovisual reminder compared with the control group (93% vs 74% median percentage taken in last 12 weeks of trial, <math>P &lt; .001</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• No significant differences occurred in clinical outcomes between the 2 groups</li> </ul>
<i>Burgess et al. 2010</i> [2] <ul style="list-style-type: none"> <li>• 4-month RCT</li> <li>• 26 patients (aged 6 to 14 years) with suboptimal asthma control</li> </ul>	<ul style="list-style-type: none"> <li>• EMD recorded date and time of actuation</li> <li>• Intervention group also received feedback based on EMD measured adherence</li> </ul>	<ul style="list-style-type: none"> <li>• Significantly higher adherence in patients who received feedback compared with the control group (79% vs 58%, <math>P &lt; .01</math>)</li> <li>• Adherence in the control group declined slightly over the study, whereas in the intervention group mean adherence was maintained (<math>P &lt; .01</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Change in forced FEV was greater in the intervention group (13.8%) than in the control group (9.8%), but did not reach statistical significance</li> </ul>
<i>Foster et al. 2014</i> [3] <ul style="list-style-type: none"> <li>• 6-month RCT</li> <li>• 143 patients (aged 14 to 65 years) with suboptimal asthma control</li> </ul>	<ul style="list-style-type: none"> <li>• EMD recorded date/time of all actuations and uploaded data monthly to a secure Web site</li> <li>• Intervention group also received IRF and/or personalized adherence discussions</li> </ul>	<ul style="list-style-type: none"> <li>• Significantly higher adherence in the IRF groups than in the non-IRF groups (73% vs 46% of prescribed daily doses; <math>P &lt; .0001</math>)</li> <li>• Adherence decreased over time in all groups, but remained twice as high in the IRF groups vs the non-IRF groups (<math>60\% \pm 38\%</math> vs <math>29\% \pm 33\%</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• 11% of patients in the IRF groups had exacerbations compared with 28% in the non-IRF groups (<math>P = .013</math>); this difference was not significant (<math>P = .06</math>) after adjustment for clustering and past self-reported prednisone use</li> </ul>
<i>Chan et al. 2015</i> [4] <ul style="list-style-type: none"> <li>• 6-month RCT</li> <li>• 220 children (aged 6 to 15 years) with prior history of asthma exacerbation</li> </ul>	<ul style="list-style-type: none"> <li>• EMD recorded date/time and number of actuations</li> <li>• Intervention group also utilized an audiovisual reminder function</li> </ul>	<ul style="list-style-type: none"> <li>• Significantly higher adherence in the intervention group compared with the control group (median 84% vs 30%, <math>P &lt; .001</math>)</li> <li>• Overall adherence fell in both groups over time, with no difference in the rate of decline (<math>P = .10</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Reduction in asthma morbidity score from baseline to 6 months was significantly greater (<math>P = .008</math>) in the intervention group (9.30 to 7.3) than in the control group (9.20 to 8.0)</li> </ul>

<i>Vasbinder et al. 2016</i> [5]	<ul style="list-style-type: none"> <li>• EMD recorded date and time of actuation</li> <li>• Intervention group also received tailored SMS reminders when a dose was at risk of omission</li> </ul>	<ul style="list-style-type: none"> <li>• Higher mean adherence in the intervention group compared with the control group (69.3% vs 57.3%; difference 12.0%, 95% CI 6.7%–17.7%)</li> </ul>	<ul style="list-style-type: none"> <li>• No differences were found between groups for asthma control, quality of life, or asthma exacerbations</li> </ul>
<i>Merchant et al. 2016</i> [6]	<ul style="list-style-type: none"> <li>• 12-month parallel arm study</li> <li>• 495 patients (aged &gt;5 years) with asthma</li> <li>• Intervention included a sensor to monitor inhaler use, an education component, reminders and alerts, data visualization and trends, and predictive analytics and feedback</li> <li>• Control group utilized sensors to monitor inhaler use along with usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Greater decrease in mean daily SABA uses per person in the intervention group (-0.41) vs routine care (-0.31), <math>P &lt; .001</math></li> <li>• Greater increase in the proportion of SABA-free days increased in the intervention group (21% vs routine care (17%), <math>P &lt; .01</math></li> </ul>	<ul style="list-style-type: none"> <li>• Improved ACT scores among adults initially lacking asthma control</li> </ul>
<i>Morton et al. 2017</i> [7]	<ul style="list-style-type: none"> <li>• EMD recorded date and time of actuation</li> <li>• Adherence data also reviewed by patient and caregiver every 3 months and reminders utilized in the intervention group</li> </ul>	<ul style="list-style-type: none"> <li>• Significantly higher adherence in the intervention group compared with the control group (70% vs 49%; <math>P \leq .001</math>) was maintained in the intervention group, but declined in the control group over 1 year</li> </ul>	<ul style="list-style-type: none"> <li>• Significant decrease in exacerbations requiring oral steroids or hospitalization in the intervention group</li> <li>• Decrease in ACQ in both groups (1.0 in control group and 0.9 in intervention group) but no significant difference between groups</li> </ul>
<b>Text messaging</b>			
<b>Study Description</b>	<b>Features</b>	<b>Effect on Adherence</b>	<b>Other Outcomes</b>
<i>Strandbygaard et al. 2010</i> [8]	<ul style="list-style-type: none"> <li>• Intervention group received daily SMS reminder to take asthma medication</li> </ul>	<ul style="list-style-type: none"> <li>• Mean medication adherence increased in the SMS group (77.9% to 81.5%) and decreased in the control group (84.2% to 70.1%)</li> <li>• The absolute difference in mean medication adherence between the 2 groups was 17.8%, <math>P = .019</math></li> </ul>	<ul style="list-style-type: none"> <li>• No between-group differences in change in exhaled nitric oxide levels, FEV1 (% of predicted), ACQ, or mini AQLQ</li> </ul>
<i>Prabhakaran et al. 2010</i> [9]	<ul style="list-style-type: none"> <li>• All patients received inpatient individualized asthma education at the beginning of the study</li> <li>• Intervention group received SMS messages to assist with asthma management, including medication use, according to a structured workflow</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in ACT scores, number of nebulizations, or ED visits between groups</li> </ul>
<i>Lv et al. 2012</i> [10]	<ul style="list-style-type: none"> <li>• Verbal asthma education (all groups)</li> <li>• Individualized asthma action plan with peak</li> </ul>	<ul style="list-style-type: none"> <li>• Medication adherence was higher in the SMS (80.0%) and traditional (74.1%) groups than in the control</li> </ul>	<ul style="list-style-type: none"> <li>• Significant increase in perceived asthma control and AQLQ in the SMS and</li> </ul>

<ul style="list-style-type: none"> <li>150 patients (aged &gt;18 years) with asthma</li> </ul>	expiratory flow monitoring and asthma diary (traditional and SMS groups) <ul style="list-style-type: none"> <li>Daily SMS reminders on how to manage asthma and option to ask questions via text message (SMS group)</li> </ul>	group (50.0%), but changes were not significant. <ul style="list-style-type: none"> <li>Follow-up appointment rates were significantly higher in the SMS (60%) and traditional (54%) groups compared with the control group (28%)</li> </ul>	traditional groups relative to control <ul style="list-style-type: none"> <li>Improved FEV1 (% predicted) in all groups, but no significant between-groups difference.</li> </ul>
<i>Petrie et al. 2012</i> [11] <ul style="list-style-type: none"> <li>9-month RCT</li> <li>147 patients (aged 16 to 45 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Treatment group received individually tailored text messages for 18 weeks based on their illness and medication beliefs</li> </ul>	<ul style="list-style-type: none"> <li>Average self-reported adherence was higher (57.8%) in the intervention group than the control group (43.2%) (<math>P &lt; .05</math>)</li> <li>Percentage taking over 80% of prescribed inhaler doses was 25.9% in the intervention group and 10.6% in the control group (<math>P &lt; .05</math>)</li> </ul>	<ul style="list-style-type: none"> <li>At 18 weeks, the text-message group was significantly higher than control on perceived necessity of preventer medication, belief in the long-term nature of their asthma, and perceived control over their asthma</li> </ul>
<i>Kolmodin MacDonell et al. 2016</i> [12] <ul style="list-style-type: none"> <li>3-month RCT</li> <li>48 African American adults (aged 18 to 29 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group received 2 computer-delivered motivational interviewing (MI) sessions with text reminders between sessions</li> <li>Control group completed asthma education matched for length, location, and method of delivery of the intervention MI sessions</li> </ul>	<ul style="list-style-type: none"> <li>Both groups missed fewer doses of controller medication at 3 months than at baseline</li> <li>The magnitude of the trend was greater for the intervention group for total doses missed, average doses missed per day, and number of days medication was missed, but did not reach statistical significance</li> </ul>	<ul style="list-style-type: none"> <li>There was a larger magnitude decrease in symptoms in the intervention vs control group in total symptoms, <math>P &lt; .05</math> and average symptoms per day, <math>P &lt; .05</math></li> <li>Intervention group improved in FEV-1 percent predicted (+4.41%) and control group decreased (-4.14%), <math>P \leq .01</math></li> </ul>
<i>Britto et al. 2017</i> [13] <ul style="list-style-type: none"> <li>6-month RCT</li> <li>64 patients (aged 12 to 22 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group received text message reminders personalized by the patient</li> <li>Ability to change, add, or delete reminders as desired</li> <li>Participants divided into intervention from baseline to month 3 or intervention from month 3 to month 6</li> </ul>	<ul style="list-style-type: none"> <li>Increased adherence to ICSs by 2.75% per month with the intervention vs without (<math>P &lt; .01</math>).</li> <li>For the group that received text messages first, adherence subsequently declined, suggesting no long-term effect</li> </ul>	<ul style="list-style-type: none"> <li>Improved ACT score after 1 month that was maintained for the 6-month duration of the study in both groups</li> <li>Asthma symptoms improved and asthma worry decreased in both groups</li> </ul>
<i>Akrom et al. 2015</i> [14] <ul style="list-style-type: none"> <li>Controlled pre- and post-intervention study</li> <li>66 patients (aged 18 to 80 years) with COPD</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group received daily text messages with motivational messages and reminders to take medication, and brief counseling</li> <li>Control group received hospital standard of care</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group experienced significant improvement in MMAS score (from 46% to 88% high compliance) from pretest to posttest; control group did not (55% to 61% high compliance).</li> </ul>	<ul style="list-style-type: none"> <li>Not measured</li> </ul>

Web-based and Mobile Applications			
Study Description	Features	Effect on Adherence	Other Outcomes
<i>Van der Meer et al. 2009</i> [15] <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 200 patients (aged 18 to 50 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Internet-based self-management program included weekly asthma control monitoring, treatment advice, online and group education, and remote communication with an asthma nurse</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Inhalation technique improved in both groups but improvements did not differ between groups (<math>P = .143</math>)</li> <li>• Self-reported medication adherence did not differ between groups</li> </ul>	<ul style="list-style-type: none"> <li>• Internet-based self-management was associated with improved asthma control and lung function</li> <li>• Asthma-related quality of life improved, but was not statistically significant in the intervention group vs control and exacerbations did not differ between groups</li> </ul>
<i>Liu et al. 2011</i> [16] <ul style="list-style-type: none"> <li>• 6-month prospective, controlled study</li> <li>• 120 patients with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Mobile phone-based interactive asthma self-care system including electronic symptoms diary and record of reliever use and PEFR</li> <li>• Control group received a written symptoms booklet and asked to record PEFR regularly</li> </ul>	<ul style="list-style-type: none"> <li>• Significant increase in mean daily dose of either systemic or ICSs in intervention group compared with control group</li> </ul>	<ul style="list-style-type: none"> <li>• Significant increase in PEFR in intervention group compared with control group at 4 and 6 months</li> <li>• Improved quality of life and fewer exacerbations in the intervention group</li> </ul>
<i>Ryan et al. 2012</i> [17] <ul style="list-style-type: none"> <li>• 6-month RCT (aged &gt;12 years)</li> <li>• 288 patients with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• Mobile phone-based system with twice-daily recording and transmission of symptoms, drug use, and peak flow, with immediate feedback</li> <li>• Control group recorded the same data using a paper diary</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in change in asthma control or self-efficacy between groups</li> <li>• No significant difference in number of acute exacerbations, prescribed steroid courses, and unscheduled HCP consultations or ED visits between groups</li> </ul>
<i>Farooqui et al. (2015)</i> [18] <ul style="list-style-type: none"> <li>• 30-day single-arm study</li> <li>• 24 patients (aged 9 to 16 years) with asthma</li> </ul>	Intervention included: <ul style="list-style-type: none"> <li>• Daily reminders for medication use</li> <li>• Personalized trigger avoidance measures</li> <li>• Algorithm-based, interactive asthma treatment plan</li> <li>• Gamification features and reward points based on medication use and interaction with the app</li> </ul>	<ul style="list-style-type: none"> <li>• Increased adherence to controller medication in 18 of 21 subjects (85%) during the intervention period compared with the 30 days immediately preceding enrollment</li> </ul>	<ul style="list-style-type: none"> <li>• Increase in measures to avoid asthma triggers after intervention period</li> </ul>
<i>Mosnaim et al. (2015)</i> [19] <ul style="list-style-type: none"> <li>• 8-week single-arm study</li> <li>• 12 African American patients (aged 11</li> </ul>	Intervention included: <ul style="list-style-type: none"> <li>• Daily visual reminders to take their ICS</li> <li>• Positive reinforcement (texts and gaming) for taking ICS</li> </ul>	<ul style="list-style-type: none"> <li>• Median ICS adherence increased from 19% at baseline to 67% at 8 weeks</li> <li>• At baseline 8% of patients met target ICS adherence (&gt;50%); at week 8, 58% of</li> </ul>	<ul style="list-style-type: none"> <li>• ACT scores increased from baseline to week 8 (18 vs 23) with 58% of participants achieving the minimal clinically important difference (3 points) in ACT score</li> </ul>

to 16 years) with persistent asthma	<ul style="list-style-type: none"> <li>• Immediate (ability to customize avatar) and long-term (\$1.00/dose-to purchase music, movies, applications, and games) rewards</li> </ul>	patients met target ICS adherence	<ul style="list-style-type: none"> <li>• SABA use decreased from a median of 3 puffs per week at baseline to 0 puffs per week at 8 weeks</li> </ul>
<i>Cingi et al. (2015) [20]</i> <ul style="list-style-type: none"> <li>• 3-month RCT</li> <li>• 136 patients with asthma (aged 25 to 41 years)</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention included physician/patient communication; health status and medication compliance tracking; sharing of motivational and educational content; and medication reminders</li> <li>• Control group received standard care</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• In the intervention group, more patients (49%) achieved a well-controlled asthma score (ACT &gt;19) compared with the control group (27%, (<math>P &lt; .05</math>))</li> </ul>
<i>Johnson et al. 2016 [21]</i> <ul style="list-style-type: none"> <li>• 3-week RCT</li> <li>• 98 patients with asthma (aged 12 to 17 years)</li> </ul>	<ul style="list-style-type: none"> <li>• Personalized health application (MyMediHealth) to help patients manage medications and receive dosing reminders</li> <li>• Control group received action lists as part of usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Significant improvement in self-reported 7-day adherence (<math>P = .011</math>) in the intervention group vs control group</li> </ul>	<ul style="list-style-type: none"> <li>• Increased quality of life (<math>P = .037</math>) and perception of self-efficacy (<math>P = .016</math>) in the intervention group compared with the control group</li> </ul>
<i>Ahmed et al. 2016 [22]</i> <ul style="list-style-type: none"> <li>• 6-month, RCT</li> <li>• 100 patients (aged 18 to 69 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• My Asthma Portal mobile application, which allowed participants to view personal health information, receive information tailored to identified knowledge gaps, and monitor and receive feedback on current self-management practices</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• No significant between-group effects on asthma-related quality of life</li> <li>• No significant effect on asthma control</li> </ul>
<i>Cook et al. 2016 [23]</i> <ul style="list-style-type: none"> <li>• Prospective single-arm, treatment-only, 4-month study</li> <li>• 60 adults (aged 17 to 82 years) with asthma</li> </ul>	Intervention included: <ul style="list-style-type: none"> <li>• Continuous patient data collection including self-assessment of asthma control and assessment of patient knowledge regarding asthma control</li> <li>• Individualized alerts, coaching, and educational materials</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>	<ul style="list-style-type: none"> <li>• Statistically significant improvement in ACT scores and FEV<sub>1</sub> (in subset of patients with available before-and-after spirometry data)</li> <li>• Nonsignificant decrease in total number of systemic corticosteroids prescribed</li> </ul>
<i>Koufopoulos et al. 2016 [24]</i> <ul style="list-style-type: none"> <li>• 9-week RCT</li> <li>• 216 patients (aged 18 to 64</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention group included access to “AsthmaVillage,” an online community for patients with asthma</li> </ul>	<ul style="list-style-type: none"> <li>• No difference in self-reported medication adherence in the intervention group vs control</li> </ul>	<ul style="list-style-type: none"> <li>• Not measured</li> </ul>

years) with asthma	<ul style="list-style-type: none"> <li>Control group did not have access to the online community, but utilized the “AsthmaDiary,” an online diary for recording ICS preventer use</li> </ul>		
<i>Kim et al. (2016)</i> [25] <ul style="list-style-type: none"> <li>8-week study</li> <li>44 patients (aged &gt;19 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group utilized an application that included: <ul style="list-style-type: none"> <li>Asthma monitoring application and peak flow meter</li> <li>Questionnaires and daily patient symptom score</li> <li>Daily alerts and action plans based on asthma control status</li> </ul> </li> <li>The control group did not use the application</li> </ul>	<ul style="list-style-type: none"> <li>Adherence improved in the intervention group (<math>P = .017</math>) but not in the control group (<math>P = .674</math>)</li> </ul>	<ul style="list-style-type: none"> <li>Lung function parameters did not significantly differ between visits or between the intervention and control groups at each visit</li> </ul>
<i>Morrison et al. (2016)</i> [26] <ul style="list-style-type: none"> <li>12-week RCT</li> <li>51 patients (aged <math>\geq 16</math> years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>“Living Well with Asthma” Web site designed to assess current level of asthma control and support optimal medication management; challenge attitudes and concerns around medication; and prompt use of personal action plan</li> <li>Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>No significant between-group difference in the percentage of recommended ICS doses self-reportedly taken, nor the equivalent beclometasone doses prescribed</li> </ul>	<ul style="list-style-type: none"> <li>No significant difference in ACQ scores and mini-AQLQ scores</li> <li>Significant improvement in PAM scores in the intervention group compared with the control group</li> </ul>
<i>Pool et al. (2017)</i> [27] <ul style="list-style-type: none"> <li>12-month RCT</li> <li>408 adults (aged 21 to 60 years) with asthma</li> </ul>	<ul style="list-style-type: none"> <li>Tailored feedback and reminders based on answers to questions (at least once per month) related to asthma symptoms, medications, provider care, and asthma management plan</li> <li>Control group received similar questions and feedback, but focused on preventive services unrelated to asthma control (eg, cancer screening)</li> </ul>	<ul style="list-style-type: none"> <li>No differences were observed in medication adherence between the intervention group and control</li> </ul>	<ul style="list-style-type: none"> <li>Greater mean improvement in ACT score in the intervention group (2.3 vs 1.2; <math>P = .02</math>)</li> <li>No differences in asthma-related health care utilization</li> </ul>
<i>Pinnock et al. 2013</i> [28] <ul style="list-style-type: none"> <li>12-month RCT</li> <li>256 adults with COPD</li> </ul>	<ul style="list-style-type: none"> <li>Intervention group recorded symptoms and medication use and monitored oxygen saturation daily</li> </ul>	<ul style="list-style-type: none"> <li>Not measured</li> </ul>	<ul style="list-style-type: none"> <li>Number and mean duration of hospital admissions for COPD did not differ significantly between groups</li> </ul>

	<ul style="list-style-type: none"> <li>• Intervention included algorithm-generated alerts to clinical team based on patient input</li> <li>• Control group utilized standard self-monitoring</li> </ul>		<ul style="list-style-type: none"> <li>• No significant effect on health-related quality of life between groups</li> </ul>
<i>Farmer et al. 2017</i> [29] <ul style="list-style-type: none"> <li>• 12-month RCT</li> <li>• 166 patients (aged <math>\geq 40</math> years) with COPD</li> </ul>	<ul style="list-style-type: none"> <li>• Intervention included daily symptom diary including medication use; Bluetooth-enabled pulse oximeter with finger probe; monthly mood screening questionnaires; and tailored videos and education based on patient entries</li> <li>• Control group received usual care</li> </ul>	<ul style="list-style-type: none"> <li>• No difference on MARS in self-reported medication adherence</li> </ul>	<ul style="list-style-type: none"> <li>• No significant difference in number of exacerbations, relative risk of hospital admission, quality of life, self-reported smoking cessation, depression, or anxiety</li> <li>• Better overall health status (measured with 5-Level EuroQol 5-Dimension Questionnaire) in the intervention group (<math>P = .03</math>)</li> </ul>

ACQ, Asthma Control Questionnaire; ACT, Asthma Control Test; AQLQ, Asthma Quality of Life Questionnaire; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ED, emergency department; EMD, electronic monitoring device; FEV1, forced expiratory volume in one second; HCP, health care provider; ICS, inhaled corticosteroid; IRF, inhaler reminders and feedback; MARS, Medication Adherence Report Scale; MI, motivational interviewing; MMAS, Morisky Medication Adherence Scale; PAM, patient activation measure; PEF, peak expiratory flow rate; RCT, randomized controlled trial; SABA, short-acting beta agonist; SMS, short message service.



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