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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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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 personalised 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 realise 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 healthcare 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.

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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 healthcare costs [1]. Complex treatment regimens for patients with asthma and 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]. Furthermore, 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 optimised adherence to maintenance medication in patients with respiratory diseases, a number of digital technologies have been developed. Strategies used to date include approaches to monitoring and improving 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 in patients with asthma and COPD that were published between 2007 and 2017, including electronic monitoring devices (EMDs), text messaging, and web and mobile applications, are summarised 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 CF, chipped-nebulisers 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 visualisation of measurements and integration into a wider dataset, such as that 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, exhaled nitric oxide fraction (F_{eNO}), physical activity and ambient pollution. These data can link adherence management with other aspects of patient self-management [40, 41] and may be used to provide appropriate information to promote healthy behaviours (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]. Taken together, digital approaches targeting adherence and advances in physiological monitoring of disease open up a range of possibilities for understanding the causes and consequences of poor adherence and, hence, a rational way to deliver effective adherence management.

Potential opportunities provided by digital technologies in respiratory medicine

Several attributes of digital technologies, which could be summarised under the headings of precision, penetration, prediction and personalisation, suggest how current and future technologies may be incorporated into the multidimensional nature of healthcare.

Precision

Longitudinal data on patients' adherence collected *via* digital applications, 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, in patients with asthma, digitally collected real-time data on adherence and symptoms can help HCPs differentiate between symptoms or changes in lung function due to low adherence *versus* those indicating refractory disease or disease progression [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 optimise 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 to 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 in terms of accurately assessing medication use, as well as in 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

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TABLE 1 Current digital strategies to improve adherence in asthma and chronic obstructive pulmonary disease (COPD)

Study description	Features	Effect on adherence	Other outcomes
Electronic monitoring devices (EMDs)			
Charles *et al.* 2007 [6] 24-week RCT 110 patients (aged 12–65 years) with asthma	EMD recorded date/time and number of actuations Intervention group also utilised an audiovisual reminder function	Significantly higher adherence in patients who received an audiovisual reminder compared with the control group (93% *versus* 74% median percentage taken in last 12 weeks of trial, p<0.001)	No significant differences occurred in clinical outcomes between the two groups
Burgess *et al.* 2010 [9] 4-month RCT 26 patients (aged 6–14 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% *versus* 58%, p<0.01) Adherence in the control group declined slightly over the study, whereas in the intervention group mean adherence was maintained (p<0.01)	Change in forced FEV_1 was greater in the intervention group (13.8%) than in the control group (9.8%), but did not reach statistical significance
Foster *et al.* 2014 [10] 6-month RCT 143 patients (aged 14–65 years) with suboptimal asthma control	EMD recorded date/time of all actuations and uploaded data monthly to a secure website Intervention group also received IRF and/or personalised adherence discussions	Significantly higher adherence in the IRF groups than in the non-IRF groups (73% *versus* 46% of prescribed daily doses; p<0.0001) Adherence decreased over time in all groups, but remained twice as high in the IRF groups *versus* the non-IRF groups (60% ±38% *versus* 29% ±33%)	11% of patients in the IRF groups had exacerbations compared with 28% in the non-IRF groups (p=0.013). This difference was not significant (p=0.06) after adjustment for clustering and past self-reported prednisone use
Chan *et al.* 2015 [5] 6-month RCT 220 children (aged 6–15 years) with prior history of asthma exacerbation	EMD recorded date/time and number of actuations Intervention group also utilised an audiovisual reminder function	Significantly higher adherence in the intervention group compared with the control group (median 84% *versus* 30%, p<0.001) Overall adherence fell in both groups over time, with no difference in the rate of decline (p=0.10)	Reduction in asthma morbidity score from baseline to 6 months was significantly greater (p=0.008) in the intervention group (mean score of 9.3 at baseline *versus* 7.3 at 6 months) than in the control group (mean score of 9.2 at baseline *versus* 8.0 at 6 months)
Vasbinder *et al.* 2016 [11] 12-month RCT 209 children (aged 4–11 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% *versus* 57.3%; difference 12.0%, 95% CI 6.7%–17.7%)	No differences were found between groups for asthma control, QoL, or asthma exacerbations
Merchant *et al.* 2016 [12] 12-month parallel arm study 495 patients (aged >5 years) with asthma	Intervention included a sensor to monitor inhaler use, an education component, reminders and alerts, data visualisation and trends, and predictive analytics and feedback Control group utilised sensors to monitor inhaler use along with usual care	Greater decrease in mean daily SABA uses per person in the intervention group compared with routine care (−0.41 *versus* −0.31, p<0.001) Greater increase from baseline in the mean percentage of SABA-free days in the intervention group compared with routine care (21% *versus* 17%, p<0.01)	Improved ACT scores among adults initially lacking asthma control
Morton *et al.* 2017 [13] 1-year RCT 90 children (aged 6–16 years) with asthma	EMD recorded date and time of actuation Adherence data also reviewed by patient and caregiver every 3 months and reminders utilised in the intervention group	Significantly higher adherence in the intervention group compared with the control group (70% *versus* 49%, p⩽0.001) Adherence was maintained in the intervention group, but declined in the control group over 1 year	Significant decrease in exacerbations requiring oral steroids or hospitalisation in the intervention group Decrease in ACQ in both groups (1.0 in the control group and 0.9 in the intervention group) but no significant difference between groups

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TABLE 1 Continued

Study description	Features	Effect on adherence	Other outcomes
Text messaging			
Strandbygaard *et al.* 2010 [14] 12-week RCT 26 patients (aged 18–45 years) with asthma	Intervention group received daily SMS reminder to take asthma medication	Mean medication adherence increased in the SMS group (77.9% to 81.5%) and decreased in the control group (84.2% to 70.1%) The absolute difference in mean medication adherence between the two groups was 17.8% (p=0.019)	No between-group differences in change in F_{eNO}, FEV_1 (% predicted), ACQ, or mini-AQLQ
Prabhakaran *et al.* 2010 [15] 12-week RCT 120 patients (aged >21 years) hospitalised for asthma	All patients received inpatient individualised asthma education at the beginning of the study Intervention group received SMS messages to assist with asthma management, including medication use, according to a structured workflow	Not measured	No significant difference in ACT scores, number of nebulisations, or ED visits between groups
Lv *et al.* 2012 [16] 12-week RCT 150 patients (aged >18 years) with asthma	Verbal asthma education (all groups) Individualised asthma action plan with PEF monitoring and asthma diary (traditional and SMS groups) Daily SMS reminders on how to manage asthma and option to ask questions *via* text message (SMS group)	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 Follow-up appointment rates were significantly higher in the SMS (60%) and traditional (54%) groups compared with the control group (28%)	Significant increase in perceived asthma control and AQLQ in the SMS and traditional groups relative to the control group Improved FEV_1 (% predicted) in all groups, but no significant between-groups difference
Petrie *et al.* 2012 [17] 9-month RCT 147 patients (aged 16–45 years) with asthma	Treatment group received individually tailored text messages for 18 weeks based on their illness and medication beliefs	Average self-reported adherence was higher in the intervention group than the control group (57.8% *versus* 43.2%, p<0.05) Percentage taking over 80% of prescribed inhaler doses was 25.9% in the intervention group and 10.6% in the control group (p<0.05)	At 18 weeks, the text message group was significantly higher than the control group on perceived necessity of preventer medication, belief in the long-term nature of their asthma and perceived control over their asthma
Kolmodin MacDonell *et al.* 2016 [18] 3-month RCT 48 African American adults (aged 18–29 years) with asthma	Intervention group received two computer-delivered motivational interviewing (MI) sessions with text reminders between sessions Control group completed asthma education matched for length, location and method of delivery of the intervention group MI sessions	Both groups missed fewer doses of controller medication at 3 months than at baseline 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	There was a larger magnitude decrease in symptoms in the intervention *versus* the control group, both in total symptoms (p<0.05) and average symptoms per day (p<0.05) FEV_1 (% predicted) improved in the intervention group and deteriorated in the control group (+4.41% and −4.14%, respectively, p⩽0.01)
Britto *et al.* 2017 [19] 6-month RCT 64 patients (aged 12–22 years) with asthma	Intervention group received text message reminders personalised by the patient Ability to change, add, or delete reminders as desired Participants divided into intervention from baseline to month 3 or intervention from month 3 to month 6	Increased adherence to ICS by 2.75% per month with the intervention *versus* without it (p<0.01) For the group that received text messages first, adherence subsequently declined, suggesting no long-term effect	Improved ACT score after 1 month that was maintained for the 6-month duration of the study in both groups Asthma symptoms improved and asthma worry decreased in both groups
Akrom *et al.* 2015 [20] Controlled pre- and post-intervention study 66 patients (aged 18–80 years) with COPD	Intervention group received daily text messages with motivational messages and reminders to take medication, and brief counselling Control group received hospital standard of care	Intervention group experienced significant improvement in MMAS score from pre-test to post-test (46% to 88% high compliance); however, the control group did not (55% to 61% high compliance)	Not measured

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TABLE 1 Continued

Study description	Features	Effect on adherence	Other outcomes
Web-based and mobile applications			
Van der Meer *et al.* 2009 [21] 12-month RCT 200 patients (aged 18–50 years) with asthma	Internet-based self-management program included weekly asthma control monitoring, treatment advice, online and group education, and remote communication with an asthma nurse Control group received the usual care	Inhalation technique improved in both groups but improvements did not differ between groups (p=0.143) Self-reported medication adherence did not differ between groups	Internet-based self-management was associated with improved asthma control and lung function Asthma-related QoL improved, but was not statistically significant in the intervention group *versus* control and exacerbations did not differ between groups
Liu *et al.* 2011 [22] 6-month prospective, controlled study 120 patients with asthma	Mobile phone-based interactive asthma self-care system including electronic symptoms diary and record of reliever use and PEFR Control group received a written symptoms booklet and were asked to record PEFR regularly	Significant increase in mean daily dose of either systemic corticosteroids or ICS in intervention group compared with control group	Significant increase in PEFR in intervention group compared with control group at 4 and 6 months Improved QoL and fewer exacerbations in the intervention group
Ryan *et al.* 2012 [23] 6-month RCT 288 patients (aged >12 years) with asthma	Mobile phone-based system with twice-daily recording and transmission of symptoms, drug use and peak flow, with immediate feedback Control group recorded the same data using a paper diary	Not measured	No significant difference in change in asthma control or self-efficacy between groups No significant difference in number of acute exacerbations, prescribed steroid courses and unscheduled HCP consultations or ED visits between groups
Farooqui *et al.* 2015 [24] 30-day single-arm study 24 patients (aged 9–16 years) with asthma; 21 patients completed the study	Intervention included: Daily reminders for medication use Personalised trigger avoidance measures Algorithm-based, interactive asthma treatment plan Gamification features and reward points based on medication use and interaction with the app	Increased adherence to controller medication in 18 out of 21 patients (85%) during the intervention period compared with the 30 days immediately preceding enrolment	Increase in measures to avoid asthma triggers after intervention period
Mosnaim *et al.* 2015 [25] 8-week single-arm study 12 African American patients (aged 11–16 years) with persistent asthma	Intervention included: Daily visual reminders to take their ICS Positive reinforcement (texts and gaming) for taking ICS Immediate (ability to customise avatar) and long-term rewards ($1.00 per dose to purchase music, movies, applications and games)	Median ICS adherence increased from 19% at baseline to 67% at 8 weeks At baseline 8% of patients met target ICS adherence (>50%), while at 8 weeks, 58% of patients met target ICS adherence	ACT scores increased from baseline to week 8 (18 *versus* 23) with 58% of participants achieving the minimal clinically important difference (3 points) in ACT score SABA use decreased from a median of 3 puffs per week at baseline to 0 puffs per week at 8 weeks
Cingi *et al.* 2015 [26] 3-month RCT 136 patients (aged 25-41 years) with asthma	Intervention included physician/patient communication, health status and medication compliance tracking, sharing of motivational and educational content, and medication reminders Control group received standard care	Not measured	In the intervention group, more patients achieved a well-controlled asthma score (ACT >19) compared with the control group (49% *versus* 27%, p<0.05)

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TABLE 1 Continued

Study description	Features	Effect on adherence	Other outcomes
Johnson *et al.* 2016 [27] 3-week RCT 98 patients (aged 12-17 years) with asthma	Personalised health application (MyMediHealth) to help patients manage medications and receive dosing reminders Control group received action lists as part of usual care	Significant improvement in self-reported 7-day adherence (p=0.011) in the intervention group *versus* the control group	Increased QoL (p=0.037) and perception of self-efficacy (p=0.016) in the intervention group compared with the control group
Ahmed *et al.* 2016 [28] 6-month RCT 100 patients (aged 18–69 years) with asthma	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 Control group received usual care	Not measured	No significant between-group effects on asthma-related QoL No significant effect on asthma control
Cook *et al.* 2016 [29] Prospective single-arm, treatment-only, 4-month study 60 adults (aged 17–82 years) with asthma	Intervention included: Continuous patient data collection including self-assessment of asthma control and assessment of patient knowledge regarding asthma control Individualised alerts, coaching and educational materials	Not measured	Statistically significant improvement in ACT scores and FEV_1 (in subset of patients with available before-and-after spirometry data) Nonsignificant decrease in total number of systemic corticosteroids prescribed
Koufopoulos *et al.* 2016 [30] 9-week RCT 216 patients (aged 18–64 years) with asthma	Intervention group included access to "AsthmaVillage," an online community for patients with asthma Control group did not have access to the online community, but utilised the "AsthmaDiary," an online diary for recording ICS preventer use	No difference in self-reported medication adherence in the intervention group *versus* control	Not measured
Kim *et al.* 2016 [31] 8-week study 44 patients (aged >19 years) with asthma	Intervention group utilised an application that included: An asthma monitoring application and peak flow meter Questionnaires and daily patient symptom score Daily alerts and action plans based on asthma control status The control group did not use the application	Adherence improved in the intervention group (p=0.017) but not in the control group (p=0.674)	Lung function parameters did not significantly differ between visits or between the intervention and control groups at each visit
Morrison *et al.* 2016 [32] 12-week RCT 51 patients (aged ⩾16 years) with asthma	"Living Well with Asthma" website designed to assess current level of asthma control, support optimal medication management, challenge attitudes and concerns around medication, and prompt use of a personal action plan Control group received usual care	No significant between-group difference in the percentage of recommended ICS doses self-reportedly taken, nor in the equivalent beclometasone doses prescribed	No significant difference in ACQ scores and mini-AQLQ scores Significant improvement in PAM scores in the intervention group compared with the control group
Pool *et al.* 2017 [33] 12-month RCT 408 adults (aged 21–60 years) with asthma	Tailored feedback and reminders based on answers to questions (at least once per month) related to asthma symptoms, medications, provider care and the asthma management plan Control group received similar questions and feedback, but focused on preventive services unrelated to asthma control (*e.g.* cancer screening)	No differences were observed in medication adherence between the intervention group and the control group	Greater mean improvement in ACT score in the intervention group compared to the control group (2.3 *versus* 1.2, p=0.02) No differences in asthma-related healthcare utilisation

Continued

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TABLE 1 Continued

Study description	Features	Effect on adherence	Other outcomes
Pinnock *et al.* 2013 [34] 12-month RCT 256 adults with COPD	Intervention group recorded symptoms and medication use and monitored oxygen saturation daily Intervention included algorithm-generated alerts to the clinical team based on patient input Control group utilised standard self-monitoring	Not measured	Number and mean duration of hospital admissions for COPD did not differ significantly between groups No significant effect on HRQoL between groups
Farmer *et al.* 2017 [35] 12-month RCT 166 patients (aged ⩾40 years) with COPD	Intervention included a daily symptom diary including medication use, a Bluetooth-enabled pulse oximeter with finger probe, monthly mood screening questionnaires and tailored videos and education based on patient entries Control group received usual care	No difference in self-reported medication adherence on MARS	No significant difference in the number of exacerbations, relative risk of hospital admission, QoL, self-reported smoking cessation, depression, or anxiety Better overall health status (measured with the five level EuroQol 5-Dimension Questionnaire) in the intervention group (p=0.03)

RCT: randomised controlled trial; FEV_1: forced expiratory volume in 1 s; IRF: inhaler reminders and feedback; SMS: short message service; QoL: quality of life; SABA: short-acting β-agonist; F_{eNO}: exhaled nitric oxide fraction; ACT: asthma control test; ACQ: asthma control questionnaire; AQLQ: asthma quality of life questionnaire; ED: emergency department; PEF: peak expiratory flow; ICS: inhaled corticosteroid; MMAS: Morisky medication adherence scale; PEFR: peak expiratory flow rate; HCP: healthcare provider; PAM: patient activation measure; HRQoL: health-related quality of life; MARS: medication adherence report scale.

circumstances. In addition, the incorporation of information on other aspects important to patients' health, such as environmental exposures and physical activity, can further support optimal patient self-management.

Penetration

Many people in remote or low-income settings are not well supported by conventional healthcare [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 healthcare [47]. For example, individuals with CF living in rural or remote areas may face challenges accessing specialist care (*i.e.* long-travel time) [50, 51]. However, for patients with CF in remote areas of Western Australia, offering tele-health clinics *via* videoconferencing 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 healthcare 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].

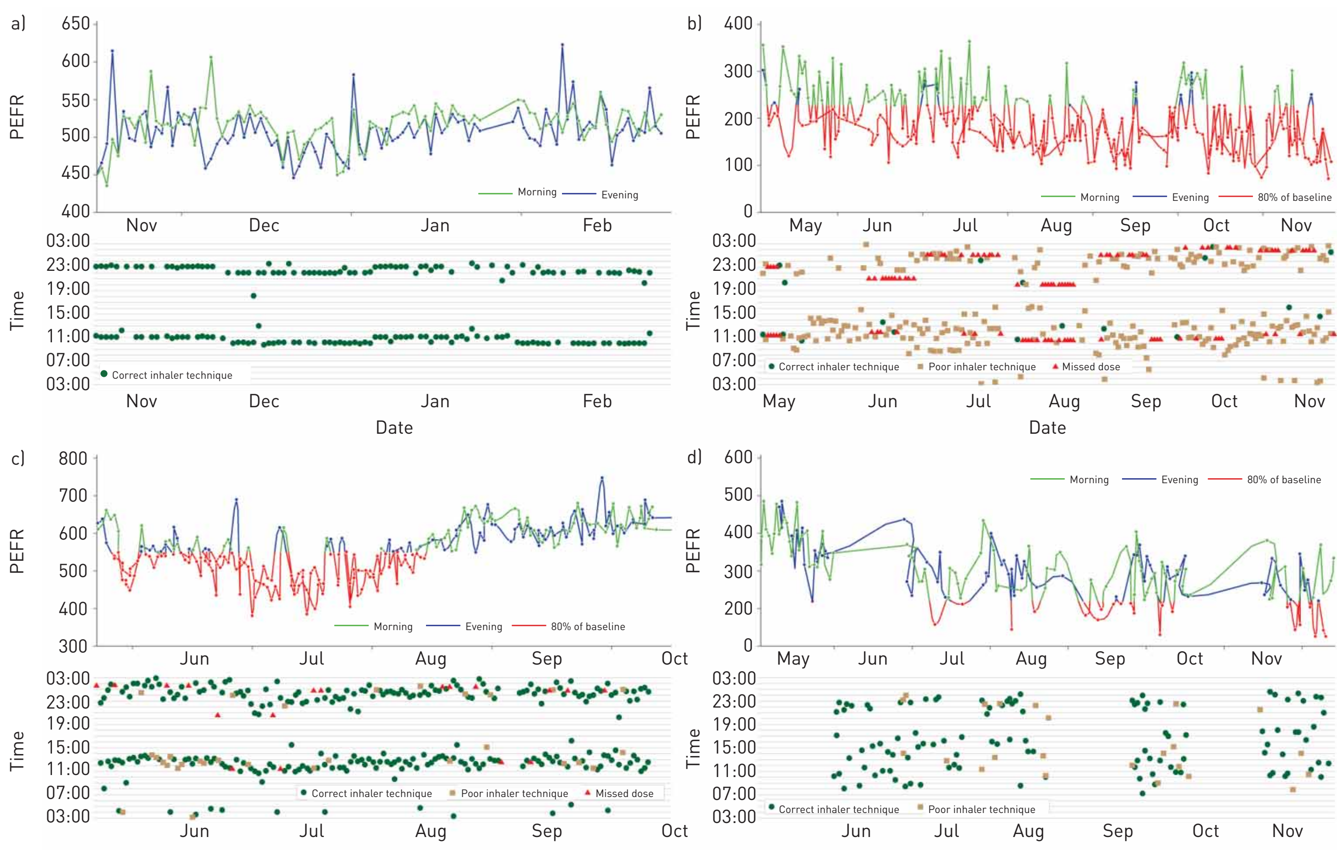

FIGURE 1 Four patterns of digitally monitored lung function, adherence and inhaler technique, as assessed by a digital audio recording device attached to the inhaler. a) A patient with well-controlled asthma with stable peak expiratory flow (PEF) and regular use of a twice daily preventer inhaler. Normal 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) A 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) A patient with initial poor lung function who subsequently improves. Improved lung function is associated with regular and correct inhaler use. d) A patient with periods of intermittent inhaler use and poor lung function, followed by periods of improved adherence and improved lung function. Drops in lung function are associated with intermittant inhaler use and appear to prompt the patient to restart use. The absence of dots on the time graph indicates that no doses were taken.

Prediction

A major strategy for improving health outcomes in respiratory patients is through decreasing the likelihood and magnitude of clinical deterioration, 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 behavioural recommendations following air quality alerts is poor and is an area where additional research is needed [61].

Personalisation

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 that is present [44, 62]. They also provide unique objective insights into the behavioural 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 such determinants. 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 CF, 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 behaviours. Digital technologies that collect patient information and provide insights into the specific barriers that drive patients' self-management behaviours can lead to meaningful communication between patients and HCPs, based on objective information [64]. Some factors cannot be changed or are difficult to modify (*i.e.* age, sex and 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 behavioural theory and focus on modifiable determinants relevant for the specific behaviours targeted [65]. Program development tools, such as the Intervention Mapping protocol, the Capability, Opportunity, Motivation, and Behaviour (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 nebuliser use in patients with CF were identified using the TDF and were used to inform development of the CFHealthHub, a digital behavioural intervention tool currently being evaluated in a large randomised trial [69, 70].

Furthermore, profiling tools that assign patients to an appropriate attitudinal cluster are promising approaches for grouping patients based on their beliefs and attitudes [71]. Personalising interventions to identify and target specific patient behaviours requires a baseline assessment of patient beliefs (*i.e.* using the BMQ or the 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 the 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 errors (*i.e.* not exhaling, not holding breath and inappropriate inhalation speed) and device-specific errors (*i.e.* 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 optimise their technique and, when used in newly diagnosed patients, could help them to 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 (*e.g.* 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 figures 1c and 1d).

The flexible nature of digital technologies provides an opportunity to develop generalisable core features and customisable elements to meet the individual patient's needs, responding to both patient preferences and the clinician's requirements. The aim would be to create interactive and adaptable digital versions of individual treatment action plans that use personal rather than population thresholds for changes in treatment, examples of which are already available [35]. Key features such as educational content could be customised to facilitate engagement based on a patient's health literacy, treatment perceptions and disease experience.

Key considerations toward successful implementation and uptake of digital applications

Digital technologies have the ability to improve the precision, penetration, prediction and personalisation of respiratory care. However, for this potential to be realised, several conditions need to be in place. A strong evidence base that represents the users is required, as are strategies for how technologies will be integrated into health systems, together with the appropriate regulatory standards.

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.

Considering the intended users of the interventions

To avoid the restricted entry criteria and rigid ecology of care issues that characterise traditional trials of medications, studies of digital interventions must reflect the user base and the usual clinical environment, and 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 might reasonably be expected in usual practice or in the control group [13]. Continuous improvement and customisation is also possible, starting from a basic user experience and incorporating user feedback features [17, 89–91].

Integrating digital technologies into existing healthcare 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 improving standardisation and facilitating transfer of information between devices and different healthcare settings (by consortia such as INTEROPen; www.interopen.org), as well as by the development of secure communication formats (by systems such as blockchain; 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 behavioural principles applied to patients: clearly define the behaviours requiring change, identify relevant determinants and incorporate behaviour change techniques that effectively target these behaviours 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. Furthermore, preparing organisations for technology-supported care of chronic conditions is likely to represent a financial burden with significant scope for 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].

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

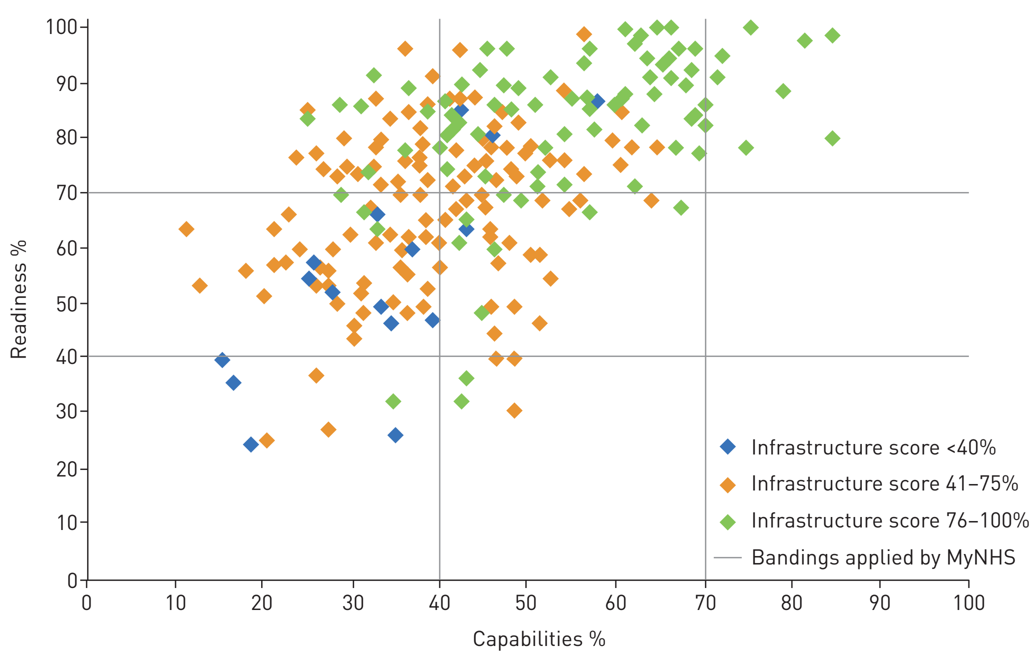

FIGURE 2 Results of the Digital Maturity Self-Assessment survey in 2016, measuring how well secondary care providers in England are making use of digital technology to achieve a health and care system that is paper-free at the point of care. Readiness indicates how well providers are able to plan and 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 was from the National Health Service (NHS), England. Reproduced with permission of the rights holder, Royal College of Physicians from [93].

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 (*e.g.* 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.

Conclusions

For patients, clinicians and researchers, digital technologies such as those addressing adherence and inhaler technique offer the opportunity to advance personalised 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 healthcare into underserved communities, where adherence is often the poorest, or of 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 healthcare 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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