

**What is the impact of innovative electronic health interventions in improving treatment adherence in asthma? The pediatric perspective.**

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**Abstract:**

Suboptimal adherence to treatment is a significant issue in the management of pediatric asthma and is a major cause of uncontrolled disease, life-threatening attacks, and increased utilization of healthcare resources. Electronic health (e-Health) solutions have the potential to positively impact self-management of children and adolescents with asthma and their families, thereby improving treatment adherence and asthma outcomes. However, there is a lack of sufficient data to support widespread adoption of e-Health tools in pediatric asthma practice. A critical evaluation of the impact of these new interventions on treatment adherence in childhood asthma must consider unmet needs, heterogeneity of trials, safety and data security issues, long-term effects, and cost-efficacy. This article explores the most relevant issues on the role of e-Health and its sub-category—mobile health (mHealth)—in promoting treatment adherence in childhood asthma, focusing on current evidence gaps and limitations, and future research perspectives.

**Key words:** asthma, children, adherence, e-Health, electronic monitoring devices, mobile applications, asthma control

**Abbreviations used**

Apps - Applications

e-Health - Electronic health

EMDs - Electronic monitoring devices

GINA - Global Initiative for Asthma

ICS - Inhaled corticosteroids

mHealth - Mobile health

RCTs - Randomized controlled trials

SABA - short-acting  $\beta$  agonist

Asthma is one of the most common chronic diseases and affects approximately 10% of children worldwide.<sup>1,2</sup> Asthma management is essentially focused on maintaining the control of the disease and reducing the risk of asthma-related exacerbations and deaths,<sup>3,4</sup> and for asthmatic children, treatment adherence is fundamental to effectively self-managing the disease. Healthcare providers are actively involved in promoting education, offering information, and establishing intervention to improve adherence in pediatric asthma, but still, patient adherence to asthma medications remains low, with adherence rates frequently less than 50% in this population.<sup>5</sup> It has been demonstrated that poor adherence compromises the effectiveness of treatment and is a major cause of uncontrolled disease, severe life-threatening attacks, and increased utilization of healthcare resources.<sup>4,6-8</sup>

Given the multidimensional complexity of nonadherence in asthma, different tools with variable accuracy have been proposed for implementation in clinical practice to assess objectively and monitor treatment adherence in children.<sup>5,10</sup> Among these, electronic health (e-Health) solutions are potentially valuable assets for children and adolescents with asthma and their families. These interventions offer opportunities to improve the efficiency of healthcare delivery and enhance patient and caregiver activation, while also engaging in medical care and shared decision making, ultimately improving treatment adherence and asthma outcomes. As part of this effort, mobile health (mHealth) devices, a sub-category of e-Health, are gaining traction as an emerging healthcare model as billions of people across the globe have quick access to an array of screens that can improve the interaction between patients and health care providers, and allow for the collection of clinical information. Devices such as smartphones, mobile applications (apps), and electronic tables fall into this category. Optimal implementation of the e-Health spectrum, as part of current asthma management, should be considered a promising strategy to enhance and maximize adherence and asthma monitoring.

### **Using e-Health modalities to promote treatment adherence**

E-Health solutions for optimal and personalized asthma management comprise a range of tools and applications for self-monitoring of symptoms and/or disease control to improve therapy adherence. They also address self-management action plans, and patient educational materials.<sup>11</sup> These modalities include digital health platforms, electronic reminders, inhaler trackers, and more (Table 1), and may collect data to improve the interaction between patients and health care providers.

Many have been developed to target the pediatric age group<sup>10</sup>, and whereas some have been studied in randomized controlled trials (RCTs) and observational studies, very recent reviews on this topic indicate a lack of conclusive data to document their effectiveness.<sup>10,11</sup> Still, the following overview suggests that e-Health modalities are worth considering.

One place to start is with the impact of e-Health on inhaler technique and adherence, a vital part of asthma management. Among adolescents, the use of electronic sensors and digital health platforms has been well accepted, as evidenced by their claims of satisfaction with the inhaler sensor device due to its portability and good functioning.<sup>12</sup> This is a step forward, as to date, evidence assessing the impact of e-Health on inhaler technique has tended to be inconclusive<sup>13</sup>, notwithstanding a recent study on adult patients with asthma or COPD suggesting that use of intelligent Spacer Data Logger systems might be helpful for improving adherence. Specifically, this device is able to measure and record whether a pressurized metered dose inhaler is adequately shaken, the time to actuation, and the volume inhaled from the spacer up to 26 seconds after actuation. Experimental results showed that the Spacer Data Logger device could accurately measure the volume inhaled from a spacer device. This encouraging finding should be confirmed in clinical trials, especially in children, where it cannot be assumed that an adequate amount of drug was inhaled from a spacer device.<sup>14</sup>

The ongoing CONNected Electronic Inhalers Asthma Control Trial 1 (CONNECT 1) will provide updated findings on feasibility and effectiveness of a so-called smart inhaler, namely an albuterol

multidose dry powder inhaler with an integrated electronic module digital system to optimize outcomes in patients with asthma who are at least 13 years of age.<sup>15</sup> Smart inhalers are defined as devices providing data wirelessly through the cloud, internet, or apps, to track medication, dosage, and time used for each inhaled dose.

An ongoing observational study by Honkoop et al, conducted in asthmatic adults ( $\geq$  age 18), is using mHealth, home-monitoring sensors and Smartinhaler devices to determine the extent to which physiological, behavioral and environmental data can be used to predict asthma exacerbation.<sup>16</sup> The outcomes may be useful for developing tailored predictive models and personalized self-management plans that can be integrated into mHealth systems. Another study focuses on an asthma digital health platform (Propeller Health) that combines inhaler sensors for passive data collection and tracking medication; patient-facing mobile applications for data transmission, education, reminders, and alerts; web-based clinical dashboards; predictive analytics; and feedback to support patients for better asthma control. In this study, Merchant et al measured the real-world effectiveness of this platform in reducing use of short-acting  $\beta$  agonist (SABA) and improving asthma control. Patients randomized to this arm versus the routine care group, in which patients received sensors but no feedback, significantly decreased SABA use, increased SABA-free days, and improved scores on the asthma control test.<sup>17</sup>

Education is another key component of treatment adherence in asthma. “Serious games”, i.e. games that do not have entertainment, enjoyment, or fun as their primary purpose<sup>18</sup>, have emerged as a new generation of videogames meant to provide education and training. In particular, serious games have been employed for improving knowledge and self-management behaviors in young people with asthma. Drummond et al. recently performed a systematic review to evaluate the impact of serious games on childhood asthma outcomes.<sup>19</sup> Twelve articles that evaluated 10

computer- or web-based serious games directed toward children were included in the analysis. It demonstrated that these games were associated with a significant improvement in children's knowledge of asthma. However, these positive results did not translate into parallel behavioral changes towards medications and, most importantly, to clinical improvement in asthma outcomes.<sup>19</sup>

There is also Mobile Adolescents' Disease Empowerment and Persistency Technology (M-ADEPT), which is an electronic medication monitor integrated with a smart app to provide educational interventions in asthmatic children and adolescents.<sup>20</sup> Its effectiveness has been explored in a small proof-of-concept study including underserved minority adolescents with asthma. This intervention demonstrated an improvement in inhaled corticosteroid (ICS) adherence and asthma control among this target population, showing a good profile of acceptability and feasibility.<sup>20</sup> A more recent study evaluating the effect of an education program (MyTherapeutic Education Program - MyTEP) that coupled multidisciplinary TEP with an mHealth Program (mHP – smartphone app) for children with mild-moderate asthma failed to find significant differences in adherence to medication between those who received MyTEP versus children who received mHP alone despite significant gains in quality of life.<sup>21</sup> This suggests that the intervention would be more beneficial in children with more severe disease or poorer disease management skills.

A Cochrane review examined the effectiveness of different interventions to improve adherence to ICS, and included children.<sup>14,22</sup> Regarding studies that investigated the role of electronic reminders and inhaler trackers in improving adherence to ICS, the results were inconsistent and inconclusive across a range of clinical outcomes, such as asthma control and exacerbations.<sup>14</sup>

Another targeted review comprehensively analyzed the effectiveness of e-Health technologies in 16 studies conducted in asthmatic children. Interactive websites showed some positive results in five

randomized controlled trials, while electronic monitoring devices (EMDs) and mobile apps had mixed findings with regard to medication adherence and asthma control.<sup>23</sup> In particular, interventions including interactive features of the websites (sometimes in combination with text messages), namely daily diary entries (i.e. daytime and nighttime symptoms, limitations in activity, and use of reliever medication); sharing of families' treatment concerns and side effects with the clinician; online asthma e-learning; and earning points redeemable for gift cards were associated with better clinical outcomes, such as improved medication adherence, asthma control. In most of these studies, caregivers actively participated through questionnaires or surveys regarding asthma control, quality-of-life of children and caregivers, beliefs and concerns about medication, and adherence. Only one study evaluated asthma-specific mobile apps within pediatric cohorts.<sup>23</sup> The clinical significance and cost-effectiveness of these interventions are yet to be determined in larger patient populations, based on asthma severity.

In the 2019 Global Initiative for Asthma (GINA) report on difficult to treat and severe asthma in adolescents and adults, electronic inhaler monitoring was recently endorsed as an objective tool for assessing adherence.<sup>24</sup> However, the small number of studies conducted in children with severe asthma showed limitations, such as a high degree of heterogeneity among adherence assessment tools, interventions and clinical outcomes. This has precluded drawing definitive conclusions and limited their applicability in daily clinical practice.<sup>25</sup> Indeed, the analysis of targeted interventions including e-Health solutions demonstrated a positive improvement in adherence rates, increasing from 28 – 67% to 49–81% in seven studies. One exception was a single study by Jochmann et al, which focused on electronic asthma medication reminders.<sup>25, 26</sup> Of four groups studied, the researchers found that only the group designated as “good adherence and good asthma control” had a significant improvement across various asthma control measures at the end of the monitoring

period, which was a median of 92 days.<sup>26</sup> To date, no official recommendations are available for younger children suffering from severe asthma.

### **Implementing e-Health into asthma practice: evidence gaps and limitations**

Despite advances in technology over the last few decades, strategies implementing e-Health for better asthma management have failed to improve adherence to treatment. Most of the available evidence suggests that this approach has not contributed to sustained improvements as adherence has been shown to decrease as the monitoring period expands. As a result, there are still insufficient data to support large-scale use of e-Health in pediatric asthma practice. Few studies assessed acceptability and feasibility in real-life practice<sup>27-31</sup>, showing that although e-Health strategies meet favorable acceptability ratings, some feasibility concerns exist, such as data transmission failure and lost devices. Indeed, barriers to treatment adherence that can occur outside of the research setting should be factored in when considering the implementation of such an intervention within the clinical setting.

The issue of age must be addressed, as different ages show different needs and challenges in treatment adherence. Younger children generally show higher prevalence of uncontrolled asthma<sup>32</sup>, even if they have been described as having better therapy adherence rates, possibly resulting from greater parental motivation in this age group.<sup>33</sup> Moreover, determinants of medication adherence may differ across age groups and over the main time points of the adherence pathway (initiation, implementation, persistence).<sup>34</sup>

Another important issue relates to socioeconomic status, which is closely associated with social challenges and lower health literacy. The worst clinical outcomes and adherence are found among minority underserved children, who are less likely to have access to e-Health interventions.<sup>35</sup> As for



children living in resource-limited settings and/or in remote sites, there may be opportunities to benefit from specialist care via telemedicine, especially in emergency situations.<sup>36</sup> ~~As an aside, the telemedicine model might be a promising tool to implement in conflict zones for providing remote supervision and training to nurses and medical staff in the field.<sup>36</sup>~~

The cost-efficacy of e-Health interventions (devices, data transfer services) in improving asthma treatment adherence also needs to be evaluated. Although the rapid and ongoing progress in technology is expected to decrease costs as well as increase reliability, these types of strategies have been viewed as too costly to be incorporated into clinical practice so far. Telemedicine, for example, could enable replacement of time-consuming visits in areas with good access, but this intervention might actually increase healthcare costs if patients would be using both telemedicine and clinical visits.<sup>37</sup> Furthermore, evidence from the literature showed that costs were not offset by a reduction in asthma exacerbations due to improved disease control despite increased adherence.<sup>38,39</sup> In conclusion, the most promising indication for e-Health strategies in clinical practice may be the management of children affected by severe or difficult-to-treat asthma as well as children with comorbid conditions where these relatively pricey interventions may improve disease outcomes, and ultimately reduce direct and indirect costs.

Other issues to consider are related to quality control processes, which involve identification of device malfunction, and maintaining information security. Use of health communication technologies has implications for physicians and their responsibility for patient safety. For instance, patients may submit incomplete data to the clinician, and on a more serious note, they may experience life-threatening situations when they do not receive an immediate response from their doctor.<sup>40</sup> Training for clinicians on the use of these tools is, therefore, essential for mitigating problems of device management and enhancing health professional-patient communication.<sup>41</sup>

Misunderstanding of information is another challenge. It can lead to serious negative consequences, so to safeguard against this, a tool intended for consumption by the general public should contain high-quality and evidence-based information presented in a way that is easily accessible and understandable for users.<sup>37</sup>

### **MHealth: updating application in childhood asthma**

MHealth has been increasingly recognized as having great potential for improving asthma care. A large number and variety of medical and health-related apps are currently available, from basic apps based on text message reminders to sophisticated ones offering multiple functions.<sup>42</sup> A potential advantage of apps over other technological interventions is that people almost always carry their smartphones, which eliminates the need to purchase another device. Today, more than 90% of teenagers use the Internet, and most of them have access to smartphones.<sup>37</sup> <sup>43</sup> Mobile communication and Internet access have also become widespread among children. Across Europe, 46% of children own a smartphone and 41% daily use it.<sup>43</sup>

Individuals continue to show interest in using Internet resources and mobile apps to access information about their health.<sup>44</sup> In this context, the large number of asthma apps developed to date likely reflects the willingness of patients to use tools that assist with symptom and medication adherence monitoring. Worth noting, however, is the fact that most of the commercially available asthma apps have not been validated in the clinical setting, nor have they been regulated or approved as medical devices. Consequently, they may result in inaccurate and even unsafe tools lacking evidence-based recommendations and reliable information for users.<sup>45</sup> In addition, concerns have been raised with regard to data reproducibility, effectiveness, and privacy issues. Therefore, clinicians should exercise caution in recommending their use to patients.<sup>37</sup>

A recent review selected 209 asthma apps, which today are available in the most popular smartphone brands.<sup>46</sup> Most of them (52%) provided teaching and training information for patients, based on alternative treatments (39%), such as yoga, acupuncture, breathing exercises; 22% helped users to monitor symptoms and medication adherence; 18% were directed to health care providers, mostly providing medical reference information; about 6% provided air quality information, and 2% served as social forums, connecting patients each other. Despite the great number of the currently available mobile apps for asthma, few effectiveness evaluations have been conducted so far.

According to a recent systematic review of 10 randomized trials, multifunctional asthma apps showed encouraging potential in the control of symptoms and in improving the quality-of-life compared with traditional interventions. However, the review included only a handful of studies on adolescents, and none on children.<sup>47</sup> When considering the use of medical apps in clinical practice, the clinician should take into account not only the correct use of the app itself, but also the possibility of its discontinued use over time, as continued use seems to wane with the passage of time from the date of the download.<sup>42</sup> Overall, the available evidence underscores the need for further research testing the use of mobile apps for asthmatic children on a large scale and over longer periods, and implementing studies able to evaluate their impact in “real-life”.

The issue of privacy and security for both data in transit and stored data remains a challenge, and is yet to be thoroughly addressed. One study showed that only 30% of the most commonly used mHealth apps had privacy policies, which generally required high level literacy for comprehension, were often not focused on the app itself, and were not informative for end users.<sup>48</sup> Maintaining the

highest standards for privacy protection is therefore a goal that must be achieved to prevent unwarranted disclosure of personal information.

With all of these limitations, it is hardly surprising that many clinicians do not feel confident in recommending the use of e-Health strategies to improve adherence to asthma treatment. Although they recognize the potential benefits of this approach in bettering the quality of care, concerns with data accuracy and protection of health information remain an unresolved issue.<sup>49</sup> Also, clinicians' attitudes toward e-Health strategies for promoting treatment adherence in childhood asthma have not been adequately explored, making further studies necessary for expanding the scant evidence and for evaluating whether this innovative approach can meet clinical needs.

### **Future directions**

Enhancing the quality of care, improving patient's adherence to treatment, and facilitating early recognition of lung function decline by means of e-Health solutions represent a revolutionary concept in asthma care. Managing asthma means taking into account patients' symptoms and environmental exposures, as well as medication use. Helping patients to recognize factors that could impact their disease and educating them about the right actions to take could be beneficial in strengthening asthma self-management.<sup>42</sup> As part of this effort, a critical evaluation of the impact of innovative e-Health interventions in improving treatment adherence in childhood asthma must consider the unmet needs, heterogeneity of trials, safety issues, long-term effects, cost-efficacy, and data safety. There are an increasing number of studies analyzing the implementation of these tools in research settings, but several aspects need to be addressed to provide pediatricians with evidence-based recommendations for their use in clinical practice. As already suggested, e-Health solutions that integrate subjective and objective parameters and adherence to drugs may help clinicians better assess medication use while also empowering patients' self-management of their

disease, ultimately improving disease control. Moreover, data on inhaler technique may be useful for identifying children who need more training or intervention to optimize inhaler use.

There is great potential for e-Health solutions in providing advanced and targeted care for children with asthma, but the unresolved issues must be carefully considered to allow their proper use in clinical practice. Strategies to promote uptake and implementation of these innovative tools need to be developed with the aim of facilitating their use over long periods, especially by minority children or in those living in underserved areas. Moreover, for such an approach to be successful, clinicians should identify patients most likely to benefit from this strategy. Indeed, use of digital technologies might be optimal for managing children with severe or difficult-to-treat asthma in which poor adherence to controller medications increases risk and severity of exacerbations.

Going forward, further research is required to develop strategies promoting e-Health integration in daily practice as well as into existing healthcare systems<sup>50</sup>, focusing on interventions that can be easily integrated into daily life of patients and clinical routine of health workers. Also, training for clinicians will be essential for ensuring both optimal device management and communication with patients. Healthcare systems will have to adapt to the increasingly digital era of personalized care, which will require budgeting for these new technologies, as well as staff training.<sup>42</sup>

In the future, it will be important to focus on the quality of asthma apps as well as on the selection process for their use by the most suitable patients. The contribution of healthcare professionals will be fundamental for their development, and finally, appropriate regulatory processes will be required in order to develop security measures for sensitive data management.

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