



# Improving adherence to asthma medications: current knowledge and future perspectives

Kathryn V. Blake

## Purpose of review

Poor adherence to asthma controller medications, particularly inhaled corticosteroids, has been well known for decades and is a major cause of uncontrolled asthma and increased healthcare utilization. This review presents recent evidence on factors leading to nonadherence in specific age groups, parents of young children, adolescents and young adults, adults, and the elderly. Novel management strategies including electronic sensors with associated smart phone applications for adherence improvement are discussed.

## Recent findings

Interventions to promote adherence must include a focus on issues important to the patient. Parents are concerned about adverse effects and the difficulty of medication administration in their child; adolescents and young adults need help with organizational skills and social barriers; adults may be more receptive to the need for daily medication after an acute exacerbation and acceptance of their disease; the elderly may have medication misuse issues associated with cognitive decline and other comorbidities related to aging. In all age groups, a trusting relationship with the provider is the key. New digital devices to track adherence may provide feedback to the patient and provider to evaluate and to promote adherence.

## Summary

Personalized approaches are required to address adherence barriers in target populations. Research on specific needs and barriers in target populations and development of appropriate strategies for use of new digital technology for adherence monitoring is needed.

## Keywords

adherence, asthma, electronic monitoring

## INTRODUCTION

Despite inhaled corticosteroids (ICS) being highly effective for improving asthma control and reducing exacerbation frequency, overall, the adherence to ICS in patients with asthma is notoriously poor. Adherence by electronic monitoring is frequently reported at less than 50% in adolescents and adults and 49–73% in young children/preadolescents [1–5]. The WHO suggests that ‘increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments’ [6]. Adherence to medications specifically refers to a patient’s fulfillment of the provider’s recommendation with respect to timing, dosage, and frequency of a medication for the duration of treatment [7<sup>•</sup>]. Poor ICS adherence is attributed to concerns for adverse effects or experiencing adverse effects, improper inhaler technique, forgetfulness, and believing (daily) use is not needed when asthma is controlled, and/or lack of knowledge of asthma and for the reason for ICS therapy

[3,8,9,10<sup>•</sup>,11]. Underutilization of ICS therapy results in poor asthma control, future risk of asthma instability, oral corticosteroid use, emergency department visits, hospitalizations, and even death [9,12–16]. Several studies in children and adults have shown that an increase in ICS adherence to between 60% and 80% results in a decrease in emergency department visits for asthma [1,2,12,17]. Identifying methods to improve patient medication adherence is a leading priority [7<sup>•</sup>,18,19]. This review presents the current understanding of adherence and the latest information on

Biomedical Research Department, Center for Pharmacogenomics and Translational Research, Nemours Children’s Specialty Care, Jacksonville, Florida, USA

Correspondence to Kathryn V. Blake, PharmD, Biomedical Research Department, Center for Pharmacogenomics and Translational Research, Nemours Children’s Specialty Care, 807 Children’s Way, Jacksonville, FL 32207, USA. Tel: +1 904 697 3806; e-mail: kathryn.blake@nemours.org

**Curr Opin Pulm Med** 2017, 23:62–70

DOI:10.1097/MCP.0000000000000334

## KEY POINTS

- Adherence to prescribed asthma medications is reported to be less than 50% in adolescents and adults and 49–73% in young children/preteens.
- Recent research using cluster analyses and focus groups has identified key issues from both the patient and healthcare provider perspective that likely influence long-term adherence.
- Newly available electronic sensors for inhalers and associated smartphone applications that transmit data in real time to a smartphone and dashboard for patient and provider monitoring, respectively, may be appealing to today's mobile-connected patient population.

electronic and digital means for assessing inhaler use.

The WHO defines several forms of nonadherence described as erratic nonadherence, unwitting nonadherence, and intelligent nonadherence [20]. Erratic nonadherence is defined as unintentional and is typically related to forgetfulness as the desire to be adherent is present. Unwitting nonadherence results from poor understanding of the intended regimen or importance for being adherent. In asthma, this is commonly manifested as confusion between reliever and controller medication regimens. Intelligent nonadherence is an intentional thoughtful decision and can be related to concerns for adverse effects, symptom resolution (and thus, no perceived need for treatment), cost benefit, or a poor relationship with the provider. These specific forms of nonadherence require different strategies for resolution. Many asthma interventions require 'restructuring of typical approaches to healthcare delivery in the United States' and, thus, are not easily sustainable for long-term implementation [7<sup>22</sup>]. Cost-effectiveness and sustainability must be incorporated into adherence interventions.

## ADHERENCE IN CHILDREN, ADOLESCENTS/YOUNG ADULTS, ADULTS, AND THE ELDERLY

The age of the patient will impact the strategy used to address nonadherence because of differences in the barriers and facilitators affecting adherence. In young children and preadolescents, the primary responsibility for medication administration relies on the parent/caregiver as only 50% of children under the age of 11 years have assumed control of their asthma medication regimen [21]. Adherence rates with ICS when measured electronically in

young children/preadolescents range from 49 to 73% [3]. The adherence relationship is more complex than in adults because the triad of caregiver/parent, child (the patient), and prescriber is involved.

In a review of perspectives from parents of young children, four primary themes were identified for adherence in asthma [22]. First, there are competing beliefs and concerns for both the treatment and condition such that fears of ICS and fears of acute exacerbations result in parents initiating treatment-free periods to determine if the ICS is still needed by their child. Second, child resistance results in non-adherence when there is difficulty administering treatment in young children (e.g., placing a face-mask on an infant) resulting in 'daily battles and caregiver fatigue'. In addition, children may also be susceptible to anxiety, inattention, and other psychosocial variables resulting in resistance to daily treatment [23,24]. Third, a caregiver's desire for their child to have a normal life may actually promote adherence in this age group [as contrasted with adolescents/young adults (AYA)] because using the medication as prescribed may allow the child to participate normally in activities. Last, the caregiver's relationship with their provider can positively or negatively influence adherence. If the caregiver and provider share the same goals, adherence is promoted but if the parent perceives risks associated with treatment, such as fears about ICS adverse effects, that the provider is unwilling to acknowledge, then adherence will suffer.

Poor asthma control and increased healthcare utilization is directly related to poor adherence in AYA [2,13,25–27]. AYA with asthma represent a vulnerable population at high risk for morbidity and mortality due to asthma [28,29]. Death rates from asthma begin to rise in mid-adolescence and those aged 15–34 years have double the mortality rate of younger children [30]. The increased risks in this age group coincide with emerging autonomy for disease management and transition to adult care and may be exacerbated by a lack of medical attention and inadequate medication use [28,31,32]. Poor adherence to ICS in AYA is consistent across race and ethnicities [5,33]. Behavioral factors in AYA which contribute to adherence barriers include, suboptimal organizational skills and self-regulatory behavior, cognitive difficulty in following instruction, social barriers, denial of symptoms, depression, risk taking behavior, as well as preference for immediate gratification, and tolerance for future uncertainty [5,33–36,37<sup>38</sup>,38–40]. Girls are less likely than boys to be taken to a provider if they have infrequent wheeze, less likely to be labeled as having asthma, and thus, less likely to receive appropriate

medication for treatment [34]. AYA also perceive that having asthma and using an inhaler makes them less normal than their peers, which results in poor adherence [34]. In addition, fear of adverse effects, busy schedules, and dislike of ICS taste promote nonadherence at this age [34].

However, a good (nonpaternalistic) relationship with their provider can promote open discussion about asthma and treatment to improve adherence [35]. Interventions with the greatest potential to improve adherence in adolescents include a multifaceted approach that combines patient preferences, education, and behavioral reminders [41]. Teens are receptive to text messaging for medication reminders that may be a low-cost means to improve adherence [42]. Although transfer to adult care begins at age 14 and may be complete by age 18, the transition process can extend through a patient's 20s [43,44]. These data suggest that AYA require continued guidance and supervision during this period of emerging adulthood to address and manage adherence barriers.

In a cluster analysis of adherence behaviors/attitudes in 392 adults (55% of participants were nonadherent by several validated measures) with a mean  $\pm$  SD age of  $48.69 \pm 14.32$  years, three clusters of nonadherent individuals were identified [37<sup>¶</sup>]. The *indifferent* cluster believed that medicines were not necessary, were not concerned about medicines, and did not believe their illness was threatening. These individuals typically were controlled, had good understanding of their disease, and had high social support. As such, they might be using lifestyle modification or avoidance of risk factors for disease control and probably are not in need of an adherence intervention. The *ambivalent* cluster had high beliefs in medication necessity but also high medications concerns and believed that their illness was threatening. These individuals were less educated, poorer, had less social support, and had uncontrolled disease. They believed that their disease was threatening but was beyond their control and that medication would not help. The *skeptical* cluster consisted of the most nonadherent and believed their disease was threatening but did not believe medications would help and were concerned about using medications. These individuals were the youngest, poor and had low social support and uncontrolled disease. Thus, interventions for individuals who are *ambivalent* or *skeptical* would likely benefit from increasing beliefs in the necessity of, and reducing concerns for, medications and disease education.

Two publications of focus group results by the same researchers explored the similarities and differences in attitudes between adult patients with

asthma (13 participants, mean  $\pm$  SD age  $52.54 \pm 15.79$  years, range 20–75 years), pulmonologist physicians (13 participants), and allied health professionals (12 participants including nurses, pharmacists, respirologists, and asthma educators) specifically on the barriers and facilitators to medication adherence [45<sup>¶</sup>,46]. The most common medication-related barrier across all three groups was the high cost of medication (resulting in stretching doses to make a controller last longer). Both patients and physicians agreed that medications were not user-friendly. Patient complaints included difficulty in determining if a full dose was inhaled, having to rinse the mouth after use, or having to use two inhalations (versus pills that normally require one tablet/capsule) [45<sup>¶</sup>]. Patient-related barriers as perceived by all three groups included attitudes and beliefs about asthma (such as, patients not realizing asthma is a chronic disease or having a hope for a 'magical cure') and concerns for adverse effects. Significantly, physicians and allied health professionals but not the patients, stated that family and friends could negatively affect a patient's perception of asthma. Patients also stated that system-related barriers included delayed appointments and waiting lists that complicated obtaining refills and follow-up care.

In the follow-up publication, the features that facilitate adherence to prescribed long-term controller medication were elicited from the same focus groups [46]. All groups believed that having lived through an asthma exacerbation due to nonadherence was a turning point to facilitating future adherence. Coincident is the patient accepting that they have a long-term disease, which patients acknowledged might be more difficult for younger adults to accept. From these factors, the three groups were in agreement that motivation for self-management, seeking asthma knowledge, improving attitudes, and having a positive trusting relationship with the provider were key factors that would enhance adherence. Thus, the best opportunity for providing an adherence intervention is after the experience of an exacerbation but when acceptance of the disease has occurred. These adult patients preferred interventions that are short, include motivational treatment, and are enjoyable; physicians and allied health professionals believed that their role is to provide encouragement and reassurance to continue treatment. In addition, physicians believed that they were in the best position to deliver the intervention but acknowledged that they had little time to do so. Rather, they suggested that asthma educators deliver the intervention and pharmacists provide continued reinforcement.

The elderly with asthma have specific health-related decline issues that can affect medication

adherence. Worsening cognitive function can affect understanding of medication purpose and use, impaired vision can affect reading medication labels, arthritis can impair the physical coordination required to use pressurized or dry powder inhalers, and multiple comorbidities and polypharmacy can contribute to confusion on timing and correct use of medications [47].

A recent study in 121 patients [88 with chronic obstructive pulmonary disease (COPD) and 33 with asthma; mean  $\pm$  SD age  $70.24 \pm 5.85$  years, range 65–88 years] found that cognitive dysfunction was present in 40.2% of patients and that cognitive level was the only parameter (out of educational status, age, sex, asthma/COPD, polypharmacy, previous year hospitalization or emergency department visit, lung function, and smoking status) associated with incorrect inhaler technique and adherence [48<sup>•</sup>]. Poor health literacy coupled with cognitive decline was also found to contribute to poor adherence. In a study of 452 patients with asthma (mean  $\pm$  SD age  $67 \pm 6.8$  years), 36% had limited health literacy skills, 27% had cognitive impairment, and only 38% were adherent to their asthma controller medication which decreased to 23% in those with limited health literacy [49]. In this study, health literacy was correlated with all measures of cognitive abilities and explained a large proportion of adherence and proper inhaler use. In a separate study of this same population, low health literacy was found to decrease adherence directly and indirectly through concerns about medications (misunderstanding about medications may induce fears of asthma controllers' adverse effects as identified from the Beliefs about Medications Questionnaire [50,51]). Cognition presented as an independent factor on adherence presumably because of the strong correlation between health literacy and cognition in older adults [51].

These studies suggest that approaches to improve adherence in the elderly need to be based on geriatric principles. Some suggested approaches include using language and images that are customary to the elderly, review connections between medication facts and behaviors, limiting the amount of information provided, using teach-back technique, and provide audio or print materials for review at home [51]. One specific strategy for inhaler technique is READY [get inhaler ready, shake the inhaler, remove the cap, and attach spacer (if used)], SET (open mouth, breath out slowly, and put lips around mouthpiece), and GO (push down on inhaler and breathe in slowly) [49]. Another strategy is 'scaffolding' in which only a small amount of information is presented at a single visit; at subsequent visits, additional information

is added which builds on what is already learned [49].

## MEDICATION ADHERENCE MEASURES

Obtaining medication use data to measure adherence is challenging. Secondary analyses of large datasets obtained from pharmacy claims data (18 456 patients 2–18 years old [1], 43 156 patients 5–12 years old [52], and 6903 patients 18 years and older [53]) are commonly used to identify aggregate adherence trends and associated healthcare utilization but are not helpful for assessing adherence in an individual patient [1,52–55]. New methods involving predictive analytics to identify individual patients with problematic adherence within a healthcare organization are in use but these methods exclude those without existing data in a health plan [56,57]. Methods to quantify an individual patient's ICS adherence include direct biochemical measure (e.g., blood or urine cortisol levels), inhaler counter monitoring, electronic health record refill requests, local pharmacy dispensing records, self-report, and electronic use capture [54,55,58,59]. Blood level measurement is not suitable nor practical for ICS, and regular dose counter monitoring on inhalers is labor intensive [20,59]. Refill and dispensing records can be inaccurate if the prescription is not picked up or multiple pharmacies are used and do not provide information on doses actually taken [53,55,60<sup>••</sup>]. Self-reported measures tend to overestimate adherence but are recognized as low cost, simplistic, and available in real time [3,5,54,61,62]. To elicit valuable information from self-report, it is important to begin the conversation with a statement that normalizes nonadherence that can be done by acknowledging that nonadherence is common, and it is difficult to take medication exactly as prescribed [63]. Using validated measures is desired but if not available, then questions can be optimized to obtain useful results [63]. For example, asking patients to make a global estimate of adherence using a Likert scale for response or percentage of doses taken, rather than asking for a report of missed doses; providing a specific timeframe for recall – a 30-day recall has been found to be better than shorter periods – and stating '30-day' rather than 'in the past month' is more meaningful to patients [63]. In addition, the individual asking about adherence should be different from the individual providing adherence counseling, and face-to-face interviews should be avoided in favor of computer or self-administered article questionnaires [63].

There are a number of adherence scales that can be used to assess adherence [54]. The Brief Medication Questionnaire, Eight-Item Morisky Medication

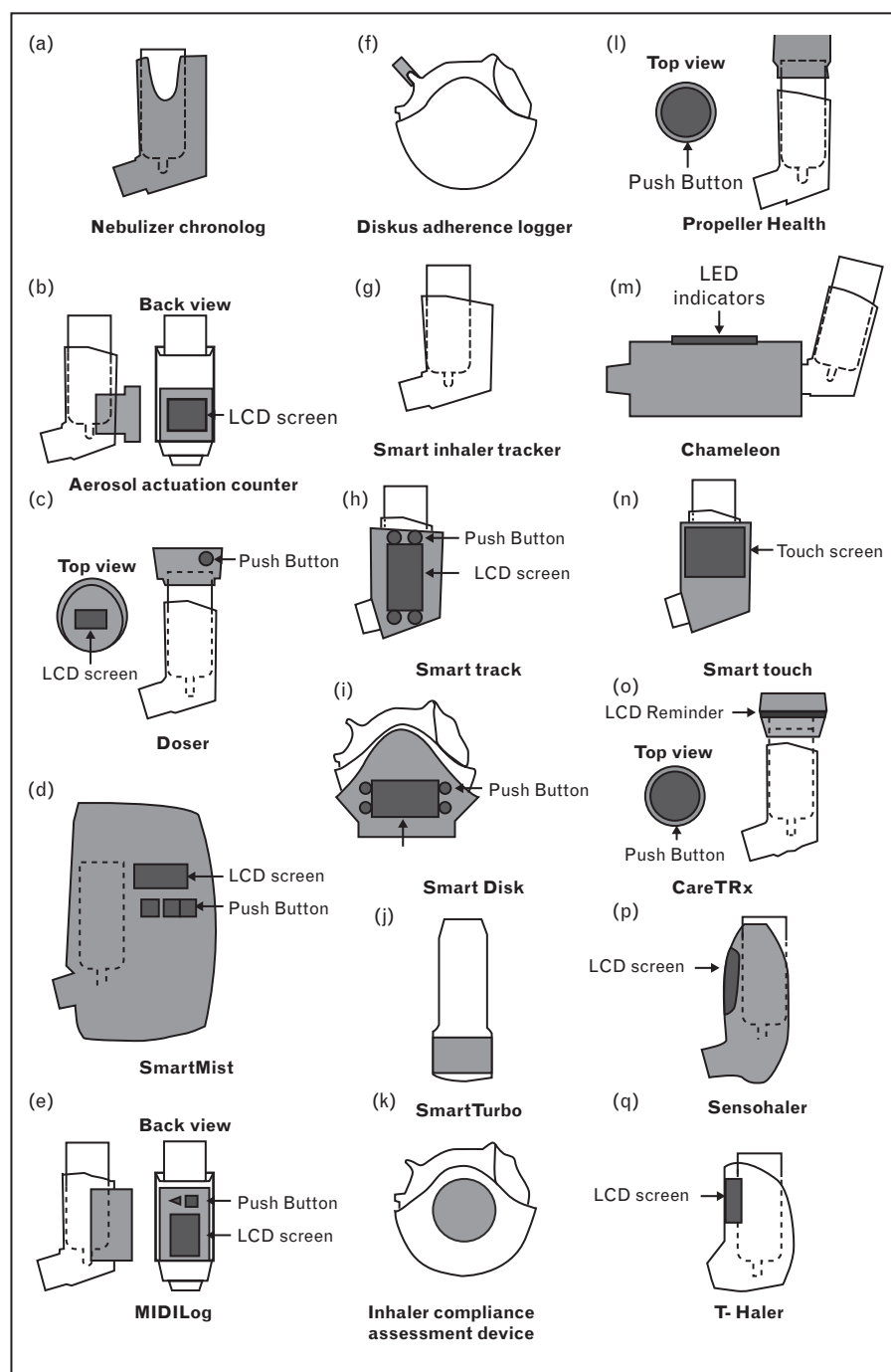


**FIGURE 1.** Evolution of the design of inhaler-based monitoring devices, indicated with gray color. Reproduced with permission from [60\*\*].

Adherence Scale, and Medication Adherence Report Scale (MARS) are the most commonly used. A shortened version of the MARS (5 items versus 10 items) was recently found to be too inaccurate for assessing adherence compared with electronic adherence capture with the SmartDisk in 133 children aged 2–13 years who were followed for 1 year [64].

Although electronic monitoring has been available for decades, newly available electronic sensors

for inhalers and associated smartphone applications (<https://www.caretrx.com/>, [www.propellerhealth.com](http://www.propellerhealth.com), <http://www.smartinhaler.com/>) are reliable, provide adherence reminders, passively collect each inhaler actuation, and transmit data in real time to a smartphone application and dashboard for provider monitoring (Figs. 1 and 2) [65–68]. These sensors cannot assure the dose was actually taken, but the recorded data can show adherence manipulation,

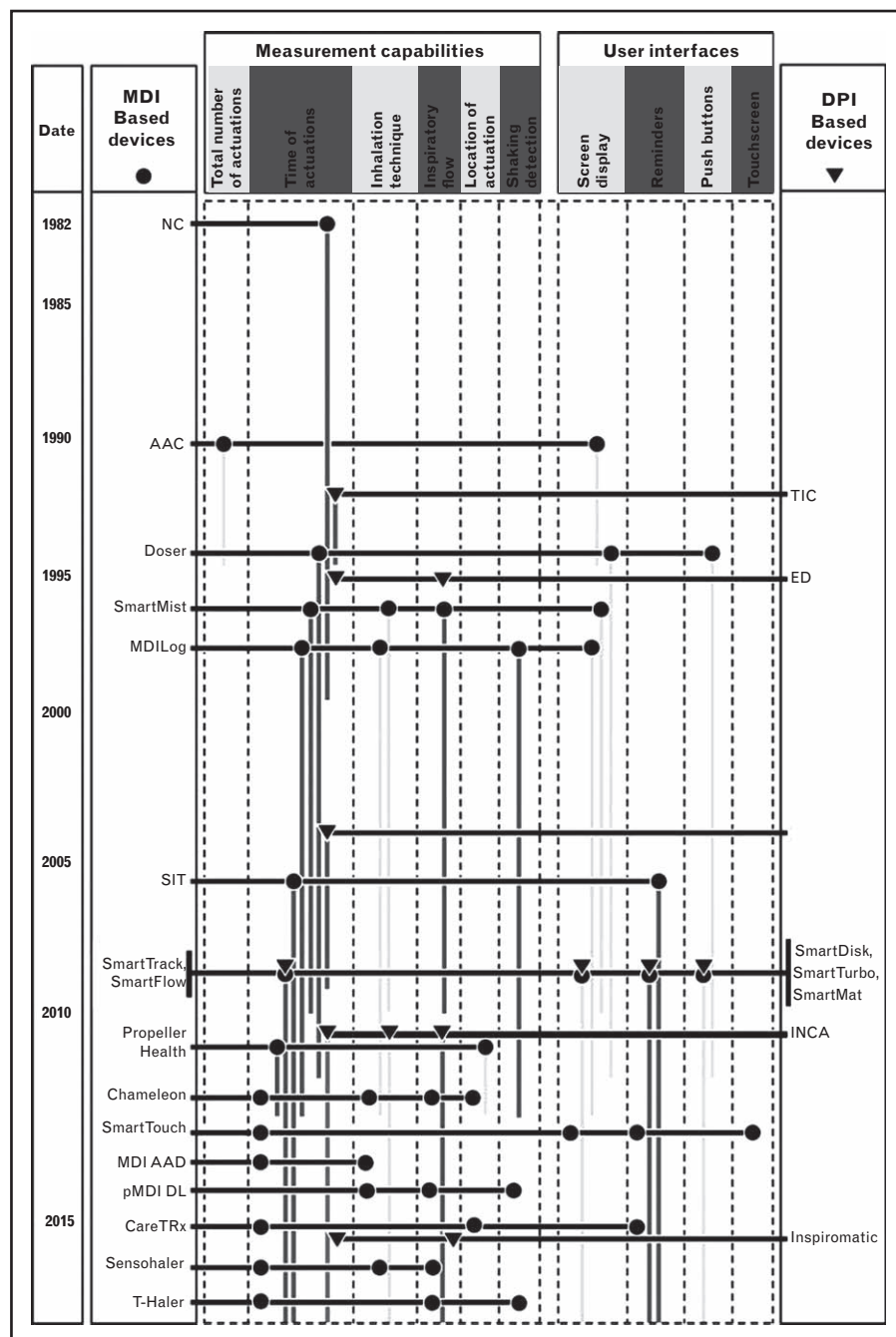


**FIGURE 2.** Evolution of technical characteristics and functionalities of inhaler-based monitoring devices. Circles and triangles on the horizontal lines indicate the functionalities of MDI-based and DPI-based devices, respectively, whereas the vertical lines show the timespan of their use in academic research. DPI, dry-powder inhaler; MDI, metered-dose inhaler. Reproduced with permission from [60].

such as dose dumping [69]. Sensors that attach as a cap over the canister may not fit on all inhalers (e.g., Symbicort is incompatible with a cap sensor due to the counter placement on the top of the Symbicort canister). Devices are developed for dry powder inhalers also (Propeller Health has a sensor for Diskus inhalers). These devices must go through the Food and Drug Administration regulatory

process for marketing. The smartphone mobile application used with the sensors for adherence tracking is novel and has significant advantages over traditional methods (paper diaries, pharmacy dispensing records) for tracking adherence which includes each activation of the sensor attached to the inhaler is passively recorded; data from the sensor attached to the ICS and rescue inhalers can

calculate daily adherence to the prescribed ICS regimen and track symptoms of asthma requiring bronchodilator use, respectively; pushed reminders on a smartphone encourage ICS adherence; and these data can be used to create a dialog between the participant and provider.

Daily monitoring of adherence with these applications would likely be impractical for busy physician providers, but review of summary data before an appointment would be feasible. However, delegating more frequent review to pharmacists, respiratory therapists, or other allied health providers who could provide adherence counseling would be a practical alternative [51]. These devices are well suited for nonadherent AYA and adult patients who are used to immediate access to information and instant gratification and are receptive to electronic means for asthma monitoring [36,70,71]. In addition, their use circumvents the annoyance of parental/spousal nagging in patients who require reminders to take daily ICS [37].

Although these smartphone-enabled devices currently lack the ability to detect inhalation as with the SmartMist inhaler developed several decades ago, these features are evolving quickly and will likely be integrated with other health wearable platforms to create an 'extended wireless body area network (WBAN)' [66]. WBAN for patients with asthma will likely include information on environmental exposures, global positioning satellite information on locations provoking symptoms recorded by patients or associated with bronchodilator use [currently available via Propeller Health (Madison, Wisconsin, USA) and CareTRx (Gecko Health Innovations, Inc., Cambridge, Massachusetts, USA)], lung function measurements, and activity levels [66]. Currently available smartphone-enabled sensors have been shown to reduce rescue inhaler use, increase asthma free days, and improve Asthma Control Scores [72,73]. In addition, the cost of these devices/subscription monitoring programs (currently under ~\$300 per device or per yearly subscription) could be offset by improvements in adherence of 50% when the direct and indirect costs of asthma are measured [67,74].

## CONCLUSION

Adherence to asthma controller medications is poor despite the availability of highly effective medications such as ICS that improve asthma control and associated activity level and function. Barriers to adherence varies by patient age group as parents of young children, AYA, adults, and the elderly will have different motivations for (not) taking medication as prescribed. The optimal time for

(re)initiating adherence intervention may be after an acute exacerbation when the patient is fully accepting the chronicity of their disease. Monitoring adherence can be obtained directly from patients through dialogue with providers and/or by newly available electronic sensors and associated smartphone applications. These latter devices will become more commonplace as additional wearable technology is integrated to deliver actionable information such as locations of environmental triggers, clinical information, and feedback on inhaler technique.

## Acknowledgements

None.

## Financial support and sponsorship

*This work was supported by the Nemours Foundation, Jacksonville, Florida, USA.*

## Conflicts of interest

*There are no conflicts of interest.*

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Herndon JB, Mattke S, Evans Cuellar A, *et al.* Anti-inflammatory medication adherence, healthcare utilization and expenditures among medicaid and children's health insurance program enrollees with asthma. *Pharmacoeconomics* 2012; 30:397–412.
  2. Williams LK, Peterson EL, Wells K, *et al.* Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence. *J Allergy Clin Immunol* 2011; 128:1185.e2–1191.e2.
  3. Morton RW, Everard ML, Elphick HE. Adherence in childhood asthma: the elephant in the room. *Arch Dis Child* 2014; 99:949–953.
  4. Krishnan JA, Bender BG, Wamboldt FS, *et al.* Adherence to inhaled corticosteroids: an ancillary study of the Childhood Asthma Management Program clinical trial. *J Allergy Clin Immunol* 2012; 129:112–118.
  5. Desai M, Oppenheimer JJ. Medication adherence in the asthmatic child and adolescent. *Curr Allergy Asthma Rep* 2011; 11:454–464.
  6. Sabate E. Adherence to long-term therapies: evidence for action. Geneva: World Health Organization; 2003.
  7. Viswanathan M, Golin CE, Jones CD, *et al.* Medication adherence interventions: comparative effectiveness. Closing the quality gap: revisiting the state of the science. Evidence report no. 208. Evidence report/technology assessment (full report). Rockville, MD: Agency for Healthcare Research and Quality; 2012: 1–685.
- Provides an excellent detailed review of adherence intervention results.
8. Ducharme FM. High inhaled corticosteroids adherence in childhood asthma: the role of medication beliefs. *Eur Respir J* 2012; 40:1072–1074.
  9. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *Eur Respir J* 2002; 19:246–251.
  10. Pelaez S, Lamontagne AJ, Collin J, *et al.* Patients' perspective of barriers and facilitators to taking long-term controller medication for asthma: a novel taxonomy. *BMC Pulm Med* 2015; 15:42.
- Using focus group data, this report provides insight into the different perspectives between the patient (the recipient), provider (the prescriber), and allied health professionals (the deliverer) on adherence strategies.
11. Darba J, Ramirez G, Sicras A, *et al.* Identification of factors involved in medication compliance: incorrect inhaler technique of asthma treatment leads to poor compliance. *Patient Prefer Adherence* 2016; 10:135–145.
  12. Lasmar L, Camargos P, Champs NS, *et al.* Adherence rate to inhaled corticosteroids and their impact on asthma control. *Allergy* 2009; 64:784–789.
  13. Jentzsch NS, Camargos P, Sarinho ES, Bousquet J. Adherence rate to beclomethasone dipropionate and the level of asthma control. *Respir Med* 2012; 106:338–343.

14. National Asthma Education and Prevention Program. Expert panel report 3: guidelines for the diagnosis and management of asthma. Publication no. 08-4051. Bethesda, MD: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute; 2007.
  15. From the Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma (GINA). 2015; Available at <http://www.ginasthma.org/>. [Accessed 17 April 2015]
  16. Suissa S, Ernst P, Benayoun S, *et al*. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000; 343:332–336.
  17. Schatz M, Cook EF, Nakahiro R, Petitti D. Inhaled corticosteroids and allergy specialty care reduce emergency hospital use for asthma. *J Allergy Clin Immunol* 2003; 111:503–508.
  18. Prioritization IoMCoCER. Initial national priorities for comparative effectiveness research. Washington, DC: The National Academies Press; 2009.
  19. Cutler DM, Everett W. Thinking outside the pillbox – medication adherence as a priority for healthcare reform. *N Engl J Med* 2010; 362:1553–1555.
  20. van Boven JF, Trappenburg JC, van der Molen T, Chavannes NH. Towards tailored and targeted adherence assessment to optimise asthma management. *NPJ Prim Care Respir Med* 2015; 25:15046.
  21. Orrell-Valente JK, Jarlsberg LG, Hill LG, Cabana MD. At what age do children start taking daily asthma medicines on their own? *Pediatrics* 2008; 122:e1186–e1192.
  22. Santer M, Ring N, Yardley L, *et al*. Treatment nonadherence in pediatric long-term medical conditions: systematic review and synthesis of qualitative studies of caregivers' views. *BMC Pediatr* 2014; 14:63.
  23. Chen E, Hermann C, Rodgers D, *et al*. Symptom perception in childhood asthma: the role of anxiety and asthma severity. *Health Psychol* 2006; 25:389–395.
  24. Koinis-Mitchell D, McQuaid EL, Seifer R, *et al*. Symptom perception in children with asthma: cognitive and psychological factors. *Health Psychol* 2009; 28:226–237.
  25. Murphy AC, Proeschal A, Brightling CE, *et al*. The relationship between clinical outcomes and medication adherence in difficult-to-control asthma. *Thorax* 2012; 67:751–753.
  26. McGrady ME, Hommel KA. Medication adherence and healthcare utilization in pediatric chronic illness: a systematic review. *Pediatrics* 2013; 132:730–740.
  27. Gamble J, Stevenson M, McClean E, Heaney LG. The prevalence of non-adherence in difficult asthma. *Am J Respir Crit Care Med* 2009; 180:817–822.
  28. Akinbami L. The state of childhood asthma, United States, 1980–2005. *Adv Data* 2006; (381):1–24.
  29. Akinbami LJ, Simon AE, Rossen LM. Changing trends in asthma prevalence among children. *Pediatrics* 2016; 137:1–7.
  30. Moorman JE, Akinbami LJ, Bailey CM, *et al*. National surveillance of asthma: United States, 2001–2010. *Vital Health Stat* 2012; 3:1–58.
  31. Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of childhood asthma in the United States, 1980–2007. *Pediatrics* 2009; 123 (Suppl 3):S131–S145.
  32. Scal P, Davern M, Ireland M, Park K. Transition to adulthood: delays and unmet needs among adolescents and young adults with asthma. *J Pediatr* 2008; 152:471.e1–475.e1.
  33. Mosnaim G, Li H, Martin M, *et al*. Factors associated with levels of adherence to inhaled corticosteroids in minority adolescents with asthma. *Ann Allergy Asthma Immunol* 2014; 112:116–120.
  34. de Benedictis D, Bush A. Asthma in adolescence: is there any news? *Pediatr Pulmonol* 2016; doi: 10.1002/ppul.23498. [Epub ahead of print]
  35. Ahmad A, Sorensen K. Enabling and hindering factors influencing adherence to asthma treatment among adolescents: a systematic literature review. *J Asthma* 2016; 53:862–878.
  36. Brandt S, Dickinson B. Time and risk preferences and the use of asthma controller medication. *Pediatrics* 2013; 131:e1204–e1210.
  37. Unni E, Shiyabola OO. Clustering medication adherence behavior based on beliefs in medicines and illness perceptions in patients taking asthma maintenance medications. *Curr Med Res Opin* 2016; 32:113–121.
- This report uses a cluster analysis approach to identify characteristics of patients at risk of poor adherence.
38. Rhee H, Belyea MJ, Brasch J. Family support and asthma outcomes in adolescents: barriers to adherence as a mediator. *J Adolesc Health* 2010; 47:472–478.
  39. Sadof M, Kaslovsky R. Adolescent asthma: a developmental approach. *Curr Opin Pediatr* 2011; 23:373–378.
  40. Bender BG. Depression symptoms and substance abuse in adolescents with asthma. *Ann Allergy Asthma Immunol* 2007; 99:319–324.
  41. Miller TA, Bannon BL, DiMatteo R. Interventions to improve treatment adherence among adolescents: a meta-analysis. *World J Meta-Anal* 2014; 2:71–77.
  42. Johnson KB, Patterson BL, Ho YX, *et al*. The feasibility of text reminders to improve medication adherence in adolescents with asthma. *J Am Med Inform Assoc* 2016; 23:449–455.
  43. Cooley WC, Sagerman PJ; American Academy of Pediatrics. American Academy of Family Pediatrics. American College of Pediatrics. Transitions Clinical Report Authoring Group. Supporting the healthcare transition from adolescence to adulthood in the medical home. *Pediatrics* 2011; 128:182–200.
  44. Stroud C, Mainero T, Olson S; Institute of Medicine; National Research Council. Improving the health, safety, and well being of young adults: workshop summary. Washington, DC: The National Academies Press; 2013.
  45. Pelaez S, Bacon SL, Aulls MW, *et al*. Similarities and differences between asthma healthcare professional and patient views regarding medication adherence. *Can Respir J* 2014; 21:221–226.
- Using focus group data, this report provides insight into the different perspectives on adherence barriers between the patient (the recipient), provider (the prescriber), and allied health professionals (the intervention deliverer).
46. Pelaez S, Bacon SL, Lacoste G, Lavoie KL. How can adherence to asthma medication be enhanced? Triangulation of key asthma stakeholders' perspectives. *J Asthma* 2016; 53:1076–1084.
  47. Ban GY, Trinh TH, Ye YM, Park HS. Predictors of asthma control in elderly patients. *Curr Opin Allergy Clin Immunol* 2016; 16:237–243.
  48. Turan O, Turan PA, Mirici A. Parameters affecting inhalation therapy adherence in elderly patients with chronic obstructive lung disease and asthma. *Geriatr Gerontol Int* 2016; doi: 10.1111/ggi.12823. [Epub ahead of print]
- This is a comprehensive review of strategies to measure medication adherence such as validated scales.
49. O'Connor R, Wolf MS, Smith SG, *et al*. Health literacy, cognitive function, proper use, and adherence to inhaled asthma controller medications among older adults with asthma. *Chest* 2015; 147:1307–1315.
  50. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health* 1999; 14:1.
  51. Soones TN, Lin JL, Wolf MS, *et al*. Pathways linking health literacy, health beliefs, and cognition to medication adherence in older adults with asthma. *J Allergy Clin Immunol* 2016; pii: S0091-6749(16)30626-1. doi: 10.1016/j.jaci.2016.05.043. [Epub ahead of print]
  52. Rusk G, Zhang S, McRoy L, Pisu M. Potential savings from increasing adherence to inhaled corticosteroid therapy in medicaid-enrolled children. *Am J Manag Care* 2015; 21:173–180.
  53. Vollmer WM, Xu M, Feldstein A, *et al*. Comparison of pharmacy-based measures of medication adherence. *BMC Health Serv Res* 2012; 12:155.
  54. Lam WY, Fresco P. Medication adherence measures: an overview. *Biomed Res Int* 2015; 2015:217047.
  55. Rand CS, Wright RJ, Cabana MD, *et al*. Mediators of asthma outcomes. *J Allergy Clin Immunol* 2012; 129:S136–S141.
  56. The Wharton Healthcare Management Alumni Association. The next phase of personalized medicine: predictive analytics and medication adherence. The Wharton Healthcare Management Alumni Association; 2016 ; Available at <http://www.whartonhealthcare.org/article.html?aid=1715>. [Accessed 21 April 2016]
  57. Rxante. 2016. Available at <https://www.rxante.com/>. [Accessed 21 April 2016]
  58. Rau JL. Determinants of patient adherence to an aerosol regimen. *Respir Care* 2005; 50:1346–1356; discussion 1357–1359.
  59. Sumino K, Cabana MD. Medication adherence in asthma patients. *Curr Opin Pulm Med* 2013; 19:49–53.
  60. Williams LK, Joseph CL, Peterson EL, *et al*. Patients with asthma who do not fill their inhaled corticosteroids: a study of primary nonadherence. *J Allergy Clin Immunol* 2007; 120:1153–1159.
- This is an excellent review of the history of electronic and digital adherence measuring devices with a look to the future.
61. Jentzsch NS, Camargos PA, Colosimo EA, Bousquet J. Monitoring adherence to beclomethasone in asthmatic children and adolescents through four different methods. *Allergy* 2009; 64:1458–1462.
  62. Brueckner JW, Marshik P, Sherman J, Hendeles L. Reliability of the Medtrac MDI Chronolog. *J Allergy Clin Immunol* 1997; 100:488–491.
  63. Stirratt MJ, Dunbar-Jacob J, Crane HM, *et al*. Self-report measures of medication adherence behavior: recommendations on optimal use. *Transl Behav Med* 2015; 5:470–482.
  64. Garcia-Marcos PW, Brand PL, Kaptein AA, Klok T. Is the MARS questionnaire a reliable measure of medication adherence in childhood asthma? *J Asthma* 2016; 53:1085–1090.
  65. Howard S, Lang A, Patel M, *et al*. Electronic monitoring of adherence to inhaled medication in asthma. *Curr Respir Med Rev* 2014; 10:50–63.
  66. Kikidis D, Konstantinos V, Tzovaras D, Usmani OS. The digital asthma patient: the history and future of inhaler based health monitoring devices. *J Aerosol Med Pulm Drug Deliv* 2016; 29:219–232.
  67. Chan AH, Reddel HK, Apter A, *et al*. Adherence monitoring and e-health: how clinicians and researchers can use technology to promote inhaler adherence for asthma. *J Allergy Clin Immunol Pract* 2013; 1:446–454.
  68. Chan AH, Harrison J, Black PN, *et al*. Using electronic monitoring devices to measure inhaler adherence: a practical guide for clinicians. *J Allergy Clin Immunol Pract* 2015; 3:335.e5–349.e5.
  69. Simmons MS, Nides MA, Rand CS, *et al*. Unpredictability of deception in compliance with physician-prescribed bronchodilator inhaler use in a clinical trial. *Chest* 2000; 118:290–295.
  70. Rhee H, Miner S, Sterling M, *et al*. The development of an automated device for asthma monitoring for adolescents: methodologic approach and user acceptability. *JMIR Mhealth Uhealth* 2014; 2:e27.

71. Mosnaim G, Li H, Martin M, *et al.* A tailored mobile health intervention to improve adherence and asthma control in minority adolescents. *J Allergy Clin Immunol Pract* 2015; 3:288.e1–290.e1.
72. Merchant RK, Inamdar R, Quade RC. Effectiveness of population health management using the propeller health asthma platform: a randomized clinical trial. *J Allergy Clin Immunol Pract* 2016; 4:455–463.
73. Foster JM, Usherwood T, Smith L, *et al.* Inhaler reminders improve adherence with controller treatment in primary care patients with asthma. *J Allergy Clin Immunol* 2014; 134:1260.e3–1268.e3.
74. Zafari Z, Lynd LD, FitzGerald JM, Sadatsafavi M. Economic and health effect of full adherence to controller therapy in adults with uncontrolled asthma: a simulation study. *J Allergy Clin Immunol* 2014; 134:908.e3–915.e3.