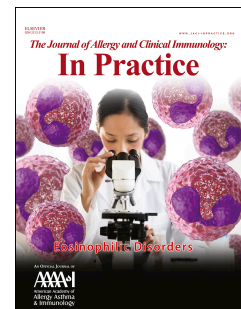


Journal Pre-proof

The impact of adherence and health literacy on difficult-to-control asthma

Sandra E. Zaeh, MD MS, Rachelle Ramsey, PhD, Bruce Bender, PhD, Kevin Hommel, Giselle Mosnaim, MD MS, Cynthia Rand, PhD



PII: S2213-2198(21)01265-4

DOI: <https://doi.org/10.1016/j.jaip.2021.11.003>

Reference: JAIP 3959

To appear in: *The Journal of Allergy and Clinical Immunology: In Practice*

Received Date: 30 July 2021

Revised Date: 25 October 2021

Accepted Date: 9 November 2021

Please cite this article as: Zaeh SE, Ramsey R, Bender B, Hommel K, Mosnaim G, Rand C, The impact of adherence and health literacy on difficult-to-control asthma, *The Journal of Allergy and Clinical Immunology: In Practice* (2021), doi: <https://doi.org/10.1016/j.jaip.2021.11.003>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2021 American Academy of Allergy, Asthma & Immunology

The impact of adherence and health literacy on difficult-to-control asthma

Sandra E. Zaeh, MD MS¹, Rachelle Ramsey, PhD^{2,3}, Bruce Bender, PhD⁴, Kevin Hommel^{2,3},
Giselle Mosnaim, MD MS,⁵ Cynthia Rand, PhD⁶

1. Division of Pulmonary, Critical Care, and Sleep Medicine, Yale School of Medicine, New Haven, CT

2. Division of Behavioral Medicine and Clinical Psychology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

3. Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio

4. Department of Pediatrics, National Jewish Health, Denver, CO

5. Division of Pulmonary, Allergy and Critical Care, Department of Medicine, NorthShore University Health System, Evanston, IL

6. Division of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD

Corresponding Author:

Sandra Zaeh, MD MS

Pulmonary, Critical Care, and Sleep Medicine, Yale University School of Medicine

300 Cedar Street TAC S-431

New Haven, CT, USA 06520

E-mail: sandra.zaeh@yale.edu

The authors declare they have no actual or potential competing interests. SZ received funding support from NIH F32HL149195-01.

Text Word Count: 3,879

Abstract Word Count: 194

Abstract

Medication nonadherence and health literacy are key factors that influence the management of difficult-to-control asthma. Adherence, or the extent to which a patient follows a treatment plan, extends beyond asthma medication use and includes appropriate inhaler technique.

Assessment of adherence is critical prior to making a diagnosis of severe asthma and stepping up asthma therapy but is challenging in the clinical context. Health literacy, or the degree to which individuals can obtain, process, and understand health information and services needed to make health care decisions, is additionally important for asthma management and has been shown to impact medication adherence.

Initiatives aiming to improve difficult-to-control asthma should address medication adherence and health literacy. Universal health literacy precautions are recommended while communicating with patients, in addition to the creation of low health literacy asthma action plans. To improve adherence, a comprehensive assessment of adherence should be conducted. Additional evidence based interventions aiming to improve adherence focus on appropriate inhaler use, improved access to medications, the use of digital platforms, school based asthma interventions, and the implementation of culturally tailored interventions. Data is limited regarding the use of these initiatives in patients with severe or difficult-to-control asthma.

Key Words: Adherence, difficult-to-control asthma, health literacy, interventions

Medication nonadherence and health literacy are key, yet under-recognized factors that influence the management of difficult-to-control asthma. This manuscript will first discuss the impact of adherence and health literacy on difficult-to-control asthma, and then provide examples of interventions that aim to improve asthma outcomes by addressing these barriers.

Impact of adherence on difficult-to-control asthma

Adherence, or the extent to which a patient follows an appropriate treatment plan from a qualified clinician, is a critical component of asthma management but is known to be suboptimal.^{1,2} Rates of adherence below 50% have been reported in children³ and rates of nonadherence ranging from 30-70% have been reported in adults.⁴ Poor adherence has been associated with increased mortality,⁵ higher rates of health care utilization, and higher risk of rescue medication use and exacerbations.^{6,7} Adherence extends beyond medication use and includes assessment of inhaler technique and side effects of medications, avoidance of allergens or irritants, and effective communication with the health care provider (HCP).^{1,8} Improving adherence in patients with asthma has been shown to improve asthma related outcomes. For example, a prospective study of children with moderate persistent asthma showed that adherence greater than 60% led to better control.⁹

Adherence to therapy is particularly important when considering difficult-to-control asthma. Current guideline-based recommendations for asthma therapy recommend checking adherence, inhaler technique, environmental factors and comorbid conditions prior to stepping up asthma medication therapy.¹⁰ The Global Initiative for Asthma suggests excluding each of these factors prior to making a diagnosis of severe asthma, defined as asthma that remains uncontrolled despite optimized treatment with a high dose inhaled corticosteroid (ICS) plus a second controller, or asthma that requires a high dose ICS plus second controller to prevent it

from becoming “uncontrolled.”^{11,12} Notably, distinguishing between poorly controlled or difficult-to-control asthma and severe asthma can be challenging within the clinical context given difficulties assessing patient medication adherence.¹³

Challenges in assessment of adherence in patients with difficult-to-control asthma

Assessment of adherence to asthma therapy is challenging as there is no standardized measurement. Mechanisms to assess adherence include biochemical measurement (i.e. for medications such as theophylline), clinical judgement, self-report, medication measurement, electronic medication measurement (EMM), and pharmacy database review.^{1,14} Objective measurements of medication adherence such as EMM have the advantage of allowing for assessment of long term patterns of adherence by recording and storing usage of medication over time, but they are more costly, making them less applicable for large scale clinical use.^{4,15} Subjective measures, such as patient self-report, are less expensive and can allow HCPs to collect information about patient beliefs, attitudes, and experiences with asthma medication, but have been shown to overestimate adherence.^{1,4,13}

Impact of severity of illness on adherence

Evidence suggests that nonadherence may be a contributing factor to difficult-to-control asthma. In a study of patients with severe asthma who were prescribed daily oral corticosteroids, 37% completing the Medication Adherence Report Scale reported suboptimal adherence and 43% did not have detectable prednisolone or metabolites in their urine.¹⁶ Another study using EMM showed that among patients with severe asthma who were eligible for novel therapies, at least half were nonadherent to preventer therapies.¹⁷

Recent studies have tried to distinguish patients with difficult-to-control asthma from those with severe asthma. Among patients with difficult-to-control asthma, 12% fulfilled strict criteria for severe asthma, 56% had difficult-to-control asthma due to poor adherence/inhaler technique, and 32% were adherent with correct inhaler technique but had unmanaged comorbidities.¹⁸ Another study using EMM of ICS adherence found that only 18% of children with good adherence had poor asthma control, suggestive of severe therapy-resistant asthma.¹³

Factors impacting adherence in patients with difficult-to-control asthma

A number of factors influence adherence in patients with asthma including issues related to medications, patient related beliefs, family factors, and interactions with HCPs.¹⁹ Notably, there has been little focus in the literature on assessment of barriers to adherence specific to patients with severe asthma. Medication related factors negatively influencing adherence include delayed effects of asthma medications, cost, and complex treatment plans.²⁰ As management of severe asthma typically includes more complicated medication regimens requiring adherence with more doses of medication, medication related barriers to adherence may be particularly relevant for patients with severe asthma.²¹ Patient related barriers, including patient attitudes towards treatment plans,²² psychological dysfunction, patient motivation, and belief in their caregiver may also impact adherence. Particularly for children with asthma, family conflict and environment can significantly impact adherence.^{23,24} Finally, factors related to the clinician, such as the patient-clinician relationship, may influence adherence.²⁰

Impact of low health literacy on difficult-to-control asthma

Effective patient-clinician communication is also critical for the delivery of quality health care for patients with difficult-to-control asthma and may contribute to poor adherence. Often, there is an

imbalance between an HCP's communication and a patient's comprehension, with evidence suggesting that patients may not understand or may misinterpret much of the information given to them.²⁵ Health literacy, defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health care decisions,"²⁶ is one contributor to this communication mismatch.

Health literacy is particularly important for asthma, a disease which has periods of worsening symptoms and which requires patient engagement in self-management.^{27,28} The National Assessment of Adult Literacy has found that only 12% of adults in the U.S. had proficient health literacy, with over one third of U.S. adults having difficulty with common health tasks (i.e. completing health insurance applications or reading a pamphlet and understanding the importance of a screening test).^{25,29} High risk groups for low health literacy include the elderly, people with limited education, ethnic minorities, individuals who spoke a language other than English in their childhood home, and individuals insured by Medicaid.²⁵ Low literacy has also been associated with poor health status, even after adjustment for sociodemographic variables.³⁰

In adult patients with asthma who required daily controller therapies, limited health literacy was associated with worse physical function, worse quality of life and increased utilization of the ED.³¹ Higher numeracy has been associated with lower lifetime risk of ED visits or hospitalizations due to asthma.³² Low health literacy in adult patients with asthma has been associated with worse asthma knowledge scores and improper inhaler use.³³ In turn, improper inhaler use has been associated with uncontrolled asthma and increased asthma exacerbations in patients on fixed dose combination therapy with an inhaled corticosteroid and a long acting beta agonist.³⁴ Low parental health literacy has been associated with greater likelihood of moderate persistent or severe persistent asthma in children and greater rates of ED visits and

hospitalizations.³⁵ Parents with low health literacy also had less asthma related knowledge, and their children were more likely to have worse asthma control.^{35,36}

Assessment of health literacy in patients with asthma

HCPs are often unable to identify patients who have limited literacy during clinical interactions³⁷ and health literacy may be dynamic during periods of high emotional stress. While quick assessments of literacy have been developed for the outpatient setting,^{38,39} most experts do not recommend the use of health literacy screening²⁸ for several reasons: 1) many patients with low health literacy are ashamed to ask for assistance or do not want their HCP to know about their difficulties with health literacy,⁴⁰ 2) health literacy screeners are often time-consuming⁴¹ and do not provide direct guidance for communication, and 3) no evidence supports that literacy screening improves the delivery of health care or health outcomes.^{42,43,44,45}

Relationship between health literacy and adherence

Finally, while adherence and health literacy are individually important factors impacting difficult-to-control asthma, evidence suggests that they are also connected. In adult patients with moderate or severe asthma, health literacy impacts adherence as well as asthma related outcomes. Better health literacy, assessed as numeracy and print literacy, was significantly related to improved electronically monitored adherence, asthma control, and asthma quality of life when controlling for age and sex.⁴⁶ Adults with moderate or severe asthma and low health literacy were found to have worse measured adherence and asthma medication inhaler technique.⁴⁷ No studies were found assessing the impact of pediatric health literacy on adherence. Initiatives aiming to improve difficult-to-control asthma therefore should address both adherence and health literacy.

Initiatives to educate and support patients with low health literacy and difficulties with adherence

Educational and behavioral interventions to improve adherence have been developed for patients with asthma with a focus on creating low health literacy asthma action plans. Given the episodic nature of asthma, many asthma management decisions are made at home by the patient, making understanding and subsequent adherence of asthma treatment plans imperative for optimal care. In addition, definitions of severe asthma and the guidelines for phenotype-specific management are all predicated on the assumption of treatment adherence,⁴⁸ making the accurate assessment and treatment of adherence crucial to not under or over-treating patients with asthma.

Health literacy precautions

While health literacy screening in regular clinical practice is not recommended, experts do encourage use of universal health literacy precautions when communicating with patients.⁴⁹ The Agency for Healthcare Research and Quality (AHRQ) toolkit offers recommendations on how to improve universal health literacy, encouraging clinicians to assess their own communications skills and how their practice engages with patients in spoken communication, written communication, patient self-management, and support systems.⁵⁰ For asthma care, universal health literacy is particularly important when selecting inhaler devices, teaching inhaler use, and counseling on use of an asthma action plan as studies have demonstrated that 70% of asthma action plans were written above a sixth-grade reading level.⁵¹ The use of professional interpreters in person or via telephone has also been shown to improve adherence and health outcomes, and reduce adverse events.^{44,45,52,53} Overall, there is limited data regarding interventions which aim to improve low health literacy in individuals with asthma,^{28,54} however

one 6-month intervention conducted in high risk children with severe asthma addressing health literacy and asthma self-management skills through weekly asthma education, literacy enhancement, and life skills training, showed a significant decline in hospitalizations and ED visits.⁵⁵ Many of the adherence interventions described below utilize tools to promote health literacy in an effort to improve adherence and health outcomes.

Adherence Assessment

Assessment of adherence can be difficult in routine clinical practice, but is a necessary component of asthma treatment requiring a systematic approach and a variety of tools. When EMM is cost prohibitive or unavailable, a comprehensive assessment of adherence should include the integration of data from medical chart review and an adherence assessment with the patient and/or caregivers.^{56,57} This clinical assessment of adherence informs the clinician while acting as an initial self-monitoring intervention. A medical chart review can provide information about adherence concerns, potential barriers to adherence, biochemical measurements and/or pharmacy/prescription refill data. Biochemical measurements are best used as a preliminary screener for nonadherence as they are not available for all medications, provide little insight into patterns of adherence, may not be sensitive enough to pick up on low levels of nonadherence, and often only represent recent adherence due to short medication half-lives.⁵⁸ Measurement of exhaled nitric oxide (FeNO) can also be used as a screener for nonadherence. Most studies reporting a single measurement or repeated measurements of FeNO find higher levels of FeNO in less adherent participants. Within these studies, FeNO levels are compared to alternative methods of measuring adherence such as patient self report or electronic monitoring devices.^{59,60,61} Notably, there is inadequate data to propose a single clinically meaningful FeNO cut-off.⁵⁹ Pharmacy/prescription refill data can also be used as a preliminary screener and to facilitate a collaborative discussion about the patient's self-management and future treatment

240 planning.⁶² Notably, filling medications on time does not imply accurate administration of
241 medication as prescribed⁶² and patients may utilize multiple pharmacies or enroll in automatic
242 refill programs.⁶³

243
244 In addition, a comprehensive assessment of adherence requires a collaborative effort by
245 clinicians, patients, and caregivers to improve health outcomes.⁶⁴ Adherence can be a
246 challenging and emotional topic to broach with patients and may result in defensiveness, worry
247 about disappointing HCPs, and efforts to avoid consequences.^{58,62,65} When discussing
248 medication adherence, a nonjudgmental interpersonal style with simple language and
249 normalization of adherence difficulties can increase the patient's comfort and validity of the
250 information received.^{62,66,67} This may be particularly true for patients with more severe asthma,
251 as adherence and health outcomes do not always have a direct relationship. Overall, it is
252 beneficial for adherence discussions to be framed as shared-decision making to improve
253 treatment planning, adherence, and health outcomes over time.⁶⁴ Adherence based discussions
254 should include four components: (1) the patient knowledge of the prescribed treatment, (2) how
255 often the patient accurately adheres to the prescribed treatment plan, (3) how often the patient
256 has missed or neglected treatment behaviors, and (4) the barriers that impede the patient's
257 adherence.⁶⁴ To improve the detail and accuracy of adherence data provided, it is important to
258 ask about a brief and recent timeframe such as a seven-day time frame for patients taking
259 twice-daily medication.^{62,64,67} Continued assessment of adherence and barriers should occur
260 over time as these may vary as the patient develops, treatment regimens are altered, or life
261 circumstances change.⁶⁸ Understanding these barriers is an integral component for treatment
262 planning and implementing adherence-focused interventions.

263
264 *Appropriate inhaler use*

Although effective asthma treatment relies on both the regular use of medications and correct inhaler technique,^{69,70,71} most children with asthma demonstrate significant deficiencies in inhaler technique.⁷¹ Key components for effectively teaching patients to use an inhaler are explaining and demonstrating the inhaler technique and repeating this instruction over time.⁷² The asthma education literature is not always clear on the extent to which programs assess or teach inhaler technique⁷² and whether they do so in a way that would be clear for patients with low health literacy. Therefore, it is not surprising that existing studies offer mixed evidence for sustained technique improvements at 12-month follow-up.⁷² Although there is a paucity of literature regarding inhaler technique specifically in severe or difficult-to-control asthma, a systematic review of 14 studies including adolescents and adults of all asthma severity levels suggested a negative correlation between advancing age and correct technique across metered dose inhalers (MDI) and varying dry powder inhaler (DPI) devices.⁷³ Poor inhaler technique may also be a marker of non-adherence.⁷⁴ Clinicians should continue to provide education in this area to all patients, including patients with severe or difficult-to-control asthma.

Assessing and addressing access to medications via pharmacy delivery

Many patients have difficulties filling pharmacy medications and when patients do not have necessary medications on hand, they are unable to be adherent. Providing discharge medication delivery service so that all patients leave the hospital with their prescribed medications has been shown to lower the odds of re-presentation to the ED within 30 days of discharge compared to patients discharged with usual care.⁷⁵ Another method for improving access to medications is to arrange pharmacy delivery so patients' medications are delivered to their homes. Improving access to medications may be the first step to improved adherence.^{76,77,78,79,80,81}

Behavioral interventions to improve adherence

Behavioral adherence interventions among adults have been shown to be efficacious in improving ICS adherence, reducing symptoms, and decreasing unscheduled health care use.^{78,79} A recent study in adults demonstrated that the more chronic care model components (e.g., teaching self-management skills, providing decision support, delivery system design) that an adherence intervention contained, the greater the impact on adherence.⁷⁹ Another study, however, found no significant associations between adherence and specific behavior change techniques in the broader asthma population. The Cochrane Review of interventions for enhancing adherence to medication among pediatric and adult participants includes 13 asthma interventions studies and documented that 6 of the interventions improved adherence in asthma.⁸⁰ None of these studies were specific to difficult-to-control asthma.^{78,79} Given the various adherence assessment methodologies utilized and the mixed findings in the general asthma literature, the authors of the Cochrane Review concluded that the data was “surprisingly weak” and that “increasing effectiveness of adherence interventions would have a greater impact than improvement in specific medical treatments.”⁴⁸

Only 1 adherence intervention study has been conducted specifically with adults with difficult-to-control asthma. Over 30% of patients with difficult-to-control asthma and recent nonadherence based on prescription refill history became adherent to their medication following a concordance interview.⁸² This interview included a conversation with patients discussing patient nonadherence and agreeing on a treatment plan to improve adherence. At 12 to 18 months of follow up, 90% of participants remained adherent and improved adherence was associated with reductions in prescribed daily dose of ICS, number of rescue courses of prednisolone and asthma related hospitalizations, and increased FEV1.⁸²

The paucity of adherence intervention studies for patients with difficult-to-control asthma extends to the pediatric asthma literature. A recent meta-analysis of 33 studies testing adherence interventions for children with asthma established that ICS adherence promotion interventions are effective among youth with asthma. However, none of the included studies specifically examined difficult-to-control asthma as a primary patient population or in secondary analyses.⁸³ Only 12 of the 33 studies documented asthma severity level for the participants, and the inclusion of moderate to severe or severe patients ranged from 10% to 94%. Although distinct from difficult-to-control asthma, a 2018 systematic review examined the impact of adherence interventions in children with severe asthma.⁸⁴ Adherence interventions for children with severe asthma included communication during pediatric visits, individualized care programs, EMM, an interactive website, and peak-flow predication with feedback. Adherence rates for children with severe asthma ranged from 28 to 67%, and interventions results in a significant improvement of adherence with rates increasing to 49-81%.⁸⁴ This review was limited by the lack of studies of adherence interventions in children with severe or difficult-to-control asthma, heterogeneity in the definitions of asthma types or severities, and the variety of adherence assessment tools utilized.⁸⁴

Use of digital platforms to support adherence

Recent advancements in technology have led to an increased number of digital interventions for adherence to improve accessibility, cost-effectiveness, and customizability of interventions. One study of African American adolescents with uncontrolled asthma and prescribed ICS demonstrated improved asthma control and ICS adherence with the use of a combination of medication reminders, rewards delivered on a smartphone application, and physician feedback.⁸⁵ Most recently sensor-based electronic monitoring systems for asthma medications and symptoms have become increasingly accessible and popular in both adults and

children.^{86,87} Often EMM works with a mHealth app to provide a combination of features such as self-monitoring, feedback, asthma education (e.g., about symptoms, medications, triggers), encouragement, and the potential to data share with the medical team. Propeller Health (Propeller Health, Madison, WI), for example, incorporates an FDA approved sensor with a mobile app providing predictive analytics and feedback to help patients and clinicians better understand and control asthma⁸⁸ based on patient adherence. In a randomized controlled trial (RCT), the use of the Propeller Health combined with clinical feedback in children with moderate to persistent asthma resulted in significantly improved asthma symptom control, caregiver quality of life and, for a smaller subset of the sample with actively transmitting sensors, adherence.⁸⁹ Similarly, in a RCT of adults with uncontrolled asthma, the use of EMM and smartphone application plus remote clinician feedback improved inhaled corticosteroid use and decreased rescue medication use compared to a control group.⁹⁰

A recent scoping review which was not limited to patients with difficult-to-control asthma demonstrated that patient-specific interactive bidirectional digital interventions reported improvements in adherence and asthma impairment in both adult and pediatric participants.⁹¹ In another review of digital asthma adherence interventions for children, 87% of the interventions demonstrated improved adherence and 53% demonstrated improved outcomes, yet approximately half of the studies did not include children with severe or difficult-to-control asthma.⁹² The studies with higher rates of moderate or severe persistent asthma (>50%) demonstrated mixed findings with an interactive web-based intervention resulting in improved adherence,⁹³ a daily electronic diary website resulting in decreased adherence that was better compared to a control group,⁹⁴ and MP3 recordings and motivational interviewing resulting in no statistical difference between the intervention and control group.⁹⁵ The mixed findings for the adherence interventions, specifically in the intervention samples including patients with more

severe asthma, highlight the need for adherence promotion interventions to be developed for patients with severe or difficult-to-control asthma.

Implementation of culturally tailored interventions

The cultural background of a patient must also be considered when implementing adherence interventions, particularly given that African Americans shoulder a disproportionate burden of the prevalence, morbidity, and mortality associated with asthma, perhaps due to lower adherence rates.^{96,97,98} Success in performing adherence behaviors consistent with a treatment plan is the result of contextual influences interacting with social, emotional, and cognitive processes.⁹⁹ A recent systematic review focused on culturally tailored ICS adherence interventions for adult African Americans with asthma found only 5 studies that met their inclusion criteria, none of which was found to be effective in improving ICS adherence, though 3 studies found improved adherence in both the intervention and control groups. Asthma criteria differed across studies included in the review, with some including participants with moderate or severe asthma, and others including participants with persistent asthma.¹⁰⁰

Interventions have been developed to specifically help overcome barriers such as access to care and poor patient-clinician communication in adults with moderate to severe asthma from low income urban neighborhoods. One example was a patient advocate (PA) intervention, in which PAs assisted patients with scheduling visits, obtaining insurance coverage, and implementing medical advice. The PA program was found to be feasible and acceptable for patients and clinicians.¹⁰¹ Adults randomized to receive six months of the PA intervention had improved asthma control and fewer ED visits compared to the control arm, although these results did not reach statistical significance.

In pediatric asthma, school-based telemedicine interventions have been developed to improve outcomes in children with uncontrolled asthma from low income, urban areas. Specifically, a school-based intervention which allowed for the delivery and supervised administration of preventative asthma medication at school as well as telemedicine visits to ensure appropriate follow-up care resulted in more symptom free days and fewer ED visits and hospitalizations for asthma compared to controls.¹⁰² Another school-based intervention for children with uncontrolled asthma found that telemedicine delivery of medical and self-management visits with a pediatric psychologist reduced asthma severity in children with higher baseline severity and improved adherence to daily medications.¹⁰³

Future Directions and Conclusions

Overall, it is imperative for clinicians to identify patients with suboptimal adherence, understand reasons for their behavior, and implement treatment approaches aimed at improving and maintaining adherence. This is specifically true in patients with difficult-to-control asthma as many patients may be impacted by low levels of medication adherence and low health literacy. There is limited literature regarding the impact of the health literacy of pediatric patients on pediatric adherence and asthma outcomes. There may be benefit to further investigation in this area. Additionally, as detailed within this manuscript, a number of initiatives have been developed to support patients like these, however, there is limited data regarding the use of these initiatives specifically in patients with severe or difficult-to-control asthma. Future research efforts should focus on designing and testing initiatives that will benefit this patient population given a higher burden of symptoms and exacerbations, additional treatment requirements, and an increased impact on work, school, and family life. Specifically, digital interventions seem promising and research should continue to examine engagement and impact of these interventions. Behavioral, educational, and digital interventions introduce added cost, but the

421 potential benefits of improved control resulting from addressing adherence and health literacy in
422 patients with severe asthma may offset such cost.

423

References

1. Bender B, Milgrom H, Rand C. Nonadherence in Asthmatic Patients: Is there a Solution to the Problem ? *Ann Allergy Asthma Immunol*. 1997 Sep 1;79(3):177–87.
2. Sabate, Eduardo. *Adherence to Long-Term Therapies: Evidence for Action*. Geneva, Switzerland: World Health Organization; 2003.
3. Milgrom H, Bender B, Ackerson L, Bowry P, Smith B, Rand C. Noncompliance and treatment failure in children with asthma. *J Allergy Clin Immunol*. 1996 Dec;98(6 Pt 1):1051–7.
4. Rand CS, Wise RA. Measuring adherence to asthma medication regimens. *Am J Respir Crit Care Med*. 1994 Feb;149(2 Pt 2):S69-76; discussion S77-78.
5. Harrison B, Stephenson P, Mohan G, Nasser S. An ongoing Confidential Enquiry into asthma deaths in the Eastern Region of the UK, 2001-2003. *Prim Care Respir J J Gen Pract Airw Group*. 2005 Dec;14(6):303–13.
6. Ismaila A, Corriveau D, Vaillancourt J, Parsons D, Stanford R, Su Z, et al. Impact of adherence to treatment with fluticasone propionate/salmeterol in asthma patients. *Curr Med Res Opin*. 2014 Jul;30(7):1417–25.
7. Engelkes M, Janssens HM, Jongste JC de, Sturkenboom MCJM, Verhamme KMC. Medication adherence and the risk of severe asthma exacerbations: a systematic review. *Eur Respir J*. 2015 Feb 1;45(2):396–407.
8. Asthma NAE and PP Third Expert Panel on the Diagnosis and Management of. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung, and Blood Institute (US); 2007.
9. Jentzsch NS, Silva GCG, Mendes GMS, Brand PLP, Camargos P. Treatment adherence and level of control in moderate persistent asthma in children and adolescents treated with fluticasone and salmeterol. *J Pediatr (Rio J)*. 2019 Jan 1;95(1):69–75.
10. Expert Panel Working Group of the National Heart, Lung, and Blood Institute (NHLBI) administered and coordinated National Asthma Education and Prevention Program Coordinating Committee (NAEPCC), Cloutier MM, Baptist AP, Blake KV, Brooks EG, Bryant-Stephens T, et al. 2020 Focused Updates to the Asthma Management Guidelines: A Report from the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group. *J Allergy Clin Immunol*. 2020 Dec;146(6):1217–70.
11. GINA-Main-Report-2021-V2-WMS.pdf [Internet]. [cited 2021 Jun 11]. Available from: <https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf>
12. Chung KF, Wenzel SE, Brozek JL, Bush A, Castro M, Sterk PJ, et al. International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma. *Eur Respir J*. 2014 Feb 1;43(2):343–73.
13. Jochmann A, Artusio L, Jamalzadeh A, Nagakumar P, Delgado-Eckert E, Saglani S, et al. Electronic monitoring of adherence to inhaled corticosteroids: an essential tool in identifying

- 463 severe asthma in children. *Eur Respir J* [Internet]. 2017 Dec 1 [cited 2021 Jun 12];50(6).
464 Available from: <https://erj.ersjournals.com/content/50/6/1700910>
- 465 14. Apter A, Bender B, Rand C. Adherence. In: Middleton's Allergy: Principles and Practice.
466 8th ed. New York: Elsevier; 2013.
- 467 15. Himes BE, Leszinsky L, Walsh R, Hepner H, Wu AC. Mobile Health and Inhaler-Based
468 Monitoring Devices for Asthma Management. *J Allergy Clin Immunol Pract*. 2019;7(8):2535–
469 43.
- 470 16. Alahmadi FH, Simpson AJ, Gomez C, Ericsson M, Thörngren J-O, Wheelock CE, et al.
471 Medication Adherence in Patients With Severe Asthma Prescribed Oral Corticosteroids in
472 the U-BIOPRED Cohort. *Chest* [Internet]. 2021 Feb 19 [cited 2021 Jun 14]; Available from:
473 <https://www.sciencedirect.com/science/article/pii/S0012369221002889>
- 474 17. Lee J, Tay TR, Radhakrishna N, Hore-Lacy F, Mackay A, Hoy R, et al. Nonadherence in the
475 era of severe asthma biologics and thermoplasty. *Eur Respir J* [Internet]. 2018 Apr 5 [cited
476 2021 Jun 15];51(4). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5884695/>
- 477 18. von Bülow A, Backer V, Bodtger U, Sørensen-Petersen NU, Vest S, Steffensen I, et al.
478 Differentiation of adult severe asthma from difficult-to-treat asthma – Outcomes of a
479 systematic assessment protocol. *Respir Med*. 2018 Dec 1;145:41–7.
- 480 19. Modi AC, Pai AL, Hommel KA, Hood KK, Cortina S, Hilliard ME, et al. Pediatric self-
481 management: a framework for research, practice, and policy. *Pediatrics*. 2012
482 Feb;129(2):e473-485.
- 483 20. Bender BG. Overcoming barriers to nonadherence in asthma treatment. *J Allergy Clin*
484 *Immunol*. 2002 Jun 1;109(6):S554–9.
- 485 21. Masaki K, Miyata J, Kamatani T, Tanosaki T, Mochimaru T, Kabata H, et al. Risk factors for
486 poor adherence to inhaled corticosteroid therapy in patients with moderate to severe
487 asthma. *Asian Pac J Allergy Immunol*. 2020 Jun 21;
- 488 22. Apter AJ, Boston RC, George M, Norfleet AL, Tenhave T, Coyne JC, et al. Modifiable
489 barriers to adherence to inhaled steroids among adults with asthma: it's not just black and
490 white. *J Allergy Clin Immunol*. 2003 Jun;111(6):1219–26.
- 491 23. Fiese BH, Wamboldt FS. Tales of pediatric asthma management: family-based strategies
492 related to medical adherence and health care utilization. *J Pediatr*. 2003 Oct;143(4):457–62.
- 493 24. Fiese BH, Everhart RS. Medical adherence and childhood chronic illness: family daily
494 management skills and emotional climate as emerging contributors. *Curr Opin Pediatr*. 2006
495 Oct;18(5):551–7.
- 496 25. Weiss, B. Health literacy and patient safety: Help patients understand. *Manual for Clinicians*,
497 Second Edition. May 2009.
- 498 26. National Institutes of Health. Current Bibliographies in Medicine: Health Literacy: January
499 1990 through October 1999. February 2000. Bethesda, MD.

- 500 27. Myers L, Murray RK. Overcoming Health Literacy Barriers to Improve Asthma Inhaler
501 Therapy Adherence. *Ann Am Thorac Soc*. 2019 Feb;16(2):182–6.
- 502 28. Rosas-Salazar C, Apter AJ, Canino G, Celedón JC. Health literacy and asthma. *J Allergy*
503 *Clin Immunol*. 2012 Apr 1;129(4):935–42.
- 504 29. U.S. Department of Health and Human Services. America's Health Literacy: Why We Need
505 Accessible Health Information. 2008.
- 506 30. Weiss BD, Hart G, McGee DL, D'Estelle S. Health status of illiterate adults: relation between
507 literacy and health status among persons with low literacy skills. *J Am Board Fam Pract*.
508 1992 Jun;5(3):257–64.
- 509 31. Mancuso CA, Rincon M. Impact of Health Literacy on Longitudinal Asthma Outcomes. *J*
510 *Gen Intern Med*. 2006 Aug;21(8):813–7.
- 511 32. Apter AJ, Cheng J, Small D, Bennett IM, Albert C, Fein DG, et al. Asthma numeracy skill
512 and health literacy. *J Asthma Off J Assoc Care Asthma*. 2006 Nov;43(9):705–10.
- 513 33. Williams MV, Baker DW, Honig EG, Lee TM, Nowlan A. Inadequate Literacy Is a Barrier to
514 Asthma Knowledge and Self-Care. *CHEST*. 1998 Oct 1;114(4):1008–15.
- 515 34. Price DB, Román-Rodríguez M, McQueen RB, Bosnic-Anticevich S, Carter V, Gruffydd-
516 Jones K, et al. Inhaler Errors in the CRITIKAL Study: Type, Frequency, and Association with
517 Asthma Outcomes. *J Allergy Clin Immunol Pract*. 2017 Aug;5(4):1071-1081.e9.
- 518 35. DeWalt DA, Dilling MH, Rosenthal MS, Pignone MP. Low Parental Literacy Is Associated
519 With Worse Asthma Care Measures in Children. *Ambul Pediatr*. 2007 Jan 1;7(1):25–31.
- 520 36. Harrington KF, Zhang B, Magruder T, Bailey WC, Gerald LB. The Impact of Parent's Health
521 Literacy on Pediatric Asthma Outcomes. *Pediatr Allergy Immunol Pulmonol*. 2015 Mar
522 1;28(1):20–6.
- 523 37. Lindau ST, Tomori C, Lyons T, Langseth L, Bennett CL, Garcia P. The association of health
524 literacy with cervical cancer prevention knowledge and health behaviors in a multiethnic
525 cohort of women. *Am J Obstet Gynecol*. 2002 May;186(5):938–43.
- 526 38. Weiss BD, Mays MZ, Martz W, Castro KM, DeWalt DA, Pignone MP, et al. Quick
527 assessment of literacy in primary care: the newest vital sign. *Ann Fam Med*. 2005
528 Dec;3(6):514–22.
- 529 39. Wallston KA, Cawthon C, McNaughton CD, Rothman RL, Osborn CY, Kripalani S.
530 Psychometric properties of the brief health literacy screen in clinical practice. *J Gen Intern*
531 *Med*. 2014 Jan;29(1):119–26.
- 532 40. Parikh NS, Parker RM, Nurss JR, Baker DW, Williams MV. Shame and health literacy: the
533 unspoken connection. *Patient Educ Couns*. 1996 Jan;27(1):33–9.
- 534 41. Davis TC, Michielutte R, Askov EN, Williams MV, Weiss BD. Practical assessment of adult
535 literacy in health care. *Health Educ Behav Off Publ Soc Public Health Educ*. 1998
536 Oct;25(5):613–24.

- 537 42. Mayer GG, Villaire M. Health literacy in primary care: A clinician's guide. New York: Springer
538 Publishing Company; 2007.
- 539 43. Apter AJ, Wang X, Bogen D, Bennett IM, Jennings RM, Garcia L, et al. Linking numeracy
540 and asthma-related quality of life. *Patient Educ Couns*. 2009 Jun;75(3):386–91.
- 541 44. Paasche-Orlow MK, Wolf MS. Evidence Does Not Support Clinical Screening of Literacy. *J*
542 *Gen Intern Med*. 2008 Jan;23(1):100–2.
- 543 45. Weiss BD. Assessing Patients' Healthy Literacy Skills Not Necessary in Clinical Practice.
544 *Am Fam Physician*. 2018 Jun 15;97(12):gma.
- 545 46. Apter AJ, Wan F, Reisine S, Bender B, Rand C, Bogen DK, et al. The association of health
546 literacy with adherence and outcomes in moderate-severe asthma. *J Allergy Clin Immunol*.
547 2013 Aug 1;132(2):321–7.
- 548 47. Federman AD, Wolf MS, Sofianou A, Martynenko M, O'Connor R, Halm EA, et al. Self-
549 management behaviors in older adults with asthma: associations with health literacy. *J Am*
550 *Geriatr Soc*. 2014 May;62(5):872–9.
- 551 48. Lindsay JT, Heaney LG. Nonadherence in difficult asthma - facts, myths, and a time to act.
552 *Patient Prefer Adherence*. 2013;7:329–36.
- 553 49. Hersh L, Salzman B, Snyderman D. Health Literacy in Primary Care Practice. *Am Fam*
554 *Physician*. 2015 Jul 15;92(2):118–24.
- 555 50. Brega AG, Barnard J, Mabachi NM, Weiss BD, DeWalt DA, Brach C, Cifuentes M,
556 Albright K, West, DR. AHRQ Health Literacy Universal Precautions Toolkit, Second Edition.
557 (Prepared by Colorado Health Outcomes Program, University of Colorado Anschutz Medical
558 Campus under Contract No. HHS290200710008, TO#10.) AHRQ Publication No. 15-
559 0023-EF. Rockville, MD. Agency for Healthcare Research and Quality. January 2015.
560
- 561 51. Yin HS, Gupta RS, Tomopoulos S, Wolf MS, Mendelsohn AL, Antler L, et al. Readability,
562 suitability, and characteristics of asthma action plans: examination of factors that may impair
563 understanding. *Pediatrics*. 2013 Jan;131(1):e116-126.
- 564 52. Flores G, Abreu M, Barone CP, Bachur R, Lin H. Errors of medical interpretation and their
565 potential clinical consequences: a comparison of professional versus ad hoc versus no
566 interpreters. *Ann Emerg Med*. 2012 Nov;60(5):545–53.
- 567 53. Juckett G, Unger K. Appropriate use of medical interpreters. *Am Fam Physician*. 2014 Oct
568 1;90(7):476–80.
- 569 54. Salim H, Ramdzan SN, Ghazali SS, Lee PY, Young I, McClatchey K, et al. A systematic
570 review of interventions addressing limited health literacy to improve asthma self-
571 management. *J Glob Health*. 10(1):010427.
- 572 55. Robinson LD, Calmes DP, Bazargan M. The impact of literacy enhancement on asthma-
573 related outcomes among underserved children. *J Natl Med Assoc*. 2008 Aug;100(8):892–6.

- 574 56. Hommel KA, Greenley RN, Maddux MH, Gray WN, Mackner LM. Self-management in
575 pediatric inflammatory bowel disease: A clinical report of the North American Society for
576 Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr*. 2013
577 Aug;57(2):250–7.
- 578 57. Quittner AL, Modi AC, Lemanek KL, Ievers-Landis CE, Rapoff MA. Evidence-based
579 Assessment of Adherence to Medical Treatments in Pediatric Psychology. *J Pediatr*
580 *Psychol*. 2008 Oct;33(9):916–36.
- 581 58. Lehmann A, Aslani P, Ahmed R, Celio J, Gauchet A, Bedouch P, et al. Assessing
582 medication adherence: options to consider. *Int J Clin Pharm*. 2014 Feb;36(1):55–69.
- 583 59. Alahmadi F, Peel A, Keevil B, Niven R, Fowler SJ. Assessment of adherence to
584 corticosteroids in asthma by drug monitoring or fractional exhaled nitric oxide: A literature
585 review. *Clin Exp Allergy*. 2021 Jan;51(1):49–62.
- 586 60. Koster ES, Raaijmakers JAM, Vijverberg SJH, Maitland-van der Zee A-H. Inhaled
587 corticosteroid adherence in paediatric patients: the PACMAN cohort study.
588 *Pharmacoepidemiol Drug Saf*. 2011 Oct;20(10):1064–72.
- 589 61. Heaney LG, Busby J, Bradding P, Chaudhuri R, Mansur AH, Niven R, et al. Remotely
590 Monitored Therapy and Nitric Oxide Suppression Identifies Nonadherence in Severe
591 Asthma. *Am J Respir Crit Care Med*. 2019 Feb 15;199(4):454–64.
- 592 62. Duncan CL, Mentrikoski JM, Wu YP, Fredericks EM. Practice-Based Approach to Assessing
593 and Treating Non-Adherence in Pediatric Regimens. *Clin Pract Pediatr Psychol*. 2014
594 Sep;2(3):322–36.
- 595 63. Hommel KA, Ramsey RR, Rich KL, Ryan JL. Adherence to Pediatric Treatment Regimens.
596 In: *Handbook of Pediatric Psychology*. Fifth Edition. New York, NY: The Guilford Press;
- 597 64. Zelikovsky N, Schast AP. Eliciting accurate reports of adherence in a clinical interview:
598 development of the Medical Adherence Measure. *Pediatr Nurs*. 2008 Apr;34(2):141–6.
- 599 65. Drotar D. Strategies of adherence promotion in the management of pediatric chronic
600 conditions. *J Dev Behav Pediatr JDBP*. 2013 Dec;34(9):716–29.
- 601 66. Hommel KA, Baldassano RN. Brief Report: Barriers to Treatment Adherence in Pediatric
602 Inflammatory Bowel Disease. *J Pediatr Psychol*. 2010 Oct;35(9):1005–10.
- 603 67. Stirratt MJ, Dunbar-Jacob J, Crane HM, Simoni JM, Czajkowski S, Hilliard ME, et al. Self-
604 report measures of medication adherence behavior: recommendations on optimal use.
605 *Transl Behav Med*. 2015 Dec;5(4):470–82.
- 606 68. Ramsey RR, Zhang N, Modi AC. The Stability and Influence of Barriers to Medication
607 Adherence on Seizure Outcomes and Adherence in Children With Epilepsy Over 2 Years. *J*
608 *Pediatr Psychol*. 2018 Mar 1;43(2):122–32.
- 609 69. Cochrane MG, Bala MV, Downs KE, Mauskopf J, Ben-Joseph RH. Inhaled Corticosteroids
610 for Asthma Therapy: Patient Compliance, Devices, and Inhalation Technique. *Chest*. 2000
611 Feb 1;117(2):542–50.

- 612 70. Burgess S, Sly P, Devadason S. Adherence with Preventive Medication in Childhood
613 Asthma. *Pulm Med*. 2011 Apr 6;2011:e973849.
- 614 71. Price D, Bosnic-Anticevich S, Briggs A, Chrystyn H, Rand C, Scheuch G, et al. Inhaler
615 competence in asthma: Common errors, barriers to use and recommended solutions. *Respir*
616 *Med*. 2013 Jan 1;107(1):37–46.
- 617 72. Geryk LL, Roberts CA, Carpenter DM. A systematic review of school-based interventions
618 that include inhaler technique education. *Respir Med*. 2017 Nov 1;132:21–30.
- 619 73. Barbara S, Kritikos V, Bosnic-Anticevich S. Inhaler technique: does age matter? A
620 systematic review. *Eur Respir Rev* [Internet]. 2017 Dec 31 [cited 2021 Jul 2];26(146).
621 Available from: <https://err.ersjournals.com/content/26/146/170055>
- 622 74. Azzi E, Srour P, Armour C, Rand C, Bosnic-Anticevich S. Practice makes perfect: self-
623 reported adherence a positive marker of inhaler technique maintenance. *Npj Prim Care*
624 *Respir Med*. 2017 Apr 24;27(1):1–6.
- 625 75. Hatoun J, Bair-Merritt M, Cabral H, Moses J. Increasing Medication Possession at
626 Discharge for Patients With Asthma: The Meds-in-Hand Project. *Pediatrics* [Internet]. 2016
627 Mar 1 [cited 2021 Jul 2];137(3). Available from:
628 <https://pediatrics.aappublications.org/content/137/3/e20150461>
- 629 76. Bender BG, Bartlett SJ, Rand CS, Turner C, Wamboldt FS, Zhang L. Impact of interview
630 mode on accuracy of child and parent report of adherence with asthma-controller
631 medication. *Pediatrics*. 2007 Sep;120(3):e471-477.
- 632 77. Viswanathan M, Golin CE, Jones CD, Ashok M, Blalock SJ, Wines RCM, et al. Interventions
633 to improve adherence to self-administered medications for chronic diseases in the United
634 States: a systematic review. *Ann Intern Med*. 2012 Dec 4;157(11):785–95.
- 635 78. Denford S, Taylor RS, Campbell JL, Greaves CJ. Effective behavior change techniques in
636 asthma self-care interventions: systematic review and meta-regression. *Health Psychol Off*
637 *J Div Health Psychol Am Psychol Assoc*. 2014 Jul;33(7):577–87.
- 638 79. Moullec G, Gour-Provencal G, Bacon SL, Campbell TS, Lavoie KL. Efficacy of interventions
639 to improve adherence to inhaled corticosteroids in adult asthmatics: impact of using
640 components of the chronic care model. *Respir Med*. 2012 Sep;106(9):1211–25.
- 641 80. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing
642 medication adherence. *Cochrane Database Syst Rev*. 2008 Apr 16;(2):CD000011.
- 643 81. Dorsey MJ, Schneider LC. IMPROVING ASTHMA OUTCOMES AND SELF-
644 MANAGEMENT BEHAVIORS OF INNER-CITY CHILDREN. *Pediatrics*. 2003 Aug
645 1;112(Supplement 2):474–474.
- 646 82. Gamble J, Stevenson M, Heaney LG. A study of a multi-level intervention to improve non-
647 adherence in difficult to control asthma. *Respir Med*. 2011 Sep;105(9):1308–15.
- 648 83. Fidler A, Sweenie R, Ortega A, Cushing CC, Ramsey R, Fedele D. Meta-analysis of
649 adherence promotion interventions in pediatric asthma. *J Pediatr Psychol*.

- 650 84. Boutopoulou B, Koumpagioti D, Matziou V, Priftis KN, Douros K. Interventions on
651 Adherence to Treatment in Children With Severe Asthma: A Systematic Review. *Front*
652 *Pediatr*. 2018;6:232.
- 653 85. Mosnaim G, Li H, Martin M, Richardson D, Belice PJ, Avery E, et al. A tailored mobile health
654 intervention to improve adherence and asthma control in minority adolescents. *J Allergy Clin*
655 *Immunol Pract*. 2015 Apr;3(2):288-290.e1.
- 656 86. Ramsey RR, Guilbert TW. Exciting Era of Sensor-Based Electronic Monitoring of Adherence
657 in Pediatric Asthma. *Pediatrics*. 2021 Jan;147(1):e2020036749.
- 658 87. Bonini M, Usmani OS. Novel methods for device and adherence monitoring in asthma. *Curr*
659 *Opin Pulm Med*. 2018 Jan;24(1):63–9.
- 660 88. Merchant RK, Inamdar R, Quade RC. Effectiveness of Population Health Management
661 Using the Propeller Health Asthma Platform: A Randomized Clinical Trial. *J Allergy Clin*
662 *Immunol Pract*. 2016 Jun;4(3):455–63.
- 663 89. Gupta RS, Fierstein JL, Boon KL, Kanaley MK, Bozen A, Kan K, et al. Sensor-Based
664 Electronic Monitoring for Asthma: A Randomized Controlled Trial. *Pediatrics*. 2021
665 Jan;147(1):e20201330.
- 666 90. Mosnaim GS, Stempel DA, Gonzalez C, Adams B, BenIsrael-Olive N, Gondalia R, et al. The
667 Impact of Patient Self-Monitoring Via Electronic Medication Monitor and Mobile App Plus
668 Remote Clinician Feedback on Adherence to Inhaled Corticosteroids: A Randomized
669 Controlled Trial. *J Allergy Clin Immunol Pract*. 2021 Apr 1;9(4):1586–94.
- 670 91. Mosnaim G, Safioti G, Brown R, DePietro M, Szeffler SJ, Lang DM, et al. Digital Health
671 Technology in Asthma: A Comprehensive Scoping Review. *J Allergy Clin Immunol Pract*.
672 2021 Jun;9(6):2377–98.
- 673 92. Ramsey RR, Plevinsky JM, Kollin SR, Gibler RC, Guilbert TW, Hommel KA. Systematic
674 Review of Digital Interventions for Pediatric Asthma Management. *J Allergy Clin Immunol*
675 *Pract*. 2020 Apr;8(4):1284–93.
- 676 93. Guendelman S, Meade K, Benson M, Chen YQ, Samuels S. Improving asthma outcomes
677 and self-management behaviors of inner-city children: a randomized trial of the Health
678 Buddy interactive device and an asthma diary. *Arch Pediatr Adolesc Med*. 2002
679 Feb;156(2):114–20.
- 680 94. Jan R-L, Wang J-Y, Huang M-C, Tseng S-M, Su H-J, Liu L-F. An internet-based interactive
681 telemonitoring system for improving childhood asthma outcomes in Taiwan. *Telemed J E-*
682 *Health Off J Am Telemed Assoc*. 2007 Jun;13(3):257–68.
- 683 95. Mosnaim GS, Cohen MS, Rhoads CH, Rittner SS, Powell LH. Use of MP3 players to
684 increase asthma knowledge in inner-city African-American adolescents. *Int J Behav Med*.
685 2008;15(4):341–6.
- 686 96. Williams LK, Pladevall M, Xi H, Peterson EL, Joseph C, Lafata JE, et al. Relationship
687 between adherence to inhaled corticosteroids and poor outcomes among adults with
688 asthma. *J Allergy Clin Immunol*. 2004 Dec;114(6):1288–93.

97. Williams LK, Peterson EL, Wells K, Ahmedani BK, Kumar R, Burchard EG, et al. Quantifying the proportion of severe asthma exacerbations attributable to inhaled corticosteroid nonadherence. *J Allergy Clin Immunol*. 2011 Dec;128(6):1185-1191.e2.
98. US Department of Health and Human Services, Office of Minority Health. Asthma and African Americans - The Office of Minority Health [Internet]. [cited 2021 Jul 2]. Available from: <https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=15>
99. Ramsey RR, Holbein C. Adherence Assessment and Intervention during Consultations in Medical Settings. In: *Clinician Handbook of Pediatric Psychological Consultation in Medical Settings*. New York, NY: Springer Publishing Company; 2020.
100. Riley IL, Murphy B, Razouki Z, Krishnan JA, Apter A, Okelo S, et al. A Systematic Review of Patient- and Family-Level Inhaled Corticosteroid Adherence Interventions in Black/African Americans. *J Allergy Clin Immunol Pract*. 2019 Apr;7(4):1184-1193.e3.
101. Apter AJ, Wan F, Reisine S, Bogen DK, Rand C, Bender B, et al. Feasibility, acceptability, and preliminary effectiveness of patient advocates for improving adult asthma outcomes. *J Asthma Off J Assoc Care Asthma*. 2013 Oct;50(8):850–60.
102. Halterman JS, Fagnano M, Tajon RS, Tremblay P, Wang H, Butz A, et al. Effect of the School-Based Telemedicine Enhanced Asthma Management (SB-TEAM) Program on Asthma Morbidity: A Randomized Clinical Trial. *JAMA Pediatr*. 2018 Mar 5;172(3):e174938.
103. Lin NY, Ramsey RR, Miller JL, McDowell KM, Zhang N, Hommel K, et al. Telehealth delivery of adherence and medication management system improves outcomes in inner-city children with asthma. *Pediatr Pulmonol*. 2020;55(4):858–65.
104. Barr RG, Somers SC, Speizer FE, Camargo CA Jr. Patient Factors and Medication Guideline Adherence Among Older Women With Asthma. *Arch Intern Med*. 2002 Aug 12;162(15):1761–8.
105. Bass PF, Wilson JF, Griffith CH, Barnett DR. Residents' ability to identify patients with poor literacy skills. *Acad Med J Assoc Am Med Coll*. 2002 Oct;77(10):1039–41.

Table 1. Factors impacting adherence.

Medication related factors
Delayed effects of asthma medications
Cost
Complex treatment plans
Adverse effects of medications
Patient related factors
Attitude towards treatment plans
Psychological dysfunction
Patient motivation
Family environment and belief in caregiver
Stigma
Underestimation of severity of disease
Patient-clinician relationship
Perceived adequacy of communication with provider
Difficulty in scheduling
Perceived clinician disinterest
Time constraints

References: 20, 21, 22

Table 2. Groups most at risk for nonadherence.

Patients with severe asthma
Advanced age
Adolescents
Lower socioeconomic status
Current smoking
Earlier onset of asthma
Patients at risk for low health literacy
Elderly
Individuals with limited education
Ethnic minorities
Non-native English speakers
Individuals insured by Medicaid

References: ^{25, 104}

Table 3. Methods of assessment of nonadherence.

Patient self report	
<i>Pro:</i> • Allows for collection of information about patient beliefs, attitudes, and experiences over time • Less expensive	<i>Con:</i> • Variable validity, may overestimate adherence • Limited by patient's memory
Medical chart review	
<i>Pro:</i> • Provides information about adherence concerns • Highlights barriers to adherence • Provides biochemical measurements • Provides pharmacy refill data	<i>Con:</i> • Concerns of nonadherence are not systematically charted • Less objective information about patient's adherence patterns
Pharmacy/refill prescription refill data	
<i>Pro:</i> • Objective data	<i>Con:</i> • Cannot assess daily pattern of medication use
Electronic medication measurement	
<i>Pro:</i> • Assess long term patterns of adherence with detailed information	<i>Con:</i> • Does not confirm medication was ingested • More costly, less applicable for large scale clinical use
Biochemical measurements	
<i>Pro:</i> • Objective data	<i>Con:</i> • Detection may depend on dose of medication, may need additional dose-ranging pharmacokinetic studies in lower doses of medication • No clear cut-off for "good" adherence
FeNO measurement and suppression	
<i>Pro:</i> • Objective data	<i>Con:</i> • No single cut-off for "good" adherence

References: 4,56,57, 58, 59, 60, 61

Table 4. Recommended interventions in difficult-to-control asthma.

Adherence	Evaluative comments
Assess adherence through discussion and chart review	Necessary components of clinical practice to ensure adherence to medications in adult and pediatric patients
Improve access to medications, self-report or electronic follow up, refill feedback, and peak flow prediction	
Utilize shared decision-making	
Utilize the objective measures of adherence, such as pharmacy refill records, electronic monitoring, written/digital tracking, or FeNO suppression	These objective measures act as both an assessment and an intervention when self-monitoring and feedback are provided
Employ or refer for behavioral interventions	Benefits include improvement in symptoms, health outcomes, and adherence
Consider use of digital platforms to enhance adherence	- Benefits adults and children - Allows for self-monitoring, feedback, asthma education
Ensure culturally sensitive interventions	Important given higher prevalence of asthma in minority groups
Provide patient navigators and other forms of assistance	Benefits adults with moderate to severe asthma in low income urban neighborhoods
Refer to school-based asthma programs	Benefits pediatric patients, specifically from low income urban areas
Health literacy	
Focus on use of universal health literacy precautions while communicating with patients	Recommended by experts in all patient communication
Provide literacy-appropriate asthma action plan	Ensure plan understood by patient
Consider culturally sensitive interventions	Use professional interpreters in person or via telephone
Provide patient navigators and other forms of assistance	Ensures accurate two-way communication
Inhaler technique	
Assess inhaler technique through effective communication	Key components for each patient visit to ensure correct inhaler technique
Demonstrate correct inhaler use	
Review at each visit	

References: 49,51,56,57,58,72,78,79, 85, 86, 87, 88, 89, 99,100, 101, 102, 103