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Medication Adherence in Children with Asthma

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Abstract: Asthma is the most common chronic disease in childhood. If untreated, asthma can lead to debilitating daily symptoms which affect quality of life, but more importantly can lead to fatal asthma attacks which unfortunately still occur globally. The most effective treatment strategy for controlling asthma is for the patient to follow a personalised asthma action plan (PAAP) which will invariably include regular use of an inhaled corticosteroid. To examine medication adherence in children with asthma, we collated recent evidence from systematic reviews in this area to address the following 5 key questions; What is adherence? Is there evidence that children are not adhering to preventer medication? Why is adherence poor and what are the barriers to adherence? Does good adherence improve outcomes in asthma? And lastly, how can treatment adherence be improved?

Keywords: asthma, adherence, inhaler, inhaled corticosteroid, children

Background on Children's Asthma

Asthma remains the most common chronic disease in childhood.¹ Most clinical guidelines refer to children with asthma in the following age categories; 2-5 years (pre-school), 5-12 years, 12-18 (adolescents; usually regarded as adults for management).

The pathophysiology of asthma involves chronic inflammation of the small and medium-sized airways (bronchi). The symptoms of asthma; wheeze, dry cough and shortness of breath, are the result of bronchoconstriction of airway smooth muscle, airway wall inflammation and mucus plugging in the bronchi which leads to airflow obstruction.

The hallmark clinical feature of small/medium airway obstruction is expiratory wheeze due to turbulent flow passing through a narrowed airway. The objective marker of this is only available for children who can perform forced spirometry (typically not until at least 5 years old). For those old enough and able to perform spirometry, one important aspect of the diagnosis of asthma is the presence of bronchial lability, represented by bronchodilator reversibility. That is, the obstructive pattern seen when performing forced spirometry is reversed following the administration of a bronchodilating agent (usually a short acting beta agonist such as salbutamol).

Measuring fractional exhaled nitric oxide (FeNO) can support an asthma diagnosis as an elevated FeNO (>20-25 ppb) is associated with increased airways eosinophilic inflammation.² Other tests which can indicate asthma as the cause of recurrent wheezing and coughing are an elevated blood eosinophilia, elevated levels of Immunoglobulin E (IgE) or positive skin prick tests to aeroallergens, all of which indicate an allergy driven response likely underpinning airway inflammation.³

In pre-school children who cannot perform the above lung function tests, the diagnosis is confirmed after a positive trial of treatment with inhaled corticosteroids. For a trial of treatment to be effective as a diagnostic test it is important that the inhaled corticosteroid has been taken and correctly delivered to the child's airways. A clear cut response is required which may be a reduction in the day-to-day symptoms or reduction in acute wheezing episodes.

If untreated, asthma can lead to debilitating daily symptoms which affect quality of life in terms of exercise tolerance and breathing difficulty, but more importantly can lead to fatal asthma attacks which unfortunately still occur globally.⁴ The aim for the treatment of asthma is to: a] reduce daily interval symptoms and b] reduce the risk of future asthma attacks.

Types of Therapy for Asthma in Children

Personalised Asthma Action Plans

Modern asthma guidelines recommend that all patients have a personalised asthma action plan (PAAP).^{5,6} Adherence to the PAAP is an essential component of asthma self-management. Patients (and in younger children, their care provider) must fully understand each aspect of the plan and be capable of implementing the treatment prescribed when the patient is well (maintenance therapy) and when the patient needs to escalate their treatment (reliever therapy).

Pharmacotherapies in Childhood Asthma

Reliever therapies (short acting beta agonists [SABAs] such as salbutamol) can easily become relied upon to relieve symptoms. Overuse of reliever therapy indicates poor asthma control and is often due to poor adherence to the patient's PAAP i.e not taking their anti-inflammatory preventer.

The most effective maintenance therapies reduce the inflammation in the airways by using inhaled (topical) corticosteroids. These work by suppressing airway inflammation and thereby reducing airway hyper-responsiveness. Inhaled long-acting beta-agonists (LABAs) added in combination with inhaled corticosteroids are now frequently used as preventer therapy and this combination is effective in controlling more severe asthma.⁷

Treatment regimens for asthma in children vary in terms of dose and frequency and are dependent on the severity of the patient's asthma. Those with more severe, less controlled disease often need higher and more frequent dosing. However, all treatments require at least daily inhalation to be optimally effective.

While the suppression of mucosal inflammation occurs within six hours, reversal of airway hyper-responsiveness takes longer (months) to reach maximal therapeutic effect. Therefore, inhaled corticosteroids must be taken regularly in the long to gain the optimal benefit.⁷

If symptom control is not achieved even with high dose inhaled corticosteroids plus a LABA then a long acting muscarinic antagonist (LAMA) such as tiotropium bromide can be added.⁶

Non-inhaled therapies for asthma are also available such as leukotriene receptor antagonists, which are commonly used in the pre-school age group and are proven to be effective (though not as effective as inhaled corticosteroids).⁸ They benefit from being easier to deliver but problems still occur with remembering to take them on a regular basis. Other non-inhaled medications such as theophylline and oral salbutamol are no longer recommended for use in controlling asthma in international guidelines,³ and so will not be considered here.

Many patients with on-going severe problem asthma improve their asthma control when the essentials of asthma care are in place (full understanding and action of PAAP, correct adherence to preventer therapy, correct inhaler technique along with trigger avoidance) and a period of optimised medication has been delivered.^{9,10} Patients failing to respond to a period of optimised therapy have Severe Treatment Resistant Asthma (STRA). For such patients, new biologic agents (namely, monoclonal antibodies to various inflammatory pathways such as IgE and Interleukins including anti-iL5 and Il4/IL13) have proven efficacy in reducing asthma exacerbation rates. As these therapies are administered by intramuscular injections, in the most part, administered as a day procedure within a hospital setting, adherence is less of an issue. The use of these biologics has enabled clinicians to reduce the exposure STRA patients have to either chronic oral steroid usage or frequent bursts of rescue steroids and thus reduce potential side-effects.

As inhaled corticosteroids (ICSs) are the most effective and widely used and thus, cornerstone treatment for asthma in children, this paper will focus on adherence to this therapy.

Single Maintenance and Reliever Therapy

The availability of a combination of a rapid long acting bronchodilator (formoterol) with an inhaled corticosteroid results in a single inhaler that can be used as Anti-Inflammatory Reliever (AIR) therapy within a Single Maintenance and Reliever Therapy regime (SMART). The recent GINA 2023 asthma guidelines now suggest that patients (older than 6 years of age), with even mild asthma, should use an ICS/formoterol inhaler as required (for relief) while those with moderate/severe asthma should use an ICS/formoterol inhaler as daily maintenance as well as when required. This strategy can be particularly effective in a patient who struggles to adhere to their daily maintenance inhaler regime as each time they take their ICS/formoterol inhaler for relief of symptoms, they are also gaining the long-term benefit of the corticosteroid. This is in comparison to the patient who overuses a SABA alone and will therefore not get the anti-inflammatory benefits of a corticosteroid.

Inhaler Devices Used to Deliver Medication

Corticosteroid containing medications are delivered in the main by two types of inhaler device in children (each with numerous variations):

- 1. Metered-dosed inhaler (MDI)
- 2. Dry powder inhaler (DPI)

The individual merits of each are beyond the scope of this paper but suffice to say that each different device from a different manufacturer, has its own specific technique which needs to be followed to ensure adequate delivery of medication to the lungs.¹¹ Steroids can also be inhaled via a nebuliser device but this is not used in routine practice for childhood asthma.

Key Questions Regarding Treatment Adherence in Children's Asthma

To examine medication adherence in children with asthma, we performed a rapid systematic review of the literature. We collated recent evidence from systematic reviews in this area to address the following key questions. Our search strategy was inclusive of systematic reviews, published since 2013 which examined adherence in children's asthma. Using Medline, our search terms included: asthma AND children/paediatric AND adherence OR inhaler use OR patient outcomes AND systematic review.

What is Adherence?

In the case of inhalers, adherence has three aspects; 1. Use of inhaler at the frequency prescribed, 2. Use of inhaler with correct technique (technique must be adequate to deliver a sufficient dose of medication to its site of action) and 3. Prescriber has adhered to appropriate asthma management guidelines.

With regards to use of an inhaler at the frequency prescribed, by convention, 80–120% is considered good adherence. In younger children (and certainly all children under 5) the responsibility for administering the inhalers is with the adult carer. As a child becomes older, they transition into more responsibility for taking their own medication.

Is There Evidence That Children are Not Adhering to Preventer Medication?

A recent study in the UK of primary care children (aged 5-16 years) with asthma addresses this question. The authors report a mean adherence of 36% to their inhaled corticosteroid.¹² In this study, adherence to treatment was calculated as the percentage of doses of medication issued to the doses prescribed in the treatment plan.

While this number is undeniably low, it is likely to still be an overestimate as a number of the patients are unlikely to be fully compliant with the prescribed regime even though the prescription was collected. Furthermore, considerable numbers of patients who use their inhaler are likely to have sub-optimal inhaler technique, and are not inhaling the required amount of drug to be effective.¹³

Why is Adherence Poor and What are the Barriers to Adherence?

Challenges in Developing a Routine

Within the normal, everyday, chaotic household, developing a routine of medication administration is challenging especially when school children are involved.

Furthermore, patient's often become reliant on, and overuse, their reliever inhaler as this provides immediate relief of symptoms which they understandably equate to better control of their disease. This is at the expense of developing a routine of using their inhaled corticosteroid on a regular basis.

Developing a routine is made more difficult when complicated inhaler regimes are prescribed. Some children are prescribed multiple inhaler types with twice daily dosing which can become cumbersome and difficult to fit into daily life.

In paediatrics, it is mostly the parents who take responsibility for making sure that the medication is administered and therefore it is the parent who needs to develop the routine. As the child enters adolescence there is a shift in responsibility and an often-difficult transitional period when the teenage patient begins to take responsibility for administering their own medication.

Patients' Health Beliefs

In the early years, a child's asthma management is reliant on their parents/care provider. Therefore, the parents' perception of the seriousness of the illness and appreciation of the importance of adherence (frequency of use and inhaler technique) can often influence medicine use by their child.¹⁴ Parents may also have concerns regarding the side effect profile of the prescribed medications, steroids in particular¹⁵ and may not initiate any therapy even after it has been prescribed and dispensed. As the child transitions to adolescence, they may not wish to have the stigma of an asthma diagnosis or the inconvenience of having to carry an inhaler on their person.¹⁴ These challenges need to be addressed during the prescribing and dispensing of medications for children with asthma.

Challenges with Inhaler Technique

A systematic review identified inhaler technique in children as often being poor and highlighted the importance of the entire health care team in educating patients and their care providers in the proper use of inhalation devices.¹³

Both MDI and DPI devices require the patient to follow a series of sometimes challenging steps (including the correct use of a spacer device with an MDI), in order to ensure adequate delivery of the drug to the lungs. This includes, for example in the case of a DPI, priming the device correctly, emptying the air from the lungs, taking a deep breath in, with correct positioning of the device and airway in doing so and an adequate breath hold. It is known that in practice, patients are not often trained sufficiently on these steps at the time of diagnosis and the correct administration method is subsequently not adhered to.¹⁶

There are many different inhaler devices available which provide the same medication. While they share many of the same attributes, there are often subtle but crucial differences in how they are used effectively. For example, an MDI requires a slow deep inhalation whereas a DPI requires a quick deep breath intake. This leads to another problem which makes adherence difficult ie patients often have their inhaler prescription changed when their control is not optimal, and this will affect their technique in using the new device.

Does Good Adherence Improve Outcomes in Asthma?

Many systematic reviews and meta-analyses have been performed to address this question. Some authors report that asthma exacerbations (requiring oral corticosteroids) are reduced by good adherence to inhaled corticosteroids.¹⁷ This has not been translated into other clinical outcomes such as asthma control, frequency of unscheduled healthcare facility visits and quality of life measures in all studies.¹⁸ This most likely reflects inadequate study design (for example inhaler use and inhaler technique not verified) and the heterogeneity in "asthma" as a diagnosis along with inconsistent outcome measures to determine clinical effectiveness.

Link Between Adherence and Objective Measures in Asthma Control

With regard to lung function, improved adherence to inhaled corticosteroids in children correlates with improved forced expiratory volume in 1 second (FEV1),¹⁹ a key marker in asthma.²⁰ FeNO levels in children with asthma, have an inverse association with adherence to ICS.²¹ FeNO is a good predictor of asthma exacerbations. Those with lower FeNO values have less exacerbations requiring fewer courses of "rescue" oral corticosteroids.²²

An interesting study of children's asthma from China investigated the effect on objective asthma measurements (FEV1, FEV1/FVC ratio, IgE and eosinophil count) of non-adherent compared with adherent patients. Followed up over 3 years, the non-adherent children showed a significant deterioration in each of these markers compared with the adherent children.²³ In this study, adherence was graded using parents self reporting and prescription pick up rates.

A randomised control trial (RCT) of over 200 children with asthma compared the adherence of those with an audiovisual reminder and those without. Adherence (in terms of frequency of medication use only, ie not taking account of inhaler technique) was recorded using an electronic monitor. The findings were unsurprising, yet interesting. The control group had 36% adherence (remarkably similar to the primary care group cited above¹²). The intervention group (with reminders), the adherence was 80%. More than half of all patients had "treatment intermissions"; that is periods of consecutively missed doses²⁴. This study also reported a significant improvement in the asthma morbidity score of those children in the intervention group (who had proven improved adherence). This study did not measure inhaler technique and so there may have been even better clinical improvement in those patients who increased the rate at which they used their inhaler device with proper technique.

Link Between Inhaler Technique and Outcomes

Studies have shown that improving inhaler technique leads to improved clinical outcomes (lung function and frequency of attacks) in children with asthma.^{25,26}

However, there is a dearth of studies measuring inhaler technique as a component of adherence and studies often rely on crude adherence markers such as prescription pick up rates, patient/parent reported adherence and electronic monitors, none of which take account of incorrect inhaler technique.

It is known that children often have incorrect inhaler technique and this results in a failure to deliver an adequate dose of inhaled corticosteroid.^{16,27} At present, the only accurate way of assessing technique is by directly observed therapy (DOT). This method has often been overlooked in study design of drug efficacy in asthma and measures of adherence.

Impact of Personalised Asthma Action Plans on Outcomes

In a systematic review of risk factors to predict early and late asthma re-admissions in children, there was no mention of long-term therapy or adherence. Rather, prior length of stay, female sex and chronic comorbidities were associated with increased risk of readmission.²⁸ However, on closer review of the papers cited in this review, one large North American study reported in 2012²⁹ does demonstrate a reduction in asthma re-admission when asthma care plans ("action plans") were implemented on discharge. Similarly, a retrospective study of children's asthma in the UK showed that the implementation of a structured asthma care pathway on discharge following an attack, with a focus on patient education and self-management, reduced the rate of attacks over the next 12 months.³⁰

Is Full Adherence Necessary?

The question of whether it really matters if a child misses occasional doses of ICS is an important but difficult one to answer. There have been some studies, in adults, which suggest that in the mild asthma range, a modified, patient led, intermittent course of ICS may be as effective as regular use.³¹ However, without accurate monitoring, it is hard to say whether the patients within the control (regular use) arm of this study were adhering with adequate frequency. Neither do they take into account inhaler technique.

While not advocating reduced compliance with the prescribed treatment regime, a study of children's asthma has shown clinical improvements when patients increase the frequency with which they use their inhaled corticosteroid, even if still below that prescribed.³⁰

Steps need to be taken to ensure that future research adopts the most appropriate outcome measures and consistent methods of measuring adherence (to include not just rate of inhaler use but also quality of inhaler technique) to accurately address this important question.¹⁷

How Can Treatment Adherence Be Improved?

A narrative systematic review was recently performed to identify which elements, within an intervention to improve adherence to ICS in children with asthma, have been successful. This review indicated that targeting patients'/carers' perceptions of their illness and treatments is important and effective. So too are more practical elements such as patient feedback, by way of rewards and reminders. Patient education on how to identify asthma triggers and instruction on how to use their inhaler were also considered effective along with means of monitoring adherence.³²

A study of the facilitators and barriers to improving asthma self-management in children identified practical barriers such as medication cost, misunderstanding of instructions, and forgetfulness (24).

Address Patient / Carers' Negative Perceptions

Parents may feel that their child's treatment is unnecessary or may be in denial about their child's asthma diagnosis. In the case of adolescent or teenage asthma patients, as they transition to adulthood and begin to take more responsibility for their asthma self-management, they also may be in denial about their illness.³³

Fears remain around the safety of long-term asthma medications. Children and their parents have identified a want to avoid "toxic" medications and a fear of tolerance and addiction to them.¹⁵ Once the child has a life-threatening asthma attack, however, this fear transiently subsides.

It is therefore important to engage in effective communication with parents and older children to facilitate a change in perception and subsequent behaviour towards managing asthma.

Motivational interviewing (MI) is a method of communication which aims to facilitate a natural process of behavioural change within the patient. MI is effective at improving medication adherence. However, its effect is more sustained when paired with other interventions and support.³⁴ In practice, however, these interventions are difficult to provide in a busy clinic or pharmacy due to a lack of time, resources and trained staff.

Shared decision-making, which involves the patient and clinician mutually sharing information regarding the patient's preferences to build a consensus on the favoured treatment plan, has also been shown to improve adherence to medications in children with asthma.³⁵ One example of this approach in paediatric practice would be to consider using the SMART regime (previously described).

Improving Self Management of Asthma

Inhaler Technique Training

While there are a variety of methods to teach inhaler technique to children, they should always involve some form of physical demonstrations to be effective. A recent scoping review of the methods used to train children how to use their inhaler device separated them into two distinct approaches: 1. brief intervention, whereby the instructor spends a limited amount of time simply demonstrating the technique to the patient without taking time to receive patient feedback and 2. "teach-back", whereby the patient must demonstrate the correct technique back to the instructor before being deemed competent at using the device (28). In a study of child asthma patients, the "teach-back" method was shown to significantly improve inhaler technique compared with brief intervention.³⁶

While interventions to improve technique have been shown to be successful, they have not yet correlated directly with consistent and sustained improvements in important clinical benefits.¹⁸ However, this is likely due to a deterioration in technique over time unless periodic reinstruction and monitoring takes place.³⁷

A hospital in the USA, used "teach-back" method to train adult patients in using their inhaler prior to discharge home following an acute admission. At 30 days post discharge there was a significantly reduced number of re-attendances in the group that received the "extra" teach-back training compared to the usual brief intervention. At 90 days, the re-attendance rate unfortunately rose but there was still a preserved reduction in inhaler misuse in those patients who received the teach-back training compared with brief intervention, suggesting a potentially longer lasting effect.³⁸

Personalised Asthma Action Plans

The implementation of structured asthma care plans (commonly referred to as personalised asthma action plans [PAAPs] in the UK)⁵ which include the education of patients (and carers) on how to self-manage their asthma, incorporating a focus on adherence to treatment, have been shown to reduce the risk of hospital re-admission following an acute exacerbation in children with asthma.^{30,39} In order for the benefits of the PAAP to be fulfilled, a teach-back approach must be used to ensure complete and sustained understanding by the patient/carer.³⁰

Lay-led or peer support to improve asthma self-management in children and adolescents is an interesting concept which may prove to be successful. As yet, the limited studies in this area have shown insufficient evidence to recommend their routine use.⁴⁰

Rationalising Dosing Schedule

Adherence can be improved by simplifying the regime from twice daily to once daily ICS in children with asthma. One study has shown that this reduction in steroid load did not negatively impact the patient time to first exacerbation. However, other important clinical outcomes were not measured.⁴¹

Some inhalers combine fluticasone furoate, a highly potent steroid with the ultra-long acting beta agonist vilanterol, and these are prescribed once daily. An adult study has shown use of this inhaler to be more effective than the equivalent steroid load given via a twice daily, divided dose regime and one of the factors in this was felt to be improved medication use adherence.⁴² In a small, retrospective study of children with asthma (>12 years old) use of fluticasone furoate/ vilanterol inhaler once daily reduced asthma attacks over a 2-year period.⁴³

Monitoring Adherence

Before considering increasing the dose of medication or adding more medications (eg expensive biologics) to an already complicated asthma plan, it is vital to assess adherence. A range of approaches are available to get information on adherence to inhaler use in children, as outlined below.

Patient / Carer Questioning

The crudest measurement of adherence to the prescribed frequency of use of an inhaler is simply asking the patient/the parent how often they use the prescribed inhalers. Unsurprisingly, patients self-reporting of adherence is often an overestimate⁴⁴ and therefore this cannot be relied upon if asthma control is sub-optimal.

Prescribing and Dispensing Data

Prescriber and/or pharmacy held prescription databases can be used in reviewing how often inhalers are being prescribed and/or dispensed. While being another crude measurement, this can often be a good screening tool (ie if the prescription has not been picked up then the patient must not be taking the medication). Of course, the opposite cannot be assumed to be true and if the index of suspicion is high or if the child's asthma control is sub-optimal then more accurate measurements of inhaler use and inhaler technique should be sought.

Electronic Inhaler Monitoring Devices (EIMDs)

Electronic inhaler monitoring devices (EIMDs) can be an effective method of monitoring adherence. EIMDs often involve an attachment to the inhaler which can determine whether the device has been actuated⁴⁵ and, in some cases, can provide feedback on the degree to which the patient has inspired adequately.⁴⁶ EIMDs improve frequency of use of inhalers and are feasible for use in children. However, they do not consistently lead to improvements in clinical outcomes such as reduced asthma exacerbations and improved lung function measures.⁴⁷ This likely reflects a persistent problem with inhaler technique (a vital aspect of treatment adherence).

Unfortunately, EIMDs also have several limitations. They are not available for every type of inhaler, they are expensive, and they generally do not measure all of the critical steps in adequate inhaler technique.

There is therefore a need for a better solution that can be used to monitor (and improve) adherence to the prescribed frequency of inhaler use and to inhaler technique simultaneously in a reliable, convenient, accessible, and cost-effective way.

Directly Observed Therapy (DOT)

By observing a patient taking their medication, DOT combines a unique assessment of adherence and of inhaler technique for monitoring and therapy improvement purposes. DOT has shown promising results with regard to improving short-term adherence in children with asthma⁴⁸ and has been shown to be an effective means of reducing asthma exacerbations.⁴⁹ The obvious drawback to DOT is that it is a resource heavy approach, relying on healthcare professionals to provide a face to face, one to one, service to each patient.

To overcome this, video directly observed therapy (vDOT) has been developed. vDOT involves a patient taking videos of themselves using their inhaler on their mobile phone and submitting it to a secure repository to be reviewed by a healthcare professional. The videos can also be taken and submitted by caregivers, for example, in the case of a young child. This allows a trained clinician to review the videos and provide personalised feedback (via text message or phonecall), for example, to improve inhaler technique and encourage use of inhaler at the appropriate frequency.

A study of children with difficult to treat asthma at a UK children's hospital which used vDOT, showed that many children who demonstrated correct inhaler technique at the clinic had major errors when at home.⁵⁰ The use of vDOT in this population was able to correct the technique and accurately monitor frequency of inhaler use in these children and in

doing so improved their clinical outcomes and avoided the incorrect diagnosis of severe treatment-resistant asthma (STRA) which may have resulted in the prescribing of expensive biologic therapies. In fact, in the 48 months before the full implementation of vDOT in the study site facility, some 17 children with asthma were escalated to biologicals, while over the 48 months with vDOT implemented that number had dropped to two patients.¹⁰

vDOT has been reported as fun and enjoyable to use for the families⁵⁰ and aids with the development of good routines and independence.⁵¹

Due to the fact that a trained healthcare professional must review individual patient videos, vDOT is often reserved for those patients with difficult to treat asthma. However, all patients prescribed an inhaler could potentially benefit from the personalised feedback vDOT provides.

At present, a study is ongoing at the Royal Belfast Hospital for Sick Children, in newly diagnosed children with asthma. Inhaler therapy is being initiated with the assistance of daily vDOT compared with standard treatment (which involves 2–3 nurse led, in-clinic reviews). This study is designed to assess the feasibility of using vDOT in a more general population and will also assess its efficacy.⁵²

Adherence to Prescribing Guidelines

When considering the topic of adherence in children with asthma, it is also important to consider whether physicians are adhering to national guidelines on best prescribing practices for children's asthma. While this is a difficult area to accurately study, one large UK investigation of primary care prescribing patterns (including over 40,000 children) showed a small proportion of patients having changes made to their steroid dose over the course of one year. The authors considered that this low number of prescription alterations over the course of a year most likely reflects a lack of adherence to published guidelines, rather than evidence that this large population of children were mostly well controlled and not in need of changes to their asthma plan.⁵³

In a systematic review of physician adherence to adult asthma guidelines, it was shown that specialist doctors (secondary care) adhered significantly better than their primary care colleagues for both chronic asthma and acute attacks.⁵⁴

Another study, in the USA, in 22 different primary care practices (including children and adult patients) showed that adherence by physicians to asthma guidelines was poor and the authors concluded that there were many opportunities for improvement.⁵⁵

Summary

Asthma is still a big problem in children. Childhood asthma is common, has an adverse impact on quality of life and can kill. Pharmacotherapy involving inhaled corticosteroids is an effective treatment when used properly.

Treatment adherence in children's asthma involves three measures: frequency of inhaler use, quality of inhaler technique and prescriber's compliance with national guidelines. Adherence to these measures remains poor and is the likely cause of ongoing asthma problems in many children.

Adherence in childhood asthma involves buy-in from the patients' parents/care providers and the patient themselves. This can be particularly challenging as patients transition through adolescence.

There are several means by which adherence can be improved. Important approaches include increasing health literacy, modifying patients' (and carer) belief systems (as appropriate), improved prescribing practices and repeated inhaler instruction based on regular adherence monitoring.

All children with asthma should be enrolled in an asthma management training program where both inhaler technique and PAAP are reviewed.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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References

- 1. Vos T, Flaxman AD, Naghavi M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380(9859):2163.
- 2. Warke TJ, Fitch PS, Brown V, et al. Exhaled nitric oxide correlates with airway eosinophils in childhood asthma. *Thorax*. 2002;57(5):383–387. doi:10.1136/thorax.57.5.383
- 3. Reddel HK, Bacharier LB, Bateman ED, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. *Am J Respir Crit Care Med.* 2022;205(1):17–35. doi:10.1164/rccm.202109-2205PP
- 4. Zhang D, Zheng J. The burden of childhood asthma by age group, 1990–2019: a systematic analysis of global burden of disease 2019 data. *Front Pediatrics*. 2022;10:113.
- 5. Society BT. Scottish intercollegiate guidelines network. Br Guideline Management Asthma. 2016;58.
- Asthma. GIf. Global strategy for asthma management and prevention, 2023; 2023. Available from: www.ginasthma.org. Accessed February 15, 2024.
 Barnes PJ. Inhaled Corticosteroids. *Pharmaceuticals*. 2010;3(3):514–540. doi:10.3390/ph3030514
- 8. Ducharme FM, Hicks GC. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. *Cochrane Database Syst Rev.* 2002;3:Cd002314. doi:10.1002/14651858.Cd002314
- 9. O'Donoghue DB, Shields MD. A Structured Multidisciplinary Approach to Managing Difficult-to-Treat Asthma in Children. Severe Asthma Children Adolescents. 2020;97–112.
- 10. Shields MD, McElnay J. Mobile video directly observed therapy can be used to improve at-home inhaler technique in children with asthma. *ERJ Open Res.* 2021;7(4):00463–2021. doi:10.1183/23120541.00463-2021
- 11. Takaku Y, Kurashima K, Ohta C, et al. How many instructions are required to correct inhalation errors in patients with asthma and chronic obstructive pulmonary disease? *Respir Med*. 2017;123:110–115. doi:10.1016/j.rmed.2016.12.012
- 12. Paracha R, Lo DKH, Montgomery U, Ryan L, Varakantam V, Gaillard EA. Asthma medication adherence and exacerbations and lung function in children managed in Leicester primary care. *Npj Primary Care Respiratory Med.* 2023;33(1):12. doi:10.1038/s41533-022-00323-6
- 13. Gillette C, Rockich-Winston N, Kuhn JA, Flesher S, Shepherd M. Inhaler technique in children with asthma: a systematic review. *Acad Pediatrics*. 2016;16(7):605–615. doi:10.1016/j.acap.2016.04.006
- 14. Rehman N, Morais-Almeida M, Wu AC. Asthma across childhood: improving adherence to asthma management from early childhood to adolescence. *j Allergy Clin Immunol Practice*. 2020;8(6):1802–1807. e1.
- 15. Miles C, Arden-Close E, Thomas M, et al. Barriers and facilitators of effective self-management in asthma: systematic review and thematic synthesis of patient and healthcare professional views. *Npj Primary Care Respir Med.* 2017;27(1):57. doi:10.1038/s41533-017-0056-4
- 16. de Groot EP, Kreggemeijer WJ, Brand PL. Getting the basics right resolves most cases of uncontrolled and problematic asthma. *Acta Paediatrica*. 2015;104(9):916–921. doi:10.1111/apa.13059
- 17. Engelkes M, Janssens HM, de Jongste JC, Sturkenboom MC, Verhamme KM. Medication adherence and the risk of severe asthma exacerbations: a systematic review. *Eur Respir J.* 2015;45(2):396–407. doi:10.1183/09031936.00075614
- Normansell R, Kew KM, Stovold E. Interventions to improve adherence to inhaled steroids for asthma. *Cochrane Database Syst Rev.* 2017;2017(4). doi:10.1002/14651858.CD012226.pub2
- 19. Tan DJ, Bui DS, Dai X, et al. Does the use of inhaled corticosteroids in asthma benefit lung function in the long-term? A systematic review and meta-analysis. *Eur Respir Rev.* 2021;30(159):200185. doi:10.1183/16000617.0185-2020
- 20. Fielding S, Pijnenburg M, de Jongste JC, et al. Change in FEV(1) and Feno Measurements as Predictors of Future Asthma Outcomes in Children. Chest. 2019;155(2):331–341. doi:10.1016/j.chest.2018.10.009
- 21. Wang Z, Pianosi P, Keogh K, et al. The clinical utility of fractional exhaled nitric oxide (FeNO) in asthma management. Int J Med. 2017.
- 22. Petsky HL, Kew KM, Chang AB. Exhaled nitric oxide levels to guide treatment for children with asthma. Cochrane Database Syst Rev. 2016.
- Zheng S, Yu Q, Zeng X, Sun W, Sun Y, Li M. The influence of inhaled corticosteroid discontinuation in children with well-controlled asthma. *Medicine*. 2017;96(35):e7848. doi:10.1097/md.00000000007848
- 24. Tibble H, Chan A, Mitchell EA, et al. A data-driven typology of asthma medication adherence using cluster analysis. *Sci Rep.* 2020;10(1):14999. doi:10.1038/s41598-020-72060-0
- 25. Chan DS, Callahan CW, Sheets SJ, Moreno CN, Malone FJ. An Internet-based store-and-forward video home telehealth system for improving asthma outcomes in children. *Am J Health Syst Pharm.* 2003;60(19):1976–1981. doi:10.1093/ajhp/60.19.1976
- 26. Minai BA, Martin JE, Cohn RC. Results of a physician and respiratory therapist collaborative effort to improve long-term metered-dose inhaler technique in a pediatric asthma clinic. *Respir Care*. 2004;49(6):600–605.
- 27. Giraud V, Roche N. Misuse of corticosteroid metered-dose inhaler is associated with decreased asthma stability. *Eur Respir J.* 2002;19(2):246–251. doi:10.1183/09031936.02.00218402
- 28. Hogan AH, Carroll CL, Iverson MG, et al. Risk factors for pediatric asthma readmissions: a systematic review. *J Pediatr.* 2021;236:219–228. e11. doi:10.1016/j.jpeds.2021.05.015
- 29. Fassl BA, Nkoy FL, Stone BL, et al. The Joint Commission Children's Asthma Care Quality Measures and Asthma Readmissions. *Pediatrics*. 2012;130(3):482–491. doi:10.1542/peds.2011-3318

- 30. Kennedy L, Gallagher G, Maxwell B, et al. Implementation of a Children's Safe Asthma Discharge Care Pathway Reduces the Risk of Future Asthma Attacks in Children-A Retrospective Quality Improvement Report. *Front Pediatr.* 2022;10:865476. doi:10.3389/fped.2022.865476
- 31. Boushey HA, Sorkness CA, King TS, et al. Daily versus as-needed corticosteroids for mild persistent asthma. N Engl J Med. 2005;352 (15):1519–1528. doi:10.1056/NEJMoa042552
- 32. Pearce CJ, Chan AH, Jackson T, et al. Features of successful interventions to improve adherence to inhaled corticosteroids in children with asthma: a narrative systematic review. *Pediatric Pulmonol*. 2022;57(4):822–847. doi:10.1002/ppul.25838
- 33. Simoni AD, Horne R, Fleming L, Bush A, Griffiths C. What do adolescents with asthma really think about adherence to inhalers? Insights from a qualitative analysis of a UK online forum. *BMJ Open*. 2017;7(6):e015245. doi:10.1136/bmjopen-2016-015245
- 34. Gesinde B, Harry S. The use of motivational interviewing in improving medication adherence for individuals with asthma: a systematic review. Perspectives Public Health. 2018;138(6):329–335. doi:10.1177/1757913918786528
- 35. Kew KM, Malik P, Aniruddhan K, Normansell R. Shared decision-making for people with asthma. *Cochrane Database Syst Rev.* 2017. doi:10.1002/14651858.CD012330.pub2
- 36. Volerman A, Balachandran U, Zhu M, et al. Evaluating inhaler education interventions for hospitalized children with asthma: a randomized controlled trial. *Ann Allergy Asthma Immunol.* 2023;131(2):217–223.e1. doi:10.1016/j.anai.2023.02.023
- 37. Baba R, Nakachi I, Masaki K, et al. Repetitive instructions at short intervals contribute to the improvement of inhalation technique. *Asia Pac Allergy*. 2020;10(2):e19. doi:10.5415/apallergy.2020.10.e19
- 38. Press VG, Arora VM, Trela KC, et al. Effectiveness of Interventions to Teach Metered-Dose and Diskus Inhaler Techniques. A Randomized Trial. Ann Am Thorac Soc. 2016;13(6):816–824. doi:10.1513/AnnalsATS.201509-603OC
- Ardura-Garcia C, Stolbrink M, Zaidi S, Cooper PJ, Blakey JD. Predictors of repeated acute hospital attendance for asthma in children: a systematic review and meta-analysis. *Pediatric Pulmonol.* 2018;53(9):1179–1192. doi:10.1002/ppul.24068
- Kew KM, Carr R, Crossingham I. Lay-led and peer support interventions for adolescents with asthma. *Cochrane Database Syst Rev.* 2017;2017(4). doi:10.1002/14651858.CD012331.pub2
- 41. Drouin O, Smyrnova A, Bétinjané N, Ducharme FM. Adherence to inhaled corticosteroids prescribed once vs twice daily in children with asthma. *Ann Allergy Asthma Immunol.* 2022;128(4):423–431.e3. doi:10.1016/j.anai.2022.01.018
- 42. Shimizu Y, Shiobara T, Arai R, Chibana K, Takemasa A. Real-life effectiveness of fluticasone furoate/vilanterol after switching from fluticasone/ salmeterol or budesonide/formoterol therapy in patients with symptomatic asthma: relvar Ellipta for Real Asthma Control Study (RERACS study). J Thorac Dis. 2020;12(5):1877–1883. doi:10.21037/jtd-19-3913
- 43. Langley R, Thompson A, Westwood J, Urquhart D. P90 Once daily inhaled corticosteroid prescribing in paediatric asthma: a single centre retrospective cohort study. *Thorax*. 2018;73(Suppl 4):A151-A152. doi:10.1136/thorax-2018-212555.248
- 44. Bender B, Wamboldt FS, O'Connor SL, et al. Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. *Ann Allergy Asthma Immunol.* 2000;85(5):416–421. doi:10.1016/s1081-1206(10)62557-4
- 45. Makhecha S, Chan A, Pearce C, Jamalzadeh A, Fleming L. Novel electronic adherence monitoring devices in children with asthma: a mixed-methods study. *BMJ Open Respir Res.* 2020;7(1):e000589. doi:10.1136/bmjresp-2020-000589
- 46. Costello R. INCA. Available from: http://www.incadevice.com. Accessed May 11, 2022.
- 47. Lee JR, Leo S, Liao S, et al. Electronic adherence monitoring devices for children with asthma: a systematic review and meta-analysis of randomised controlled trials. *Int J Nursing Studies*. 2021;122:104037. doi:10.1016/j.ijnurstu.2021.104037
- 48. Halterman JS, Riekert KA, Fagnano M, et al. Effect of the School-Based Asthma Care for Teens (SB-ACT) program on asthma morbidity: a 3-arm randomized controlled trial. J Asthma. 2022;59(3):494–506. doi:10.1080/02770903.2020.1856869
- Pertzborn MC, Prabhakaran S, Hardy A, Baker D, Robinson MA, Hendeles L. Direct observed therapy of inhaled corticosteroids for asthma at school or daycare. *Pediatr Allergy Immunol Pulmonol.* 2018;31(4):226–229. doi:10.1089/ped.2018.0912
- Shields MD, ALQahtani F, Rivey MP, McElnay JC. Mobile direct observation of therapy (MDOT)-A rapid systematic review and pilot study in children with asthma. PLoS One. 2018;13(2):e0190031. doi:10.1371/journal.pone.0190031
- 51. McIntire K, Weis B, Litwin Ye L, Krugman S. Feasibility of video observed therapy to support controller inhaler use among children in West Baltimore. J Asthma. 2021;1–12.
- 52. Ferris K. Optimising Inhaler Technique and Asthma Self-Management in Children and Young People. Royal Belfast Hospital for Sick Children; 2023.
- Gayle A, Tebboth A, Pang M, et al. Real-life prescribing of asthmatic treatments in UK general practice over time using 2014 BTS/SIGN steps. Npj Primary Care Respiratory Med. 2019;29(1):25. doi:10.1038/s41533-019-0137-7
- 54. Mathioudakis AG, Tsilochristou O, Adcock IM, et al. ERS/EAACI statement on adherence to international adult asthma guidelines. *Eur Respir Rev.* 2021;30(161):210132. doi:10.1183/16000617.0132-2021
- 55. Yawn BP, Rank MA, Cabana MD, Wollan PC, Juhn YJ. Adherence to Asthma Guidelines in Children, Tweens, and Adults in Primary Care Settings: a Practice-Based Network Assessment. *Mayo Clin Proc.* 2016;91(4):411–421. doi:10.1016/j.mayocp.2016.01.010

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