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Adherence to asthma treatment in childhood and adolescence – a narrative literature review

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ABSTRACT

Objectives: We provide a narrative literature review on surveys used to assess the level of medication adherence in children and adolescents with asthma, the attitudes of these patients and their parents toward asthma therapy, and their expectations concerning asthma and available treatment.

Methods: A PubMed search and manual selection of the retrieved papers was conducted to identify studies using surveys or interviews that addressed one of the three topics of interest.

Results: Adherence to asthma medication varies across age groups and with the type of measurement used. Levels of 49–71% were observed in children and adolescents by objective measurements. Subjective measurements overestimate the level of adherence compared to objective measurements. A considerable percentage of parents expressed fear of side effects of inhaled corticosteroids, although the impact of these concerns on adherence is unclear. Many adolescents and parents adapt inhaled corticosteroids use according to the prevalence of asthma symptoms, by reducing or eliminating controller medication in the absence of symptoms. Pediatric asthma patients and their parents tend to overestimate the level of asthma control, either by underestimating asthma severity or by assuming that a better control is not possible. The knowledge of parents and adolescents concerning asthma management is suboptimal; moreover, insufficient knowledge about inhaled corticosteroids was linked to poor adherence.

Conclusion: Medication adherence is crucial for a good control of asthma symptoms. Additional research concerning the triggers of non-adherence is still needed. Educating both the patients and their parents on proper asthma care might improve adherence.

KEYWORDS

Adherence; inhaled corticosteroids; patient attitude; patient expectations; education

Introduction

Asthma is a chronic inflammation of the airways affecting over 300 million people, with prevalence increasing over the last few decades [1]. A worldwide survey conducted in 2002–2003 showed that prevalence of asthma symptoms ranged between 3% (Indonesia) and 38% (Costa Rica) in the 6–7 years age group, and between 3% (Albania) and 27% (Costa Rica) in the 13–14 years age group, with higher incidences in more affluent countries [2]. Another study in over 33,000 children aged 11–15 years from 6 European countries showed large differences in prevalence rates of diagnosed asthma (9–21% in boys, 7–19% in girls) [3].

Asthma prevalence might be better assessed through prevalence of asthma-like symptoms; surveys addressing only diagnosed asthma may underestimate real prevalence. In a survey in 932 Belgian children (mean age: 11 years) and their parents, 5% of the children reported to be diagnosed with asthma, compared to 7% of the parents. However, questions concerning

asthmatic symptoms revealed an additional prevalence of possible asthma (children's questionnaires: 6%, parental questionnaires: 4%), resulting in a prevalence of 11% according to the children's questionnaires and 10% according to the parental questionnaires [4]. Similarly, the European study cited earlier detected a large group of adolescents with 'asthma-like symptoms' but without asthma-diagnosis (up to 22%), indicating a significant rate of undiagnosed or less-severe asthma [3].

Inhaled corticosteroids (ICS) remain the main treatment for children with persistent asthma, being preferred over leukotriene receptor agonists [5]. In poorly controlled asthma, leukotriene receptor agonists or long-acting β_2 -agonists may be added to the ICS therapy [6,7]. However, before changing the medication regimen, it is essential to realize that an important reason for poor disease control is suboptimal adherence. In a recently proposed taxonomy, medication adherence is defined as the process of taking medication as prescribed during initiation, implementation, and discontinuation

of treatment [8]. Non-adherence is largely responsible for the differences in efficacy of medications seen in clinical practice versus the efficacy reported in clinical trials (Figure 1) [9]. Strategies for measuring asthma medication adherence can be classified into objective measurements (pharmacy refill data, use of metered dose inhalers, or electronic measuring devices) and subjective measurements (self-reported adherence using questionnaires provided to patients, diaries, or physician assessment) [10,11]. A review of studies using electronic adherence monitoring showed that half of these reports mean adherence rates of 50% or below, and the majority report rates below 75% [12].

Three different patterns of non-adherence exist: intentional non-adherence, unplanned non-adherence due to family-related barriers, and unplanned non-adherence due to the transfer of excessive responsibility to children [13]. Intentional non-adherence included parents balancing the positive and negative effects of the prescribed medication, and deviating deliberately from the pediatrician's advice (increasing the dose during a 'bad' season, or giving a single daily dose instead of the recommended two). Family-related barriers comprised refusal of the child to take the medication, the absence of daily medicine-taking routines, or the acceptance of the current level of adherence as the best possible level that their child can achieve. The third pattern of excessive responsibility for the child supports the importance of parental guidance to achieve optimal adherence; this was also observed in a study in France, in which children with good adherence were those whose parents ensured that they always had their medications with them [14].

Similar reasons for suboptimal adherence were identified by a systematic review of qualitative studies on treatment adherence in children with various long-term conditions, including asthma. Caregivers reported balancing various concerns, including their beliefs about a condition and its treatment, managing

child resistance, preserving family relationships and promoting a 'normal life' for their family. Simplifying treatments and discussing strategies to address child resistance with the parent were proposed to improve adherence [15].

In assessing medication adherence, self-reporting remains the most cost-efficient method, despite its disadvantages [16], and also allows collection of information on patients' attitude and beliefs. Future surveys may be designed based on previous experience, to maximize the quality and volume of information obtained, and to become a more useful tool in evaluation of adherence. With this in mind, we provide a narrative review of the literature on surveys assessing adherence of children and adolescents aged 0–18 years to asthma medication, focusing on ICS; the attitude of the patients and their parents toward asthma treatments; and expectations of the patients and their parents concerning asthma and the available therapies.

Search strategy and selection criteria

References were identified through PubMed searches using the keywords in Supplementary Table 1, and also Google and PubMed searches using Dutch and French keywords, to retrieve Belgian studies. Searches for worldwide data were limited to 2009–2014; searches performed to assess the Belgian situation were extended to 2003–2014, due to limited data available. A few more recent, relevant references were also included. A further selection of articles was performed manually based on their abstracts, to include only studies using surveys or interviews addressing one of the following three topics: (1) adherence to ICS of children and adolescents with asthma; (2) attitude of children, adolescents, and their parents toward asthma treatment; and (3) expectations of children, adolescents, and their parents concerning asthma and the available treatments.

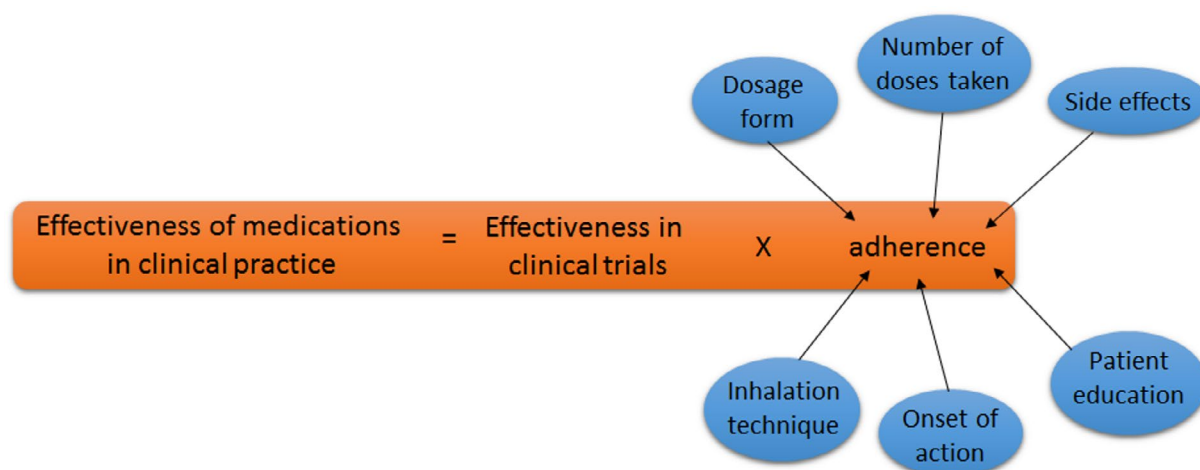


Figure 1. Impact of adherence on the effectiveness of medications.

Medication adherence in asthmatic children and adolescents

Adherence to ICS

Several studies have shown that objectively measured adherence to ICS is suboptimal in children, ranging between 49–71% (Table 1). Adherence levels decrease over time: in a 4-year study, mean adherence during the first year was 69%, compared to 52% during the fourth year [17]. Early discontinuation is also a problem; in the US, more than half of the assessed children and adolescents had no refill claim, and 63% had discontinued their asthma medications within 3 months after the first prescription. The risk was higher for ethnic minorities and disadvantaged households [18].

Higher adherence rates have been observed in children below 6 years of age compared to older children, possibly as a result of more parental motivation in the younger age group [19]. Similarly, in African-American or Hispanic adolescents aged 11–16 years, older age was significantly associated with lower adherence [20]. In a study including 285 children aged 5–11 years and 211 adolescents aged 12–18 years, a low level of adherence to the US asthma guidelines was assessed based on medical records; older age was associated with poorer adherence to non-medication elements of the asthma guidelines [21].

Measurement of medication adherence

Subjective measurements tend to overestimate the level of adherence compared to objective measurements. In 5- to 12-year-old children with mild or moderate asthma, the level of agreement between self-reported adherence (using daily diary cards) and objectively measured adherence (the number of doses left in the study inhaler) was poor, with objectively measured adherence being significantly lower than self-reported adherence (percentage of doses taken: 61% vs. 94%, $p < 0.0001$) [17]. Moreover, inadequate adherence (less than 80% of doses taken) was reported by only 6% of the children, while objective measurement revealed inadequate adherence in 75% of the children (Figure 2) [17]. Similarly, in a study comparing parental report of adherence and dose counter-measured adherence [22], 42% of the parents reported complete adherence whereas only 10% of the children had complete adherence according to the

dose counter (Figure 3(a)). However, parents accurately reported complete non-adherence: 4% of parents reported 0% adherence, as compared to 6% of children showing complete non-adherence by dose counter (Figure 3(b)). On average, 58% of the expected puffs were taken during the 30-day follow-up in that study, as measured by the dose counter [22]. In a third study, the percentage of doses taken was also overestimated in parents' verbal reports (85%) and questionnaire responses (84%), compared to medication use determined by an electronic monitoring device (71%) [23]. Similarly, parents of US preschoolers with asthma reported a significantly higher adherence than objectively measured by pharmacy refill data (mean adherence: 92% vs. 57%) [24].

Physicians' estimates of children's medication use were generally lower than the parents' reports (70% vs. 85%), but the correlation between the physicians' estimates and data from the electronic monitoring devices was weak. Moreover, physicians were unable to determine which parents correctly estimated their child's use of medication [23].

Factors affecting adherence

For children between 18 months and 7 years of age, parents reported 'forgetting' and 'their child's reaction to being given medication' as the most common reasons for missing doses [23]. For adolescents, additional factors could play a role; in a study in US adolescents (12–18 years), about half of non-adherence instances took place in the presence of friends [25]. The ease of use of medication devices can also influence adherence; most interviewed adolescents (11–18 years) in the UK did not use their spacer device to take inhaled medication [26], likely leading to reduced drug delivery. In addition, most adolescents did not take responsibility for their asthma, relying on their parents instead. Forgetfulness has also been linked to non-adherence in teens [27,28].

Attitudes toward asthma therapy

Of 100 Egyptian parents of asthmatic children who were interviewed to determine their concerns regarding use of ICS, 53% reported fear for side effects, including non-specific side effects (35%), addiction (9%) or weight gain (6%). Moreover, 46% mentioned encountering

Table 1. Objectively measured adherence in children with asthma.

	Region	Age group	Study period	Adherence measurement	Adherence level
Krishnan [17]	US	5–12 years	4 years	Doses left in Turbuhaler	Mean: 61%
Reznik [22]	US	2–9 years	1 month	Metered-dose inhaler	Mean: 58% (SD: 31%)
Burgess [23]	Australia	18 months – 7 years	1 month	Electronic monitoring device	Median: 71% (range 21.4–100%)
Vasbinder [47]	The Netherlands	1–11 years	3 months	Real Time Medication Monitoring system	Mean: 49% (SD: 31%)
Bollinger [51]	US	2–8 years	18 months	Prescription fills	49% of prescriptions filled
Armstrong [24]	US	2–5 years	9 months	Pharmacy refill data	Mean: 57% (SD: 31)

Note: SD, standard deviation.

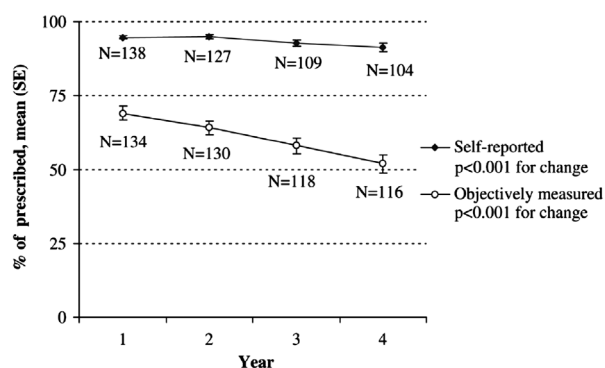


Figure 2. Subjectively versus objectively measured adherence. Notes: Objective and self-reported adherence by study year within the ancillary study. Self-reported (solid diamonds) and objective (open circles) adherence at years 1, 2, 3, and 4 of the study are shown. The number of children in whom adherence data were available each year is shown adjacent to each data point. N, number of children; SE, standard error. Source: Reprinted from Journal of Allergy and Clinical Immunology, Vol. 129, Krishnan et al. Adherence to inhaled corticosteroids: An ancillary study of the Childhood Asthma Management Program clinical trial, p. 112–118, Copyright (2012), with permission from Elsevier [17].

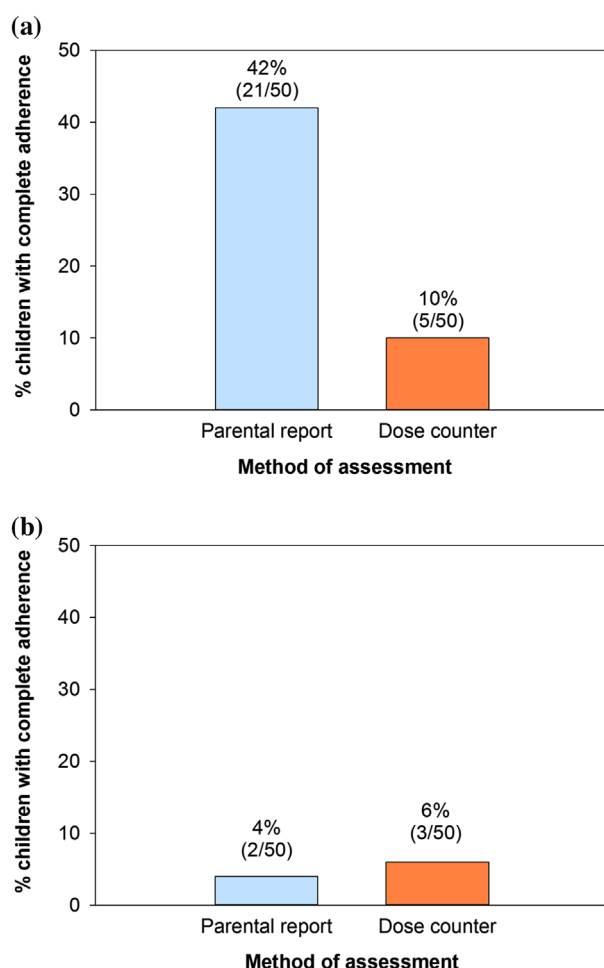


Figure 3. Complete adherence (a) and complete non-adherence (b) to ICS according to parental report and dose counter measures. Source: Figure adapted from Reznik et al. J Allergy 2012 [22].

difficulties in using ICS, such as expensive cost, problems with the use of inhaler devices, and the need for higher doses [29]. A study discussing the beliefs of parents of

both asthmatic and healthy students aged 8–16 years in Brazil also reported that over 20% of parents were afraid of asthma medication use and more than 40% believed that using inhalers leads to drug dependence [30].

The impact of such concerns and fears on medication adherence is unclear. In an interview-based study, parents reported deliberately deviating from the pediatrician's advice and adjusting the ICS dose according to their expectations or impressions about their child's level of asthma control; their main reasons for lowering the ICS dose were concerns about side effects or resistance against medication in general [13]. For asthmatic preschoolers, medication adherence decreased as negative health beliefs of their parents increased [24]. In another study, parental concerns about medication use were associated with therapy adherence when performing univariate analyses, but the association was no longer observed in the multivariate analysis performed to assess independence of the adherence-associated factors [19]. A fourth study found that concerns about side effects did not affect guideline-recommended use of ICS [31]. Nevertheless, a higher risk for uncontrolled asthma has been reported in children whose parents had concerns about medication [32,33].

The adjustment of ICS dosing has also been observed in adolescents, who often reported decreasing their use of the controller when they had less symptoms [25,28]. Moreover, adolescents did sometimes not use their controller or rescue inhaler even though they had asthma symptoms, because they did not believe they needed it or did not have their inhaler with them [25].

Parental beliefs about the necessity of medication to maintain the child's health have been associated with good medication adherence [19,32]. Surprisingly, strong parental beliefs about medication use have also been associated with a two times higher risk of uncontrolled asthma; a potential explanation could be that strong parental beliefs about the necessity of medication reflect more severe asthma in the child, which is difficult to control [32]. Beliefs about medicines were also associated with adherence in adolescents; adherence rates were higher for patients classified as accepting than for those classified as ambivalent or skeptical [28].

An evaluation of the psychosocial implications of asthma in Belgian French-speaking children revealed that children with asthma were assessed by their parents as having significantly more internalizing problems (e.g. anxiety, depression, or somatic complaints), social and attention problems, and fewer competences in their activities than healthy children. Boys with asthma appeared more vulnerable to psychological and social difficulties, but had better school competences than girls with asthma. No significant relationship was found between the level of asthma control and psychological, social or school difficulties [34].

Lahaye et al. explored the relationship between emotional competence and quality of life in children with

asthma, as well as the effect of coping strategies. In children with asthma, high scores on 'differentiating emotions' and 'bodily awareness' and low scores on 'analyses of emotions' were related to a reduction in 'ignoring asthma' and 'worrying about asthma'; this reduction increased the children's quality of life [35].

Expectations concerning asthma treatments

A focus group study in Sweden revealed that parents and adolescents expected to be treated by a competent health care professional, but this did not always occur. Parents also mentioned that they would prefer getting repeated education in asthma care; for example, when they have a second child being diagnosed with asthma, the health care professional should not assume that the parents already have all the necessary information. Asthma nurses were appreciated by both parents and adolescents. Interestingly, parents also wished that school teachers had more knowledge about caring for a child with asthma [36]. A Turkish study found asthma knowledge among elementary school teachers to be poor; the teachers had inadequate information about the main characteristics of asthma, how to recognize symptoms and triggers, and asthma treatment. Moreover, many teachers were not aware of asthmatic students in their class [37].

In various studies, low knowledge about ICS has been linked to poor adherence [20,31,38]. Additionally, low parental education level has been associated with uncontrolled asthma [32]. The type of education source may be more important for good adherence than the number of education sources; Delgado et al. found no relationship between the number of used education sources and the risk for non-adherence, but did observe a trend toward decreased risk for non-adherence for parents who indicated their primary care provider as a source of helpful information [39]. Also, multimedia education using text, sound, pictures, and video has been reported to increase parents' knowledge and self-efficacy [40].

Children and their parents overestimated the level of achieved asthma control [41–43]. This could be due to patients or parents assuming that better control is not possible and thus accepting lower levels of control than recommended. Another explanation could be the underestimation of asthma severity and subsequent under-treatment, leading to a lower level of disease control [42]. Parental knowledge about asthma was found to be important for recognizing and reporting asthma symptoms, especially nocturnal symptoms; however, parents still failed to identify these as a sign that their child's asthma was not well controlled [43].

Parental knowledge about asthma medication has been reported to be suboptimal. In a survey performed in the Netherlands, only 53% of the parents agreed with the statement 'anti-inflammatory drugs/maintenance medication must be taken every day, also when the child

is doing well.' Parental knowledge about how asthma medication should be given was found to be a major determinant of guideline-recommended use. Of the parents who knew that anti-inflammatory drugs should be taken every day, 84% reported that they actually gave their child the medicines every day, compared to only 25% of the parents who did not have this knowledge [31]. Deis et al. found that many parents have an inadequate understanding of the differences between ICS and rescue medications, and more than half of them reported that they would like more information about those differences [38]. Moreover, 62% of these parents would like to know more about common triggers of asthma exacerbations.

Better adherence has been reported in children with good understanding of asthma and who think that treatment can control their asthma [14]. Also in adolescents, sufficient knowledge about asthma medication has been associated with better adherence rates [20,28].

In the UK, most adolescents did not take responsibility for their asthma nor for interacting with health professionals, but relied on their parents instead. Adolescents also had a poor understanding of their medication [26].

A recent study conducted in Australia in parents of children 2–10 years old showed that a Triple P parenting intervention on childhood asthma-related behaviour problems can enhance family quality of life and ameliorate symptom severity, by improving medication adherence [44]. A school-based educational intervention in Thailand, targeting 47 asthmatic students 6–15 years of age, 14 caregivers and 5 teachers, was shown to significantly improve asthma knowledge and control, and the rates of ICS use [45]. A significant decrease in asthma exacerbation was also observed following a motivational intervention in Italian patients 5–18 years and their parents [46].

Discussion and conclusions

Our narrative review of the literature data showed that medication adherence in asthmatic children and adolescents is suboptimal, and both patients and their parents are biased toward overestimating asthma control. Patient knowledge on this condition needs to be improved to achieve better treatment adherence.

Adherence to asthma medication varies across age groups and with the type of measurement used. Objectively measured levels of adherence of 49–71% were observed in children and adolescents, although self-reported adherence is usually higher. Thus, adherence to ICS in these age categories is suboptimal. Children and parents were also found to often overestimate the achieved level of asthma control; subsequently, many children and adolescents have a lower level of asthma control than could ideally be reached with an optimized treatment.

Reasons for non-adherence may differ between children and adolescents. For instance, non-adherence in adolescents often took place in the presence of friends. For younger children, parents are usually also more involved in medication taking, whereas adolescents are responsible themselves for taking their medication.

Surveys addressing attitudes of children and parents toward asthma and asthma therapy found that an important percentage of parents expressed concerns regarding daily use of ICS, translated mainly into fear of the side effects. However, the impact of such concerns on adherence is unclear. One of the problems is the fact that the use of ICS is often adapted according to the prevalence of asthma symptoms, with doses being reduced or controller medication not being taken at all when the child or adolescent experiences no symptoms (Table 2).

Both patients and their parents expect to be treated by competent health care professionals, who can provide them with information and continuous guidance regarding asthma therapy. Various surveys showed that knowledge about asthma medication was suboptimal both in parents and adolescents [26,31,38]. Insufficient knowledge about asthma and its therapies has been linked to non-adherence and lower disease control [20,31,38], supporting the importance of improved patient education. This education could be provided by asthma nurses, whose support is appreciated by the parents [36]. In the case of children attending school, a need was observed to provide the school with sufficient information and knowledge, so that teachers know how to react in case of an asthma attack. In Belgium, a form has been developed for parents to provide the necessary information about their child's asthma to the school, including asthma severity, risk factors, the symptoms that indicate an asthma attack, and information about the medication [47].

Educating patients and their parents on the importance of controller medication and the difference

between controller and rescue medication may also improve their self-efficacy in assessing asthma symptoms and accurately estimating their level of disease control.

Increased knowledge about asthma with older age does not translate into better adherence. A study in young university students under 23 years of age showed that individuals experiencing embarrassment and concern about medication, immediate gratification seekers and those with lower risk tolerance are less likely to adhere to asthma medication, despite increased knowledge of the disease [48]. These elements are more likely to be encountered in adolescents than children and might largely contribute to the difference observed in medication adherence. Subsequently, different strategies may be needed to improve adherence in young children and in adolescents. Because adolescents are more susceptible to social influence and peer pressure, using social media and mobile technology is likely to be a suitable strategy in asthmatic adolescents, although the effectiveness of such measures is yet to be demonstrated [49].

A potential limitation of this study is its focus on publications using surveys to gather information about the assessed topics. This method would have captured most studies concerning attitudes toward asthma treatment, and the expectations of parents and asthmatic children concerning asthma and the available treatments. However, we have probably missed studies which did not use surveys but only other ways of measuring adherence, such as prescription refills or electronic monitoring devices. It was difficult to compare findings in children and adolescents, as few publications reported data in adolescents; this could constitute a limitation of this review. The literature search was executed using only Google and PubMed, so it might not be exhaustive.

In conclusion, adherence to therapy is crucial for a good control of asthma symptoms. However, additional research is still needed, especially concerning the triggers of non-adherence. One potential way to improve medication adherence and asthma control may be through adequate education of asthmatic children and adolescents and their parents. Interventions to improve adherence may also need to be adapted according to the patient's age, as different factors may play a role in non-adherence in different age groups.

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Disclosure statement

No potential conflict of interest was reported by the authors.

Table 2. Key findings of the literature search.

Adherence to ICS is suboptimal in children and adolescents with asthma

- Subjective measurements tend to overestimate the level of adherence.
- The use of ICS is often adapted according to the asthma symptoms.
- Parental beliefs about asthma medication have been associated with uncontrolled asthma and medication adherence.

Children/adolescents and parents tend to overestimate their asthma control

- They may assume that better control is not possible and therefore accept lower levels of control than recommended.
- Another potential explanation could be the underestimation of asthma severity, leading to under-treatment and thereby a lower level of disease control.

Insufficient knowledge about ICS is linked to poor adherence

- The knowledge of parents and adolescents concerning asthma medication is suboptimal.
- Surveys revealed that parents would like to have more information, as well as repeated education in asthma care.
- Increasing patient knowledge could be a way to improve adherence.

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