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Factors that Affect Adherence with Long-Term Controller Medications Used to Manage Asthma in Children

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FACTORS THAT AFFECT ADHERENCE WITH LONG-TERM CONTROLLER MEDICATIONS USED TO MANAGE ASTHMA IN CHILDREN

by

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A thesis submitted in partial fulfillment of the requirements
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Abstract

Problem: Asthma affects one out of every ten children in the United States. It is recommended that children with persistent asthma take long-term controller (LTC) medications to achieve control. However, adherence varies, and many children do not take their LTC medication at all. The average cost for hospitalization of a child with asthma is $8,406. Asthma in children also contributes to school absenteeism and a decrease in quality of life.

Objective: A literature review was performed to examine factors that affect adherence to LTC medications used to control asthma in children.

Method: A literature review was performed using the CINAHL, ERIC, Medline, Psych Info, and Academic Search Premier databases. Keywords included asthma AND child* OR pediatric* AND adherence OR compliance AND corticosteroid* OR "leukotriene modifier*" OR "mast cell stabilizer*" OR "monoclonal antibod*" OR "long-acting beta agonist.*" After applying exclusion criteria 35 articles were included in this review.

Results: A variety of factors that affect adherence were identified. Internal factors included age, sex, and race/ethnicity. External factors included socioeconomic status, environment, health perception, lack of motivation, parental education, disease/medication beliefs, family dynamics and planning, responsibility, severity, and exacerbations. Interventional factors included caregiver-family communication, asthma knowledge, specialty care, white coat adherence, number of prescriptions, asthma action plans, medication regimens, and technology.

Conclusion: It is recommended that healthcare providers use a four-step process during inpatient and outpatient asthma visits. The steps include assess and educate, collaborate, problem-solve,

and follow-up. Collectively, this method can help healthcare providers overcome many of the barriers that were identified.

Dedication

This journey was a long one for me. There were many doubts and even more late nights and early mornings. Throughout everything I have been able to rely on my family for support. They have taken me to school when I didn't have a car. They have paid my bills when I didn't have enough money to live. They have motivated me and encouraged me when I didn't have faith in myself.

That being said, I would like to dedicate my thesis to my family. On my own I could have accomplished much. But with my family I can accomplish anything.

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Introduction

Pathophysiology

Symptoms exhibited by people with asthma are a manifestation of underlying inflammatory processes. The airways of people with asthma contain excessive amounts of inflammatory cells including: mast cells, eosinophils, neutrophils, and macrophages. These cells and many others have been identified in the pathophysiology of asthma. Immunoglobin E (IgE) are antibodies that are abundant during allergic responses that may trigger asthma. They activate other cells including mast cells. Mast cells contribute to bronchoconstriction. Smaller airways decrease the amount of air that is able to traverse through the bronchioles (National Heart, Lung, and Blood Institute [NHLBI], 2007.

Macrophages in the airways are also activated by IgE antibodies, and they increase inflammation. Eosinophils and epithelial cells that line the airways also contribute to inflammation. The inflammation can have a negative effect on the smooth muscle in the airways causing hypertrophy which may decrease the size of the airways and contractions that can obstruct airflow (NHLBI, 2007).

Inflammation involved in the pathophysiology of asthma is complex and not fully understood. What is understood is that inflammation contributes to bronchoconstriction, airway hyper-responsiveness and obstruction. This causes the hallmark symptoms of asthma which are coughing, wheezing, breathlessness, and chest tightness. Over time, permanent changes to the airway, known as airway remodeling, can also occur (NHLBI, 2007).

Asthma Today

According to the most recent data, there are 25.7 million people in the United States that have asthma, and its incidence is increasing. It is more common among women than men, and is more prevalent in the poor. There is also racial disparity with 16% of Porto Ricans, 11% of blacks, 8% of whites, and 5% of Mexicans having asthma.

In one year, asthma accounted for more than 10 million outpatient visits, more than 2 million emergency department (ED) visits, and more than 450,000 hospital admissions (National Center for Health Statistics [NCHS], 2012).

There are seven million children in the United States that currently have asthma. It is more prevalent among boys than girls. Children account for more ED visits and hospitalizations than adults even though the number of adults with asthma far surpass that of children. More than half of the children with asthma had an exacerbation in the year preceding data collection. More than half of the children also missed school due to the disease (NCHS, 2012).

Background

The most recent guidelines for the diagnosis and treatment of asthma were published by the NHLBI in 2007. According to these guidelines, the purpose of asthma treatment is to achieve specific goals. The first goal is to prevent symptoms such as coughing, wheezing, and shortness of breath. The second goal is to reduce the use of rescue medications to less than two times per week. The third goal is to maintain lung function as close to normal as is possible. The fourth goal is to maintain normal physical activity. The fifth goal is to prevent exacerbations and subsequent ED visits or hospitalizations. The next goal is to prevent any lessening in lung growth. The final goal is to provide optimal therapy with minimal side effects. Healthcare providers (HCPs) can determine if these goals are met when they assess asthma control.

Asthma control is classified as "well-controlled," "not well-controlled," or "poorly controlled." For children, control is based on frequency of symptoms, frequency of nighttime awakening, frequency of rescue medication use, frequency of exacerbations that require oral corticosteroids, and how much symptoms interfere with physical activity (NHLBI, 2007).

For children above the age of five, control is also based on an objective assessment of lung function. For children above the age of 12, control is also based on data collected in a questionnaire. Optimally, asthma should be well-controlled. The regimen used to control asthma also depends on disease severity (NHLBI, 2007).

Asthma can be further classified based on disease severity. Asthma severity is classified as either intermittent or persistent. Persistent asthma is further classified as "mild," "moderate," or "severe." Severity is based on the same parameters used to determine asthma control. The

best way to control persistent asthma is by incorporating the use of long-term controller (LTC) medications into the plan of care. LTC medications are taken regularly to prevent exacerbations and improve control (NHLBI, 2007).

Guidelines identify several medications that are indicated for long-term control of asthma. All medications have some effect on inflammatory processes. The first and most effective class of medications include the inhaled corticosteroids (ICSs). They are not the same as the oral corticosteroids which produce a systemic effect (NHLBI, 2007).

The next class of medications are mast cell stabilizers including cromolyn sodium and nedocromil. They are used as alternative medications, and are not preferred therapies. The next class of medications are the immunomodulators. Included in this class is omalizuab which is a monoclonal antibody. This class is only recommended if other regimens are unsuccessful (NHLBI, 2007).

The next classification of medications are the leukotriene modifiers. These medications are also designated for use as alternative medications, and are not preferred therapies. The next classification includes inhaled long-acting $beta_2$ agonists (LABAs). They are not recommended as monotheraphy, and should be used in conjunction with another medication (NHLBI, 2007).

The final classification of medications are methylxanthines including theophylline. Again it is suggested that these medications be used as an alternative, and not preferred therapy. These medications are used to control persistent asthma and achieve therapeutic goals (NHLBI, 2007).

Problem

Poor Adherence

Many children with asthma do not take their medication at all. Statistical data collected by the NCHS in 2012 determined that 60% of children with asthma had persistent asthma. Another 38% of children with asthma had uncontrolled asthma. Only 40% reported that they had used a LTC medication in the three months prior to data collection, and 19% overused rescue medications.

This was consistent with data collected in 2011 when Arellano, Arana, Wentworth, Vidaurre, and Chipps evaluated prescription fill patterns for 659,159 children with asthma. They determined that 40% of the participants never received their initial prescription. Children in this study were between the ages of 6-18, and all of them were insured. This is also consistent with a study published by Wijga et al. in 2014. Parents of 229 children with asthma participated in the study. There were 170 children who were taking ICSs. In a questionnaire given to parents it was determined that 15% of parents avoided giving their child the medication, and another 25% of parents discontinued the medication.

Schultz et al. (2012) determined that when caregivers report adherence it is unreliable. They monitored medication adherence in 132 children with asthma using inhalers with electronic monitoring capability. Adherence was as low as 0% and as high as 100%. Generally, parents who reported that they missed doses missed at least half of them. Also, parents that reported that they did not miss any doses missed at least 20% of them.

Duchame et al. (2012) reported that when medication is used to control asthma, it is not used consistently with caregivers only claiming 51% of their child's ICSs. In 2014, Mosnaim et

al. electronically monitored adherence in minority children with asthma. They found that 76% did not even take half of their prescribed doses. Chan et al. (2015) showed that adherence in children taking ICSs was as low as 8%. Inconsistent adherence was also observed by Al-Muhsen et al. (2015) when they interviewed the caregivers of 297 children with asthma in an ED. Seventy-three percent of the caregivers reported that they stopped giving their child ICSs when symptoms improved.

Al-Muhsen et al. (2015) found that 40% of caregivers either started or increased the dosage of ICSs when their child was having an exacerbation. This was also observed by Wijga et al. in 2014. Forty percent of caregivers only gave their child ICSs when their child was symptomatic. This was also observed by Sloan, Gebretsadik, Wu, Michel, and Hartert (2012). They evaluated prescription fill patterns among children with asthma. Their data showed that there was a trend in which ICSs were obtained at the same time that caregivers were obtaining rescue medications used to treat an exacerbation. Poor adherence is problematic because it can contribute to poor control.

Poor Adherence and Poor Control

In 2014, Baddar, Jayakrishnan, and Al-Rawas examined asthma control in 218 participants. They found that 83% of the participants that had poor medication adherence also had poor asthma control. This was supported by Klok, Kaptein, Duiverman, and Brand in 2014 who electronically monitored adherence in 81 children with asthma, and determined that children with well-controlled asthma had a median adherence above 80%.

In 2015, Al-Muhsen et al. found that if caregivers started or increased ICS usage when their child was having an exacerbation, that child was three times more likely to have

uncontrolled asthma. Children who were not taking an ICS were also more likely to have uncontrolled asthma. Poor medication adherence and the resulting poor control contribute to increased healthcare utilization including emergency services.

Poor Adherence/Poor Control and the Corresponding Increase in Healthcare Utilization

Emergency department.

Deis, Spiro, Jenkins, Buckles, and Arnold (2010) found that medication adherence was a factor in ED utilization. They included caregivers of 108 children with persistent asthma. When asked about their use of ICSs 49% percent of caregivers reported that they did not use ICSs daily.

Rust, Zhang, and Reynolds (2013) evaluated the ratio of LTC medications to total asthma medications and its effect on ED utilization among children with asthma covered by Medicaid. Children who used more rescue medications were 21% more likely to have an ED visit and 70% more likely to be admitted than children who used more LTC medications than rescue medications.

Supporting evidence was provided by Al-Muhsen et al. (2015) who found that children with uncontrolled asthma visited the ED more that those with controlled asthma. Despite this, the majority of caregivers were not giving their child the medication necessary to achieve control. Emergency department utilization remains a costly problem for children with asthma.

Costs of emergency department.

Wang, Srebotnjak, Brownell, and Hsia published data in 2014 that determined just how costly. They received data from almost 3 million ED visits in which costs ranged from $19 to $12,601. Participants were between the ages of 0-85. Yet, children between the ages of 0-19

made up 48% of the sample. The average costs for an ED visit among children with asthma are displayed in Table 1.

Average Cost for Emergency Department Visits by Insurance Type in Children Aged 0-19			
Medicare	Medicaid	Uninsured	Private
$414	$1,108	$1,120	$1,263

Table 1 ED Costs

Hospitalization.

Exacerbations may require frequent hospitalization. In 2014, Auger, Kahn, Davis, and Simmons examined hospital readmission among 601 children with asthma between the ages of 1-16. The five year study found that children were more likely to be readmitted if their caregivers reported any lapse in medication adherence or if they did not answer questions related to adherence at all.

Costs of hospitalization.

In 2013, Hasegawa, Tsugawa, Brown, and Camargo evaluated the costs of asthma hospitalizations from 2000-2009. According to the data collected, the costs have increased from 1.3 billion in 2000 to 1.6 billion in 2009. In 2009, there were 305,000 admissions that were an average of two days. The average cost of hospitalization was $8,406.

Poor Control and Quality of Life

Besides monetary repercussions, poor asthma control has also been shown to have a negative effect on quality of life in children. Almost half of the children with asthma had missed school due to their asthma, and 60% of people with asthma limit their physical activity (NCHS,

2012). In 2013, Li et al. published a study to determine if asthma control affected sleep in 160 children. They found that poor asthma control was also associated with daytime sleepiness.

Summary of Problem

To summarize the concepts presented, the primary problem is that adherence to medications used to control asthma is poor. Some children do not take any medication at all. Those who do often fall short of the 80% that is recommended to maintain asthma control. Children that do not adhere to LTC medications are more likely to have uncontrolled asthma. Those with uncontrolled asthma are more likely to visit the ED or be hospitalized. This results in increased costs and decreased quality of life.

Purpose

The purpose of this research is to determine the different factors that affect adherence to LTC medications used to manage asthma in children. A literature review was performed to examine the current evidence. Factors will be identified that either increase or decrease adherence, and the findings will be discussed.

The secondary purpose of this research is to make recommendations for current practice and future practice based on the findings in this study. The final purpose of this research is to make recommendations for future research based on the findings of this study.

Overall, the purpose of this research is identify a method to improve the way that HCPs care for children with persistent asthma in order to decrease costs and increase the quality of life.

Method

A literature review was performed using the CINAHL, ERIC, Medline, Psych Info, and Academic Search Premier databases. Keywords included asthma AND child* OR pediatric* AND adherence OR compliance AND corticosteroid* OR "leukotriene modifier*" OR "mast cell stabilizer*" OR "monoclonal antibod*" OR "long-acting beta agonist.*" This produced a list of 305 articles. Articles were included only if they met specific criteria.

Articles were included only if the publication was in English. Articles that were written in foreign languages were excluded. Any duplicate articles were also excluded.

Articles that were published in or after 2010 were included in this review. Articles published prior to 2010 were excluded.

Primary sources were included in this review. Randomized, controlled trials, controlled trials without randomization, case-studies, cohort studies, and qualitative studies were included. Secondary sources were excluded to prevent further degradation of content.

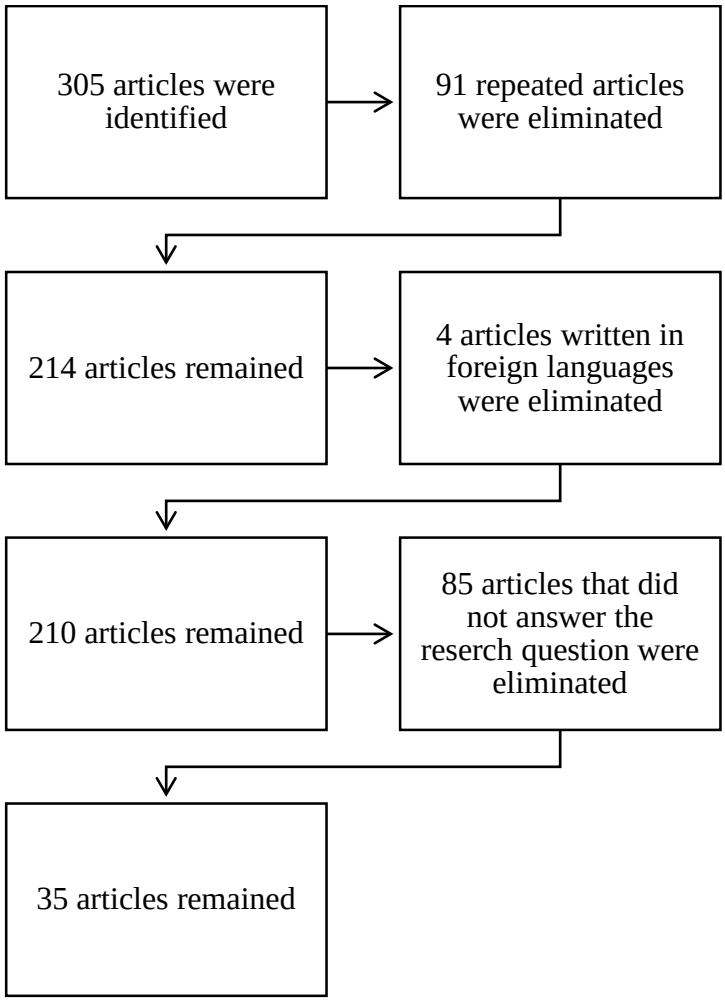
Articles that contributed to the research question were included in this review. Articles had to identify factors associated with adherence to long-term medications given to control asthma in children. Articles were excluded if they did not identify specific factors. Articles were also excluded if they focused on healthcare provider adherence to recommendations.

Articles that included pediatric participants between the ages of 0-18 were included in this review. Any articles that included adult participants were excluded from this review even if pediatric participants were also involved in the research.

Articles that included children diagnosed with asthma were included in this review. Articles that included children also diagnosed with other diseases were also included in this review. Articles were excluded if participants had respiratory distress or wheezing, but were not diagnosed specifically with asthma.

The search yielded 305 results. After apply exclusion criteria 270 articles were eliminated. The remaining 35 articles were included in the literature review.

Figure 1 Method



Findings

Over 20 factors were identified that affect adherence to LTC medications used to manage asthma in children. They have been organized into three categories that include internal factors, external factors, and interventional factors. Inherent characteristics were classified as internal. Factors that were neither inherent nor controlled by HCPs were classified as external. Factors that HCPs have control over were classified as interventional.

Internal Factors

Age.

Several different studies have evaluated age and its correlation with adherence to LTC medications. Studies included various age ranges and populations.

In 2014, Capo-Ramos, Duran, Simon, Akinbami, and Schoendorf examined prescription fill patterns to ascertain adherence among children with Medicaid. Participants were between the ages of 2-17, and they were taking LTC medications used to treat persistent asthma. There were a total of 4,262 participants with the majority being male and white. The researchers determined that adherence declined over time, and only 15% of the participants were still receiving medications 190 days after the initial prescription was filled.

Capo-Ramos, Duran, Simon, Akinbami, and Schoendorf (2014) also found that there was a higher likelihood of non-adherence among toddlers between the ages of 2-4 and adolescents between the ages of 12-17. Herndon et al. (2012) also found an association between children between the ages of 2-4 and non-adherence.

Contradictory to these studies, Elkout et al. (2012) showed higher adherence among children aged 0-4 taking ICS when compared to all other age groups.

Koster, Raaijmakers, Vijverberg, and der Zee (2011) evaluated ICS adherence among children with asthma in the Netherlands between the ages of 4-12. They found that adherence was higher in the children under the age of six when compared with older children. To complicate the findings more, Vasbinder et al. (2014) did not show a statistically significant difference in adherence among children between the ages of 1-11. One weakness in this study was that participants knew that they were being monitored, and they may have adjusted their behavior based on this knowledge.

Mosnaim et al. (2014) evaluated adherence to ICSs in 93 minority adolescents between the ages of 10-16. The average age for adherence greater than 50% was 12. The average age for adherence less than 50% was 13. This corresponds with data published by Capo-Ramos et al. in 2014 that found an association between older adolescents and non-adherence.

Overall, results vary between the different studies. There is one consistency. That is the association with older adolescents above the age of 13 and non-adherence. This may be due to problems with delegation of responsibility which are evaluated later on in this review.

Sex.

Childhood asthma disproportionately affects boys (NCHS, 2012). Most of the studies included had more male participants, consistent with this unequal distribution.

In 2010, Sawicki et al. evaluated adherence in 425 children with asthma who were prescribed ICSs. The study spanned five years, and adherence declined over the span of the study. Adherence was self-reported and classified as consistent, variable, intermittent, or none.

After the first year it was determined that consistent adherence occurred more frequently in girls. One limitation was that adherence was self-reported (Schultz et al., 2012).

In 2012, Elkout, Helms, Simpson, and McLay investigated adherence to LTC medications in 3,172 children with asthma. Adherence to various LTC medications was determined by medication possession. In this study, adequate adherence was medication possession between 80-120% of the prescribed regimen. The researchers determined that adequate adherence was higher in boys for all classes of medication. Overall, 58% of those with adequate adherence were male. However, 62% of their participants were boys. That is indicative of higher adherence in girls.

In 2014, Mosnaim et al. examined adherence to ICSs in 93 minority adolescents between the ages of 10-16. Adherence was determined by medication possession. Their study population was 44% male. However, only 24% of males had adherence greater than 50%. Data collected in this study showed that girls were statistically associated with higher adherence.

Herndon et al. (2012) had varying results. They evaluated adherence among 18,456 children with Medicaid using claims data. Higher adherence was found in 60% of the boys taking ICSs. However, boys accounted for 60% of the participants taking ICSs. They also evaluated adherence to leukotriene modifiers. Boys accounted for 64% of the participants who were taking leukotriene modifiers, but they accounted for 64% of the participants with higher adherence. For leukotriene modifiers boys were slightly more likely to have better adherence.

Overall, there are multiple studies that indicate that adherence in girls is superior to that of boys with the exception of adherence to leukotriene modifiers.

Race/Ethnicity.

In 2011, Koster et al. evaluated ICS adherence among children in the Netherlands between the ages of 4-12. There were 527 children who participated in the study. Data obtained determined that good adherence was reported more often in native Dutch children when compared with other children. One limitation was that adherence was self-reported (Schultz et al., 2012).

In 2014, Vasbinder et al. also examined adherence to ICSs in children between the ages of 1-11 in the Netherlands. The purpose of the study was to determine if there were differing levels of adherence between native Dutch participants and Moroccan participants. They measured adherence electronically. They found that adherence among the native Dutch was higher than that of Moroccan children. Adherence among the native Dutch was 56%. The average adherence for Moroccan participants was 42%.

There have also been studies that evaluate how race and ethnicity affect adherence here in the United States. Herndon et al. (2012) evaluated adherence among 18,456 children in the United States using Medicaid claims data. Adherence was lower in the black and Hispanic participants when compared to white participants. This trend was repeated in the study by Capo-Ramos et al. in 2014. They evaluated adherence among 4,262 children with Medicaid using prescription fill patterns. They also found that adherence was lower in the black and Hispanic participants when compared to the white participants.

Another contributory study by Martin, Olson, Mosnaim, Ortega, and Rothschild (2012) specifically examined 101 Puerto Rican children with asthma living in the United States. Overall, adherence was poor. It was determined that 69% of the children in the study did not

have well-controlled asthma in the preceding month. However, only 29% of them reported that they used a medication to control asthma, and had the medication in the house.

The studies consistently showed that adherence is higher in white children when compared to other races and ethnic backgrounds. Barriers to adherence may be different depending on the different populations.

External Factors

Socioeconomic status.

In 2012, Elkout et al. examined adherence among 3,172 children with asthma. Adherence was determined using medication possession. They did find an association between socioeconomic status and adherence. Socioeconomic status was determined using the Sottish Index of Multiple Deprivation (SIMD). Results that were between 0-5 indicated low socioeconomic status, and results that were between 6-10 indicated high socioeconomic status.

Among those with adequate adherence, 54% were of high socioeconomic status. The lower adherence observed in participants with lower socioeconomic status may be due to the higher costs associated with asthma. In 2010, Barnett and Nurmagambetov determined that asthma costs an individual approximately $3,259 annually including $1,680 in medication expenses.

Environment.

Herndon et al. (2012) also found an association between environment and adherence. Using Medicaid claims data, they found that among their 18,456 participants 35% of the participants living in rural areas had poor adherence. Poor adherence among participants living in urban areas was almost twice as much.

Health perception.

Herndon et al. (2012) showed that the higher participants perceived their health the lower their compliance. This study involved 18,456 children with asthma who were covered by Medicaid. Capo-Ramos et al. (2014) did not see this trend repeated in their research. They also evaluated children with asthma who were covered by Medicaid. Their study included 4,262 participants. They found no correlation between health perception and adherence.

Lack of motivation.

In 2014, Vella, Bezzina, and Urpani published data collected in a survey of children with asthma. There were 131 participants between the ages of 7-15. Among those who reported non-adherence, 76% reported that their lack of adherence was due to indifference. This study differs from the other studies that incorporate surveys into their research, because it gives the sole perspective of the older child with asthma, rather than data reported by caregivers.

Parental education.

In 2011, Koster et al. studied 527 children from the Netherlands between the ages of 4-12. Adherence in this study was self-reported. Results from this study showed that, among participants that reported good adherence, there was an equal distribution of parents with higher and lower levels of education. However, they did not specify what was considered a high education, and what was considered a low level of education. Another weakness was that adherence levels were reported subjectively (Schultz et al., 2012).

Capo-Ramos et al. (2014) did find an association between adherence and parental education. They evaluated adherence among 4,262 participants with Medicaid. Continued

adherence was more likely if parents had at least some college education. Parents were more likely to discontinue LTC medications if they completed no higher than high-school education.

This was supported by Vasbinder et al. in 2014. Their study included 87 participants in the Netherlands. Adherence was monitored electronically. Children had higher adherence if their parents had completed college or university education when compared with children whose parents had completed no higher than vocational education, 59% and 45% respectively.

Disease/Medication beliefs.

In 2011, Koster, Raaijmakers, Vijverberg, and der Zee evaluated adherence to ICs among 527 children in the Netherlands. They found an association between medication beliefs and adherence. Among those who reported good adherence, 67% highly believed that the medication was necessary. One weakness was the use of self-reports (Schultz, 2012). However, this concept has been reinforced by several other studies.

In 2012, Klok, Kaptein, Duiverman, and Brand examined the effect that medication beliefs had on electronically monitored adherence among 93 children in the Netherlands between the ages of 2-6. Overall adherence was high with a median of 92% adherence. They also found that high adherence was associated with medication beliefs. Parents were more adherent if they believed two things: the medication was necessary for their child, and there was little risk for harm.

This concept was also identified by Wijga et al. in 2014. Adherence to LTC medications was assessed in 229 participants. Reported adherence was higher when parents felt that the medication was important for their child. However, self-reports were again used (Schultz, 2012).

Klok, Kaptein, Duiverman, and Brand (2014) observed that parents were more adherent if they believed that their child needed the medication and the risk of harm was minimal. Non-adherence occurred if parents were concerned about the side effects of the medications. Those parents would intentionally give their child less medication when symptoms improved.

Schultz et al. (2012) evaluated 132 families, and adherence was electronically monitored. Parents were interviewed to determine barriers to adherence. Parents in this study reported that they intentionally stopped administering the medication to see if their child needed it. That supported previous data that indicated that adherence is improved when parents believe that their child needs the medicine.

Parental concerns about medications was also determined to affect adherence when Armstrong, Duncan, Stokes, and Pereira (2014) studied adherence among 43 preschoolers with asthma in the southern United States. The children included in this study were predominantly white and male. Adherence was determined using subjective data, and then compared to prescription fill patterns. Medication beliefs were determined using a questionnaire developed in prior asthma research. Data obtained showed that negative medication beliefs were associated with non-adherence. As negative medication beliefs increased adherence decreased.

Vella et al. (2014) assessed adherence among 131 children between the ages of 7-15 taking ICSs. Twenty percent of children who reported non-adherence reported that it was because they felt the medications were unnecessary. Eighteen percent of the participants also believed that it was okay to stop the medication in the summer, and an additional 7% reported that they reduced the dosage. According to Al-Muhsen et al. (2015), these children are three

times more likely to have uncontrolled asthma, and children with uncontrolled asthma are more likely to visit the ED. They provided the perspective of the older children, many of whom have taken responsibility for their own medication administration.

Contradicting all of the previous studies, Vasbinder et al. (2014) did not find an association with medication beliefs and adherence when they evaluated 87 children with asthma in the Netherlands. Results from this study did not show statistically significant adherence among participants whose beliefs ranged from skeptical to accepting.

Overall, most of the included studies emphasized the importance of assessing medication beliefs when planning care for children with asthma. In 2010, Zedan, Regal, Osman, and Fouda interviewed the parents of 100 children with asthma. Fifty-three percent of parents were concerned about medication side effects. HCPs need to educate parents and older children about the medications that they are taking and overcome this powerful barrier to adherence.

Family dynamics and planning.

In 2012, Schultz et al. published a study in which adherence to ICSs were unknowingly monitored electronically for 132 children with asthma. Parents that missed doses generally missed at least half of the prescribed doses. Parents were then asked about their adherence. Parents then identified reasons for their inconsistency.

The most frequent responses were due to forgetfulness, child refusal, or being too busy. Some parents reported that their children fell asleep prior to medication administration. Others reported that medication may not be administered properly when the child is with another

caregiver. These concepts identify the importance for the HCP to anticipate these problems, and assist with problem-solving and planning (Schultz et al., 2012).

In 2014, Klok, Lubbers, Kaptein, and Brand evaluated reasons behind medication adherence and non-adherence among children with uncontrolled asthma in the Netherlands. There were 135 families that participated in the study, and children were between the ages of 2-12. Researchers fist objectively monitored adherence electronically. Afterwards they interviewed ten families that had adherence above 75% and ten families with adherence below 75%.

In families with non-adherence there were a lot of the same reasons that have already been identified. Parents reported that they may forget to give a dose, or skip a dose when their child refuses it. Among families with higher adherence there was more planning. For example, parents would create a routine in order to avoid forgetting to give the child their medication (Klok, Lubbers, Kaptein, and Brand, 2014).

Capo-Ramos et al. (2014) also found an association between children non-adherence and family dynamics, although their results were different from those that were already discussed. Single-parent families, with three or more children, had a higher risk for non-adherence when compared to families that had two parents and less than three children.

This was studied to a lesser extent by Renov in 2014. There were 58 families included that were taking ICSs. The study found no statistically significant difference in adherence when comparing single parent families to dual parent families. However, this research did not examine the number of children in the families.

Armstrong et al. (2014) did not find a statistically significant correlation between parental stress and medication adherence when they studied the families of 43 preschoolers with persistent asthma.

HCPs should anticipate these potential problems. They also need to collaborate with families and identify any barriers to medication administration. This collaboration can help to increase adherence (Rohan et al., 2013).

Responsibility.

Klok et al. (2014) objectively monitored medication adherence among 135 children with asthma between the ages of 2-12. Afterwards they split participants into two groups. One group had adherence greater than 75%. The other group had adherence less than 75%. Researchers interviewed the families to determine reasons for non-adherence. They found that many older children were given the responsibility to take their own medications.

Families with additional stressors gave their children the responsibility at a younger age. Among the families that had adherence greater than 75% responsibility was given to older children gradually. Parents also continued to supervise medication administration. In situations where parental supervision caused conflict they would be more subtle about overseeing their child's medication administration (Klok et al., 2014).

Klok et al. (2014) also determined that in families with adherence less than 75% some parents were unaware of their child's non-adherence. Others relied on their doctor to intervene. The data showed that the shift in responsibility from parent to child can be hazardous time for

medication adherence. It should occur gradually, and parents should resume responsibility if the child is unable to maintain adherence.

This is supported by Rohan et al. (2013). Adherence among all of the children in the study improved with the exception of a nine-year old whose parent did not resume responsibility for medication administration when adherence began to decline. Adherence for this child continued to decline.

The positive effect of a gradual shift in responsibility is supported by Duncan et al. (2012). They examined the effectiveness of an intervention used to increase medication adherence in 48 children with asthma between the ages of 9-15. The purpose of the study was to determine if the gradual shift in medication responsibility using a teamwork approach between parents and older children would improve adherence.

Children were divided into three groups. Group one utilized the teamwork intervention led by therapists. This intervention involved teaching parents and children about development, independence, expectations, communication, and teamwork. At the beginning of the intervention children were supervised, and gradually medication responsibility was transferred depending on their level of adherence. Group two provided an educational intervention in which families were educated about asthma. Group three was the control group. Over the 20 weeks of the study adherence declined in all three groups. However, adherence in group one was the highest. Initially, it was 90%, and it was reduced to a low of 81% after 20 weeks. In group two adherence was 59%. It was gradually reduced to 33% after 20 weeks. Adherence in the control group was 67%. It gradually decreased to 37% after 20 weeks. Overall, the teamwork

promotion intervention resulted in the highest levels of medication adherence. This intervention shows that adherence can be maintained above 80% when the child gradually assumes responsibility for medication administration (Duncan et al., 2012).

Severity.

In 2010, Sawicki et al. studied adherence in 425 children with asthma who were prescribed ICSs. The study spanned five years, and adherence declined over the span of the study. Adherence was self-reported and classified as consistent, variable, intermittent, or none. After the first year, consistent adherence was determined to occur more in those with moderate to severe asthma.

These results were supported by Zhang, Taylor, Sazonov, Thomas, and Price in 2011. They included 2,220 children with asthma between the ages of 2-14. Adherence was determined using prescription fill patterns, and it was monitored for a year. Children with mild persistent asthma had the worst adherence. Fifty-five percent of them had discontinued medication by the end of the year. Adherence was better in children with moderate persistent asthma, and adherence was best in children with severe persistent asthma. Only 41% of them had stopped receiving medication by the end of the year.

These results were replicated by Klok, Kaptein, Duiverman, and Brand in 2014. They electronically monitored adherence in 81 children with asthma. Overall adherence in this study was high, between 74-95%. Adherence among children with mild intermittent symptoms was lowest, 74%. Adherence in children with uncontrolled moderate to severe symptoms was highest, 95%.

These studies have all determined that adherence improves as disease severity increases. This may be because medication is more likely to be perceived as necessary in children who are more symptomatic.

Exacerbations.

In 2013, Sloan, Gebretsadik, Wu, Michel, and Hartert examined adherence to ICSs among 51,725 children with asthma covered by Medicaid. During this five-year study, adherence was determined using prescription fill patterns. The researchers determined that 37% of ICS were dispensed at the same time that rescue medications were dispensed. Based on this data, they determined that adherence to LTC medications increased when there was an exacerbation, and was reactive rather than proactive.

Elkout, Helms, Simpson, and McLay (2012) evaluated adherence to LTC medications among 3,172 participants. They found an association between higher adherence and those who obtained greater than six rescue medications annually. Sloan et al. (2013) determined that 37% of LTC medications were dispensed at the same time that SABAs were dispensed, and adherence was triggered by an exacerbation. The higher adherence that was observed by Elkout et al. is likely because children receiving greater than six rescue medications annually have more exacerbations than those who require less.

Interventional

Caregiver-Family communication.

Communication and problem-solving may contribute to increased adherence to LTC medications over time. This was demonstrated by Sleath et al, in 2012. They examined 259 children between the ages of 8-16 with persistent asthma. First, they recorded a visit with the

family and their HCP. They were trying to determine if HCPs complied with national guidelines that recommend that family input be included when developing a plan of care.

They found that the child's input was only asked for in 8% of visits and the caregiver's input was only asked for in 9% of the visits. A month after the visit the family was interviewed to assess adherence. Adherence was self-reported. Researchers found that there was statistically significant higher adherence in the families if HCPs asked for their input when developing the plan of care (Sleath et al, 2012).

This was also demonstrated by Rohan et al. in 2013. Pediatric psychologists taught HCP how to provide feedback about ICS adherence and problem-solve with families. Eleven families were included in the study and children were between the ages of 5-14. Families were divided into the intervention group in which HCP incorporated their training about adherence feedback and problem-solving. The other participants were divided into the control group.

In the intervention group, routine asthma care involved feedback about electronically monitored adherence, identification of barriers to medication administration, and problem-solving. Adherence increased from a baseline adherence of 31% to an intervention adherence of 57%. After completion of the intervention adherence dropped to 26% (Rohan et al., 2013).

Adherence and problem-solving can be an effective tool to increase adherence. This is supported by Wijga et al., (2014) who reported that parents reported higher adherence when they felt that had received enough information from their HCP. However, enhanced communication cannot be used independently to increase adherence above 80%.

Asthma knowledge.

In 2012, Duncan et al. instilled an educational intervention to determine if it had any effect on adherence. Participants were between the ages of 9-15 and adherence was electronically monitored over 20 weeks. In children who received an educational intervention, adherence gradually declined from 59% to 33%. In the control group, adherence gradually declined from 67% to 37%. However, the study did not evaluate the knowledge of the participants.

In 2014, Mosnaim et al. examined adherence to ICSs among minority adolescents with asthma. There were 93 participants between the ages of 10-16. Adherence was electronically monitored over two weeks and children were divided into a group that took more than half of their prescribed medication and a group that took less than half of their prescribed medication. Children who took more than half of their medication scored higher on a questionnaire used to determine knowledge about ICSs.

This was also demonstrated by Wijga et al. in 2014. The study included 229 participants and their families. A questionnaire was used to determine parental knowledge about ICSs. Reported adherence was 84% for parents who knew that the ICSs should be taken daily. Reported adherence was only 25% for parents who did not now that the ICSs should be taken daily. Unfortunately, adherence in this study was self-reported (Schultz et al., 2012).

In 2010, Klok, Brand, Bomhof-Roordink, Duiverman, and Kaptein evaluated adherence among children with asthma who were going to primary or secondary care facilities. For the purposes of this study primary care represented a general pediatric facility, and secondary care

represented a pediatric asthma facility. There were 44 participants, and children were between the ages of 2-12.

Reported adherence was higher in the secondary group. Parents in the secondary group believed that the medication was necessary to suppress asthma and prevent exacerbations. Parents in the primary group believed that the medication would lose its effectiveness if given regularly. Parents in the secondary group knew more about asthma medications which may contribute to their increased adherence (Klok, Brand, Bomhof-Roordink, Duiverman, and Kaptein, 2010).

These studies suggest that knowledge about LTC medications used to manage asthma may be superior to general asthma knowledge in increasing adherence.

White coat adherence.

Keemink, Klok, and Brand examined white coat adherence in 2014. White coat adherence is described as adherence that increases in the time period directly preceding a scheduled visit to the doctor. The study was conducted in the Netherlands, and there were 78 children included.

Participants were between the ages of 2-6 and taking ICSs for asthma. Adherence was electronically monitored, and the median adherence was 85%. In 22% of the participants adherence did increase in the week prior to the scheduled outpatient visit. However, adherence also decreased for 21% of the participants in the week prior to the visit. This study shows that adherence may increase or decrease directly before a scheduled visit to the doctor (Keemink,

Klok, and Brand, 2014). White coat adherence can account for the increase. However, there was no explanation about the decreased adherence.

Specialty care.

In 2010, Klok et al. evaluated adherence among children with asthma who were going to a general pediatric facility and children who were going to a pediatric asthma facility. There were 44 participants, and children were between the ages of 2-12. Reported adherence was higher in the group that went to the asthma clinic.

Bollinger et al. (2013) also evaluated how a specialist may affect adherence. There were 53 participants with persistent asthma included in this study. They were between the ages of 2-8. The majority of the participants were black. There were more males and most of the participants had Medicaid. Prescription fill patterns were used to determine adherence. They determined that 30% of the medications prescribed by the allergist were never filled. However, non-adherence was at least 10% lower in those who saw other HCPs.

Both of these studies suggest that adherence is higher in children who see specialists rather than primary care providers. However, one study reported that medication knowledge was higher in the group that saw the specialist (Klok et al., 2010) which may be the main factor contributing to the increased adherence.

Number of prescriptions.

In 2010, Pando et al. examined adherence to ICSs in children between the ages of 5-15. There were 2,355 participants in their Canadian study. They determined adherence based on the amount of medication obtained compared with the amount of medication prescribed. Almost half of the participants were not prescribed a refill. Among those who were given one

prescription adherence was 100%. Adherence dropped to 61% for participants who were given 2-6 prescriptions. Those who were given greater than seven prescriptions had the lowest adherence of 37%.

Based on this study, the higher the amount of prescriptions the lower the adherence. Data is consistent with other studies that show a gradual decrease in adherence over time. Healthcare providers should schedule follow-up visits periodically in order to assess adherence, and determine if there are any barriers or problems with the medications that need to be overcome.

Asthma action plans.

An asthma action plan (AAP) is a written document that is created by a healthcare provider. It is an individualized medication plan that is either symptom based, peak-expiratory flow based, or both. Medication instructions are given to the patient and the family dependent on symptoms or PEF. National guidelines recommend that all patients with asthma receive an AAP. This plan should be updated at every opportunity (NHLBI, 2007).

In 2011, Ducharme et al. examined how receipt of an AAP affected adherence to ICSs over 28 days. There were initially 219 participants between the ages of 1-17. The majority of the participants were white, and there was an even distribution of public and private insurance. All of the participants were not prescribed ICSs over the entire timespan, and results were based on the amount of time medications were prescribed.

Participants were divided into two groups. The first group received a prescription and an AAP. The control group only received a prescription. Adherence was monitored using dose

counters. Over the course of the 28 days there was higher adherence in the group that received the asthma action plan, and the gap increased over time.

Over the first two weeks, adherence was 89% for those with the AAP compared to 86% in the control group. Over the last two weeks adherence was 79% for those with the asthma action plan compared to 25% for those in the control group (Ducharme et al., 2011). Based on these results, an AAP may be a key tool in increasing adherence, but it cannot be used independently to maintain adherence above 80%.

Medication regimens.

There are several studies that suggest that adherence varies depending on medication. In 2011, Zhang, Taylor, Sazonov, Thomas, and Price examined adherence among children with asthma in the United Kingdom. There were 2,220 children included, and they were between the ages of 2-14. They used prescription fill patterns to monitor adherence for a year. Adherence was best for children taking fluticasone. At the end of the year 59% of children were still receiving medication.

Lesser adherence was observed among children taking beclomethasone. At the end of the year 45% of children were still receiving this medication. Budesonide had the least adherence. At the end of the year there were just 42% of children still receiving medication. Out of all of the included ICSs fluticasone had the best adherence (Zhang, Taylor, Sazonov, Thomas, and Price, 2011).

Herndon, Mattke, Cuellar, and Hong (2012) examined LTC medication adherence among 18,456 children with asthma. Children were Medicaid recipients and between the ages of 2-18.

Adherence was determined using prescription fill patterns. Data obtained from this study showed that medication adherence was higher among children taking leukotriene modifiers when compared to children taking ICSs. Adherence was 28% for those taking leukotriene modifiers and 20% for those taking ICS. These results were consistent with those of several other studies.

In 2012, Spray examined adherence to LTC medications among 244 families that had a child with asthma between the ages of 7-15. Spray also found varying adherence depending on the type of medication prescribed. Adherence for ICSs was 37%, and adherence for leukotriene modifiers was 56%.

Elkout et al. (2012) also had similar results when they did a study that evaluated how medications may affect adherence. Adequate adherence was defined as medication possession of 80-120% of the prescribed regimen. Thirty-nine percent of participants taking leukotriene modifiers had adequate adherence. Adherence was lower among participants taking LABSs in conjunction with ICSs. Less than 30% of them had adequate adherence. The worst adherence was observed among participants taking ICSs as monotherapy. Only 15% had adequate adherence.

These results replicated by Durcharme, Noya, Allen-Ramey, Maiese, and Blais in 2012. They used claims data to monitor adherence among 227 children with asthma between the ages of 2-17. Children included in the study were taking either ICSs or leukotriene modifiers. Fifty-one percent of the prescribed ICSs were claimed. However, 74% of the leukotriene modifiers were claimed. Once again, there was higher adherence among those taking leukotriene modifiers.

Bollinger et al. expanded on this in 2013. They evaluated adherence using prescription fill patterns for 53 children between the ages of 2-8. They found that 40% of children prescribed ICSs in conjunction with LABAs never filled their initial prescription. For those prescribed monotherapy ICSs 31% never filled their initial prescription. Consistent with previous literature, just 21% of those prescribed leukotriene modifiers did not fill their initial prescription. This data shows that there is a medication regimen with less adherence than ICSs: ICSs with LABAs.

Capo-Ramos et al. in 2014 also evaluated adherence with different medication modalities. They included 4,262 children with asthma between the ages of 2-17. Children were all enrolled in Medicaid, and adherence was determined using prescription fill patterns. They found that adherence was greater in participants who were prescribed ICSs in conjunction with leukotriene modifiers when compared to other medications.

Data in these studies provide evidence that the prescribed medication does affect medication adherence among children with asthma. Adherence is consistently highest for regimens that contain leukotriene modifiers. Adherence is consistently lowest for monotherapy ICSs. This represents a difficult situation for HCPs, because ICSs are the most effective medication for treating persistent asthma (NHLBI, 2007).

Lower adherence for ICSs may be due to negative medication beliefs which do contribute to non-adherence (Armstrong et al., 2014). Concerns about steroids among the parents of children with asthma may be as high as 53% (Zedan et al., 2010). That represents a significant barrier that HCPs will need to anticipate and overcome to improve adherence.

Symptom Diaries

In 2014, Arga, Sahbaz, Bakirtas, Turktas, and Demirsoy incorporated the use of symptom diaries into asthma management. There were 340 children between the ages of 6-17 that were included in the study. They found that children who kept symptom diaries were more likely to take LTC medications regularly. Eighty-one percent of the children who kept symptom diaries took medications regularly as opposed to 58% of the children who did not keep symptom diaries. One significant weakness of this study is that medication adherence was self-reported (Schultz et al., 2012).

Technology.

In 2012, Feldman et al. evaluated the effect of peak expiratory flow (PEF) feedback among minority children between the ages of 7-15 living in the Bronx, New York. PEF is an objective way to monitor lung function. Children received an electronic peak flow device that gave audible reminders when it was time to check PEF. In the intervention group, children estimated their PEF prior to using the device, and data was stored. Afterwards, they used their device and compared their estimate to their actual PEF. Children in the control group were unable to see their PEF. The entire study included 192 children.

Adherence to ICSs was monitored electronically in 95 of the included children. In the intervention group that used the electronic peak flow device adherence to ICS was 49%. In the control group the average adherence was 28%. Incorporating the use of this technology increased adherence in minority children who had lower rates of adherence when compared to white children (Feldman et al., 2012).

Giselle et al. (2013) evaluated a different kind of technology in an attempt to improve medication adherence among minority adolescents between the ages of 11-16 taking ICSs.

There were 34 participants, and they were divided into an intervention group and a control group. The intervention group received mp3 players and attended weekly peer group support meetings. After the meeting, the adolescents recorded supportive messages that were incorporated into the mp3 playlist. The intervention lasted for 10 weeks.

Adherence gradually declined from baseline in the intervention group and in the control group. At five weeks adherence for the intervention group was 19%, and adherence for the control group was 16%. At ten weeks adherence for the intervention group was 7%, and adherence for the control group was 14% (Giselle et al., 2013).

This technology was not shown to be effective in increasing adherence. There are a couple of factors that may have contributed. One, in particular, is that the intervention depended on children listening to the supportive messages on their mp3 players. Children who skipped over the messages or did not listen to their mp3 players at all would not have benefitted from this intervention. While this intervention was not successful, there are some more recent studies that have been able to get better results.

In 2015, Bender et al. conducted a randomized control trial to determine if using voice recognition phone calls would improve adherence to LTC medications used to manage persistent asthma. There were 899 participants between the ages of 3-12. Participants were divided into the intervention group and the control group.

The intervention group received a series of phone calls that were triggered when medication refills were two weeks overdue. The phone calls reminded parents about the importance of medications, asked if they needed some assistance with medication refills, and

also gave them the option of contacting a pharmacist or an asthma nurse with questions. The control group did not receive phone calls. The study was continued for two years. Adherence was determined by prescription fill patterns.

Adherence in the control group was 36% and adherence in the intervention group was 45%. The use of voice recognition phone calls did improve adherence, and 84% of parents who took the survey said that their child's asthma was better controlled because of the intervention (Bender et al., 2015).

In 2015, Chan et al. examined adherence to ICS among children between the ages of 6-15 in New Zealand. The researchers conducted a randomized control trial that included 220 participants. Children in the intervention group received an inhaler that had audiovisual reminders. The inhaler was programmed to know when the LTC medications should be taken. If the medication was taken within six hours of its scheduled time there was no reminder. However, if it was not taken a ringtone reminder would play. The ringtone would stop after the medication was taken or after 15 minutes. Children in the control group did not receive the electronic reminders.

The average adherence for the intervention group was 84%. The average adherence for the control group was 30%. Research has shown that children with well-controlled asthma had a median adherence above 80% (Klok et al., 2014), and this intervention was able to change behavior enough to achieve those results. This study suggests that technology may play a pivotal role in changing the way that we manage asthma in the future.

Summary

A summary of the findings is presented in Table 2.

Table 2 Findings

Internal	External	Interventional
Age Older adolescents have less adherence **Sex** Females have more adherence **Race/Ethnicity** Adherence is less among blacks and Hispanics	**Socioeconomic Status** Adherence is higher among those with higher SES **Environment** Adherence is lower in urban areas **Motivation** Indifference contributes to non-adherence **Parental Education** Children whose parents have higher education have higher adherence **Disease Beliefs** Adherence is higher if parents believe that their child needs the medication for control **Medication Beliefs** Adherence is lower among those who have negative beliefs about the medications **Family Dynamics/Planning** Adherence was higher in families that planned medication administration and were able to problem-solve **Responsibility** Adherence was higher among families that gradually gave responsibility to older children, and supervised medication administration **Severity** The more severe the disease the higher the adherence Exacerbations Adherence increases during an exacerbation	**Communication** Enhanced HCP-family communication increases adherence **Medication Knowledge** Knowledge about medications increases adherence **Doctor Visits** Adherence may increase or decrease just prior to a scheduled doctor visit **Specialist** Adherence was increased in those who saw a specialist **Medications** Adherence is higher among those prescribed leukotriene modifiers and lowest among those prescribed ICSs **Multiple Prescriptions** Adherence declines over time when multiple prescriptions are given at once **Asthma Action Plans** AAP increase adherence **Symptom Diaries** Symptom diaries may increase adherence **Technology** Incorporation of some types of technology have increased adherence

Discussion

It is imperative that all children with persistent asthma receive guideline-based care. However, the internal and external factors identified can help HCPs recognize when additional barriers can be anticipated. This foresight can enable HCPs to increase adherence and overall quality of life for children with asthma. It can also lead to reduced costs associated with emergency care utilization.

Interventional factors identified can help HCPs determine what methods are effective and what methods are ineffective before making any changes to current practice.

Communication

Multiple studies have concluded that improved communication between families and HCPs can increase adherence. That is discussed frequently in the subsequent sections.

Time

Multiple studies have suggested that adherence declined over time. One study reported that the more prescriptions provided initially, the lower the adherence. HCPs should schedule follow-up appointments to prevent this trend, especially after a new medication regimen is initiated. During the follow-up HCPs can reassess control, reiterate the importance of the medications, and also determine if any new barriers have been identified.

Race/Ethnicity

Data reported that there was less adherence among black and Spanish children when compared to white children. HCPs should anticipate cultural barriers among these populations. They should anticipate differing perceptions of health and healthcare. For this reason it is important for HCPs to make sure that families agree with the plan of care. If there are any

cultural discrepancies HCPs should compromise and work on a plan that everyone can agree on. HCPs should also anticipate language barriers in families if English is not a first language or not spoken at all. In these situation a translator should be used.

Socioeconomic Status

The data indicated that medication adherence was lower in families that had a lower SES. These families may see money as a barrier, and HCPs should know what community resources are available to help these families with medical expenses as well as transportation to obtain the prescribed medications.

Urban or Rural Environment

One study reported that adherence was lower in urban areas when compared to rural areas. This is possibly due to the more established relationship that rural families have with their HCPs. Communication may be more effective, and better HCP-family communication has been shown to have a positive effect on adherence. Particularly in urban areas, HCPs should work to establish relationships with their families and improve communication.

Parental Education

The data also reported that medication adherence was lower in families if parents had lower levels of education, although some of the data did not specify what was considered lower levels of education. This may be directly related to SES. If parental education is higher families are more likely to have higher SES and not perceive money as a barrier. If HCPs determine that money is preventing families from adhering to medication regimens then they should connect the family with local resources, as mentioned before. If knowledge and understanding is the reason for non-adherence then they should provide education.

Family Dynamics

Family dynamics is about planning. Objective and subjective data was included on this topic. Families had less adherence if they were single-parent families with at least three kids. Other families had less adherence if they forgot medication or had problems giving the medication, such as child refusal. HCPs can help the families plan medication administration and overcome these barriers. For example, they might suggest that families set an alarm if forgetfulness is the problem.

Older Adolescents and Responsibility

Some of the data suggested that toddlers had less adherence when compared to older children. However, there were some studies that did not support this. More data needs to be obtained to form a conclusion.

The data did consistently point out that older adolescents have less adherence when compared to younger adolescents and children. Data from subjective studies also found that adherence declined when parents gave responsibility to older children and adolescents without supervision. In order to overcome this barrier it is suggested that parents be instructed to gradually give responsibility to older children and adolescents and to maintain supervision. It is also important for HCPs to incorporate these children when educating families about medications and making the treatment plan, because they are also responsible for medication administration.

Motivation and Disease Beliefs

These factors are related, and they can all be affected by the HCP to a certain extent. Objective and subjective data was obtained for these topics. Children who were not motivated to take their medications stopped taking them. If parents felt that their child did not need the

medication they did not give their child the medication. HCPs should determine if these children do need the medication to obtain control. If they do then HCPs should educate them about how the medication can improve quality of life and decrease the number of exacerbations. Understanding may improve motivation and parents may agree that their child does need the medication.

Medication Knowledge and Beliefs

These factors are also related and can also be affected by the HCP. Objective and subjective data was also obtained for these topics. Parents in multiple studies expressed concerns about the medications. Adherence was improved if parents knew more about the medications. HCPs should anticipate that if families do not have concerns about the medications they will develop concerns after consulting other sources. That is why HCPs should educate all families about the medications that they are prescribed even if there are no questions asked. Many of the parents did not know that LTC medications should be taken regularly rather than initiated when there is an exacerbation.

Medications

Data from the studies consistently suggest that adherence is higher among medication regimens that contain leukotriene modifiers and lower among regimens that contain ICSs. That supports the data obtained from objective and subjective studies that indicate that parents do not feel comfortable giving their children ICSs. Unfortunately, data also suggests that ICSs are more effective than leukotriene modifiers. One promising fact is that families with more education about ICSs did have higher adherence. HCPs should specifically educate families about these medications, and alleviate any fears or misgivings.

Severity and Exacerbations

Data suggests that adherence increases during an exacerbation and when children have more severe asthma. These children are more symptomatic, and families see that the benefits of administering the medication outweigh the risks. However, HCPs can teach families that it is possible to prevent these exacerbations and control the symptoms when medication is given regularly.

Asthma Action Plan (AAP)

Data suggest that AAPs were beneficial in improving adherence. AAPs are recommended according to national guidelines and should be updated by HCPs at every opportunity.

Specialist or Primary Care

Data suggests that adherence improved when families went to a specialist rather than a general pediatric practitioner. Also, one subjective study reported that knowledge about the medications was also greater if families went to a specialist. The increased adherence may be because parents were more knowledgeable about the medications which has also been shown to increase adherence. HCPs in any setting should ensure that families are knowledgeable about their medications and plan of care.

Symptom Diary

Data suggests that symptom diaries were beneficial in improving adherence. However, the only data available was based on self-report. It is recommended that more data be obtained before incorporating symptom diaries into patient care.

Technology

Peak flow meters that electronically measured peak expiratory flow after an estimate were reported to have a positive effect on adherence. MP3 players with recorded messages providing encouragement did not have a positive effect on adherence. Data reported that voice recognition phone call reminders and inhalers with electronic monitors did have a positive effect on adherence. HCPs should incorporate technology into current practice if it is practical.

Recommendations for Current Practice

It is recommended that HCPs in inpatient and outpatient settings incorporate this four-step process into management of children with persistent asthma to overcome the majority of the barriers that have been identified. To ensure that all of these steps occur routinely it may be beneficial to use a prompting form. An example of a prompting form can be found in the appendix.

1. Assess and Educate

In this step, HCPs should assess asthma severity and control using guidelines established by the NHBLI. They should also assess knowledge about previously prescribed LTC medications and administration technique if applicable. HCPs should also assess adherence to LTC medications used to control persistent asthma. If relying on patient or caregiver report, HCPs should assume that adherence is over-reported. If patients that are prescribed LTC medications have poor asthma control, HCPs should assume that poor adherence is a factor. They should also assess for any barriers that may contribute to poor adherence. As HCPs are assessing, they should also be educating, if appropriate.

2. Collaborate

This step includes planning or revising a current plan. This is where the asthma action plan can be created. HCPs should collaborate with the families when making the plan because parents consider themselves to be the ultimate decision makers when it comes to caring for their children. If older children or adolescents are responsible for medication administration, they

should be included in creating the plan. HCPs should compromise if there are any disagreements.

3. Problem-Solve

In the first two steps, barriers to adherence may be identified by families. In the third step, problem solving should be incorporated into the plan. Identify possible solutions to any obstacles that have been identified. It may be helpful to write this out for parents to reference later. Know the local resources available for parents who cannot afford medications or do not have transportation to pick up medications.

4. Follow-up

Anything can happen after the family leaves. That is why it is important for HCPs to make follow-up appointments at the time of the visit. Adherence may decline after the visit for innumerable reasons, and it is recommended that adherence be assessed regularly. Also, a follow-up appointment is necessary for HCPs to determine if the prescribed regimen is effective.

By using these four steps collectively HCPs can potentially overcome most of the barriers to adherence that were identified in this review of literature.

Recommendations for Future Practice

In the future, it is recommended that HCPs use data obtained from electronic inhalers to objectively monitor adherence rather than relying on reported adherence to modify plans. The reasoning is simple. If asthma control is poor, and medication adherence is also poor, changing the medication regimen is not going to solve the problem. In order to determine if adherence is the problem, HCPs need to be able to monitor adherence objectively.

Electronic inhalers are more expensive than traditional inhalers. However, the objective data obtained from the electronic inhalers can help HCPs identify that there are barriers to medication adherence even if the families do not readily communicate this. HCPs could use this information to possibly identify barriers to adherence. If they are able to improve adherence asthma control will improve as will quality of life. Costs from asthma care will also decrease. Overall, the benefits outweigh the costs.

Recommendations for Future Research

This review has identified different factors that affect adherence to LTC medications used to manage asthma in children. However, it has not effectively determined why all of these factors affect adherence. Future research should evaluate this.

It is recommended that some of the studies presented be repeated to validate the results. A study should be done to see if symptom diaries improve adherence when adherence is monitored objectively rather than through self-report. It is also recommended that the study that incorporates inhalers that use audio and visual reminders be repeated on a larger scale and with various demographics to make the results more generalizable.

Future research should also evaluate the effectiveness of using the suggested four-step plan to improve adherence to medications.

Limitations

Many research studies excluded participants who did not speak English. This is a limitation because non-adherence caused by cultural or language barriers may be overlooked because those participants were excluded. Also, each study included had its own unique criteria for inclusion. Some studies focused specifically on minorities while other studies focused primarily on the Medicaid population. This increased the generalizability, but it decreased the strength of the comparisons.

Another limitation is that the different studies also had varying measurements of adherence. One study may define adequate adherence as greater than 48% whereas another study may define adequate adherence as greater than 80%. In many studies adherence was determined based on prescription fill patterns. One weakness to that is that receipt of medication does not guarantee administration of the medication. Adherence is likely over-reported in those studies.

Another limitation is that different studies also defined statistical significance differently. One study may have described statistically significant data as $p=<0.05$, and another study may described it as $p=<0.01$. This decreased the strength of the comparisons as well.

Appendix: Example of a Prompting Form That Can Be Used by Healthcare Providers Caring for Children With Asthma

MY NAME IS:
MY Health Care Provider is:

ASTHMA

ASSESSMENT

- Are my symptoms controlled?
- Am I able to play and exercise without having trouble breathing?
- Am I sleeping well?
- Do I have any concerns about the medicines?
- Do I have any problems taking the medicines?

My Asthma is:

- ☐ Intermittent
- ☐ Mild Persistent
- ☐ Moderate Persistent
- ☐ Severe Persistent

My Control Is:

- ☐ Well Controlled
- ☐ Not Well Controlled
- ☐ Poorly Controlled

PLAN

I have no symptoms I can play and exercise I am sleeping well	I have some symptoms I can play and exercise most of the time I am waking up at night sometimes	I have symptoms often I can play and exercise some of the time I am waking up at night often	My symptoms do not stop I cannot play or exercise at all I cannot sleep
I will take: at this time:	I will take: at this time:	I will take: at this time:	I will take: at this time:
I will take: at this time:	I will take: at this time:	I will take: at this time:	I will take: at this time:
			Contact your healthcare provider, and for emergencies call 9-1-1

CHECKLIST

- ☐ I know why my medicine is important
- ☐ I know how my medicines work
- ☐ I know when to take my medicine
- ☐ I can use my inhaler the right way
- ☐ I understand this plan
- ☐ I agree with this plan

PROBLEM-SOLVE

- ☐ I know whose responsibility it is
- ☐ I know where to get my medicine
- ☐ I have access to transportation to get my medicines
- ☐ I have enough money to pay for my medicines

FOLLOW-UP

My next appointment is:

_____

If I have any problems with my medicines or questions I can call:

_____

Designed by Brittany Bowks

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