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## Determinants of adherence to inhaled corticosteroids in children with asthma

Klok, Teunis

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# Determinants of adherence to inhaled corticosteroids in children with asthma

**Ted Klok**

Visit <http://www.tedklok.nl/> for updates and personal information

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**Determinants of adherence to inhaled  
corticosteroids in children  
with asthma**

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Promotores:

Prof. dr. P.L.P. Brand  
Prof. dr. A.A. Kaptein  
Prof. dr. E.J. Duiverman

Beoordelingscommissie:

Prof. dr. A.M. van Dulmen  
Prof. dr. J.C. de Jongste  
Prof. dr. G.H. Koppelman

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# 1

## Introduction



## **INTRODUCTION**

Asthma is the most common chronic disease of childhood, with an increasing prevalence worldwide over the last decades.<sup>1,2</sup> The keystone of current asthma management is the regular use of inhaled corticosteroids (ICS), the effectiveness of which has been shown by large trials, starting from the seventies of the last century.<sup>3</sup> Although these studies were widely confirmed, physicians and patients were slow to adopt the use of ICS, perhaps because their effects on the airways were delayed compared with those achieved with bronchodilators.<sup>3</sup> However, over time, it became clear that ICS were effective in asthma treatment and safe relative to the use of systemic corticosteroids. Therefore, all evidence-based asthma guidelines now recommend the prescription of ICS to children with persistent asthma. Despite the effectiveness and widespread use of ICS, many asthmatic children continue to suffer from uncontrolled asthma.<sup>4</sup> Because poor adherence to ICS is the rule rather than the exception (table 1),<sup>5,6</sup> this is thought to be a major cause of the limited effectiveness of ICS in achieving asthma control in most children.

Improving adherence to ICS in children with asthma probably is the most effective method through which health care providers can reduce the burden of uncontrolled asthma. Knowledge of the reasons for such poor adherence, however, is required to improve adherence. Therefore we designed a series of studies on determinants of adherence to ICS in children with asthma. This thesis reports the results of these studies. In this introduction, I will provide a broad overview of the state of research on adherence in paediatric chronic conditions, based on work summarized in several reviews on adherence.<sup>7-11</sup> The introduction will be followed by a description of the theoretical framework underlying this thesis. At the end of this chapter, the scope of this research project is presented in more detail together with the further outline of this thesis.

## **ADHERENCE: A DEFINITION**

Adherence to a medication regimen is generally defined as the extent to which the amount of medication patients take corresponds with agreed recommendations from

a health care provider.<sup>5</sup> Children with persistent asthma are recommended to use ICS daily throughout the year as a preventer medicine.<sup>12</sup> When parents of those children administer the medication once daily instead of a recommended two doses per day, adherence is 50%. A child whose parents decide to administer the medication only in episodes with symptoms (instead of the whole year), for example for 20 weeks annually, will have an adherence of  $20/52 \times 100\% = 38\%$ . These two different patterns of non-adherence behaviour illustrate the multi-faced character of non-adherence (table 2). The term adherence, therefore, does not hold any explanation of the pattern and reasons of medicine taking behaviour of patients (and their parents), and is intended to be a non-judgmental statement of fact rather than a declaration of blame of the patient or parent.<sup>9</sup>

**Table 1. Overview of adherence studies in asthmatic children using electronically measurement of medication use.**

First author year	Sample size	Age (yrs)	Study duration (months)	Correlates/predictors of adherence*	Adherence rates
Bender <sup>23</sup> , 2000	27	7-12	6	Patient related factors	Mean 50%
Berg <sup>24</sup> , 2007	48	8-12	0,5	Patient and Asthma related factors, <i>Child's perception of hope</i>	Median 71%
Burgess <sup>25</sup> , 2008	51	2-17	1	Patient related factors	Median 71%
Celano <sup>26</sup> , 2010	143	6-11	0,5	Patient related factors	Mean 57%
Fiese <sup>27</sup> , 2005	72	5-18	12	Patient related factors	Not reported
Gibson <sup>28</sup> , 1995	29	1-5	2	Patient and Asthma related factors	Median 77%
Ho <sup>29</sup> , 2003	155	7-17	12	Patient and Asthma related factors	Mean 50%
Jentzsch <sup>30</sup> , 2012	102	5-14	3	Asthma related factors	Median 44%
McNally <sup>31</sup> , 2009	63	5-17	12	Asthma related factors	Mean 33%
McQuaid <sup>32</sup> , 2003	106	8-16	1	Child's reasoning about asthma	Median 48%
Modi <sup>33</sup> , 2006	36	6-13	3	Patient and Asthma related factors	Not reported
Schultz <sup>34</sup> , 2012	132	2-6	12	Qualitative assessment of correlates	Median 60%
Vasbinder <sup>35</sup> , 2012	90	1-11	3	Patient related factors and <i>medication beliefs</i>	Mean 49%

\*Correlates and predictors of adherence divided into:

1. Patient related factors such as socio-economic status, ethnicity, family routines or knowledge about asthma.
2. Asthma related factors such as asthma control and health utilisation.
3. Parental views or child's perspectives about asthma or treatment in italics in the table

**Table 2. Different patterns of non-adherence (adapted from<sup>21</sup>)**

erroneous non-adherence	Caused by poor instructions by health care providers or insufficient understanding of the treatment rationale on the part of the patient.
unplanned non-adherence	Related to barriers to adherence such as child-raising issues, limited family (medicine taking) routines and lack of motivation.
intentional non-adherence	Refers to patients who deliberately choose not to follow the doctor's recommendations.

## ADHERENCE: THE PROBLEM

Low adherence with prescribed treatments is very common, in particular with long-term therapies. Typical adherence rates for prescribed medications are about 50%, and rates of adherence among patients with asthma range from 30% to 70% (table 1).<sup>5</sup> Poor adherence to long-term therapies severely compromises the effectiveness of treatment and accounts for substantial worsening of disease, death, and increased health care costs.<sup>8</sup> It is clear that the full benefit of the many effective medications that are available (e.g. ICS in children with asthma) will be achieved only if patients follow prescribed treatment regimens reasonably closely. There is growing evidence to suggest that because of the alarmingly low rates of adherence, increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatment.<sup>5</sup> Without a system that addresses the determinants of adherence, advances in biomedical technology will fail to realize their potential to reduce the burden of chronic illness.<sup>5</sup>

## IMPROVING ADHERENCE: THE EVIDENCE

Studies on interventions to improve adherence to long-term therapies have shown only small, if any, improvement in adherence, with only a minority of interventions leading to improvement in at least one treatment outcome.<sup>9</sup> Almost all effective interventions improving adherence to long-term therapies were complex and, therefore, costly.<sup>8,10</sup> In asthma, educational interventions alone are insufficient to promote adherence in children and adolescents.<sup>10</sup> Incorporating a behavioural component (e.g. monitoring and goal setting, reinforcing medication taking with rewards, problem solving and linking medication taking with established routines) to adherence interventions is needed to increase potential efficacy.<sup>10</sup> The disappointing effects of many adherence interventions, combined with the slow progress adherence research has made over thirty years, has motivated researchers to delve further into the reasons why some adherence interventions are effective and others are not, the underlying theoretical frameworks which might help to explain these differences in efficacy, and what research and development is needed to develop more effective interventions and health

care practices to optimize adherence.<sup>7</sup> In a comprehensive review of reviews on adherence, van Dulmen and coworkers noted that only two reviews included studies with a follow-up of at least 6 months. This limited the authors' ability to draw meaningful conclusions on interventions capable of fostering long-term improvements in adherence. Together with the complexity of many adherence interventions and the lack of studies explicitly comparing components of adherence interventions, effective components within promising theories could not be identified.<sup>7</sup> This may also be related to the multi-faceted character of non-adherence which is not taken into account in most adherence studies (table 2).<sup>13</sup> Because of the different forms of non-adherence, probably no single theoretical framework can explain the non-adherence phenomenon.<sup>13</sup> Therefore, experts encouraged a more fundamental shift in focus, moving away from conceptualizing non-adherence as a fault of the patient. Future adherence studies should focus on patients' perspectives and the support needed by patients to find their way in self-management: 'patients should be supported, not blamed'.<sup>5,13</sup> This concept of patients self-managing their illness is discussed in the next section, together with a theoretical framework that takes the role of patients' perspectives into account.

## **ADHERENCE, A PERSPECTIVE OF SELF-MANAGEMENT AND SELF-REGULATION**

Self-management is the key to successful management of chronic illness. It can be estimated that an 'average' patient will have direct face-to-face contact with a health professional in the health care system about one hour per year, which means that during the other 8759 hours of the year the patient has to manage his or her illness without health care providers.<sup>14</sup> Barlow and colleagues have defined self-management as follows:

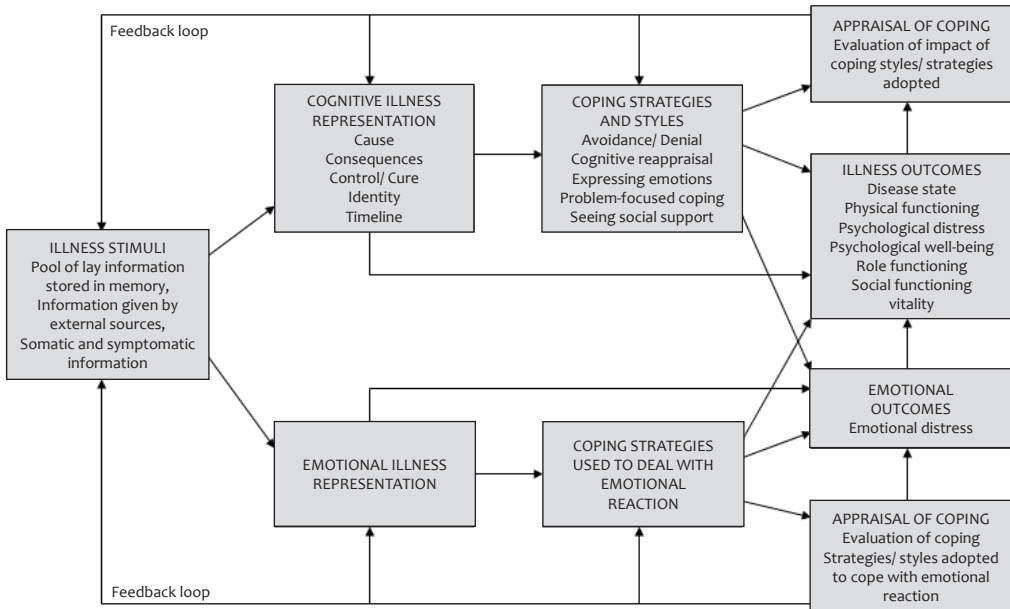
*"... the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and life style changes inherent in living with a chronic condition. Efficacious self-management encompasses ability to monitor one's condition and to effect the cognitive, behavioural and emotional responses necessary to maintain a satisfactory quality of life."<sup>15</sup>*

Self-management skills are diverse and include behaviours such as gathering information, managing medication (including adherence), symptoms and psychological consequences, adjusting lifestyle, mobilizing and drawing on social support, and communicating effectively.<sup>14</sup>

Recent research on self-management and adherence in various chronic conditions lends support to a theoretical model which has become known as the 'Common Sense Model' (fig.1).<sup>14</sup> In this model, the central tenet pertains to people making sense of

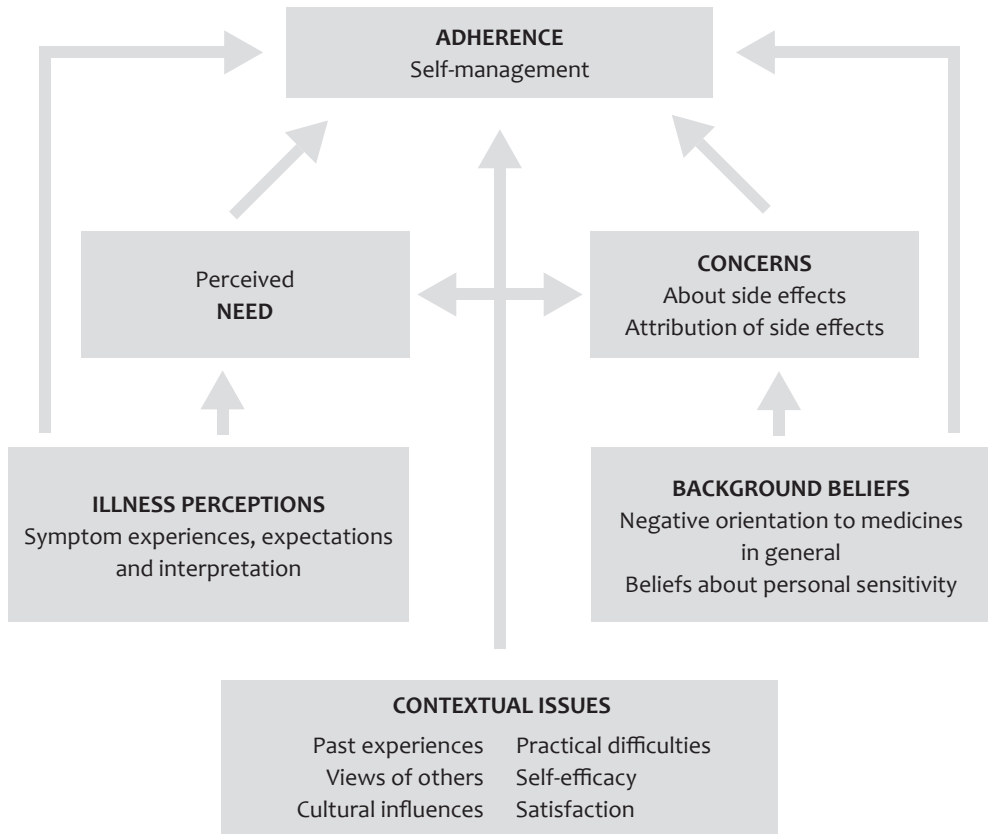
physical sensations, and the steps they take as a result of this process of sense making.<sup>11</sup> A patient with asthma who perceives the asthma to have an episodic nature will not perceive the necessity to take preventive medication. This ‘no symptoms, no asthma’ behaviour will lead to inadequate control of asthma.<sup>16,17</sup> On the other hand, a patient who perceives the asthma to be a chronic condition that necessitates maintenance medication will adhere to medication use, therefore, and will have a higher chance of controlling her asthma. Patients create their own personal cognitive representation of their illness which include beliefs about what may have caused the illness, the consequences the illness will have on their lives, how long the illness will last, and whether or not it is controllable or curable. In parallel, they also develop emotional responses to the threat. The cognitive and emotional representations of symptoms and illnesses are called illness perceptions.<sup>11</sup> “Illness perceptions are shaped by early experiences with illness-related episodes (e.g. flu, fall), in which children learn how to respond to pain and discomfort from their parents, and by imitating siblings and other children, for example, stay home or continue daily activities as much as possible. In addition, public images of how to respond to various complaints and illnesses are learned by watching television, surfing the Internet, lay press publications, and by listening to stories of parents, teachers and physicians. Illness perceptions, therefore, are strongly influenced by cultural, social and psychological factors, and are hardly, if at all, determined by the ‘objective’ medical severity of the symptoms or by age, gender, intellectual capacity or socio-economic class of the patients.”<sup>14</sup> Such illness perceptions have been found to determine self-management behaviour and outcomes (fig. 1).<sup>14</sup>

**Figure 1. The Common Sense Model, (adapted by Orbell & Hagger)<sup>15</sup>**



An extended self-regulatory theory that includes treatment beliefs as well as illness perceptions has been put forward in particular by Horne et al., whose research showed strong correlations between treatment beliefs and adherence (fig 2).<sup>18</sup> In adult patients with asthma, self-reported non-adherence was associated with doubts about the necessity for preventer medication to maintain health and with concerns about the potential adverse effects of this medication.<sup>19</sup> Necessity beliefs and concerns appeared to be separate constructs and not opposite poles of a more general attitude towards prescribed medication.<sup>19</sup> Horne et al.'s observation that treatment beliefs were substantially and independently related to adherence is consistent with findings in a range of chronic illness samples.<sup>18</sup> In agreement with these findings, a number of qualitative studies suggested that parental perceptions about illness and medication are major determinants of the use of controller medicines in their children.<sup>20,21</sup> An overview of (most very recent) quantitative studies supporting this, is provided in the general discussion of this thesis together with the results of the present project. Before discussing the scope and outline of this thesis, first an overview of limitations in present studies on adherence in children with asthma is provided.

**Figure 2. A theoretical model of the relationship of illness perceptions, medication beliefs and adherence as presented by Horne.<sup>22</sup>**



**Limitations in studies on adherence in children with asthma.**

- Most studies on adherence in children with asthma have focused on the role of disease severity, asthma knowledge, and socio-economic factors in explaining adherence (table 1). There is a paucity of studies conceptualizing adherence from a self-regulation perspective, with illness perceptions and treatment beliefs as key predictors of adherence.
- Many studies on determinants of adherence in childhood asthma were of relatively short duration, while long-term adherence is the focus of interest.
- Most studies rely on subjective measures of adherence such as self-report by parents or children or on estimation of adherence by physicians. Research has consistently shown such subjective measures to be highly unreliable, overestimating the rate of adherent patients which interferes with study results.<sup>36</sup> Canister weight and electronic monitoring are the most accurate measurements of adherence.<sup>37</sup> Of the studies relying on such objectively measured adherence, only a few conceptualized adherence from a self-regulation perspective (table 1).
- Adherence studies in preschool children with asthma are very rare.

There appears to be an urgent need, therefore, to improve the knowledge on long-term adherence to maintenance treatment, and its determinants, in children with asthma. In particular, the importance of illness beliefs and treatment beliefs in determining adherence should be explored in more detail. Such studies should rely on objectively measured adherence. Developing this research further will be helpful in constructing applicable interventions to optimize adherence, and thus improve asthma control.

**AIMS AND METHODS OF THIS STUDY**

This study was designed to examine determinants of long-term adherence to daily maintenance treatment, measured objectively and reliably, in children with chronic persistent asthma. The primary objective was to test the hypothesis that illness perceptions and treatment beliefs are more important in determining adherence than demographic and socio-economic factors, or the severity of the disease. The project was primarily set in a secondary care asthma clinic, because adherence to therapy was assumed to be more important in patients with more severe disease, as compared to children with mild intermittent disease being treated and monitored in primary care. The results of the initial focus group study of this research-project, in which parents whose children were being followed up in primary and in secondary care, respectively, reported striking differences in the organization of health care and in illness per-

ceptions and treatment beliefs between primary care and secondary care, suggested that the organization of health care was a significant determinant of adherence. This prompted us to extend this study to primary care practices in the catchment area of the hospital-based asthma clinic.

The project consists of three complementary studies. In study 1, illness perceptions and medication beliefs of parents of asthmatic children were explored in semi-structured focus group interviews. In study 2, adherence to daily inhaled corticosteroid use was examined over a 12-months period with electronic adherence logging device, in a large sample of children, 2-12 years of age, with chronic persistent asthma, both in primary and in secondary care. Patients and their parents were characterized extensively to identify factors associated with both poor and good adherence. The illness perceptions and treatment beliefs of parents were assessed with validated and standardized questionnaires. We also studied the importance of adherence in determining long-term asthma control. Asthma control was assessed by parents and physicians, in chart review and by measuring lung function, as proposed by international asthma guidelines.

Study 3 was a qualitative study designed to explore additional reasons for non-adherence. Parents who consented to de-blinding of study results after completing study 2 were interviewed about their medicine-taking behaviour.

## **OUTLINE OF THIS THESIS**

In chapter two, the results of the focus group interviews (study 1) are presented. The results of study 2 are presented in four different chapters. First, preliminary results of 3-months adherence in children 2-6 years are presented in chapter 3. The inclusion of children with persistent asthma in primary care was hampered by liberal prescription of ICS by general practitioners to children with nonspecific respiratory symptoms, as described in chapter 4. The main analysis of determinants of long-term adherence in primary care and secondary care is reported in chapter 5. The role of long-term adherence in acquiring and maintaining well-controlled asthma in children is described in chapter 6. Results of the interviews with parents who completed the 1-yr follow-up on their reasons and motives to adhere or not to adhere to daily maintenance medication (Study 3) are presented in chapter 7. Chapter 8 provides a general discussion of all study results.



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# 2

## Parental illness perceptions and medication perceptions in childhood asthma, a focus group study

T. Klok  
P.L.P. Brand  
H. Bomhof-Roordink  
E.J. Duiverman  
A.A. Kaptein

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## **ABSTRACT**

### *Aim*

Asthma treatment according to guidelines fails frequently, through patients' non-adherence to doctors' advice. This study aimed to explore how differences in asthma care influence parents' perceptions to inhaled corticosteroids (ICS).

### *Methods*

We conducted six semi-structured focus groups, including 44 parents of asthmatic children (2–12 years of age, treated in primary or specialist care). Verbatim transcripts were analysed with standard qualitative research methods.

### *Results*

Parents decided deliberately whether ongoing ICS use was useful for their child. This decision was based on their perceptions about illness and medication. In primary care, this issue was hardly ever discussed with the health care provider because regular scheduled follow-up was unusual. In specialist care, regular scheduled follow-up was usual, and parental perceptions about illness and medication were discussed and modified when needed. Parent-reported adherence was lower in primary care than in specialist care.

### *Conclusion*

This focus group study illustrates how strongly parental perceptions of illness and medication influence adherence to health care providers' advice and that such perceptions can be modified within a strong doctor–patient partnership, improving adherence.

## INTRODUCTION

Low adherence to inhaled corticosteroid (ICS) treatment in children with asthma is one of the main reasons why asthma is still associated with significant morbidity, and goals set in the GINA guidelines are frequently not met.<sup>1-3</sup> Reasons for poor adherence to ICS are not fully understood, but patients' perceptions about illness and medication appear to be at least as important as external, non-modifiable factors such as socio-economic status and race.<sup>4-8</sup> Because most health care providers do not discuss patients' perceptions of their illness and its medical management during the consultation, they are frequently unaware of differences between the parents' perception and the professional model of the disease.<sup>9</sup> This makes it impossible to focus on such differences. Building a partnership with patients (and their parents), as suggested by the most recent revision of the guidelines, may improve awareness of different perspectives between patients and physicians.<sup>10</sup> However, the way such partnership is reached is different between primary care and specialist care caused by differences in organization. Most asthma care takes place in primary care, where patients and physicians tend to have a long-standing relationship. Most primary care physicians provide asthma care without specific support from specialized asthma nurses, and planned follow-up visits are uncommon – the decision to visit the doctor is primarily made by the parents.<sup>11</sup> According to their guidelines, primary care physicians refer patients to specialist care when asthma control is not achieved by low-dose ICS maintenance treatment. In our paediatric specialist clinic, asthma care is delivered by paediatric chest physicians together with asthma nurses, and all newly referred patients receive comprehensive and tailored asthma education.<sup>12</sup> We schedule frequent follow-up visits until guideline goals for treatment are met. This study aimed to explore how these differences in asthma care influence parents' perceptions about asthma, its treatment and how they qualify the relationship with their health care providers. A qualitative approach was chosen because this allows a rich interpretation of patients' perspectives, experiences and roles.<sup>13</sup> By organising focus groups, we aimed to reach dynamic conversations where the interaction between parents would provide supplemental information.

## METHODS

We performed a focus group study according to published guidelines.<sup>14</sup> Six focus groups of parents of children with asthma were convened: three from the paediatric asthma clinic at our hospital and three from five primary care practices in the catchment area of our hospital. These practices represented city and rural area, and small and large practices. The family physicians involved had contributed to previous research of our paediatric asthma clinic; they had expressed an interest in childhood asthma care and were supportive of regional guidelines for the management of asthma. Parents of children aged 2–12 years with a doctor's diagnosis of mild to moderate persistent asthma who had received at least one prescription for ICS in the last year were eligible for inclusion in the study. From an alphabetic list, consecutive parents were approached, and after giving informed consent, they were included until groups were full (eight parents). No pre-set characteristics of parents or children were used for inclusion, because characteristics that determine parental perceptions are unknown.

Each focus group interview, which lasted approximately 2 h, followed a semi-structured interview guide of 10 open-ended questions, asking parents about their perceptions of asthma and its treatment, and on the organization of care. The interviews were led by a professional journalist without specific medical knowledge, who encouraged parents to express their views freely and who clarified views and expressions where needed. One of the authors (TK) attended the sessions, took field notes and debriefed the moderator after each interview to record her impressions of emerging themes. This information was used to structure the subsequent focus group interviews. After reviewing the transcripts of six focus groups, it was concluded that saturation had been reached.<sup>14</sup> Each focus group was audio-taped and transcribed verbatim prior to data analysis.

Before conducting the focus groups, a codebook was put together, including items from the beliefs about Medicines Questionnaire.<sup>15</sup> New codes were added for emerging themes from field notes, debriefing and during the coding process itself, to allow capturing all relevant data. The transcript of the first focus group interview was coded independently by two researchers (TK, HR). Cohen's Kappa was 0.78 (where 0 = no agreement and 1 = perfect agreement), indicating good agreement for classification by code. Subsequent transcripts were coded by one of the researchers (HR) and cross-checked by another (TK). Differences in coding were resolved by consensus. Codes were grouped into three themes: parental perceptions about illness and medication, self-management including self-reported adherence and issues relating to asthma care and health care providers. A provisional theoretical model explaining the results was developed by two researchers and modified and extended in discussions between all authors.

The Medical Ethics Review Board of our hospital judged that this study, because it involved only adult volunteers, did not require formal ethical approval under Dutch law.

## RESULTS

From the primary care practices, parents of 38 children were invited to participate. Parents of 20 children consented, and 24 parents, representing 18 children, attended. From the paediatric asthma clinic, parents of 42 children were invited to participate, parents of 17 children accepted and 20 parents representing 16 children participated. All parents had full health insurance (which is mandatory in the Netherlands), most were Caucasian (which comprises >90% of patients in the catchment area of our hospital) and most were from (upper) middle class backgrounds. The mean age of the children of the parents in the focus groups was 5.7 years, ranging from 2 to 12 years. Fourteen children were under the age of five and had primarily viral-induced wheeze exacerbations. Most preschool viral-induced wheeze patients from secondary care were hospitalized for an exacerbation, whilst none of the patients from primary care had ever been referred or admitted to hospital. All children 5 years of age or older had mild to moderate persistent asthma; the large majority were atopic. The principal findings of the focus group interviews are presented separately for primary care and specialist care. These findings are illustrated by quotes about common perceptions of illness and medication and about health care providers (Table 1).

### Primary care

Parents reported that after the initial visits to the health care provider, during which a diagnosis was made and maintenance medication was prescribed, they did not receive regular follow-up appointments. Parents would receive repeated inhaled corticosteroid prescriptions for their child without seeing a health care provider for up to three years, with parents managing their child's asthma on their own. Parents would only visit the health care provider when they could not manage their child's asthma problems by themselves anymore. Parents considered this method of self-management without consulting a health care provider as entirely logical. They were comfortable with it, because they viewed themselves as being responsible for making decisions on issues such as medication use. These decisions were based on their perceptions about illness and medication (Table 1). Consequently, they used the prescribed medication depending on how they valued their child's need for medication and on their concerns regarding medication use. If parents were convinced of the necessity of using ICS, this was mostly because they had observed an improvement of their child's symptoms after starting ICS, or it was based on an experience in the family that patients with asthma benefit from ICS. Although some of these parents would give ICS on a daily basis to



**Table 1. Parental quotes from the interviews illustrating the key findings**

<b>Similarities in primary care group and secondary care group</b>	
<i>Views on the partnership with the health care provider for taking decisions on treatment</i>	
<p>‘The paediatrician suggested to lower the dose, but I said; he is now doing well, let’s keep the dosage at two times a day’.</p> <p>‘When my son has an asthma attack, I know he will receive oral prednisone when we visit the doctor. But I prefer he recovers without. Therefore, together with my husband we decide when the problems with breathing are severe enough to visit the doctor for receiving a prescription for oral prednisone’.</p> <p>‘I think the time changed that doctors are the ‘all-knowing’. Therefore, nowadays it is more a two-way conversation. Again, it is your child, you know the best if he is ill’.</p> <p>‘In general, we don’t have to debate very much, the doctor takes usual the decision we had in thought’.</p> <p>‘When I say I want to stop de medicines, the asthma nurse does not automatically reject my idea. Her reaction is that the complaints of my child can return in a very severe way, so she keeps mentioning the importance of the medicines. But she does not say I can’t do that. This in contrary with the general practitioner’.</p>	
<i>Perceptions about resistance to medicines in general</i>	
<p>‘It is poison’/‘It is trash’/‘Medicines are bad’.</p> <p>‘I don’t like medicines altogether’.</p> <p>‘That doctor said that there are no side effects when using this medicine for a long period of time, but in the past they were saying that about a lot of medicines, and they turned out to be wrong’.</p>	
<b>Differences between primary care group and secondary care group</b>	
<i>Perceptions about asthma and the treatment with ICS in the primary care group</i>	<i>Perceptions about asthma and the treatment in the secondary care group</i>
<p>‘Most illnesses in children disappear by themselves’</p> <p>‘If you continue preventive medicine you can never find out whether the child can do without’</p> <p>‘I compare it with a sprained ankle: maybe you need crutches first, but for full recovery you have to walk without them’</p> <p>‘We wanted to find out how he would do without his medicine. Well, he was fine. So now we only give the medicine when he needs it’</p> <p>‘I don’t want to burden my child with medicine of which I am not sure it will help. With salbutamol, it is clear, but with fluticasone, you just have to assume that it works. And that is really difficult’ ‘It doesn’t work as well when you use it on a daily basis’</p>	<p>‘Her asthma may not disappear, but with the medicines you can suppress it’</p> <p>‘The well-being of my daughter depends on the use of the medication’</p> <p>‘First I thought that periods with no symptoms means she had control over the asthma by herself and medicines were no longer needed. Now I have learned this is the wrong assumption’</p> <p>‘The fluticasone is a preventive medicine, I try to say, just take your meds, you can reach the age of one hundred years using them’</p> <p>‘If you are thinking about the kind of medicines you put into your child, sometimes it upsets you, but asthma upsets you more. So, you have to give the medicines’</p> <p>‘He uses it on a daily basis, it prevents complaints’</p>

their child, most would use ICS only intermittently or stop it altogether, arguing that their child's asthma was not severe enough to justify daily use of medication. Most of these parents expressed resistance against medicines in general; the feeling that children should use as few medications as possible was common. Persistent asthma symptoms in the children were described frequently. Parents regarded these symptoms as belonging to having asthma and not as a reason to visit the health care provider or to step up medical treatment. Parents described the asthma care and the amount of information received as minimal, but adequate, and they were satisfied with their primary care practitioner.

### **Specialist care**

Parents reported that in specialist care, all children received regular follow-up by the paediatric chest physician and by the asthma nurse, with a frequency of at least two visits a year. All parents were convinced of the necessity of ICS, preventing their children from having symptoms. This belief was consistent between parents, although concerns about the use of medication in general were common. These parents expressed the opinion that their child's need of being treated with ICS outweighed their concerns regarding the risks of daily use of ICS. Although all parents reported to be adherent to the advice of daily use of ICS, those with strong concerns about medication were eager to diminish the dose. As follow-up was regular, they felt free to discuss this topic with the health care provider, and in their opinion changing the medication dosage was a shared decision between parents and the medical team. Parents were very satisfied with the asthma care. They particularly valued the fact that they were taken seriously and that they were acknowledged as the people knowing their child best. The asthma nurses were highly valued as being easily approachable, well-trained and because they provided lots of practical advice. Parents felt free to discuss issues such as their concerns about medicines or the use of alternative and complementary treatment with these nurses. Many parents expressed strong criticism about the health care providers in primary care. They did not feel having been taken seriously by these health care providers in their concerns about their children. Consequently, their view on their child's symptoms and treatment differed from that of the health care providers, and this prompted parents to ask for referral to specialist care. Parents emphasized that they had to be very assertive to receive the treatment that they felt their child needed. Another complaint about primary care was the limited amount of information patients received, making it difficult to self-manage their child's asthma.

*Feedback of study findings to participating physicians*

The results of our focus group studies were discussed with the family physicians and paediatric chest physicians in a group meeting. All participating physicians confirmed that the parents' reports of asthma care were a representative description of current asthma care in their practices.

**DISCUSSION**

This focus group study with parents of children with asthma provides important clues to understanding how differences in asthma care facilitate or hamper adherence to ICS treatment in children with asthma. Two main results emerged from the inductive analysis of the focus group interviews.

First, parents play a pivotal role in the management of their child's asthma. Health care providers can not force asthma treatment upon these children; parents decide whether they will follow medical advice for their child's condition. This parental decision is based on their own perceptions about illness and medication. Even a satisfying long-term relationship with the primary care physician does not prevent parents from critically approaching prescriptions for maintenance medication for their child. This is in accordance with previous qualitative studies' findings showing how parents take the medical care of their child's asthma into their own hands by balancing the perceived need for ICS against their concerns about (side effects of) medication.<sup>4,16-18</sup> This finding emphasizes the importance of parental perceptions about illness and medication and illustrates how strongly such perceptions influence parental behaviour regarding health care providers' advice.<sup>4,6,8</sup>

Second, the results of this study strongly suggest that these powerful parental perceptions about illness and medication can be modified by health care providers during close and intensive follow-up. In contrast to parents in primary care, most parents in specialist care adopted the professional model of asthma (Table 1). The regularly scheduled follow-up in specialist care and the involvement of asthma nurses offer the opportunity to listen carefully to parents, to explore and understand their views on illness and their attitudes towards asthma medication, which is needed to develop a true patient/parent-doctor partnership. Being aware of the family's needs and perceptions, tailored information can be given.<sup>19</sup> Our results support the hypothesis that such close follow-up allows modification of these parental perceptions about illness and medication.<sup>20</sup> This underscores the importance of building a partnership with parents, characterized by listening to their views and perspectives on illness and medication and by shared decision making. Modifying parental illness and medication perceptions during long-term close follow-up allows better self-management and improved adherence to health care providers' advice. This helps to understand how quality impro-

vement strategies for childhood asthma care, including communication education of physicians or group discussions with parents based on the concept of concordance, improve asthma outcome.<sup>21,22</sup>

Although our findings strongly suggest that the observed differences in parental perceptions about illness and medication between primary care and specialist care were caused by the different organization of care, other explanations must be considered. It could be argued that a higher degree of asthma severity or poorer asthma control in patients from specialist care increased the parental sense of usefulness of maintenance medication for their child. Although we did not formally assess asthma severity and control level in the children with asthma whose parents we interviewed, the overall impression from the focus groups was that the degree of asthma severity was similar between children from primary and specialist care, the only difference being a larger history of hospitalizations in the secondary care group children. Although this may have affected parental perceptions on usefulness of medication in the preschool children concerned, it can not explain the large differences in parental perceptions between the whole secondary care group when compared to the primary care group. Furthermore, children in primary care appeared to have poorer asthma control with frequent asthma symptoms, and this did not affect the parents' view on the usefulness of maintenance medication. Previous studies from the USA and from the Netherlands have also shown little difference in childhood asthma severity between primary and specialist care.<sup>11,23</sup>

Focus group methodology was chosen because this is superior to quantitative surveys in exploring parents' perspectives and beliefs on the management of asthma.<sup>13</sup> However, the time- and labour-intensive nature of qualitative research imposes the limitation that it can only be conducted with small samples. As a result, findings are not immediately generalizable to the larger population, in particular because most parents were Caucasian middle class with good access to health care and full health insurance. However, in a study among low-income urban families, caregiver and child perceptions about illness and medication were also found to be a major barrier to asthma care.<sup>8</sup> Other studies showed that such perceptions hamper adherence more in low-income, minority populations.<sup>4,7</sup> Although it might be tempting to think that such misperceptions about illness and medication are the result of ignorance and would be more common in lower socioeconomic strata, our results, remarkably, show that such counterproductive parental perceptions about illness and medication are an important barrier to adherence to maintenance treatment, even in a group of affluent and well-educated parents. This stresses the importance of a strong doctor–parent partnership where such perceptions can be discussed and modified.

A final limitation is that we had no objective data on adherence in our study group, which could corroborate the parental reports of adherence. Given the cross-sectional

nature of our study, monitoring adherence with electronic logging devices or by weighing canisters was not possible. It has been shown that checking pharmacy dispensing data on inhaled corticosteroids in children is as unreliable as parental reporting of adherence.<sup>24</sup> Therefore, it is unlikely that we could have improved the accuracy of our assessment of adherence in the context of this study. Although it is likely that parental reporting of adherence is an overestimate of true adherence, it is unlikely that this overestimation differed between the groups of parents that we studied.

In summary, this study shows the pivotal role parents have in the management of childhood asthma. Parental decisions about the treatment of their children are highly influenced by their perceptions about illness and medication. This study suggests that health care providers can modify such perceptions by offering regular follow-up in which consultations are characterized by collaboration between health care providers and parents. This approach may help to improve adherence and increase asthma control.

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# 3

## High inhaled corticosteroids adherence in childhood asthma: the role of medication beliefs

T. Klok  
A.A. Kaptein  
E.J. Duiverman  
P.L.P. Brand

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## **ABSTRACT**

### *Aim*

To study determinants of adherence in young asthmatic children over a 3-month period, including the role of parental illness and medication perceptions as determinants of adherence.

### *Methods*

Consecutive 2-6-yr-old children with asthma, using inhaled corticosteroids (ICS), followed-up at our paediatric asthma clinic (where patients are being extensively trained in self-management, and are followed-up closely) were enrolled. Adherence was measured electronically using a Smartinhaler® and calculated as a percentage of the prescribed dose. We examined the association of adherence to a range of putative determinants, including clinical characteristics and parental perceptions about illness and medication.

### *Results*

Median (interquartile range) adherence, measured over 3 months in 93 children, was 92% (76-97%), and most children had well controlled asthma. 94% of parents expressed the view that giving ICS to their child would protect him/her from becoming worse. Adherence was significantly associated with asthma control and with parental perceptions about medication.

### *Conclusion*

The high adherence rate observed in our study was associated with parental perceptions about ICS need. The high perceived need of ICS may probably be ascribed to the organisation of asthma care (with repeated tailored education and close follow-up).

## INTRODUCTION

Adherence to maintenance therapy is of key importance in determining the success of treatment of chronic diseases, such as childhood asthma.<sup>1,2</sup> Adherence to maintenance treatment, however, is poor, and this is a major cause of uncontrolled asthma.<sup>1,3,4</sup> Improving adherence to inhaled corticosteroids (ICS) in children with asthma is probably the most effective method through which health care providers can reduce the burden of uncontrolled asthma.<sup>1</sup> In contrast with the common belief among healthcare providers, parental asthma knowledge is hardly associated with adherence, and isolated educational efforts to improve asthma knowledge are ineffective in improving adherence.<sup>1,5</sup> Socio-demographic factors and the severity of asthma are also of little importance in determining adherence to maintenance treatment in this disorder.<sup>1</sup> Conversely, although adherence to ICS is notoriously poor among the urban-ethnic minority youth in the USA, with adherence rates between 37 and 50%, high adherence can be achieved, even in such underprivileged populations, when patients are repeatedly educated about self-managing their chronic disorder and followed-up closely.<sup>6,7</sup> This suggests that it is not the education per se, but rather the intensity, quality and frequency of education about self-management and follow-up that help to improve adherence. Studies aimed at interventions to improve physician-patient communication have shown better adherence and asthma control in children and adults with asthma.<sup>8,9</sup>

The association between such interventions and adherence maybe partially mediated by parental and patient's illness and medication perceptions. Patients (and parents of paediatric patients) create their own personal cognitive representations of their illness, including beliefs about what may have caused the illness, the consequences the illness will have on their lives, how long the illness will last and whether or not it is controllable or curable. The cognitive and emotional representations of symptoms and illnesses are called illness perceptions.<sup>10</sup> Similarly, medication perceptions comprise the patient's (or parent's) cognitive and emotional representations of the medication prescribed; including method of action, desired effects and side effects.<sup>11</sup> Studies in adults have

shown that perceptions about illness and medication are important drivers of adherence. However, in childhood asthma care, the association between illness/medication perceptions and adherence has only been examined in qualitative or cross-sectional studies, and the importance of such perceptions as determinants of ICS adherence has not been studied in a quantitative fashion. Although asthma is very common in preschool children, only a few studies examined adherence to maintenance therapy and its determinants in this age group.<sup>1,11-15</sup> Most of these studies did not focus exclusively on young children, only two used electronic adherence monitoring, and parental illness and medication perceptions received little attention. We designed this study to assess adherence, measured electronically, and its determinants, in children aged 2-6 yrs with asthma during close follow-up in a paediatric asthma outpatient clinic. We hypothesized that adherence to ICS maintenance treatment in these patients would be associated with parental perceptions about illness and medication.

## METHODS

For this study the parents of all children aged 2-6 yrs with asthma, and currently treated with ICS, attending the Amalia Children's clinic (Zwolle, the Netherlands) for regular follow-up, were asked to participate in the study. All children had a doctor's diagnosis of asthma based on more than three recurrent episodes of wheezing and dyspnoea, and all were referred to our clinic by their general practitioner because of troublesome, severe, or frequent symptoms. In our clinic, we prescribe ICS to children with asthma as daily controller therapy, in accordance with the Dutch national guidelines on paediatric asthma, which are adapted from the Global Initiative for Asthma guidelines.<sup>2</sup> Education and follow-up focuses on building and maintaining a strong partnership with patients and parents. We provide repeated tailored asthma self-management education, discuss parents' perceptions about asthma and its treatment, ensure concordance on treatment (goals) with parents, train correct inhalation technique and stress the importance of adherence to daily ICS treatment.<sup>16</sup> To achieve this, patients and their parents visit the clinic four to six times during their first year of follow-up, and two to four times per year afterwards.

Exclusion criteria were limited knowledge of the Dutch language and severe comorbidity. We collected clinical and demographic data by structured interview and chart review. Lung function was assessed before and after inhaling salbutamol 400 µg: flow-volume curves in children 5 yrs of age and older, and resistance of the respiratory system measured by the interrupter technique was used for children < 5 yrs of age (Microrint<sup>®</sup>), according to European Respiratory Society/ American Thoracic Society guidelines.<sup>17</sup> Results were expressed as Z-scores.

Upon entry into the study, a number of validated questionnaires were applied; details

including references are presented in the online depository. Parental illness perceptions were assessed by the Brief Illness Perception Questionnaire (B-IPQ), and medication perceptions by the Beliefs about Medicines Questionnaire (BMQ), which also provides the balance between parent-perceived necessity and concerns about ICS, and the Treatment Satisfaction Questionnaire for Medication (TSQM).<sup>11,18,19</sup> In addition, we applied the I Worry scale, which scored parental worries about their child having asthma and using daily ICS; the Medication Adherence Report Scale (MARS), which assessed self-reported adherence; the Satisfaction with Information about Medicines Scale (SIMS), the Paediatric Asthma Caregiver Quality Of Life questionnaire (PAC-QOL), and an asthma knowledge questionnaire.

Asthma control was assessed by a parent-completed Asthma Control Questionnaire (ACQ).<sup>20</sup> The attending physician rated asthma control on a visual analogue scale ranging from 0 (worst asthma control possible) to 10 (complete asthma control) at a 3 month follow-up visit.

Patients used ICS by metered dose inhaler/ spacer combination during the 3-month follow-up period. Adherence was monitored by Smartinhaler<sup>®</sup>, a validated electronic device logging date and time of each ICS actuation.<sup>21</sup>

### *Analysis*

Adherence was calculated as the number of Smartinhaler-recorded inhaled doses expressed as a percentage of the number of doses prescribed, and censored at 100% of the prescribed dose. We assessed the association of ICS adherence (both as a continuous variable and dichotomized as good (>80%) and poor (< 80%) adherence of prescribed doses used) to all putative determinants (defined a priori with a focus on parental perceptions about illness and medication) in non-parametric univariate analyses (because adherence had a highly skewed distribution).<sup>12</sup> We chose to refrain from adjustments for multiple comparisons because of the exploratory and observational nature of our study.

### *Ethical considerations.*

This study was approved by the hospital ethics review board and all parents provided written informed consent.

## RESULTS

Out of a total of 137 consecutive eligible patients, 103 children (75%) entered the study after informed consent was obtained, and 93 children (90% of those enrolled) completed the 3 month follow-up (figure 1). Most parents who did not participate in or withdrew their child from the study did so because of serious illness in a family member or other pressing circumstances. Clinical characteristics of participating and non-participating children were comparable (table 1). Most participating children had well controlled asthma while on ICS maintenance therapy. Reliable and reproducible lung function results could be recorded in 66 (71%) children, and sensitisation to inhaled allergens was available for 86 children (table 1).

**Figure 1. Inclusion of patients**

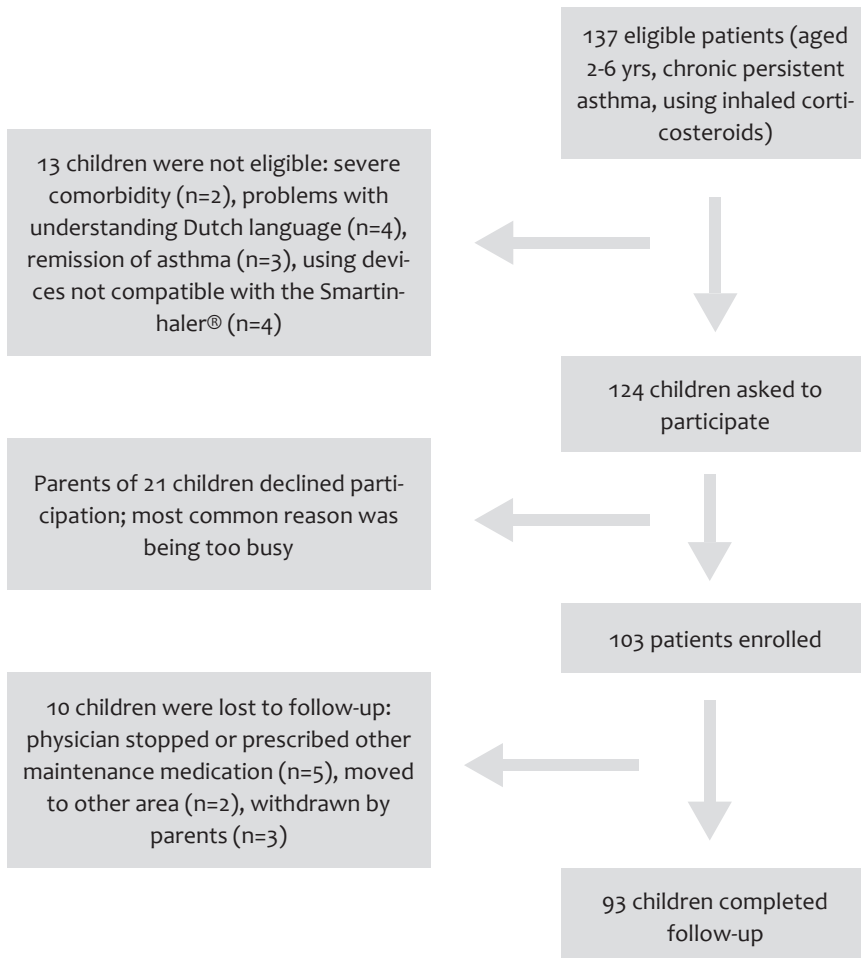
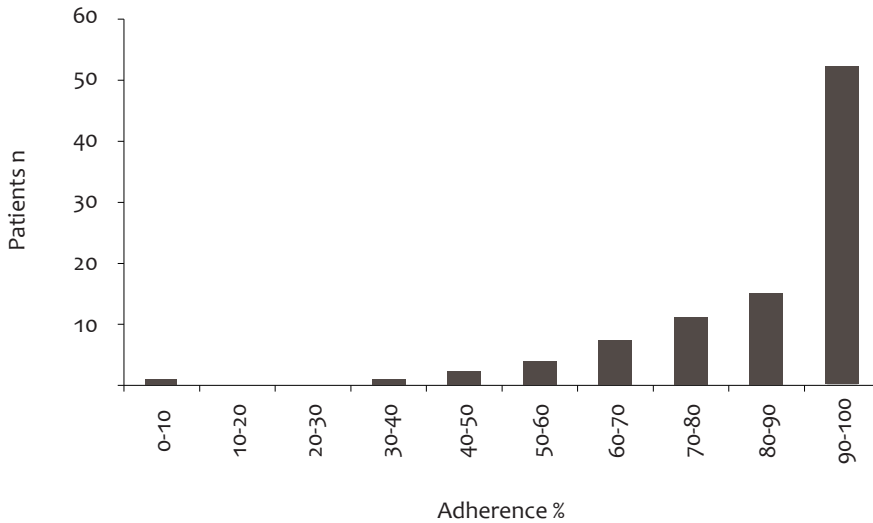


Table 1. Characteristics of all eligible study patients

	Patients with complete follow up	all other eligible patients	p-value
<b>Subjects n</b>	93	44	
<b>Male</b>	56 (61)	26 (60%)	0.90
<b>Age (yrs)</b>	4.5 (2.2 to 6.8)	4.6 (2.1 to 6.9)	0.67
<b>Duration of outpatient clinic asthma care before study (months)</b>	17 (8 to 27)	17 (9 to 28)	0.58
<b>Maintenance medication:</b>			
• inhaled corticosteroids (ICS)	86 (92)	42 (95%)	0.51
• ICS and long-acting bronchodilators	7 (8)	2 (5%)	0.51
• ICS (fluticasone) dose ( $\mu\text{g}$ )	250 (125 to 500)	250 (125 to 500)	0.73
<b>Scheduled visits to outpatient clinic in year before study</b>	5 (4 to 6)	4 (2 to 5)	0.007
<b>Hospitalisations in year before study</b>	0 (0 to 5)	0 (0 to 1)	0.007
<b>ACQ baseline (&lt;0.75 = well-controlled asthma, &gt;1.5 = not well-controlled asthma)</b>	0.5 (0.2 to 1.3)	NA	NA
<b>PACQoL baseline (score 1 to 7, with 1 is low and 7 is high quality of life)</b>	6.2 (5.3 to 6.8)	NA	NA
<b>Smoking parent(s)</b>	28 (30%)	NA	NA
<b>Educational level of mother (1 = low and 7 = high)</b>	5 (4 to 7)	NA	NA
<b>Positive specific IgE to common inhalant allergens</b>	43 (50) <sup>¶</sup>	24 (65) <sup>‡</sup>	< 0.001
<b>FEV1 baseline<sup>#</sup></b>	0.66 $\pm$ 1.1	NA	NA
<b>FVC baseline<sup>#</sup></b>	0.29 $\pm$ 1.3	NA	NA
<b>Rint baseline<sup>#</sup></b>	1.90 $\pm$ 2.8	NA	NA
Data are presented as n (%), median (interquartile range) or mean $\pm$ SD, unless otherwise specified; ACQ: Asthma Control Questionnaire20; PACQoL: pediatric asthma caregiver quality of life questionnaire; Ig: immunoglobulin; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; Rint: respiratory resistance by the interrupter technique; NA: not available. #: z-score, n=33; ¶: n=86; ‡: n=37.			

The frequency distribution of adherence to daily ICS is presented in figure 2. Median (interquartile range (IQR)) adherence was 92% (76% to 97%). Sixty-seven children (72%) had good adherence (>80% of prescribed dosages); adherence rates below 60% were recorded in only eight (9%) children (figure 2). There was a small, non-significant decrease in adherence from the first to the third months of follow-up (median (IQR) -1% (-8% to 1%);  $p=0.483$ ). Adherence rates were comparable between children aged 2-4 yrs (median 92%) and children aged 5-6 yrs (median 92%,  $p=0.899$ ).

**Figure 2. Adherence to ICS measured by electronic loggers**

The association of adherence to the individual item responses on each questionnaire is presented in the online depository. Parental perceptions about illness were not associated with adherence, but perceptions about medications were. Parents who believed that ICS maintenance treatment is needed for their child's health, those who viewed ICS administration as convenient, and those who expected little harm of medicines in general had higher adherence rates to ICS (table 2). The other putative determinants that showed significant ( $p < 0.05$ ) or near-significant ( $p < 0.1$ ) association to adherence are presented in table 3. Not unexpectedly, parental self-reported adherence (as assessed by MARS) was strongly related to electronically measured adherence. In addition, good asthma control was positively related to adherence measured electronically. Parental characteristics such as educational level, asthma knowledge and smoking habits were not significantly associated with adherence.

For 84 (93%) parents, BMQ scores indicated that the perceived necessity outweighed concerns about ICS (table 4). This was mainly due to the large majority of parents expressing the view that giving ICS to their child would benefit his/her health, even when they had concerns about the use of ICS. The results from other questionnaires were consistent with this finding (see online depository for details). For example, only three parents responded negatively to the TSQM question "Overall, how confident are you that taking this medication is a good thing for your child?".

**Table 2. Associations between parental perceptions about illness and medication and electronically measured adherence**

	Rank correlation coefficient		comparison between children with high (>80%) and low adherence (<80%) of prescribed dosages taken
	$\rho$	p-value	p-value
<b>Brief Illness Perception Questionnaire</b>			
consequences	0.00	0.969	0.870
timeline	-0.09	0.425	0.289
personal control	0.11	0.319	0.760
treatment control	0.11	0.294	0.526
identity	-0.05	0.663	0.598
concern	0.00	0.970	0.835
understanding	-0.08	0.440	0.260
emotional response	0.13	0.203	0.961
<b>Beliefs about Medicine Questionnaire</b>			
Specific part: perception of necessity	0.22	0.035*	0.299
Specific part: concerns	-0.01	0.949	0.368
Need-concern ratio	0.09	0.414	0.394
General part: perceptions of overuse	0.18	0.082	0.418
General part: perceptions of harm	0.23	0.025*	0.253
<b>Treatment Satisfaction Questionnaire for Medication</b>			
effectiveness of daily use of ICS	-0.10	0.342	0.633
side effects of daily use of ICS	-0.01	0.963	0.838
convenience of administering ICS to child	-0.25	0.020*	0.212
global satisfaction about ICS	0.19	0.067	0.522

\* =p&lt;0.05



**Table 3. Other putative determinants which showed a (near) significant ( $p < 0.1$ ) association with electronically measured adherence over 3-month period**

	Rank correlation coefficient		comparison between children with high (>80%) and low adherence (<80%) of prescribed dosages taken
	$\rho$	$p$ -value	$p$ -value
<b>MARS</b>	0.53	<0.001	0.001
<b>VAS asthma control by physician</b>	0.26	0.028	0.009
<b>ACQ at 3 months</b>	-0.19	0.105	0.036
<b>Rint baseline<sup>†</sup></b>	-0.33	0.060	0.056
<b>Rint % change after bronchodilator<sup>†</sup></b>	0.41	0.016	0.006
<b>FEV<sub>1</sub> change after bronchodilator<sup>†</sup></b>	-0.33	0.069	0.085

MARS: Medication Adherence Report Scale; Rint: respiratory resistance by the interrupter technique; FEV<sub>1</sub> change: difference in forced expiratory volume in one second before and after salbutamol; VAS: visual analogue scale; ACQ: asthma control questionnaire; <sup>†</sup>n=33

**Table 4. Parental beliefs about medication measured by the Beliefs about Medicines Questionnaire<sup>†</sup>**

	Agree	Neutral	Disagree
<b>5 questions about need</b>			
My child's health, at present, depends on his/her medicines	8.33	7.8	8.9
My child's life would be impossible without his/her medicines	26.7	35.6	37.8
Without his/her medicines my child would be very ill	51.1	23.3	25.6
My child's health in the future will depend on his/her medicines	24.7	43.8	31.5
My child's medicines protect him/her from becoming worse	94.4	4.4	1.1
<b>5 questions about concern</b>			
My child having to take medicines worries me	39.3	6.7	53.9
I sometimes worry about long-term effects of my child's medicines	44.4	17.8	36.7
My child's medicines are a mystery to me	4.5	7.9	87.6
My child's medicines disrupt his/her life	1.1	3.3	95.6
I sometimes worry about my child becoming too dependent on his/ her medicines	28.9	10.0	61.1
<b>Balance between need and concern</b>			
necessity beliefs higher than concerns	93.4	2.2	4.4

Data are presented as %

## DISCUSSION

This study shows that high adherence to daily maintenance treatment with ICS along with good asthma control can be achieved in preschool children with asthma and that high adherence is associated with parental beliefs about the necessity of ICS therapy. The median adherence rate in our study remained stable over 3 months of follow-up at 92%, which is considerably higher than in earlier studies (adherence ranging from 44% to 72%, decreasing strongly over time). For example, a recent study showed that adherence to an ICS prescribed after an emergency visit for acute asthma deteriorated from 90% to 50% during the first two weeks after the acute asthma attack.<sup>22</sup> This confirmed earlier population-based observations that most patients with asthma fail to continue ICS use after an initial prescription.<sup>23</sup> Although some large studies showed lower adherence rates for adolescents than for school- and preschool-aged children, age is not consistently related to treatment adherence.<sup>1</sup> Even in pre-adolescent children, adherence to ICS of >75% of prescribed dosages has rarely been described, neither in observational, nor in intervention studies.<sup>14</sup> We emphasize that the very high adherence we observed was not the result of an intervention aimed at improving adherence, but was obtained during routine care in our paediatric asthma outpatient clinic.

The large majority of parents of the preschool children with asthma in our study expressed the belief that ICS therapy for their child's asthma was both useful and necessary (table 4). This is in contrast with previous studies examining medication beliefs in asthma. Studies in adults with asthma have shown lower BMQ "need" scores and higher "concern" scores.<sup>11,24</sup> In a study of 622 parents of children with asthma in the USA, concern scores exceeded need scores in 17% of parents, compared to only 4% in our study.<sup>15</sup> Such concerns about the daily use and safety of ICS in children are a major reason for parents to withdraw this medication in their children.<sup>25</sup> Because the distributions of ICS adherence (figure 2) and parental medication perceptions (table 4) were strongly skewed towards high adherence and ICS necessity, with relatively little variance, the power of our study to identify determinants for adherence was lower than expected. This may help to explain why we only identified a few parental perceptions significantly associated with adherence rates, and why these associations were relatively weak (tables 2 and 3).

We found a significant association between ICS adherence and asthma control, with poorer asthma control in patients with lower adherence, suggesting that this association does not only play a role at the severe end of the asthma spectrum, but also in patients with relatively well controlled asthma, and that every effort to optimise adherence to ICS maintenance therapy is worthwhile.

It is interesting to explore potential reasons why the parental medication beliefs and the high adherence rates in our study population differed from those previously reported. Selective enrolment of parents with high need and low concern scores should be considered. However, we feel that this is unlikely, because consecutive outpatients at our clinic were approached for the study, the large majority of whom were enrolled (figure 1). Furthermore, the high need scores for ICS in this study are in agreement with a previous qualitative study from our clinic, in which parents accepted that their child needed ICS to control asthma, although parents universally expressed reservations about having to give daily medication to their child. Parents whose children were treated in primary care, however, expressed beliefs of the high concern-low need pattern. These findings prompted us to hypothesise that parental medication beliefs can be modified by repeated tailored education and close follow-up in a specialized asthma clinic, resulting in high adherence.<sup>26</sup>

The young age of the children in our study may have increased the likelihood of good adherence, because most medication in this age range is given by the parents. However, previous studies have shown poor adherence rates to inhaled medication in young children with asthma, even when parents knew that adherence was being monitored.<sup>14</sup> Therefore, parental awareness of monitoring adherence does not seem a likely cause of the high adherence rates observed. This is supported by the finding that adherence rates did not deteriorate significantly over time in our study. Further follow-up of this cohort will allow us to examine whether the high adherence rates observed can be maintained over longer periods of time.

It should also be noted that access to health care and ICS medication is available to all Dutch citizens, because health insurance is mandatory in the Netherlands. Studies in urban US populations have shown that poor insurance and financial issues may play a major role in poor adherence in such populations.<sup>1,6</sup> Although it is conceivable that excellent insurance coverage may have improved adherence in our study, poor adherence has been shown in earlier Dutch studies of asthmatic children, suggesting that this is not a major determinant.<sup>4,26</sup>

In the absence of other logical explanations for the high adherence and constructive parental medication beliefs observed, we hypothesise that the organisation of our asthma care may be a contributing factor. The fact that our clinic is run by paediatric asthma specialists may be of importance in that respect. Previous studies have shown superior asthma control, better lung function and higher adherence to treatment and self-management plans when asthma care was provided by specialist physicians (paediatric allergists or paediatric pulmonologists, depending on country and setting) compared by general paediatricians or family physicians.<sup>3,27,28</sup> A recent systematic review showed that more intensive follow-up, with multiple educational sessions using

combinations of instructional modalities, was associated with higher adherence and improved outcomes for children with asthma.<sup>3</sup> In our clinic, such a comprehensive asthma management consists of frequent follow-up visits to both asthma specialist physicians and dedicated asthma nurses, providing repeated tailored education to parents and patients, and extensively training and checking correct inhalation technique.<sup>16</sup> In earlier studies, we reported the added value of easy accessibility of asthma nurses which was highly appreciated by parents of children with asthma.<sup>26,29</sup> This was recently confirmed in a study from a referral centre for children with difficult-to-treat asthma, where the important role of nurse-led home visits to address parental perceptions, contextual and psychosocial issues was highlighted.<sup>30</sup> Taken together, these results suggest that intensive multi-disciplinary education about self-management, along with close follow-up in a specialised clinic setting, helps to improve adherence to ICS in children with asthma, with parental perceptions about medication being an important mediator.

It should be stressed, however, that a causal relationship between our model of care and the high adherence we observed cannot be established based on our data because this was an observational study. Ideally, a randomized controlled trial should be performed to test the hypothesis that comprehensive asthma management and close follow-up, as described, leads to high adherence to maintenance medication. However, it has been argued that randomized trials on the effects of complex interventions, such as our model of asthma management, are fraught with difficulties.<sup>16</sup> A prospective study in which both adherence and parental perceptions about medicines are followed-up over longer periods of time from the time of referral to a specialised asthma clinic would also be worthwhile.

#### *Strengths and limitations*

The main strengths of our study include the objective, validated, quantitative assessment of adherence over a considerable period of time, and the extensive characterization of patients' and parents' characteristics using validated methodology. The real-life setting avoids any adherence-improving effects of clinical trial interventions, other than the potential adherence-improving effect of participating in a study. This effect is an unavoidable drawback of electronic adherence monitoring.

The most important limitation of our study lies in its generalisability. We limited our study to 3 month adherence in children aged 2-6 yrs in a specialised asthma clinic. Further follow-up of this cohort and additional studies in other settings are needed to substantiate our observation that high adherence combined with well-controlled asthma is possible in other patient groups. Recent studies from other groups support the idea that more intensive asthma care enhancing patient-provider partnership improves adherence and asthma control, and decreases hospitalisation rates and asthma expenditures.<sup>7,28</sup>

*Conclusions*

This study shows very high 3-month adherence rates to ICS maintenance treatment in children aged 2-6 yrs with asthma. This high adherence was associated with improved asthma control, and with parental medication perceptions, which are in agreement with the chronic illness model of asthma. We hypothesise that this desirable combination of high adherence and constructive parental medication beliefs can be ascribed to the organisation and content of asthma care, with repeated tailored self-management training and close follow-up, which helps to build and maintain a strong partnership between patients/parents and the medical team.<sup>2</sup> Further studies are needed to examine the relationship of such guideline-driven comprehensive asthma treatment and high adherence.

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# 4

## General practitioners' prescribing behaviour as a determinant of poor persistence with inhaled corticosteroids in children with respiratory symptoms: mixed methods study

T. Klok  
A.A. Kaptein  
E.J. Duiverman  
F.S. Oldenhof  
P.L.P. Brand

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## **ABSTRACT**

### *Aim*

To evaluate general practitioners' (GPs') prescribing behaviour as a determinant of persistence with and adherence to inhaled corticosteroids (ICS) in children.

### *Methods*

This was a prospective observational study of persistence with and adherence to ICS followed by a focus group study of the GPs prescribing this treatment. Participants were 134 children aged 2–12 years, who had been prescribed ICS in the year before the study started by their GPs. Main outcome measures were patterns and motives of GPs' prescribing behaviour and the relationship with persistence with and adherence to ICS.

### *Results*

GPs' prescribing behaviour was characterized by prescribing short courses of ICS to children with various respiratory symptoms without follow-up for making a diagnosis of asthma. This was driven by the GPs' pragmatic approach to deal with the large number of children with respiratory symptoms, and by beliefs about ICS which differed from currently available evidence. This prescribing behaviour was the main reason why 68 (51%) children did not persist with the use of ICS. In children with persistent use of ICS and a GP's advice to use ICS on a daily basis, the median (IQR) adherence was 70% (41–84%), and was similar for patients with persistent asthma and children lacking a diagnosis or symptoms of asthma.

### *Conclusion*

Inappropriate prescription of ICS to children by GPs is common and drives the lack of persistence with ICS therapy in primary care. This finding should be taken into account when interpreting data from large prescription database studies. Improving primary healthcare providers' knowledge and competence in diagnosing and managing asthma in children is needed.

## INTRODUCTION

Childhood asthma guidelines are unanimous in recommending daily inhaled corticosteroids (ICS) maintenance treatment only for children with persistent asthma.<sup>1-3</sup> Maximal efficacy of such treatment can only be achieved by high adherence rates above 80% of prescribed dosages and by persistence with this therapy over long periods.<sup>4</sup> To ensure this, close follow-up of children with asthma is recommended.<sup>1-3</sup>

In daily practice, however, both persistence with ICS prescriptions and adherence to their daily use is usually poor. Only half of the children having received a first prescription of ICS have an ongoing prescription 1 year later (poor persistence), and adherence rates to daily ICS use range from 30% to 70% in different studies.<sup>5-7</sup> Patients and their parents are usually held responsible for the poor persistence and adherence to ICS treatment,<sup>8,9</sup> and interventions to enhance medication adherence are focused on how health care providers can improve patients' and their parents' adherence behaviour.<sup>10</sup>

In disagreement with childhood asthma management guidelines, most children with asthma are not being followed up regularly in primary care,<sup>11,12</sup> and many children with an ICS prescription have not been diagnosed with persistent asthma.<sup>7,13</sup> Although these observations suggest that physician's prescribing behaviour and primary health care organization issues also may be important in determining poor persistence with and adherence to ICS treatment in children with asthma, this has received little attention in the literature to date. In particular, the reasons why primary care physicians choose to deviate from their childhood asthma management guideline have not been explored to our knowledge. We designed this study to evaluate primary health care providers' prescribing behaviour, both quantitatively and qualitatively, and the role of this behaviour in persistence with and adherence to ICS prescriptions in children with asthma in primary care.

## METHODS

This was a sequential mixed-methods study, starting with a quantitative study on ICS prescriptions and adherence to ICS use in children 2-12 years of age in primary care,

followed by a qualitative study in which general practitioners (GPs) were interviewed about the motivation underlying their prescription patterns.

#### *Participating GPs*

Nineteen GPs in the catchment area of our hospital, both from rural and urban region primary care practices, were willing to participate in the study. GPs who had participated in a previous study from our clinic were approached, after which these GPs recruited colleagues. The mean age of the participating GPs was 50 years (range 35-65 years), and they had been in practice for a mean of 15 years. There were 16 men (84%); most GPs (16, 84%) worked in group practices. The six GPs initially approached because of their previous participation in a study were known for their interest in childhood asthma care, the other GPs did not follow specific courses on the management of childhood asthma.

#### *Inclusion of children*

The quantitative part of our study was a 12-month longitudinal study in which adherence was measured electronically in children with persistent ICS use. GPs provided details of all 2-year-old to 12-year-old children who had received an ICS prescription in the last 12 months. These children were eligible for inclusion in our study. We excluded children who had been referred to secondary care for respiratory symptoms, those with severe comorbidity, and children whose parents had insufficient knowledge of the Dutch language. We approached no more than 20 children per GP to prevent overreliance of study results on GPs with high ICS prescription rates, and included only one child per family. Patients who had not used ICS and had had no asthma symptoms in the last 6 months, and patients with occasional intermittent ICS use (less than 2 weeks/year) were excluded from the 12-month longitudinal study.

#### *Interviews with parents*

To obtain a cross-sectional assessment of ICS prescription patterns in primary care, parents who agreed to participate were interviewed in a structured fashion about respiratory symptoms, ICS use and bronchodilator use of their child in the past 12 months.

#### *Assessing adherence*

In patients with persistent use of ICS by metered dose inhaler (MDI)/spacer combination or dry powder inhalator (DPI), adherence was monitored during the 12-month longitudinal follow-up study by the Smartinhaler<sup>®</sup>(MDI) or the SmartDisk<sup>®</sup> (DPI), electronic devices logging date and time of each ICS actuation.<sup>14,15</sup> Patients were excluded from adherence analysis if their ICS were withdrawn and stopped within 3 months of entry into the longitudinal follow-up study. In all other patients, adherence

was calculated as the number of SmartInhaler-recorded or SmartDisk-recorded inhaled doses expressed as a percentage of the number of doses prescribed, and censored at 100% of the prescribed dose.<sup>15</sup> At the end of the 1-year follow-up study, respiratory symptoms were recorded by validated questionnaire,<sup>16</sup> supplemented with parental information about doctor's prescription of ICS and bronchodilators, and about the GP's advice on how to use these medications. Data on follow-up visits and organisation of asthma care were obtained by chart review.

### *Interviews with GPs*

After completing the 1-year follow-up in all the patients, the aggregated adherence results and data on follow-up and organisation of asthma care were discussed in a 2.5 h focus group interview to which all participating GPs were invited, eight of whom (representing all primary practices involved in the study, mean age 54 years, range 39–65 years) participated.

Patterns of prescription of asthma medication to children and deviations from the primary care childhood asthma practice guideline were discussed. Reasons and motives for this behaviour were explored in a non-judgmental manner, along with a discussion of perceived advantages and drawbacks of the GPs' prescribing behaviour. This interview was audio recorded and analysed using standard methods of qualitative studies, as in earlier work from our group.<sup>17</sup> At the end of the focus group interview, a theoretical framework of the views discussed was developed by the senior researcher based on a recapitulation of the main findings, which was discussed and modified through discussion with all participating GPs until everyone present agreed with the final framework. The transcript was charted according to this theoretical framework, focused on detection of quotations not supporting the original framework or providing new categories or themes. The five themes that emerged from the data comprised: 'bridge a period with symptoms', 'difficulties in establishing a diagnosis of asthma', 'a pragmatical way of working', 'organisational issues', and 'perceptions about asthma and ICS'. The final interpretation of the data and the analysis of their possible explanations were checked by one of the attending GPs.

### *Ethical considerations*

This study was approved by the hospital ethics review board; all the parents provided written informed consent.

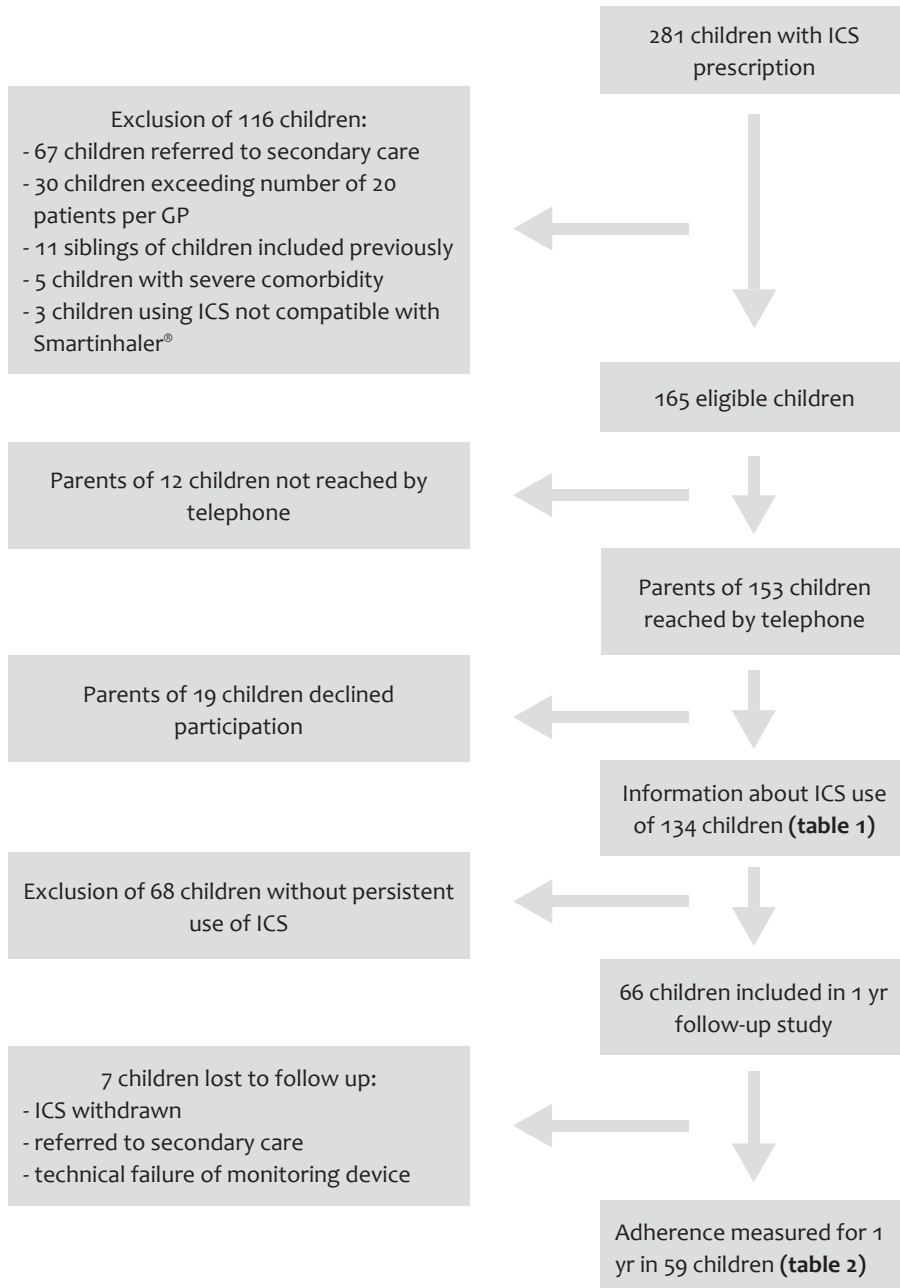
## **RESULTS**

### *Patients*

Patient recruitment is presented in figure 1. The 19 GPs had a mean of 11 (range 3–28) patients between 2 and 12 years of age who had received a prescription of ICS in the last year, had no severe comorbidity and had never been referred to secondary

care. Of the 165 eligible children, parents of 12 children could not be reached by telephone and 19 declined participation, leaving a total of 134 children whose parents provided information about ICS use. Only 66 of these children (49%) fulfilled the criteria of persistent ICS use. Their adherence to ICS maintenance therapy was measured electronically for 1 year.

**Figure 1. inclusion of patients**



*Result of interviews with parents of children being prescribed ICS*

Of the 134 patients (median age 5.7; IQR 4.0 to 9.8 yrs) whose parents were interviewed, ICS were stopped completely or used during less than 2 weeks per year in 68 (51%). Parents of 43 (63%) of these patients with non-persistence with ICS reported that they had been using ICS in short courses at the GP's advice, and 14 of these parents (21%) reported that their child had been using only one single course of ICS ever (table 1). Parents of 21 children (31%) reported chronic cough as the main symptom of their child; 18 parents (26%) reported that their child had never been prescribed a bronchodilator. Three children had been using ICS for episodes of croup.

*Symptoms and medication use during 1-yr follow-up*

Of the 59 children (median age 7.3, IQR 5-10.8 years) completing the 1-year adherence monitoring period, 26 (45%) never received a diagnosis of asthma, according to the parents (table 2). Based on parental report and chart review, 15 (26%) and 11 patients (19%) had never wheezed or suffered from breathlessness, respectively, and parents of 10 patients (17%) reported that ICS had been prescribed for persistent cough. During the 1-yr follow-up period, 13 children (22%) remained completely free from wheezing or breathlessness. Bronchodilators had never been prescribed to 6 patients (10%); 8 others (14%) had been recommended to use their bronchodilator on a daily basis (table 2). Although older children more frequently had a diagnosis of asthma (56% vs 21%,  $p=0.008$ ) and were more often advised to use ICS regularly (78% vs 43%,  $p=0.001$ ), differences between age groups in reported symptoms supporting an asthma diagnosis or the frequency of such symptoms were small (all  $p$  values  $>0.1$ , table 2).

**Table 1. Persistence of ICS use based on cross-sectional parental report (n=134)**

	all children (n=134)		children 2-4 years of age (n=47)	
<b>Non-persistent use</b>				
Use of ICS only in periods with symptoms (as prescribed by GP, for various respiratory symptoms), > 6 months no symptoms	43	(32%)	24	(51%)
Short course of ICS once in first wheezing episode	14	(11%)	6	(13%)
Daily use of ICS stopped at GP's advice because of remission of symptoms	11	(8%)	6	(13%)
<b>Persistent use</b>				
Persistent use in children	66	(49%)	11	(23%)

*Determinants of adherence during 1-yr follow-up*

During the 1-year follow-up, electronic adherence measurements were collected for a median (IQR) of 238 (121-350) days. Missing days were caused by children stopping ICS at their GP's advice during a "good" season with little symptoms, children in whom ICS therapy was stopped altogether because of clinical remission, and by technical device failures. Parents of 13 patients reported that their GP had recommended using ICS episodically when the child was symptomatic, but parents of four of these children administered ICS to their child on more than 50% of days.

In the 46 children who were prescribed long-term daily ICS, the median (IQR) adherence rate was 70% (41-84%); 32 children (70%) had adherence rates below 80%. Adherence was not determined by the presence of symptoms supporting an asthma diagnosis or by frequency of symptoms (table 2).

**Table 2. Characteristics of 59 children in whom adherence was measured electronically for 1 year**

		all children (n=59)	children 2-4 years of age (n=14)	Median adherence for children advised to use ICS on a daily basis (IQR)
<b>GP's advice</b>	use ICS daily	46 (78%)	6 (43%)	70% (41-84%)
	use ICS in symptomatic episodes only	13 (22%)	8 (57%)	Not calculated
<b>Symptoms not supporting asthma diagnosis</b>	never wheezing	15 (25%)	4 (28%)	70% (31-82%)
	never breathlessness	11 (19%)	3 (21%)	66% (53-81%)
	ICS as treatment for persistent cough	10 (17%)	5 (36%)	71% (60-85%)
<b>no GP diagnosis of asthma</b>		26 (44%)	11 (79%)	67% (22-85%)
<b>Frequency of wheezing/breathlessness in patients ever wheezing and/or breathless</b>	this year no symptoms	13 (22%)	5 (36%)	61% (54-87%)
	this year 1-3 periods with symptoms	25 (42%)	5 (36%)	70% (30-81%)
	this year >3 periods with symptoms	21 (36%)	4 (28%)	73% (26-87%)
<b>Use of bronchodilator</b>	used daily	8 (14%)	1 (7%)	76% (52-87%)
	never prescribed, never used	6 (10%)	4 (28%)	77% (70-86%)

*Focus group interview with GPs*

All GPs recognized the poor persistence with ICS and intermittent use of ICS as representative patterns of their prescription behaviour. As a general rule, they would prescribe a short ICS course to children with respiratory symptoms ranging from obvious wheezing and breathlessness to mild wheezing or persistent cough. Prescription of ICS in this way was accompanied by instruction to parents to return with their child after 6 weeks if symptoms persisted (which rarely occurred), or to stop ICS if symptoms resolved. GPs explained this prescription behaviour as a practical strategy to manage children with a range of respiratory symptoms without having to focus on making or excluding specific diagnoses.

**GP 3:** “It is not a conscious process; it is determined by the way we work.”

For children with symptoms likely to be self-limiting, such as chronic cough, the main reason for ICS prescription was to ‘bridge a period with symptoms’. In particular when parents were expecting or demanding a therapy, this strategy was used. In the GPs’ opinion, this satisfied most parents and prevented lengthy discussions about the lack of effective treatment options for cough, and about the need for referral to secondary care.

**GP 4:** “Parents and children are satisfied, that’s great. The diagnosis doesn’t really matter.”

**GP 1:** “I sometimes think back to the good old days when we were still allowed to use oral anticholinergics to help bridge a period of symptoms”

If symptoms returned in children with more obvious wheezing disorders, parents were encouraged to start another short ICS course themselves or the GP would prescribe it once again. Although GPs realized that they did not follow-up these patients or evaluated treatment effect, many considered these repeated ICS bursts as serial ‘treatment trials’, building up to an eventual asthma diagnosis in some children. Most GPs expressed lack of confidence in their ability to diagnose asthma, particularly in young children.

**GP 8:** “It is symptom treatment, really. On and off, you know, without thinking about a diagnosis”

**GP 5:** “A diagnosis of asthma is rarely made by me; I guess this happens mainly in secondary care. They have better diagnostic tools there, like lung function”



Besides the two main reasons for prescribing short courses of ICS (bridging a period of symptoms and working on establishing a diagnosis of asthma), GPs expressed additional perceptions about ICS and asthma that supported their prescribing behaviour. Most GPs viewed a 6-week course of ICS as an effective treatment option for children with chronic cough or intermittent wheezing. For some GPs this view was driven by their perception that these symptoms could be presenting symptoms of asthma.

**GP 6:** “Cough is also an expression of inflammation, which ICS may help to control.”

This prescribing behaviour was also driven by the GPs’ desire not to undertreat asthma. In their opinion the pros of this approach (not undertreating asthma) outweighed the cons (overtreatment of nonspecific cough and mild intermittent wheezing with ICS), because they viewed short ICS courses as harmless. They remarked that the reactive organization of primary health care for children (i.e., seeing the child only when symptoms occurred) instead of being proactive (with scheduled follow-up) enhanced this prescribing behaviour.

**GP 3:** “Most important lesson of this study for me? Making asthma care more proactive!”

## DISCUSSION

This study shows a common practice of prescribing short courses of ICS to children with various respiratory symptoms in primary care. This prescribing behaviour, which deviates from primary care childhood asthma management guidelines, is driven by a pragmatic approach aimed at symptom-treatment rather than making or excluding the diagnosis of asthma, and is enhanced by the reactive organization of primary care, where children are mainly being seen when symptoms occur, instead of being followed up regularly. Many GPs expressed perceptions about ICS and asthma which are in disagreement with the currently available evidence, stimulating the overtreatment of children with nonspecific or mild intermittent respiratory symptoms. The very low persistence with ICS in children is largely explained by this prescribing behaviour. Of the 59 children with persistent use of ICS, 20% used ICS only during symptomatic episodes (at the GP’s advice) and a similar proportion had no asthmatic symptoms ever but used ICS on a daily basis. Children with persistent wheeze were also commonly treated with intermittent courses of ICS.

The high ICS prescription rates in children without persistent asthma and low persistence with ICS that we found confirm results from previous studies in various coun-

tries. In two Dutch primary care studies, ICS were frequently prescribed to children and adults without a diagnosis of persistent asthma, and ICS persistence over a 1-yr follow-up period was only 50%.<sup>7,18</sup> In a large Dutch birth cohort study, 36% of children 2-8 years of age used ICS without having reported a single episode of wheezing in the past two years.<sup>19</sup> Several UK studies also reported high ICS prescription rates to children without persistent asthma, but with intermittent wheeze or chronic cough, together with low persistence with ICS therapy.<sup>4, 13, 20</sup> A recent Swedish study reported the same pattern of poor persistence with ICS, although the authors did not consider liberal ICS prescription by physicians.<sup>21</sup> Although it has been speculated that low ICS persistence rates could be explained by the use of ICS as a diagnostic treatment trial in children with nonspecific respiratory symptoms, previous studies never examined the reasons for ICS prescription behaviour of GPs.

Our focus group interview with GPs now provides unique and innovative insights into the pragmatic way in which GPs deal with the large number of children presenting with various respiratory symptoms. In agreement with our results, previous studies reported that primary care paediatricians in the USA and Spain recommended short-course ICS therapy for fictional patients with asthma, virus-induced wheeze, and bronchiolitis.<sup>22-24</sup> In these studies, primary care physicians with limited experience in respiratory disorders were most likely to show this erratic prescribing behaviour. Our study indicates that such limited experience is associated with lack of confidence in making or excluding a diagnosis of asthma, particularly in young children, and with non-evidence based perceptions about the effects of short-course ICS therapy on cough and on mild intermittent wheezing, confirming findings from a previous study.<sup>25</sup>

Because establishing the diagnosis of asthma may indeed be difficult, in particular in young children,<sup>26</sup> and because most respiratory symptoms in young children are transient, the pragmatic approach of GPs to treat nonspecific respiratory symptoms with short courses of ICS is understandable, particularly when considering their view that short ICS courses are harmless and their desire not to undertreat asthma. Nevertheless, there are numerous reasons to discourage this practice. First, even though most of these children inappropriately being prescribed ICS used the medication only briefly, some of these children were unnecessarily exposed to daily ICS for long periods of time, increasing the risk of exposure to high doses of ICS and their associated side effects.<sup>27</sup> Second, under this regime, children with asthma were also treated intermittently with ICS instead of the recommended daily use.<sup>1-3</sup> Third, inappropriate ICS treatment may distract from appropriately diagnosing and treating the real cause of their respiratory symptoms, such as a lower respiratory tract infection or allergic rhini-

tis.<sup>28</sup> Fourth, prescribing ICS to satisfy parents and to avoid lengthy discussions about referral or the lack of effective treatment for cough, although helpful in running an efficient clinic in the short term, may jeopardize a constructive physician-patient-parent relationship in future consultations. Finally, unnecessary ICS treatment for nonspecific cough generates considerable societal costs (an estimated €1 million per annum in our country of 17 million inhabitants).

Our study has considerable implications both for research and for clinical practice. ICS persistence and adherence studies are usually based on large pharmacy databases, with limited information about physician's considerations, beliefs, and prescribing practices. Such studies rely heavily on appropriate diagnosing and prescribing behaviour of physicians, while our study illustrates how important it is to take the physicians' prescribing behaviour into account to interpret and understand these data. The GPs in our study acknowledged the problem of lacking proactively organized primary care for children with respiratory symptoms, and suggested using specialized nurses as an important solution to ensure scheduled follow-up for these patients. Previous studies from our group have shown that children with a confirmed diagnosis of asthma can effectively and cost-efficiently be followed up by asthma nurses.<sup>29</sup> The GPs themselves, however, are responsible for solving the problem of inappropriately prescribing ICS to children without persistent asthma and advising short courses of ICS to children with asthma. The presence of erratic perceptions suggests the need for additional targeted training in asthma diagnosis and management for GPs. Such training has been shown to be effective in improving asthma care to children.<sup>30</sup>

### *Strengths and limitations*

The main strength of this study is that we collected detailed information about the patients' symptoms and ICS use, and on the reasons and motivations for GPs' prescribing behaviour, which not only highlighted important areas for improvement in primary care for children with asthma, but also provided a novel explanation for the previously described poor ICS persistence in children. The main limitation is the generalizability of this study because we studied only GPs willing to participate in the study of which a number with specific interest to childhood asthma care. Because of this interest of these GPs, it is not likely other GPs perform better in prescribing ICS and following asthma guidelines. Considering the similarities of our findings with previous reports of prescribing patterns of ICS in primary care in several countries,<sup>5,7,13,20-24</sup> we believe our findings can be applied to most settings of primary care.

A second limitation is recall bias because parental report of asthmatic symptoms in their children was recorded retrospectively, at the end of the follow-up period. However, because the questionnaire we used for this purpose was validated and has been

used extensively in previous work, it is unlikely that this had a major influence on our findings.<sup>16, 19</sup>

## **CONCLUSION**

Inappropriate prescription of ICS to children by GPs is common and is driven by a pragmatic approach to treat symptoms rather than making or excluding a diagnosis of asthma, erratic perceptions about the efficacy of ICS in reducing persistent cough and mild intermittent wheeze, and a reactive organisation of primary care where scheduled follow-up is exceptional. The inappropriate prescribing behaviour of GPs that we observed drives the lack of persistence with ICS therapy in primary care and this finding should be taken into account when interpreting data from large prescription database studies. The large number of inappropriate ICS prescriptions together with intermittent therapy in children with asthma stresses the need to improve GPs' knowledge and competence in diagnosing and managing asthma in children in primary care.

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# 5

Physician's adherence to guidelines and parent's adherence to inhaled corticosteroids in children with asthma: 1-year observational study in primary and secondary care

T. Klok  
A.A. Kaptein  
E.J. Duiverman  
P.L.P. Brand



## ABSTRACT

### *Aim*

To study patient- and physician-related determinants of 1-year electronically measured adherence to inhaled corticosteroids in children with asthma in primary and secondary care.

### *Methods*

This was an observational study with one year follow-up in a hospital-based outpatient clinic providing comprehensive asthma care and seven primary care practices providing basic asthma care. Participants were children 2-12 years of age with asthma and a prescription of inhaled corticosteroids. Long-term adherence to inhaled corticosteroids was electronically measured. A broad range of putative determinants were assessed, including parental illness perceptions and medication beliefs, and patient-centeredness of consultations, by validated questionnaires.

### *Results*

Median (interquartile range) adherence was significantly higher in secondary (84%, 70 to 92%) than in primary care (66%, 32 to 86%,  $p < 0.001$ ). Parents from secondary care expressed higher ICS need for their child; they also rated patient-centeredness of consultations higher than parents in primary care. The relationship of these findings and the level of asthma care was potentially biased by less severe asthma in children from primary care, but children from primary care and secondary care had similar high median rates of asthma control.

### *Conclusion*

Patient-centred, guideline based comprehensive asthma care with repeated scheduled follow-up is associated with considerably higher adherence than basic asthma care with single-session education and lack of scheduled follow-up. Modification of parental medication beliefs appears to be an important moderator of this association. Improvement of asthma care can make a pivotal contribution to improving adherence and reducing the burden of uncontrolled asthma.

## INTRODUCTION

Adherence to daily medication is of critical importance in determining the success of treating chronic conditions such as childhood asthma.<sup>1</sup> Poor adherence to maintenance medication is the rule rather than the exception, however.<sup>1</sup> Knowledge of the reasons for such poor adherence may help to improve adherence, and the effects of treatment.

The most basic form of non-adherence is when patients (and their parents, if the patient is a child) do not understand the rationale for treatment (unwitting non-adherence).<sup>2</sup> Although this can be easily overcome by providing appropriate information, studies consistently show that education alone is insufficient to improve adherence, indicating that other factors are more important in driving non-adherence.<sup>3</sup> These can be divided into two groups. First, unplanned non-adherence is related to limited family (medicine taking) routines, and child raising issues.<sup>2,4</sup> Second, intentional non-adherence refers to patients who deliberately choose not to follow the doctor's recommendations, based on their illness perceptions and medication beliefs.<sup>2</sup> Such perceptions and beliefs have consistently been shown to be strong determinants of adherence.<sup>5,6</sup>

Currently available research on non-adherence has primarily examined patient related factors.<sup>1</sup> Accumulating evidence, however, shows that the organization of health care and the health care provider's behaviour have major impact on adherence in a range of chronic conditions.<sup>1,7-9</sup> Children from underprivileged backgrounds exposed to numerous risk factors for non-adherence can achieve good adherence and asthma control when enrolled in a programme of self-management education and close follow-up.<sup>10</sup> Such a programme of comprehensive self-management education and follow-up, while common in hospital-based secondary care, is rare in primary care.<sup>11-14</sup> In a recent qualitative study, we observed considerable differences in illness perceptions and medication beliefs between parents of asthmatic children in primary and secondary care, suggesting that comprehensive care allows modification of these important determinants of adherence.<sup>14</sup> In the present longitudinal observational study, we monitored adherence and its patient- and physician-related determinants in patients in primary and secondary care.

## METHODS

**Design and setting.** This was an observational study with one year follow-up of asthmatic children aged 2-12 years, receiving asthma care in our hospital-based outpatient clinic (with comprehensive asthma education and close follow-up, as described previously)<sup>15</sup> or in one of seven participating primary care practices in the catchment area of our hospital (with mostly single-session education and follow-up as needed by patients and parents).<sup>14</sup>

### *Inclusion*

In primary care, general practitioners provided a list of all 2-12 year old children who had received an ICS prescription in the last 12 months. Children who had ever been referred to secondary care for their asthma were excluded, and the number of patients per GP was limited to 20. Parents of all other children were approached by telephone (as described previously).<sup>16</sup> Children were eligible for inclusion in the 1-yr follow-up study if they had persistent ICS use. This was defined as parents reporting having received the advice (from their GP) to give ICS to their child on a daily basis, having indeed been using the ICS during the last 6 months for recurrent wheezing and breathlessness (not isolated cough), and expecting to continue using ICS during the next three months.

In secondary care, parents of all children aged 2-12 years with paediatrician-diagnosed asthma and persistent ICS use attending the outpatient clinic for regular follow-up were asked to participate in the study. Only one child per family was included. Exclusion criteria comprised limited knowledge of the Dutch language and severe comorbidity.

### *Follow-up and assessment of adherence to ICS*

Throughout the 12-months follow-up, adherence was monitored by electronic devices logging date and time of each ICS actuation: Smartinhaler<sup>®</sup> for metered dose inhaler (MDI)/spacer combination, SmartTracker<sup>®</sup> for MDI with dose counter, and SmartDisk<sup>®</sup> for Diskus/Accuhaler.<sup>15,17</sup> At each follow-up visit, or during home visits when time to the next scheduled follow-up visit exceeded 5 months, data recorded by the electronic devices were uploaded and proper recording function checked. Adherence was calculated as the number of electronically recorded inhaled doses expressed as a percentage of the number of doses prescribed, censored at 100% of the prescribed dose.<sup>4</sup>

### *Putative determinants of adherence*

We collected clinical and demographic data by structured interview and chart review. Upon entry into the study, a number of validated questionnaires were administered to parents and children. Parental illness perceptions were assessed by the Brief Illness

Perception Questionnaire (B-IPQ),<sup>18</sup> and medication perceptions by the Beliefs about Medicines Questionnaire (BMQ, which also provides the balance between parent-perceived necessity and concerns about ICS)<sup>19</sup>, and the Treatment Satisfaction Questionnaire for Medication (TSQM).<sup>20</sup> In addition, we applied the 'I Worry scale' (scoring parental worries about their child having asthma and using daily ICS),<sup>21</sup> the Satisfaction with Information about Medicines Scale (SIMS),<sup>22</sup> and an asthma knowledge questionnaire.

At baseline and at 6 and 12 months follow-up, asthma control and parental quality of life were assessed by parent-completed Asthma Control Questionnaire (ACQ) and the Paediatric Asthma Caregiver Quality Of Life questionnaire (PACQOL), respectively.<sup>23,24</sup> Participating children aged 8-12 years completed children's versions of each questionnaire, without input from their parents, under supervision by the investigator (TK). At the end of 1-yr follow-up, we asked the parents to assess the degree of patient centeredness the physician had employed during the study period with a questionnaire focusing on physician's exploration of parental views and concerns about the illness and the medication and on achieving mutual agreement about treatment.<sup>25</sup>

### *Analysis*

We assessed the association of ICS adherence to all putative determinants (defined a priori with a focus on parental perceptions about illness and medication) for primary care and secondary care separately, and for the total population, in nonparametric univariate analyses (because of skewed distribution of adherence) using SPSS version 17.0. We chose to refrain from adjustments for multiple comparisons and from multivariate analysis because of the exploratory and observational nature of our study.

## **RESULTS**

### *Patient recruitment and follow-up*

Inclusion in primary care was hampered by lack of persistent ICS use: 50% of the children who had had an ICS prescription during the last 12 months had not been using ICS in the last 6 months (figure 1).<sup>16</sup> In primary care and secondary care, 42 children (86% of those enrolled) and 135 children (90% of those enrolled) completed the study, respectively. Of these children, 167 (94%) were followed for 1 year, 10 children were followed-up until medication was stopped by the physician after at least 3 months participation in the study (figure 1).

Electronic adherence data were collected for a median of 286 days (interquartile range 152-362 days). Reasons for missing data included technical failure of the electronic monitoring devices, parents not bringing back the devices or returning damaged devices, and parents failing to use the device (e.g. leaving the electronic device at home during vacations).

Figure 1. Inclusion of patients (part 1 of 2)

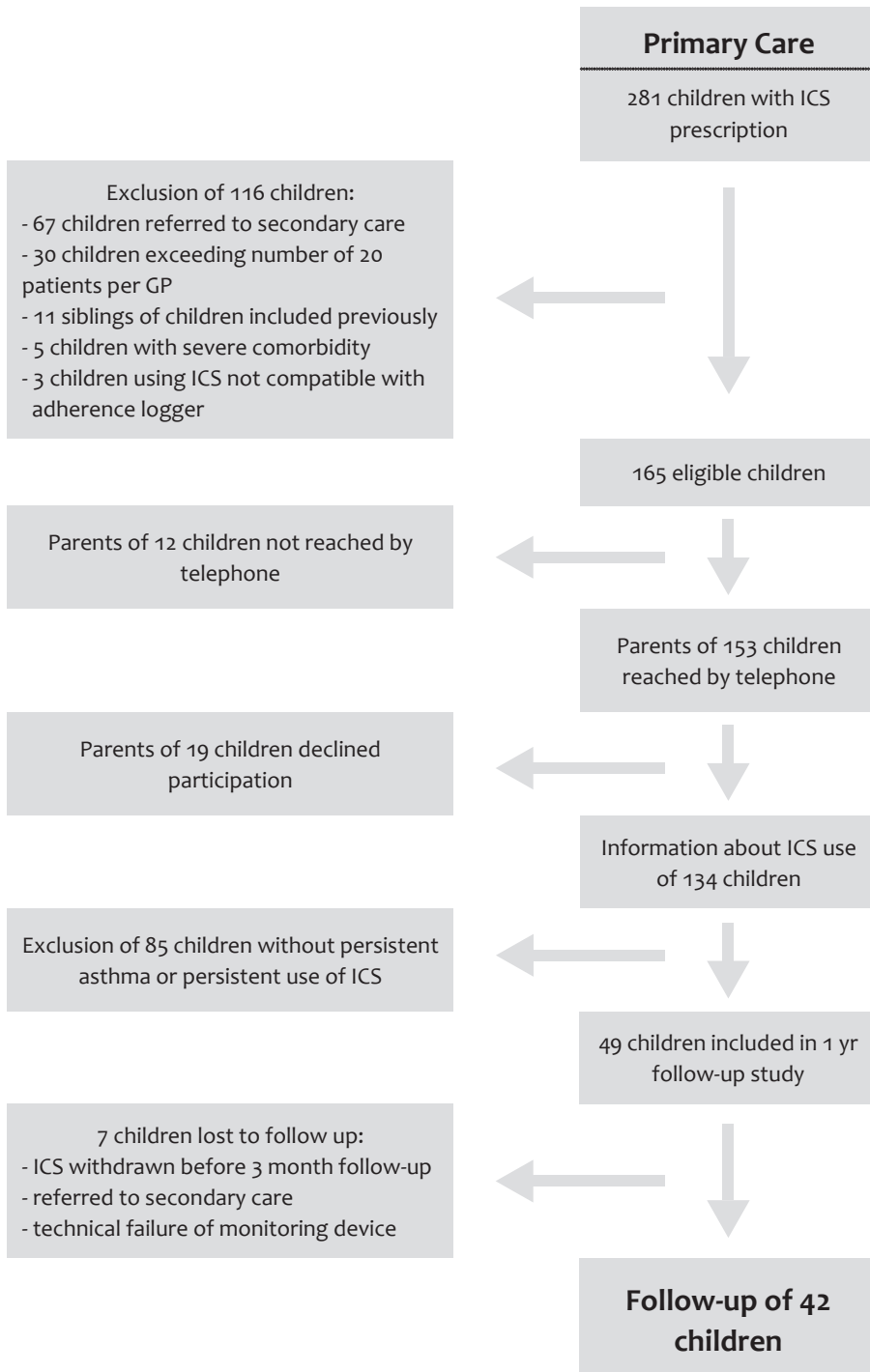
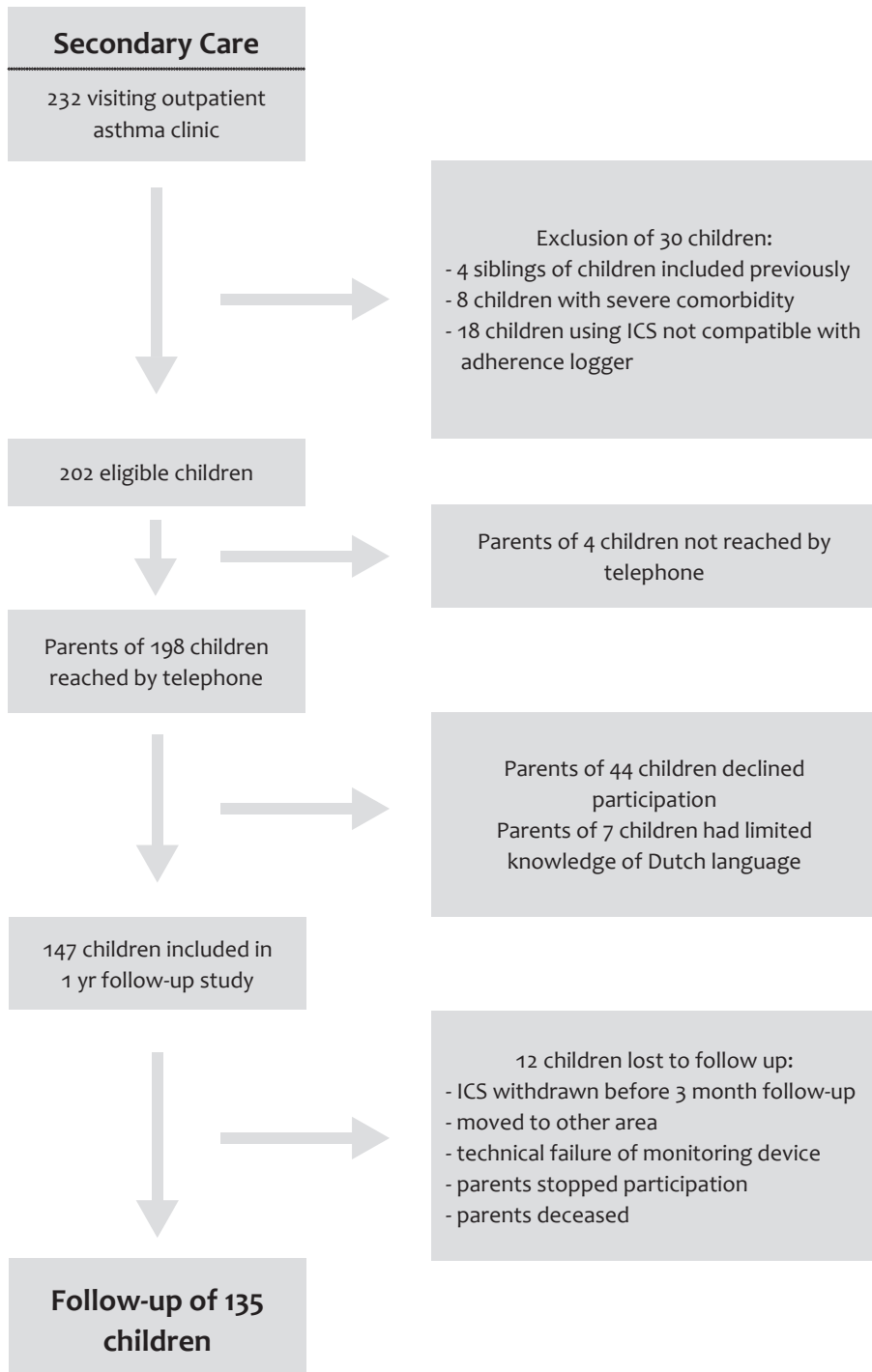


figure 1. Inclusion of patients (part 2 of 2)



*Differences between participants in primary and in secondary care*

Children from primary care were older, used a lower daily ICS dose, had slightly better quality of life, and had been less frequently hospitalized before study entry than children from secondary care (table 1). Asthma control as assessed by ACQ was comparable, with good asthma control at baseline and throughout 1-yr follow-up in most children (table 1). Parental quality of life remained high in both groups throughout the study. In primary care, patients were seen less frequently for follow-up, parents were less satisfied with the information about medicines, and physicians' patient-centeredness was rated lower than in secondary care (table 1).

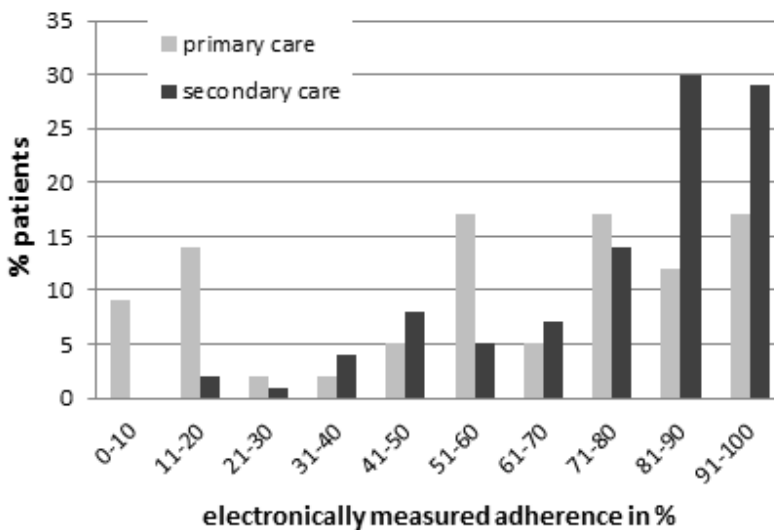
*Differences in parental illness perceptions and medication beliefs between primary and secondary care*

Parents from secondary care perceived higher influence of asthma on their child ( $p=0.038$ ) and reported higher levels of concerns ( $p=0.002$ ) and emotions ( $p<0.001$ ) regarding their child's asthma. The maximum difference in the mean scores of illness perceptions (score 1 to 10) was 2 points. Parental perceived ICS necessity was significantly higher in secondary care, where ICS concerns superseded necessity in only 12 parents (9%), as compared to 10 parents (26%) in primary care ( $p<0.001$ ).

*Adherence rates in primary and secondary care*

Adherence was considerably higher in secondary than in primary care (figure 2), with median (interquartile range, IQR) adherence of 84% (70-92%) and 66% (32% to 86%), respectively ( $p<0.001$ ). The proportion of children with adherence > 80% of

**Figure 2. Electronically measured adherence in primary care and secondary care.**



**Table 1. Characteristics of study patients, their parents and parental assessment of asthma care (n=177)**

	Patients from general practi- ces (n=42)	Patients from outpatient clinic (n=135)	p-value
<b>Patients</b>			
Age (mean; range; yrs)	8 (2 to 12)	6 (2 to 12)	<0.001
Maintenance medication:			
-inhaled corticosteroids (ICS)	100%	90%	0.065
-ICS and long-acting bronchodilators (%)	0%	10%	
-ICS dose (fluticasone®; mean; range; µg)	175 (50 to 250)	250 (125-500)	0.014
Nr of children hospitalised in year before study (%)	2 (5%)	37 (27%)	0.004
Nr of children requiring prednisolone for asthma exacerbations	4 (10%)	25 (19%)	0.256
ACQ baseline (<0.75 = well-controlled asthma, >1.5 = not well-controlled asthma)	0.67 (0.33 to 1.13)	0.50 (0.17 to 1.17)	0.498
ACQ at 6 months	0.67 (0.00-1.34)	0.33 (0.00-1.00)	0.303
ACQ at 12 months	0.50 (0.00-0.83)	0.50 (0.00-1.17)	0.551
<b>Parents</b>			
Educational level of mother (1 = low and 7 = high)	5 (4 to 7)	5 (5 to 6)	0.823
Parental diagnosis of asthma	40%	40%	0.932
PACQOL (1 = low and 7 = high quality of life)	6.7 (6.1 to 6.9)	6.3 (5.5 to 6.9)	0.008
PACQOL at 6 months	6.7 (6.4-7)	6.7 (6.1-6.9)	0.129
PACQOL at 12 months	6.9 (6.4-7.0)	6.7 (6.3-6.9)	0.062
<b>Asthma care</b>			
Number of visits to GP or outpatient clinic in study year (range)	1 (0 to 3)	4 (2 to 4)	<0.001
SIMS (0 = low and 9 = high level of satisfaction)	8 (6 to 9)	9 (7 to 9)	0.024
Patient-centeredness questionnaire (1 = low and 5 = high)	3.1 (2.9 to 4.0)	4.0 (3.4 to 4.6)	<0.001
Data are presented as mean ± SD, or as median (interquartile range) unless otherwise stated; ACQ: Asthma Control Questionnaire; PACQOL: paediatric asthma caregiver quality of life questionnaire; SIMS: Satisfaction with Information about Medicines Scale. <sup>22-24</sup>			



**Table 2. Determinants that showed statistically significant correlation with adherence**

	Rank correlation coefficient between independent variables and adherence in:					
	primary care (n = 42)		secondary care (n = 135)		total population (n = 177)	
	$\rho$	p-value	$\rho$	p-value	$\rho$	p-value
<b>Characteristics of children</b>						
Child's age	-0.27	0.086	-0.15	0.082	-0.23	0.002
ACQ at 6 months	-0.19	0.247	-0.21	0.020	-0.23	0.004
ACQ at 12 months	0.12	0.503	-0.23	0.016	-0.13	0.128
TSQM, children's global satisfaction of daily use of ICS (n=28)	NA		0.51	0.006	NA	
<b>Characteristics of parents</b>						
Educational level mother	0.16	0.354	0.17	0.060	0.15	0.046
<b>Characteristics of care</b>						
Parental asthma knowledge questionnaire	0.39	0.012	0.08	0.380	0.17	0.027
Patient-centeredness questionnaire	0.43	0.008	0.01	0.948	0.18	0.035
<b>Parental perceptions about illness &amp; medication</b>						
BMQ, specific part, subscale necessity of ICS	0.40	0.012	0.07	0.437	0.20	0.009
BMQ, specific part, need-concern ratio	0.29	0.070	0.08	0.355	0.15	0.045
BMQ, perceptions about harm and over-use of medication in general	-0.13	0.421	-0.18	0.041	-0.16	0.038
TSQM, subscale convenience of daily use of ICS	0.20	0.212	0.26	0.003	0.23	0.003
TSQM, subscale global satisfaction of daily use of ICS	0.29	0.074	0.17	0.059	0.19	0.011
B-IPQ, emotional response on child's asthma	0.03	0.843	0.06	0.484	0.15	0.047
B-IPQ, feeling of understanding child's asthma	-0.27	0.090	-0.12	0.159	-0.19	0.013
#: in all items higher scores represent higher level of measured concepts, with the exception of Asthma Control Questionnaire in which high scores represent poor asthma control; ACQ: Asthma Control Questionnaire; TSQM: Treatment satisfaction questionnaire for medication; BMQ: Beliefs about Medicines Questionnaire; B-IPQ: Brief Illness Perception Questionnaire.18-20, 23						

prescribed doses was 29% in primary and 59% in secondary care ( $p=0.001$ ); the median (IQR) number of days on which children received no ICS was 17% (4% to 49%) in primary and 6% (1%-19%) in secondary care ( $p=0.004$ ).

#### *Determinants of adherence*

Determinants significantly associated to adherence differed between primary and secondary care (table 2). In primary, but not in secondary care, asthma knowledge, ICS necessity, and patient-centeredness were strong determinants of adherence. In both groups, parents who viewed ICS administration as convenient, who reported high global satisfaction with ICS, and who expected little harm of medicines in general had higher ICS adherence rates (table 2). The only factor significantly associated with adherence from the children-completed questionnaires was global satisfaction with ICS therapy (table 2).

## **DISCUSSION**

This study shows that adherence to daily ICS use in children with asthma was considerably lower in patients followed up in primary care than in secondary care. In secondary care, children's asthma was more severe at study entry than in primary care, with more hospitalizations, higher ICS dose, and lower quality of life. Asthma control scores and exacerbation rates, however, were comparable in the two groups throughout follow-up. The higher adherence in secondary care was accompanied by a higher parental perceived need of the daily use of ICS. Parents rated patient-centeredness of consultations higher in secondary than in primary care. Medication beliefs were associated with adherence rates in both settings. In addition, asthma knowledge and patient-centeredness were strong determinants of adherence in primary care. Of all studied modifiable patient-related factors, parental medication beliefs were the only determinants of the measured adherence that differed between primary care and secondary care. This suggests that such medication beliefs are the moderator of the relationship of quality of asthma care and adherence to ICS.

#### *Strengths and weaknesses*

The main strengths of this study are the electronic measurement of adherence, the follow-up of 1 year, the comparison between primary and secondary care, and the comprehensive collection of putative determinants of adherence. The poor persistence with ICS in primary care hampered the inclusion of children from primary care, causing a relatively small study population in this setting. The cross-sectional measurement of parental illness perceptions and medication beliefs does not allow firm inference of causality that these cognitions were modified by comprehensive asthma care. An alternative explanation for the observed higher perceived necessity of ICS in the

secondary care group could be differences in asthma severity or the age of the children between the two settings. Previous studies, however, have shown poor adherence in children with asthma irrespective of asthma severity, and no association of asthma disease characteristics and adherence.<sup>26</sup> It appears unlikely, therefore, that the differences we observed in medication beliefs and adherence between primary and secondary care are caused by selective recruitment of high-necessity, highly adherent parents in secondary care. Similarly, the small difference in age between the populations is too small to be responsible for the large difference in adherence we found.

### *Comparison to other studies in the field*

The strikingly high adherence rate of the children with asthma in secondary care in this study (median 84%) far exceeds that previously reported in long-term quantitative adherence studies (40-70%),<sup>4, 27-30</sup> which were comparable to the adherence found in our primary care group (66%). This is clinically highly relevant because of the strong relationship between adherence and asthma control (table 2).<sup>31, 32</sup> These findings illustrate that characteristics of healthcare organization and delivery are important determinants of adherence,<sup>1</sup> and that good adherence can be achieved in the large majority of children receiving comprehensive guideline-based asthma care.<sup>10, 33</sup> The key components of comprehensive asthma care being delivered by asthma specialists in secondary care appear to be regular follow-up and repeated tailored self-management education. In contrast, the asthma management in primary care was characterized by mostly single-session education and haphazard or absent follow-up. This is not unique to our study, as this phenomenon has been reported in several countries in Europe and North America.<sup>11, 12, 34-36</sup>

International guidelines including the Dutch primary care guideline, however, recommend regular follow-up and self-management education.<sup>37-39</sup> Poor adherence by primary care professionals to asthma guidelines is therefore common, and is associated with poor adherence to maintenance medication by patients and parents in this study. In accordance with previous studies,<sup>2, 26, 40</sup> parental medication beliefs were the main determinant of non-adherence to ICS (table 2). The significantly higher ICS necessity perception in parents in secondary care as compared to those in primary care suggests that counterproductive medication beliefs (concerns exceed perceptions of benefit) can be modified into constructive and useful beliefs (benefits outweigh concerns) as the result of comprehensive guideline based asthma care. This is supported by the few previous studies which have examined whether illness and medication beliefs can be modified.<sup>6, 41</sup> This appears to be dependent on whether the health care professional is able to explore the patient's (or parents') illness perceptions and medication beliefs, and is able to build sufficient rapport and trust to discuss these cognitions constructively,<sup>42</sup> aiming at making a shared decision on treatment.<sup>43, 44</sup> In a randomized control-

led trial of adults with asthma, individualized text messaging, tailored to each patient's specific information based on a discussion of their illness perceptions and medication beliefs, modified these cognitions and improved self-reported adherence.<sup>41</sup> Therefore, it appears not to be the regular follow-up in itself, but the physician's communication behaviour during follow-up that determines long-term adherence to daily maintenance medication in children with asthma.

#### *Practice and research implications*

The results of this study have important implications both for clinical practice and research. Our findings underscore the need to enhance implementation of guideline-based comprehensive asthma care, with close follow-up and repeated tailored self-management education. Children with asthma should be managed in a setting in which such care can be guaranteed. This is likely to improve adherence to maintenance medication, and reduce the burden of uncontrolled asthma in the community. The implications for future adherence research are twofold. Firstly, because of its high level and limited variation, a quantitative study such as ours has limited power in detecting the determinants of adherence in children receiving comprehensive asthma care. Unravelling the components of comprehensive asthma care responsible for high adherence, therefore, needs a different, probably qualitative study design. Second, prospective studies are needed to study how parents' and children's illness perceptions and medication beliefs develop and change from enrolment into comprehensive asthma care.

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# 6

It's the adherence,  
stupid! (that determines  
asthma control in  
preschool children)

T. Klok  
A.A. Kaptein  
E.J. Duiverman  
P.L.P. Brand



## **ABSTRACT**

### *Aim*

To explore the relationship between adherence to inhaled corticosteroids and long-term asthma control in young children with asthma.

### *Methods*

Eighty-one 2–6-yr-old asthmatic children, using inhaled corticosteroids (ICS), enrolled in a program with extensive self-management training and close follow-up were enrolled. Adherence was measured daily for 12 months using Smartinhaler<sup>®</sup> devices. Long-term asthma control was assessed by parents and physicians and included clinical assessment, asthma control questionnaire, and lung function. We examined the association of adherence to short-term and long-term asthma control, adjusting for seasonal influences and clinical characteristics.

### *Results*

Median (interquartile range) adherence was 87% (70-94%), and 64 (79%) children had well-controlled asthma throughout follow-up. Adherence >80% was associated with better asthma control, and we found no important confounders of this association. Children with persistent mild symptoms had lower adherence rates ( $p=0.028$ ).

### *Conclusion*

Guideline-based asthma care was associated with good asthma control in most children. Adherence to inhaled corticosteroids was an independent strong predictor of long-term asthma control, with highest levels of asthma control found in children with adherence >80% of doses prescribed.

## INTRODUCTION

Daily low-dose inhaled corticosteroid (ICS) therapy significantly improves asthma control, both in school-aged and in pre-school children with persistent asthma.<sup>1,2</sup> Poor adherence to this therapy decreases the effectiveness of ICS, but studies on the relationship of adherence and asthma control are complicated by the different methods used to assess adherence. Electronic monitoring devices recording date and time of each inhaler actuation have been shown to be the most accurate measurement of adherence.<sup>3-5</sup> The few studies using this methodology in children showed an increased risk of uncontrolled asthma or an asthma exacerbation in children with lower adherence over the preceding 1- or 3-month period, respectively.<sup>6,7</sup> Although these studies therefore show an association between adherence and asthma control at group level over short periods of time, no studies to date have examined the relationship between long-term asthma control and adherence in individual patients. A number of factors may influence this relationship over longer periods of follow-up. First, short-term adherence is likely to increase when parents know that adherence is being monitored, or when a follow-up visit is approaching, while long-term adherence decreases over time.<sup>6,8</sup> Secondly, individual characteristics such as significant comorbidity and seasonal changes in asthma control may influence the relationship of long-term asthma control and adherence.<sup>9</sup> Thirdly, the focus of guideline-based comprehensive asthma care is not only on adherence, but also on improving inhalation technique, elimination of exposure to relevant allergens and irritants (including environmental tobacco smoke) and treating comorbidities such as allergic rhinitis, all of which may contribute to improved asthma control.<sup>10</sup> Previous studies have shown that such comprehensive asthma care with regular follow-up was associated with achieving and maintaining well-controlled asthma in inner-city asthmatic children.<sup>11,12</sup> Although the authors suggested that adherence may explain the relationship between comprehensive asthma care and asthma control, adherence in these studies was assessed by health care providers instead of being monitored electronically.

We previously showed very high median electronically measured adherence rates and a significant association between adherence and asthma control in 2-6 year old children

with persistent asthma followed up at our hospital-based paediatric asthma clinic for 3 months.<sup>13</sup> In the present study, we examined the association between daily electronically measured adherence and asthma control during 12 months of follow-up, which allowed us to take several potential confounders into account.

## METHODS

### *Design and setting*

This was an observational study with one year follow-up of asthmatic children aged 2-6 years, who were being monitored and followed up at our hospital-based paediatric asthma outpatient clinic. To enter our asthma management program, children have to be referred by their primary care practitioner because of troublesome, severe, or frequent symptoms. After the diagnosis of persistent asthma had been made by the attending paediatrician, ICS by metered dose inhaler/ spacer combination were being prescribed as daily controller therapy, irrespective of the wheezing phenotype (episodic viral or multiple trigger wheeze), in accordance with the national paediatric asthma guidelines.<sup>14</sup> Details of the asthma management program in our clinic have been published previously,<sup>13,15</sup> and comprise extensive training of correct inhalation technique, home-visits to assess and reduce exposure to relevant allergens and tobacco smoke and treatment of relevant comorbidities.

### *Inclusion and collection of baseline data*

For this study, parents of all children aged 2-6 years with persistent asthma currently treated with ICS attending the outpatient clinic for regular follow-up were asked to participate in the study. Exclusion criteria comprised limited knowledge of the Dutch language and severe comorbidity. All included children whose ICS were withdrawn at the physician's advice during or immediately after completion of the study were excluded from analysis, because asthma control in these children was considered to be unrepresentative because of clinical asthma remission. We collected demographic and clinical data by structured interview and chart review. At baseline, lung function, asthma control, and parental quality of life were also recorded. Lung function was assessed before and after inhaling salbutamol 400 µg: flow-volume curves in children 5 years of age and older, and respiratory resistance (Rint) by Microrint® in children < 5 years of age (Microrint®; Micro Medical Ltd, Rochester, UK), according to European Respiratory Society/American Thoracic Society guidelines.<sup>16</sup> Results were expressed as Z-scores. Asthma control was assessed by parent-completed Asthma Control Questionnaire (ACQ), and parental quality of life by the Paediatric Asthma Caregiver Quality Of Life questionnaire (PACQOL).<sup>17, 18</sup>

*Assessment of adherence to ICS*

Throughout the 12-months follow-up, adherence was monitored by Smartinhaler<sup>®</sup>, a validated electronic device logging date and time of each ICS actuation.<sup>13,19</sup> At each follow-up visit to the clinic, the data recorded by the Smartinhaler<sup>®</sup> were uploaded and proper recording function checked. To prevent considerable loss of data in case of malfunctioning devices and to assess asthma control regularly, a home-visit was made by a researcher to upload the Smartinhaler<sup>®</sup> and record parental assessment of asthma control, when time to the next scheduled follow-up visit exceeded 5 months.

*Assessment of asthma control, lung function, and parental quality of life during follow-up*

At each follow-up visit, asthma control was assessed by the attending physician and paediatric asthma nurse on a visual analogue scale ranging from 0 (completely uncontrolled asthma) to 10 (completely controlled asthma), based on a review of symptoms, limitations, and exacerbations since the previous visit.<sup>20</sup> The prescribed daily dose and dosing frequency of maintenance treatment for asthma and any identified comorbid disorder was documented in the patient's chart at each follow-up visit, and recorded for study purposes. At each visit, parents completed an ACQ about their child, and reported any exacerbations that had occurred since the previous visit. After 6 and 12 months of follow-up, parents also completed the PACQOL, lung function was performed as described above, and a single-breath fraction of nitric oxide in exhaled breath (FeNO) measurement was carried out with a hand-held electrochemical analyser (NIOX Mino; Aerocrine, Solna, Sweden) with an expiration time of 6 s.<sup>21</sup> After completion of the study, hospital and family physician charts were reviewed to double-check the reliability of the data, and to identify any prescriptions of oral prednisolone during the study period.

*Analysis*

Adherence was calculated as the number of Smartinhaler<sup>®</sup>-recorded inhaled doses expressed as a percentage of the number of doses prescribed, either between midnight and midday or between midday and midnight for morning and evening doses, respectively, or at any time during the day for once-daily dosing. Adherence was censored at 100% of the prescribed dose. We assessed the association of adherence during the two months preceding each follow-up visit to each indicator of asthma control at the follow-up visit, using nonparametric methods because of the highly skewed distribution of adherence.

Because a number of children used a lower ICS dose, or no ICS at all, during summertime, and because we expected asthma control to deteriorate during winter months because of viral infections, we performed separated analyses for summer (May to September) and winter (October to April) seasons, expecting the relationship of adhe-

rence to asthma control to be stronger in winter. To compare the effects of moderate and good long-term adherence on asthma control, we also assessed the association of asthma control to the 12-month adherence dichotomized as good (>80%) and moderate (50-80%) adherence.

Based on all the collected information about asthma control, the child's long-term asthma control was classified as 'well-controlled asthma' (no or infrequent mild symptoms during the study period), 'mostly well-controlled asthma' (well controlled asthma, except for 1 or 2 episodes with moderate to severe symptoms sometimes requiring a course of prednisolone), 'mild uncontrolled asthma' (recurrent periods with mild to moderate asthma symptoms), and 'uncontrolled asthma' (recurrent periods with moderate or severe asthma symptoms including one or more exacerbations needing prednisolone).

Correlations between asthma control and clinical and demographic variables were assessed using Spearman's rank correlation coefficient. Because this yielded no statistically significant correlations, we refrained from multivariable analyses between adherence and asthma control, adjusting for other clinical and demographic variables.

#### *Ethical considerations*

This study was approved by the hospital ethics review board and all parents provided written informed consent.

## **RESULTS**

Of the 138 eligible patients, 104 children (75%) entered the study after informed consent was obtained, and 81 children (78% of those enrolled) with persistent prescription of ICS completed the 12-months follow-up (figure 1). The clinical and demographic characteristics of these patients are presented in table 1. Most participating children had well-controlled asthma using only low dose ICS maintenance therapy. Reliable and reproducible lung function results were recorded in 60 patients (74%), and inhalant allergen sensitisation results were available in 77 (95%, table 1).

The frequency distribution of adherence to daily ICS is presented in figure 2. Median (interquartile range, IQR) adherence was 87% (70% to 94%). 51 children (63%) had high adherence (>80% of prescribed dosages); adherence rates below 50% were recorded in only 10 children (12%, figure 2).

Figure 1. inclusion of patients

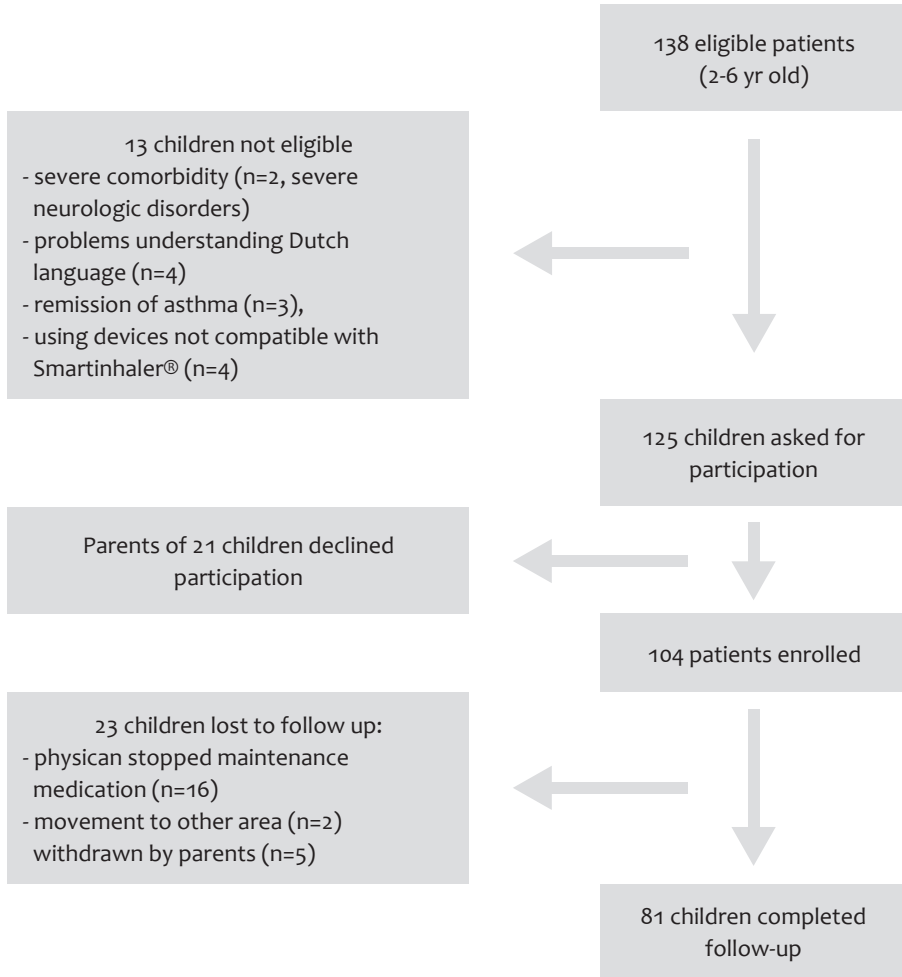
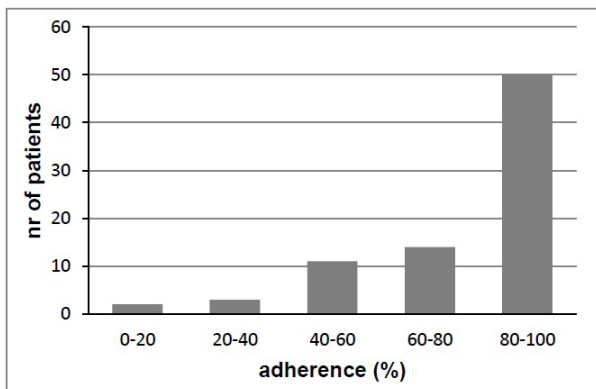


Figure 2. Electronically measured adherence to inhaled corticosteroids (n=81)



**Table 1. Characteristics of study patients at baseline (n=81)**

<b>Demographic and clinical characteristics</b>	
Age (mean; range; yrs)	4.6 (2.2 to 6.9)
Male gender (%)	51 (63%)
Parental diagnosis of asthma	33 (41%)
Household smoking (%)	24 (30%)
Maternal educational level (1 = low and 7 = high)	5 (4 to 7)
Positive specific IgE to inhalant allergens (n=77)	43 (56%)
Hospitalisation ever for asthma exacerbation (n, %)	40 (49%)
Duration of outpatient clinic asthma care before study (months)	17 (8 to 26)
FEV1 (z-score, n=33)	0.67 ± 1.1
FVC (z-score, n=33)	0.26 ± 1.4
Rint (z-score, n=27)	1.70 ± 3.1
ACQ	0.5 (0.2 to 1.3)
PACQOL	6.2 (5.3 to 6.8)
<b>Baseline medication</b>	
Inhaled corticosteroids (ICS)	73 (90%)
ICS and long-acting bronchodilators (%)	8 (10%)
ICS dose (fluticasone®; mean; range; µg)	250 (125 to 500)
nasal corticosteroids	19 (23%)
oral antihistamine	20 (25%)
Data are presented as mean ± SD, or as median (interquartile range) unless otherwise stated; ACQ: Asthma Control Questionnaire (<0.75 = well-controlled asthma, >1.5 = not well-controlled asthma); PACQOL: paediatric asthma caregiver quality of life questionnaire (1 is low and 7 is high quality of life), <sup>17, 18</sup> ; Ig: immunoglobulin; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; Rint: respiratory resistance by the interrupter technique	

Overall, asthma control during the 12-month study period was high and lung function was normal (table 2). Only 2 children were hospitalized because of an asthma exacerbation during the study period. The fifteen children (19%) that received a prednisolone course during the study period had similar long-term adherence (median 87%, IQR 54% to 92%) compared to children not receiving prednisolone (median 87%, IQR 72% to 94%,  $p=0.463$ ). Exacerbations requiring prednisolone courses were not associated with low adherence in the two months preceding the exacerbation ( $p=0.552$ ). In two children, however, exposure to lower ICS dose was associated with exacerbation occurrence: the exacerbation requiring prednisolone followed a physician-prescribed decrease of ICS dose in one child, and a pharmacy error (delivery of MDIs with lower ICS dose than prescribed) in the other.

**Table 2. Indicators of asthma control and their association with electronically measured adherence during the 2 months before asthma control was assessed, and with 12 month adherence**

		Rank correlation coefficient (adherence in the 2 months before clinic visit)		Comparison between children with good (>80%, n=51) and moderate (50-80%) 12-months adherence (n=20)
		$\rho$	p-value	p-value
ACQ winter (n=172/154/149)	0.58 (0.00 to 1.17)	-0.16	0.048	0.003
ACQ summer (n=118/106/97)	0.50 (0.00 to 1.00)	-0.31	0.001	0.001
PACQOL winter (n=95/79/83)	6.6 (5.8 to 6.8)	0.22	0.053	0.081
PACQOL summer (n=54/51/46)	6.6 (5.9 to 6.9)	0.30	0.034	0.024
VAS asthma control physician winter (n=85/76/88)	89 (82 to 95)	0.22	0.063	0.002
VAS asthma control physician summer (n=79/71/59)	88 (82 to 94)	0.24	0.044	0.003
FVC at 6 months (z-score, n=39/38/33)	-0.3 (-1.2 to 0.7)	0.36	0.028	0.032
FEV1 at 6 months (z-score, n=39/38/33)	0.0 (-0.6 to 0.9)	0.29	0.079	0.040
FVC at 12 months (z-score, n=42/41/36)	0.3 (-0.8 to 1.3)	0.30	0.060	0.047
FEV1 at 12 months (z-score, n=42/41/36)	0.7 (-0.5 to 1.1)	0.29	0.065	0.008
FeNO at 6 months (n=17/17/12)	15 (9 to 21)	-0.36	0.162	0.808
FeNO at 12 months (n=19/19/17)	12 (8 to 19)	-0.56	0.013	0.037

Data are presented as mean  $\pm$  SD, or as median (interquartile range) unless otherwise stated; ACQ: Asthma Control Questionnaire (<0.75 = well-controlled asthma, >1.5 = not well-controlled asthma); PACQOL: paediatric asthma caregiver quality of life questionnaire (score 1 to 7, 1 is low and 7 is high quality of life)<sup>17, 18</sup>; FEV1: forced expiratory volume in one second; FVC: forced vital capacity; Rint: respiratory resistance by the interrupter technique.

The relationship of adherence to asthma control, lung function, and FeNO values is presented in table 2. Adherence was associated with several indicators of asthma control, and asthma control was significantly better in children with good than in those with moderate adherence (table 2).

Against our expectations, the association between adherence and parent-assessed asthma control was stronger in summer than in wintertime (table 2). When filling out



the ACQ, many parents made remarks about having difficulties to attribute symptoms (cough) to viral respiratory tract infections or to asthma; this may have interfered with the association between adherence and asthma control. Children with high adherence had better spirometry results and lower FeNO levels, but no association was found between adherence and Rint results (table 2).

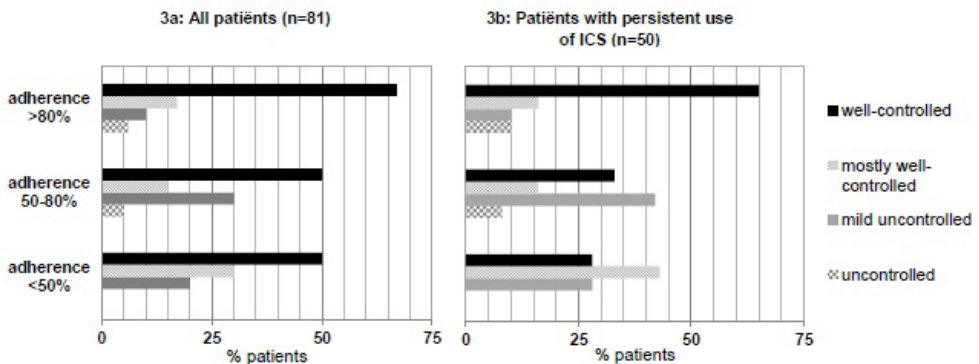
In table 3, adherence levels in different categories of asthma control are being compared. Four patients had severe uncontrolled asthma, 3 of which had very high adherence to ICS/long acting bronchodilator combination therapy, along with a prescription of nasal steroids and antihistamines for comorbid allergic rhinitis. Compared to patients with (mostly) well-controlled asthma, children with mild uncontrolled asthma had significantly lower adherence rates (95% CI of difference in median adherence rates 3% to 28%,  $p=0.008$ ), and mild uncontrolled asthma was rare among children with good adherence levels (figure 3). Good adherence was accompanied by well-controlled asthma in 67% of the children, but not associated with a lower likelihood of mild uncontrolled asthma or uncontrolled asthma (figure 3a). To adjust the relationship between adherence and asthma control for the potential confounding by overtreatment of mild episodic asthma symptoms or asthma in clinical remission, we repeated this analysis taking only those patients into account who were still using ICS two years after completion of the 12-months follow-up of adherence. The results are presented in figure 3b. There was a clear trend of higher levels of asthma control with higher levels of adherence ( $p=0.032$ ), and patients with moderate levels of adherence (50-80%) were significantly more likely to have mild uncontrolled asthma ( $p=0.028$ ). Of all other clinical and demographic characteristics, only inhaled allergen sensitization showed a trend to an association with good asthma control although it did not reach statistical significance ( $p=0.075$ ), and sensitization prevalence was comparable in adherent (>80%) and non-adherent (<80%) patients. Therefore no other confounders of the relationship of adherence and asthma control were identified.

**Table 3. Level of long-term asthma control in the study population\***

	N	Median (IQR) adherence	Difference with well-controlled asthma
Well-controlled asthma: no symptoms or infrequent mild symptoms during study period	49 (60%)	88% (72 to 94%)	
Mostly well-controlled asthma: Most of the time well-controlled asthma, but up to three episodes with symptoms	15 (19%)	88% (57 to 92%)	p=0.302
Mild uncontrolled asthma: persistent mild to moderate severe symptoms, most children none exacerbation	13 (16%)	74% (53 to 84%)	p=0.008
Uncontrolled asthma: persistent moderate to severe symptoms including exacerbations	4 (5%)	95% (70 to 98%)	p=0.288

\*: asthma control based on parental reports, physician's assessment and chart review; IQR: interquartile range

**Figure 3. Relationship between asthma control and adherence in all patients (figure 3a) and in those patients in whom ICS were continued for at least two years after completing the 12-month study period because of persistent asthma symptoms (figure 3b)**



## DISCUSSION

This study demonstrates the key role of adherence to ICS in achieving and maintaining asthma control in young children. In the large majority (79%) of these patients, asthma could be well-controlled most of the time over 12 months of guideline-based comprehensive asthma care. Only 4 children (5%) had uncontrolled asthma, one of which had poor adherence to ICS. In comparison to earlier studies of long-term adherence in childhood asthma,<sup>6,22</sup> median adherence was remarkably high (87%) in our study cohort. Despite the overall high levels and associated limited variability of both adherence and asthma control, a significant and consistent association was found between the two variables. Asthma control was significantly better in children with good (>80%) than in those with moderate adherence (50-80%) (table 2, figure 3), and this association was independent of clinical and demographic characteristics. In particular children with persistent mild asthma symptoms had lower adherence rates (table 3). Exacerbations requiring oral prednisolone and mild intermittent asthma symptoms were not associated with poor adherence in this cohort with overall high adherence and good asthma control.

Previous studies have also shown a high prevalence of well-controlled asthma during comprehensive guideline-based asthma care.<sup>11,12,23</sup> Because such comprehensive care comprises several components that may promote asthma control, including reduction of allergen and irritant exposure, identification and treatment of relevant comorbidity, and ensuring proper inhalation technique and self-management, the independent role of adherence in determining asthma control remained uncertain in these studies. Our finding of a significant association of electronically measured adherence to both short-term and long-term asthma control, including lung function, in this population of young asthmatic children, independent of treatment of comorbidity and other clinical characteristics, shows that adherence to ICS plays a key role in achieving and maintaining asthma control. In previous studies, substantially different levels of adherence needed to achieve asthma control have been reported, ranging from 40-60% to higher than 80%.<sup>6,22</sup> In these studies, however, a high prevalence of children with short-term asthma control despite low adherence to ICS was observed, suggesting ICS overtreatment of mild intermittent symptoms or asthma in clinical remission. To adjust for this potential confounder, we reanalysed the relationship between adherence and asthma control in a subgroup of children from our study who were still using ICS for persistent asthma two years after completion of the present study (figure 3b). Because the association between adherence and asthma control was stronger in patients with on-going persistent asthma (figure 3b) than in the whole population comprising both on-going persistent asthma and asthma in clinical remission (figure 3a), clinical remission of asthma in young children may help to explain why asthma can be

well-controlled in this age group despite poor adherence. Our results show that the relationship between good adherence and good asthma control is particularly strong in children who need ICS maintenance treatment for prolonged periods of time, thus emphasizing the pivotal role of optimal adherence to achieve asthma control in children with chronic persistent asthma.

International guidelines recommend stepping up maintenance therapy in case of insufficient asthma control in the preceding months.<sup>10</sup> Our results suggest that adherence should be considered as a potential cause of such reduced asthma control, in particular when parents report that their child has frequent mild asthmatic symptoms (table 3). In clinical practice, many physicians will not step up maintenance therapy after a short episode of uncontrolled asthma while children have well-controlled asthma most of the time, and our results suggest that this pattern is not a marker of poor adherence to ICS.

### *Strengths and limitations*

The main strengths of our study include the longitudinal comprehensive assessment of asthma control and the objective, validated assessment of adherence over 12 months of follow-up. Asthma control is a multidimensional clinical construct which is not easily captured by a single questionnaire, particularly in children.<sup>24</sup> The assessment of asthma control by different methods in our study, using parental and physician assessment, validated questionnaires, and lung function, is most likely to capture the clinical concept of asthma control described in asthma guidelines. Previous studies on the relationship between asthma control and adherence are hampered by a limited assessment of asthma control, use of less reliable methods of measuring adherence, or short follow-up. Our long-term follow-up allowed us to analyse the influence of seasonal changes in adherence and asthma control, along with a range of potential clinical and demographic confounders, which enhances the robustness of the relationship between adherence and asthma control that we found.

The most important limitation of our study lies in its generalizability. Most parents and children in our study population came from Caucasian middle-class families, and the study was performed in a dedicated, secondary care, specialized asthma clinic. However, previous studies pointed out the importance of ICS adherence in determining good asthma control in inner-city populations from ethnic minorities.<sup>11,12</sup> In addition, the relationship between adherence and asthma control in our study was not influenced by demographic and clinical characteristics of the study population. This suggests that adherence is a key factor in determining asthma control, irrespective of study setting and ethnic or social background of the population studied. Finally, the limited variability of asthma control and adherence in this study population may limit the study's power to identify determinants of either variable.

## **CONCLUSION**

In most young children with asthma, well-controlled asthma can be achieved by comprehensive guideline-based asthma care. The role of adherence to ICS in this relationship was crucial, because even in this highly adherent, well-controlled population, adherence was the only determinant significantly associated with asthma control, irrespective of other clinical or demographic characteristics. Persistent mild symptoms were a marker of suboptimal adherence. Adherence to ICS is a crucial factor to achieve and maintain asthma control in young children and should be a key focus of asthma care in this age group.

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# 7

Every parent tells a story:  
Why non-adherence  
may persist in children  
receiving guideline-based  
comprehensive asthma  
care

T. Klok  
S. Lubbers  
A.A. Kaptein  
P.L.P Brand



## **ABSTRACT**

### *Objective*

Effective self-management and adherence to inhaled corticosteroids are points of particular interest in comprehensive asthma care. In spite of this care, however, a number of parents and children remain non-adherent. The reasons for this non-adherence have up till now been unknown, because previous adherence studies have based their findings either on populations with poor adherence or on unreliable self-reported adherence. This study was designed to explore factors that contribute to persistent non-adherence to inhaled corticosteroids in children ranging between two and twelve years of age receiving comprehensive asthma care.

### *Methods*

This qualitative study was based on in-depth interviews which took place in the homes of parents whose children had completed a one-year follow-up of electronically measured adherence to inhaled corticosteroids. Rich and comprehensive descriptions of parents' own accounts of self-management behavior were obtained by using active listening techniques. Each interview was recorded and transcribed verbatim followed by data analysis using standard methodology for qualitative studies.

### *Results*

Twenty children's parents (mean age 5.9 years) were interviewed. Distinctive patterns of modifiable barriers to adherence emerged, including a novel finding of parents misjudging of their children's capacities to manage the daily use of medication by themselves. Persistence of non-adherence appeared to be caused by a number of maintaining factors. Most noticeable factors were unawareness of non-adherence with both parents and health care providers, a lack of drive in parents to achieve high adherence and ineffective parental problem-solving behavior.

### *Conclusions*

This study has identified known and novel barriers to adherence. Overcoming these barriers should start with objectifying non-adherence. Interventions should focus on parental motivation and problem-solving behavior.

## INTRODUCTION

Over the last decade, several studies have explored determinants of adherence to inhaled corticosteroids (ICS) in children with asthma.<sup>1</sup> In most studies, children only received between 30 to 70 percent of the prescribed doses. Adherence appeared to be particularly poor in ethnic minorities from lower socioeconomic status.<sup>1-4</sup> These fixed demographic determinants of poor adherence, however, are largely mediated by modifiable risk factors for low adherence, such as parental illness perceptions and medication beliefs.<sup>1-3,5</sup> If these modifiable risk factors are addressed in guideline-based comprehensive asthma care,<sup>6</sup> high adherence and good asthma control can be achieved even in this group of underprivileged children with asthma.<sup>7</sup>

We have recently shown a comparable pattern of high median adherence in pre-school children from middle class families receiving regular, comprehensive, multidisciplinary asthma care.<sup>8</sup> This was associated with most parents expressing illness perceptions and medication beliefs in accordance with the medical model of asthma.<sup>9</sup> However, even in populations with such high median adherence, variability in adherence remains. In our study in pre-school children whose median adherence was 92% over a three-month period, a third of the children received less than 75% of the prescribed doses of ICS.<sup>8</sup> Reasons for such “persistent non-adherence” in spite of comprehensive guideline-based asthma care are unknown. Previous adherence studies have focused on populations with poor adherence, or have relied on parental or patients’ self-reported adherence which highly overestimates objectively measured adherence.<sup>10</sup> This study was designed to explore determinants of persistent non-adherence to inhaled corticosteroids in parents and children receiving comprehensive guideline-based asthma care. We used electronically measured adherence, which ensures capturing unreported and unwitting non-adherence. We intended to explore every potential reason for non-adherence and did not want to limit ourselves to identifying established barriers to adherence. We therefore chose a qualitative study design, allowing for a rich and detailed description of determinants of adherence.<sup>11</sup>

## METHODS

### *Setting and design*

We have recently completed a one-year observational follow-up study of electronically measured adherence to ICS maintenance therapy. We followed a group of 2-12-year-old children with asthma in our secondary care pediatric asthma outpatient clinic.<sup>8,9</sup> To ensure optimal asthma management and adherence, our asthma care comprises repeated teaching of tailored asthma self-management, including:<sup>6,12</sup>

- Discussing parents' perceptions about asthma and its treatment.
- Establishing and maintaining a partnership between health care providers and the patient/parent dyad.
- Ensuring concordance on treatment and its goals with parents and those children old enough to participate in the discussion.
- Stressing the importance of adherence to daily ICS treatment.

To achieve this, patients and their parents visited the clinic four to six times during their first year of follow-up, and two to four times per year afterwards.

Our study aimed to explore determinants of non-adherence persisting in spite of such comprehensive care. In order to achieve this, we interviewed parents about their medicine-giving behavior as electronically measured during the follow-up study. Even though we focused on non-adherence, we included children's parents from the whole adherence spectrum. The interviews with adherent parents served the purpose of enriching our analysis by allowing us to contrast the ways medicines were used between parents with low and high adherence.

### *Selection of eligible patients and parents*

For this qualitative study, all 2-12-year-old children who had completed a one-year follow-up of electronically measured adherence to ICS (details of which were published previously)<sup>8</sup> were eligible for inclusion. The consecutive eligible children's parents were asked to allow debinding of the results of long-term adherence measurements and to participate in an in-depth interview on their (non-)adherence behavior. Based on the results of electronically measured adherence over the completed one-year follow-up period, parents who had given informed consent were divided into two groups of at least ten parent couples. These groups represented those with adherence below 75 percent and those with adherence above 75 percent.<sup>13</sup> In both groups, random number tables were used to rank the children, stratified for age (younger than six and 6-12-year-olds). From the top of each of these ranked lists, parents were included for interviews until saturation for each group had been reached (i.e. additional interviews were not expected to yield new information on patterns of non-adherence).

Parental educational level was assessed by recording the highest level of education completed, and was classified on a 7-point scale, ranging from 1 (high school drop-outs; only completed primary education) to 7 (completed college or university education).

### *Interviews*

Two researchers (TK and SL) visited parents at their homes for a semi-structured in-depth interview lasting approximately one hour. We started each interview by asking the parents to estimate the one-year ICS adherence achieved in their child, after which we revealed the results of one-year electronically measured adherence. The similarity or difference between the parent-estimated and actually measured adherence was used as a starting point to explore parental (non-)adherence behavior without passing judgment. Active listening techniques were used to obtain a rich and comprehensive description of the parents' explanation for following or deviating from the health care team's recommendations of ICS dose and dosing frequency. As the character of the interviews was home-based, children aged eight to twelve commonly engaged in the interview themselves. When the interviewers felt they had obtained a comprehensive and accurate overview of parental and children's (non-)adherence behavior, they summarized it, inviting modification by parents until they accepted it as accurate and complete. Following the principle of grounded theory methodology, findings of previous interviews were used to guide subsequent interviews in exploring patterns of adherence behavior.<sup>11</sup> Explanations for non-adherent behavior were also specifically discussed with parents with high adherence. This served the purpose of finding out if such explanations were less prevalent in adherent families. It also improved understanding of the reasons why parents confronted with the same problem (e.g. a child unwilling to take medication) showed different behaviors.

### *Analysis*

Each interview was recorded and transcribed verbatim and analyzed using standard methodology for qualitative studies.<sup>8,9</sup> The transcripts of the first two interviews were coded independently by two researchers (TK, SL) using qualitative analysis software (Kwalitan<sup>®</sup>, Kwalitan advice, Malden, the Netherlands) with good agreement (Cohen's kappa values 0.80 and 0.90, respectively). Subsequent transcripts were coded by one researcher (SL) and cross-checked by another (TK). Differences in coding were resolved by consensus. Three distinct patterns of non-adherence behavior and conceptual ideas underlying the persistence of each of these non-adherence behaviors were identified. These concepts were modified and extended during discussions between all authors.

*Ethical considerations.*

This study was approved by the hospital ethics review board; all parents provided written informed consent.

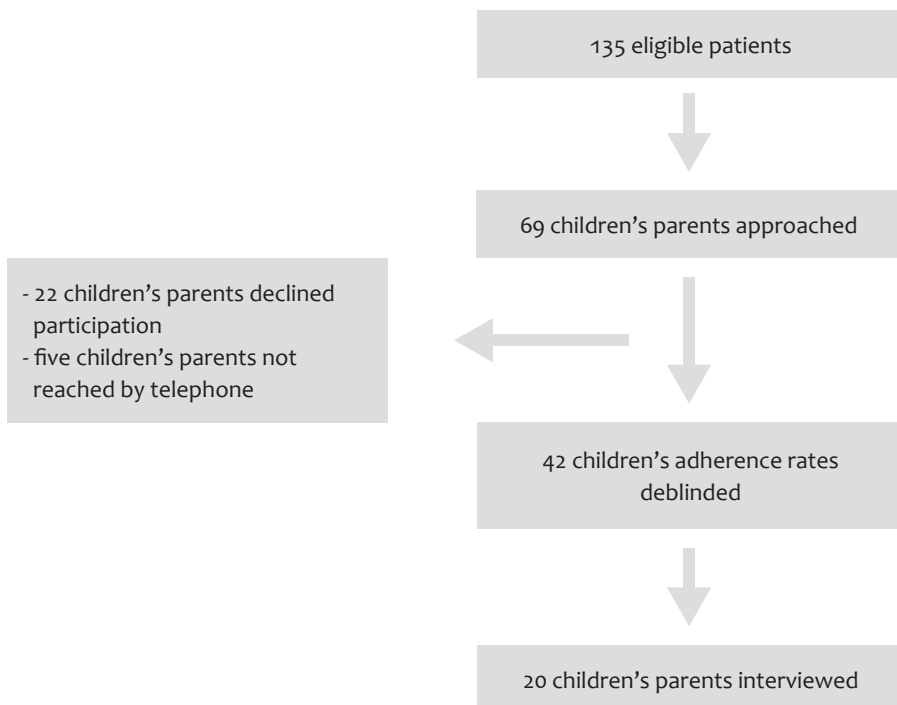
**RESULTS**

42 out of 69 children's parents (61 percent) who had been asked to participate in our study gave informed consent to deblind study results for the interview (figure 1). Refusal of deblinding consent was equal in adherent and non-adherent parents. Saturation was reached after ten children's parents with poor adherence (below 75 percent) and ten with high adherence (above 75 percent) had been interviewed. The mean age of the children whose parents were interviewed was 5.9 years. Median education level of parents was 5 (range 3-7).

*Individual stories, recognizable patterns*

The interviews were all set around a kitchen or dinner table, allowing for a low-profile atmosphere. Parents were all happy to discuss the way they managed giving medicine in detail. Each single interview provided us with a unique story about how parents and children cope with the child's asthma and the recommendation of daily ICS use.

**Figure 1. inclusion of patients**



With the exception of one family, all interviews could be summarized with a clear and mutually agreed description of how medication was taken. All of the parents reported that they had been recommended to provide daily ICS to their child. Even though some parents reduced the dose, all expressed the intention to use ICS regularly in order to achieve good asthma control in their child. We were able to identify three patterns of non-adherence behavior (table 1). Within these patterns, a number of barriers as well as factors contributing to the persistence of these barriers were identified (table 1).

### *1. Intentional non-adherence*

One group of parents deliberately deviated from the pediatrician's advice. They adjusted the ICS dose according to what they thought was the desired or obtained level of asthma control in their child. Based on their own experience, these parents increased the dose during a 'bad' season, or when their child showed increased symptoms. These parents were all convinced they were self-managing their child's asthma well.

Most commonly, children were given a single daily dose instead of the recommended two. In these children, electronically measured adherence could thus be as low as 50 percent, with parents readily confirming the accuracy of this number. They did not discuss their dose-reducing behavior with the pediatrician, unless the pediatrician explicitly asked them about their ICS use. Parents' main reasons for lowering the ICS dose were concerns about ICS side effects or resistance against medication in general. These parents were convinced their child needed ICS treatment, but their aim was to optimally balance the pros and cons of ICS.

Parents with good adherence differed from these non-adherent parents in two ways. Some of these highly adherent parents expressed few if any concerns about (side effects of) ICS and therefore did not deliberately balance pros and cons of ICS. Other highly adherent parents did express a high level of concerns about ICS use, but were convinced that their child needed the ICS two times a day nevertheless.

### *2. Family related barriers*

Parents in this group tended to give a higher estimation of the level of adherence than the electronically measured adherence would show. Unaware of their non-adherence, these parents would not discuss this with their pediatrician. Different families were confronted with different sets of barriers that kept them from regular ICS use. Barriers such as relational or economic issues or parental psychiatric illnesses seemed fixed or difficult to modify at first sight. After exploring parental and children's adherence behavior in more detail, however, in most families barriers appeared modifiable. Child raising issues, for example, were often found to be important barriers, as in cases where parents would skip a dose when children refused the use of their inhaler simply

**Table 1. Patterns of barriers to adherence and factors contributing to the persistence of these barriers.**

Patterns of barriers	Quotes from the interviews
<p><b>Intentional non-adherence:</b></p> <ul style="list-style-type: none"> <li>• concerns about medication</li> <li>• resistance against meds in general</li> </ul>	<p>“I was rather skeptical about the meds, but I also saw my daughter’s breathlessness. Well, then you weigh your options in your mind”</p> <p>“No, I don’t follow each of the pediatrician’s recommendations. I look at my child, whether he needs the meds or not.”</p>
<p><b>Unplanned non-adherence associated with family-related barriers:</b></p> <ul style="list-style-type: none"> <li>• Child raising issues</li> <li>• Missing family routines</li> </ul>	<p>“Do I have to upset him completely, only for such an inhalation? How hard should you push? That’s a difficult decision sometimes.”</p> <p>“I have this experience with my daughter (also an asthmatic), of controlling her like a cop. That’s something I don’t want to go through again.”</p> <p>“I should stick to the rules that we decided on, but that’s not what happens”</p>
<p><b>Unplanned non-adherence associated with self-management of children.</b></p> <ul style="list-style-type: none"> <li>• Parental misperceptions about children’s capacity of self-management</li> <li>• Children incapable of self-managing daily use of medication</li> </ul>	<p>“When he received the powder inhaler, when he was eight, we thought he could take the meds on his own.”</p> <p>“He’s already 9 years; he has to figure out for himself what he wants, and how to get things done.”</p> <p>“The meds are just annoying. I see the inhaler when I go to bed, but I don’t take it”</p>
<b>Maintaining factors</b>	
<p><b>Parent related:</b></p> <ul style="list-style-type: none"> <li>• unawareness of non-adherence</li> <li>• not reporting of non-adherence</li> <li>• lack of motivation to achieve high adherence</li> <li>• ineffective problem-solving behavior</li> </ul>	<p>“That he takes his meds only half of the time, that’s quite shocking to me.”</p> <p>“Giving the meds every day once a day, that’s so obvious to me, and the right thing to do. I think that’s the reason I don’t report this to the pediatrician.”</p> <p>“Well, I do notice he doesn’t take his meds. I see the counter of the inhaler still on the same number, just like some days before. Then you think: okay.... but, you know, I have to deal with a lot of problems...”</p> <p>“In the evening, he usually falls asleep on the couch. Then I don’t wake him up for his meds.”</p>
<p><b>Physician related:</b></p> <ul style="list-style-type: none"> <li>• unawareness of non-adherence</li> <li>• not (specifically) asking about the use of ICS</li> <li>• unawareness about young children self-managing their medication</li> </ul>	<p>“He (the pediatrician) never informed about the details of using the medication: about who is responsible, and how we are doing it”</p>

to avoid upsetting their child. Augmented by the absence of daily medicine taking routines, families were prone to simply forget giving the medication altogether. Parents were aware of these barriers, but accepted them to avoid family stress.

Compared to the self-management of parents with good adherence, two differences emerged. First, parents with good adherence were dedicated to use ICS regularly, whereas parents with poor adherence regarded the achieved adherence rates as the best they could possibly do. Highly adherent parents put giving medication before avoiding to upset their child. Secondly, parents with good adherence showed good problem-solving skills by having developed medicine taking routines to avoid forgetting the medication.

### *3. Transferring excessive responsibility to children*

In this group, children were given full responsibility for taking their own medicine. Children from eight to ten years of age used their inhaler without parental supervision. A number of these children's parents were astonished to find out that the adherence rates that had been recorded for a year turned out to be much lower than they had expected. These parents had been convinced that eight to ten year-old children could take such a responsibility. In families struggling with relational or economic problems, children were given the responsibility for taking their own medicine at an even younger age, in order to reduce the number of issues that needed tackling. Even though aware of their child's non-adherent behavior, some parents decided to ignore it in their wish to avoid a fight about taking medicine. Their decisions to do so were either based on the assumption that too much pressure on the child would lead to more resistance, or on the belief that giving the child full responsibility would foster their independence. Lacking the drive to achieve good adherence as well as ineffective ways of solving problems, however, lie at the bottom. Parents that were aware of their child's non-adherence relied on the pediatrician to try and change their child's behavior.

In children with high adherence, parents were much more involved in supervising their children's ways of taking medication. These parents were more dedicated to achieve good adherence and expressed the view that children could not be expected to self-manage their own medication before the age of 12.

## **DISCUSSION**

Through in-depth interviews, which took place in the domestic environment of children with asthma that remained non-adherent in spite of receiving guideline-based comprehensive asthma care, we gained insight into three groups of barriers that kept these patients from being adherent and into determinants that explained why these



barriers could not be overcome. Some parents faced non-adherence even though they were conscientiously dealing with medication. They were adequately self-managing medication by giving the lowest possible ICS dose. Other parents, however, poorly planned medication. They were either overwhelmed by complex family, social or child-raising issues, or gave responsibility for medication to the children themselves without supervising them. Further probing suggested that in those parents a lack of drive or ineffective problem-solving skills lay at the bottom of why barriers would not be overcome. These factors, together with parental as well as health care provider's unawareness of the degree of non-adherence were identified as the underlying causes of persistent non-adherence.

Parents who deliberately balanced the pros and cons of prescribed medication use, based on their own illness perceptions and medication beliefs, formed the group of 'intentional non-adherers'. Previous studies have described this as a cause of problematic non-adherence: not taking medication at all or only if symptomatic.<sup>14-16</sup> This is the first study to demonstrate that intentional non-adherers may also show adequate self-management, aiming to achieve good asthma control with the lowest possible dose of daily ICS. The parents in this group in our study expressed constructive illness perceptions and medication beliefs, concordant with the medical model of asthma, after receiving comprehensive self-management education.<sup>9</sup> To avoid misclassifying such parents as being problematically non-adherent, physicians and parents need to reach concordance on the ICS dose and on modifying this dose based on the level of asthma control achieved.<sup>17</sup> Finally, physicians should actively check the current dose being given at each follow-up visit.

This study confirmed previous findings that unplanned non-adherence is common, in particular in families with relational or economic issues.<sup>2,18</sup> As reported by previous studies, this relationship is mediated by potentially modifiable barriers, including a lack of medication taking routines and ineffective child raising strategies.<sup>2, 14,18-20</sup> Given that parents and physicians are usually unaware of the degree of unplanned non-adherence, current guideline-based comprehensive asthma care is not sufficient.<sup>10,19,21</sup> Factors contributing to the persistence of these potentially modifiable barriers emerged in our study. These included the lack of motivation to achieve good adherence and the presence of ineffective problem-solving behavior. The latter has been noted in a survey of diabetes educators. They reported that appropriate problem-solving was the most difficult skill to teach patients.<sup>22,23</sup> A large trial in asthmatic adults showed no benefits of problem-solving education, and the authors suggested that patients' lack of motivation to achieve high adherence was the main reason for this failure.<sup>24</sup> Similarly, an asthma outreach program in inner-city children with asthma in the USA

was of limited benefit when parents lacked the motivation to participate.<sup>25</sup> Apparently these maintaining factors represent determinants of self-management that are difficult to modify, supporting our analysis about the role of such underlying factors in the persistence of modifiable barriers.

Perhaps the most striking novel finding of our study was the excessive responsibility given by parents to children at a relatively young age to self-manage the daily use of their own medication, without parental supervision. This represented a major cause of non-adherence. An increase in shared responsibility for asthma self-management has been reported from the age of 8 years,<sup>26,27</sup> particularly for daily preventer medication use.<sup>28,29</sup> Until now, the effect of this practice on adherence has been unknown. The only previous study investigating this effect (reporting no effect) used parental-reported adherence.<sup>26</sup> Results were highly unreliable for two reasons. Both parents and children are generally hesitant to disclose poor adherence and parents can also be unaware of their child's poor adherence. In contrast to common belief,<sup>14</sup> children below the age of 10 to 12 years seem to be unable to take responsibility for their own taking of medicine.<sup>30,31</sup> To identify and overcome this barrier to adherence, parental belief about the self-management responsibility of their child should be discussed during follow-up visits, along with the associated lack of motivation to achieve good adherence and ineffective problem-solving behavior. Parents should likewise receive counseling in supervising their child's taking of medicine at least until their child reaches the age of 12.

### *Clinical implications*

This study has shown the importance of assessing non-adherence objectively. Many parents and physicians appear to be unaware of the extent of non-adherence. Non-adherence needs to be identified before barriers underlying it can be discussed and modified. It has been shown that feeding back results of objectively measured adherence improves adherence, but only for a short period.<sup>32,33</sup> This may reflect a lack of parental motivation or ability to control asthma, in particular in families with competing priorities and problems. Whether motivation enhancing techniques such as motivational interviewing may change long-term adherence in such patients remains to be established. Short-term benefits of this approach have been established in inner-city asthmatic adolescents.<sup>34</sup> In families struggling with many and complex daily life issues, a child's asthma may be a minor problem not getting priority. An open discussion about the complex issues of coping with daily life and about the child's ability to self-manage the daily use of their medication may help to achieve concordance with parents on the degree of achievable asthma management and control in these patients. At all costs, reproaching these parents' non-adherence must be avoided.

*Strengths and limitations*

The main strength of this study lies in the qualitative design, which allowed for an in-depth exploration of barriers to adherence during guideline-based comprehensive asthma care. A home-based environment for the interviews appeared to be the ideal environment to explore and discuss parental explanations for following or deviating from the pediatrician's recommendation to give daily ICS to their child. The use of electronic devices ensured detection of unwitting non-adherence. The limitation of this study is that it is still impossible to make generalizations. Whether our findings, in particular our finding of excessive medication responsibility given to children, are applicable to populations of children with asthma in primary care and different settings remains to be established.

**CONCLUSIONS**

This study shows that persistence of non-adherence in spite of comprehensive asthma care can be related to both adequate and inadequate asthma self-management. Adequate self-management that nevertheless leads to non-adherence is related to parents' intentions to achieve optimal asthma control with the lowest possible ICS dose. Inadequate self-management is caused by potentially modifiable barriers, of which child-raising issues and lack of family routines are barriers that have been identified before. In this study, a novel barrier to adherence was identified: full responsibility given to children at a young age to self-manage their daily use of ICS. The persistence of barriers was related to limitations in parental problem-solving behavior and a lack of motivation to achieve high adherence as well as unawareness of non-adherence with both parents and health care providers. Barriers to non-adherence may be overcome by first objectifying non-adherence behavior, after which an open discussion with parents and children about their self-management behavior should take place, preferably in their own homes. Effectiveness of interventions to improve adherence may well prove limited if parental motivation and problem-solving skills are not addressed.

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# 8

## General discussion

## STUDY DESIGN AND HYPOTHESIS

“The study described in this thesis was designed to identify determinants of long-term adherence to daily maintenance medication in children with asthma. Before this study was undertaken, there was a paucity on studies of long-term adherence in children with asthma, which is striking because asthma is a chronic disease which usually requires maintenance treatment taken for many years. Previous studies on adherence in children with asthma were also hampered by the lack of objective and reliable assessment of adherence. Most studies used self-report or pharmacy refill rates, both of which have been shown to be unreliable. Very few studies using electronic data loggers have been performed in children with asthma, and most of these studies used only short-term follow-up.

When the study was designed, parental illness perceptions and medication beliefs were hypothesized to be the main determinant of long-term adherence in children with asthma. Therefore, these illness perceptions and medication beliefs were assessed comprehensively when patients were enrolled into the study, with a range of validated questionnaires designed for this purpose. Numerous other putative determinants of adherence were also assessed, along with a careful characterization of asthma control during follow-up. The study employed a mixed methods design, with both quantitative methods (measuring adherence electronically throughout 1-yr follow-up, and analysing the effects of various determinants on adherence measured in this way) and qualitative research methodology (focus group and individual interviews aimed at acquiring a rich and detailed description of parental views on the necessity of maintenance medication, their concerns about this treatment, and their strategies and behaviour regarding daily maintenance medication).

## MAIN RESULTS OF THE STUDY

This study showed:

1. a very high median adherence during 3-months follow-up of 92% in children with asthma 2-6 years of age (chapter 3) and a similarly high median adherence during

- 12-months follow-up of 84% in asthmatic children 2-12 years of age followed up in secondary care (chapter 5). Considerably poorer adherence was measured in a group of asthmatic children in primary care (median 66%, chapter 5).
2. striking differences in the illness perceptions and medication beliefs between parents from primary and secondary care as revealed by the focus group interviews (chapter 2) and confirmed by the quantitative assessment of these perceptions and beliefs (chapter 5). Compared to parents from primary care, parents from secondary care had illness perceptions more concordant to the medical model of asthma and higher perceived necessity of ICS.
  3. medication beliefs to be important determinants of adherence to ICS, both in parents from primary care and in parents from secondary care (chapters 2, 3, and 5).
  4. major differences in the organization and content of asthma care between primary and secondary care (chapters 2 and 5). Whilst children in primary care received education and instruction only once, and were seen for follow-up only when things were not going well, children and parents in secondary care received repeated and comprehensive self-management education, and were seen regularly for follow-up.

Taken together, these main results confirm our primary study hypothesis: parental medication beliefs are important determinants of adherence to ICS in children with asthma in this study. In addition, this study showed major differences in quality of asthma care, medication beliefs and adherence between primary asthma care and secondary asthma care.

The general discussion in this chapter focuses on the implications of these observations: that good adherence can be achieved in most children with asthma, that modifying parental medication beliefs into adherence-promoting constructive beliefs is a key determinant of such good adherence, and that patient-centred asthma care is required to modify these perceptions and improve adherence. This discussion is followed by a description of the present lack of patient-centred care, and of the barriers to the implementation of such care. We will also discuss the contribution of patient-centred communication to achieve good adherence. Towards the end of this chapter, the thesis's implications for practice and suggestions for future research will be presented. The main implication for clinical practice is that asthma, being a chronic disease, requires chronic attention and follow-up from the health care providers, with a focus on self-management education and discussing parental illness perceptions and medication beliefs, and modifying these beliefs when required. In adherence research, the focus up to now was always on the patients, driven by the question 'why don't patients take medications as prescribed by the physician?'. The results of this thesis



strongly suggest, however, that future research should (also) be driven by the question ‘How can a widespread adoption of patient-centred communication in chronic health care be realized?’.

## **THE COMMON SENSE MODEL: MEDICATION BELIEFS DETERMINE ADHERENCE**

We found large differences in illness perceptions and medication beliefs between parents from the primary care group and those from the secondary care group, associated with different rates of self-reported adherence to ICS (chapter 2). These qualitative findings were supported quantitatively by the results of the 1-yr follow-up study (chapters 3 and 5), which showed a high medication necessity perception in parents in secondary care, accompanied by very high median adherence, measured electronically. The limited variability in adherence to ICS hampered the study’s power to detect determinants of adherence. Even at this high median level and limited degree of variation of adherence, however, medication beliefs were the strongest predictors of adherence. Finally, the interviews with parents who completed the study also showed an association of medication beliefs to adherence behaviour (chapter 7). The results of these 3 studies therefore demonstrate a consistent pattern of parental medication beliefs determining adherence to ICS in children (figure 1). This main outcome of the thesis, therefore, confirms our study hypothesis, and is in agreement with several studies which showed the pivotal role of medication beliefs in determining adherence to ICS in adults and in children with asthma (table 1).<sup>1-5</sup>

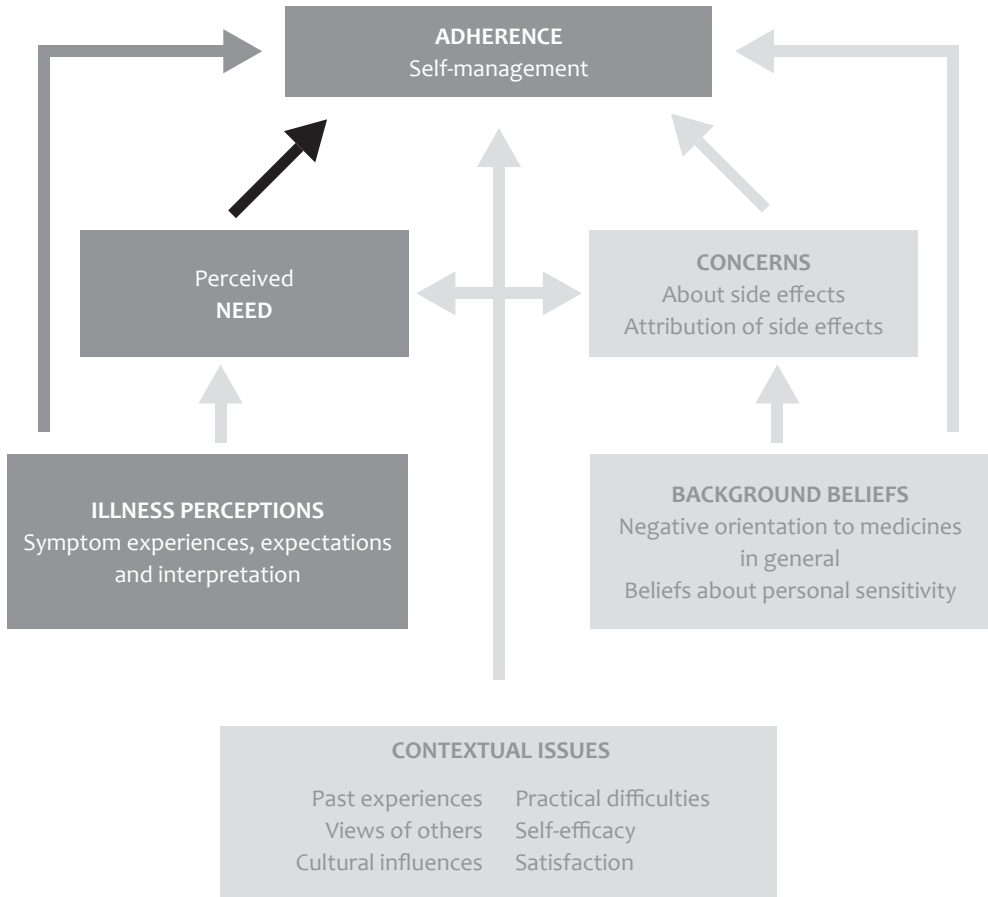
The results of this study are in agreement with the self-regulation theory (or Common Sense Model) and the extended version of this theory, which added medication beliefs to the model. This model highlights the pivotal role of illness perceptions and medication beliefs as key determinants of self-management and illness outcome, as was discussed in the general introduction. The model is not only strongly founded in medical psychological theory, but is also supported by numerous empirical observations in a range of chronic conditions (reviewed in the introduction).<sup>6-8</sup> As a result, the Common Sense Model provides a solid theoretical framework to discuss the highlights of this thesis.

**Table 1. Quantitative studies on the relationship between parental medication beliefs and adherence to controller medication in children with asthma.**

First author, year, country	Nr. patients, age	Assessment of parental medication beliefs	Assessment of adherence/ underuse of controller medication	Results
Conn <sup>58</sup> 2007 USA	622 children 2-16 yrs	BMQ*	Parental self-report	Mean adherence scores increased as the necessity-concern differential increased.
Koster <sup>59</sup> 2011 the Netherlands	170 children 8 yrs	BMQ*	Parental self-report	Parents with strong need beliefs towards their child's medication use showed higher therapy adherence rates.
Koster <sup>60</sup> 2011 the Netherlands	527 children 4-12 yrs	BMQ*	Parental self-report	Parental necessity beliefs about medication were associated with higher adherence.
McQuaid <sup>61</sup> 2012 USA and Puerto Rico	277 children 7-16 yrs	BMQ*	Electronically measurement and counter teller	Parental belief regarding medication necessity was associated with adherence.
Riekert <sup>62</sup> 2003 USA	318 children 5-12 yrs	5-item questionnaire <sup>¶</sup>	Parental self-report	More overall positive attitudes toward asthma management associated with concordance to prescribed medicines.
Smith <sup>63</sup> 2008 USA	754 children 2-13 yrs	5-item questionnaire <sup>¶</sup>	Parental self-report	High score on medication concerns summary measure associated with underuse of controller medication.
Van Dellen <sup>64</sup> 2008 the Netherlands	232 children 7-17 yrs	2 questions <sup>‡</sup>	Pharmacy records and parental self-report	Significant association between the positive subjective view to ICS of the parents and poor adherence.
Vasbinder <sup>65</sup> 2012 the Netherlands	90 children 1-1 yrs	BMQ*	Electronically measurement	Medication beliefs showed a borderline association with adherence in the univariate analysis.
Yoo <sup>21</sup> 2007 USA	228 children 5-12 yrs	AIRS <sup>#</sup>	Parental self-report	Parents whose attitudes to medication was more concordant with the professional model of asthma had children who were more likely to be on an adequate medication regimen.

\*: Beliefs about Medicines Questionnaire; <sup>¶</sup>: higher scores reflect a more positive attitude toward preventive care, increased confidence to manage asthma attacks, and fewer concerns about side effects; <sup>‡</sup>: It keeps the asthma of my child under control, it reduces the risk of having an asthma attack; <sup>#</sup>: The Asthma Illness Representation Scale.

**Figure 1. Patient adherence influenced by individual judgement and the role of asthma care as shown in this study**



Patient adherence to medication is influenced by a number of factors relating to how the individual judges the necessity of their treatment relative to their concerns (as described by Horne<sup>57</sup>). Factors which can be modified by comprehensive asthma care, as suggested by the results of this thesis, moderating the reported association of asthma care and high adherence, are presented in black.

## **INTERVENTIONS BASED ON THE COMMON SENSE MODEL**

Following international asthma management guidelines, self-management education nowadays is a major component of comprehensive asthma care.<sup>9</sup> This is justified because self-management education has been shown to be effective in improving illness outcomes in a range of chronic conditions, including childhood asthma.<sup>10-13</sup> Such education is primarily focused on improving patients' and parents' knowledge and self-management skills by providing unidirectional education (from the health care provider to patient and parents). The relationship of such self-management education

and asthma outcomes may be moderated by improving knowledge and self-management skills such as understanding the disease mechanism of asthma and its triggers, proper inhalation technique, early recognition of impending exacerbations, and the treatment of such events. Because this kind of education provides the basics needed for proper self-management, it can be concluded that it has incorporated the reality that patients (or their parents) have to manage their illness by themselves most of the time. However, increased knowledge and improved self-management skills per se are not associated with high adherence to inhaled corticosteroids, as illustrated by findings from a recent large review.<sup>5</sup> Apparently, adherence to medication can only be improved to a limited degree by information-based and skills-based self-management education.

This may be caused by the pivotal role of illness perceptions and medication beliefs in determining self-management in general and adherence in particular. As discussed in chapter 1 of this thesis, such individual perspectives are strongly influenced by cultural, social and psychological factors, and are hardly, if at all, determined by 'objective' medical information. The results of our study suggest that addressing and modifying illness perceptions and medication beliefs is of key importance in determining the success of self-management education in particular in achieving high adherence.

It is therefore important to examine the evidence on the effectiveness of interventions in the context of the central tenet of the common sense model. If illness perceptions determine outcome, then changing illness perceptions should lead to changes (i.e., improvements) in self-management and, therefore, in outcome. When medication beliefs determine adherence, changing counterproductive beliefs into constructive and useful medication beliefs may improve adherence. A number of intervention studies support this hypothesis, in particular regarding the change of illness perceptions. For example, Jansen et al. described an intervention programme focused on changing both misperceptions and negative perceptions of illness and treatment. This programme increased the patients' self-efficacy and stimulated social support, and showed encouraging results on short-term outcome in patients with end-stage renal disease.<sup>14</sup> Comparable promising results of interventions targeted on changing illness perceptions have been reported for patients with cardiac disease, diabetes and chronic low back pain.<sup>15-17</sup> Very few studies, however, have examined interventions focused on modifying medication beliefs to improve adherence. To our knowledge, only Petrie et al. studied such an intervention by sending participants tailored text messages based on their illness and medication beliefs. In the intervention group, the perceived necessity of preventer medication increased, and this was associated with higher self-reported adherence to ICS compared to the control group.<sup>18</sup>

## **TAILORED SELF-MANAGEMENT EDUCATION MAY MODIFY ILLNESS PERCEPTIONS AND MEDICATION BELIEFS**

Because of the observational design of this study and because illness perceptions and medication beliefs were assessed only once, this study provided no insight in individual changes in these perceptions and beliefs from the moment of referral to secondary care throughout the comprehensive self-management education programme and follow-up. Although the study therefore does not directly demonstrate that illness perceptions and medication beliefs can be modified during comprehensive guideline-based asthma care in our secondary care setting, it does provide a considerable amount of circumstantial evidence supporting this hypothesis. It also suggests that these changes in parental perspectives largely contributed to the high adherence rates we measured in the secondary care group.

First, the focus group study (chapter 2) showed remarkable differences in medication beliefs between populations from primary and secondary care, and these differences in the perception of the necessity of ICS between parents from primary care and secondary care were confirmed at enrolment into the 12-month follow-up study (chapter 5). Because it can be assumed that parents in secondary care, at the time of referral to secondary care by their GP, had similar illness perceptions and medication beliefs as the parents from primary care examined in our study, it is likely that the adherence-supporting constructive illness perceptions and medication beliefs developed during long-term management and follow-up in secondary care.

Second, because of the haphazard primary asthma care, without regular follow-up, a repetitive discussion of parental perspectives was impossible. Secondary asthma care comprised extensive self-management education and regular follow-up, providing the opportunity to discuss parental perspectives repeatedly. Third, the perceived degree of patient-centeredness was considerably higher in secondary than in primary care (chapter 5), suggesting a more collaborative physician-patient-parent partnership in secondary care, which is likely to increase the likelihood that parents and patients accept and internalize the adherence-promoting constructive medication beliefs that the health care providers present. This is supported by work by Petrie et al. who showed that patients' medication beliefs can be modified by providing information tailored to the patient's need after exploring their medication beliefs.<sup>18</sup>

Taken together, these observations support the hypothesis that exploring parental illness perceptions and medication beliefs, and providing tailored self-management education based on this, may help to modify medication necessity beliefs. This is the most likely explanation of the strong association between guideline based comprehensive asthma care and high adherence (figure 1). It suggests it is not the regular follow-up itself, or the provision of information-based and skills-based self-management

education, but that modification of parental medication beliefs determines adherence. The discussion of patients' and parents' perspectives, however, is missing in many consulting rooms, as will be discussed next.

## THE REALITY OF THE CONSULTING ROOM

We observed very limited self-management education and no regular follow-up for most patients in primary asthma care, both in the narratives provided by parents and by the GPs themselves (chapters 2 and 4). Previous studies in primary care settings in several countries, including the Netherlands, have shown comparable deviation from asthma guideline-based care.<sup>19-21</sup>

Moreover, this finding is not unique for asthma, but has also been reported for a range of other chronic illnesses. Recent surveys indicate that many physicians fail to provide self-management education on a regular basis, although there is now consistent evidence supporting the effectiveness of such education in patients with chronic illness.<sup>8,22-24</sup> The lack of attention to adherence in follow-up consultations in daily practice is even more striking,<sup>25,26</sup> to such an extent that it has been called a 'conspiracy of silence'. Our observations suggest that the conspiracy of silence also includes insufficient attention to discussing illness perceptions and medication beliefs. This is in agreement with several studies showing a lack of exploration of the patient's perspective in many medical consultations.<sup>26-31</sup> The reality of patients self-managing their illness, as determined by their illness perceptions and medication beliefs, is therefore not acknowledged in many consulting rooms. This is unfortunate as the results of this study strongly suggest that collaborating with parents of children with a chronic disease such as asthma, taking their perspectives on the disease and its treatment into account, may help to improve adherence and to control asthma successfully. This approach has been termed "patient-centred care", and consists of three key elements (box 1).<sup>32,33</sup>

### Box 1. Domains of patient-centered care (adapted from <sup>32,33</sup>)

- discovering the patient's perspective
- shared control of the consultation
- activating the patient to ask questions, prepare for consultations, and take initiative

Accumulating evidence suggests that patient-centred care is associated with improved health outcomes.<sup>32,34</sup> Most patients and parents prefer consultations which are organized along the principles of patient-centred care. Although patient-centred care consultations are therefore associated with increased patient satisfaction and improved health outcomes,<sup>32,35</sup> many physicians experience obstacles to its adoption in daily practice.

## ‘ACUTE CARE MODEL’ OR ‘COMMON SENSE MODEL’?

*“Most medical students have images of their future professional lives as young physicians, dressed in white coats that flutter while running through empty hallways late at night – heading for the emergency room where they will perform heroic, complex medical miracles, after which the patient will go home the next morning, completely recovered. To many of them, it comes as quite a shock to learn about the ‘epidemiological transition’: the shift from ‘cure’ to ‘care’, and the shift from acute illness to chronic disease”<sup>36</sup>*

Although most practicing physicians will acknowledge that they are more involved in care than cure, the health care provided to patients with a chronic illness does not meet the patients’ needs, as outlined above. This may be related to organizational issues. The GPs in our study reported that the care provided in their practices was largely reactive in nature, aimed at delivering acute care to patients with current symptoms, but less tailored to chronic health care in children aimed at preventing future symptoms (chapters 2 and 4). Time constraints are also frequently mentioned as a reason to avoid discussing adherence.<sup>26,37</sup>

Research has shown that patient-centred consultations indeed take slightly longer than traditional doctor-centred consultations.<sup>38</sup> Because of the limited time available to physicians in a single consultation, comprehensive self-management education is often outsourced to specialized nurses. In the primary care practices in our study, however, asthma nurses were not available for children with asthma (chapter 2); most specialized nurses in primary care focus on disease management in chronic conditions of (elderly) adults, such as COPD and diabetes. The failure of the financial health system to reimburse self-management education contributes to the persistence of such organizational issues.<sup>39</sup>

A major barrier to providing patient-centred care and to discussing illness perceptions, medication beliefs, and adherence, is the absence of training of such communication skills in current graduate and postgraduate medical education. Most medical students are now being sufficiently trained in basic communication skills, including eliciting the patient’s perspective and preferences.<sup>40</sup> However, when these students enter clinical practice, they experience that many of their role models show different professional communication behaviour altogether. Instead of eliciting the patient’s perspective and agenda, most senior consultants perform their consultations in a doctor-centred fashion, and they do so with great confidence and efficiency.<sup>41</sup> This lack of training in and role-modelling of patient-centred care may help to explain the ignorance and denial of the patients’ perspective illustrated by the following quote that I took from a colleague paediatric registrar in my training department:

*“Parents come to the outpatient clinic with their child, because they want help with their child’s symptoms. I do my job well, by providing a diagnosis and prescribing medication. Why then don’t they follow my advice? They came to me because they wanted help! I give them good advice, what else do they want?”*

Recognizable and understandable as this colleague’s heart cry may be, it does not reflect the reality that parents take decisions on the treatment of their children based on their own illness perceptions and medication beliefs. Unfortunately, such ignorance is common among physicians. In a recent European study among GPs, large variations were noted between physicians, not only on their perspectives on asthma and its management, but also on how the doctor-patient relationship can be used optimally to treat the condition effectively.<sup>42</sup> In the focus group interview with the GPs in our study, we recorded several beliefs about ICS which were not concordant with the current state of the evidence, and these physician’s beliefs determined their prescription behaviour (chapter 4). In another Dutch study, GPs reported the belief that they could not modify patients’ attitudes to the use of medication as an important reason to refrain from discussing adherence.<sup>26</sup>

Such individual perspectives are major determinants of behaviour, comparable to the main focus of this thesis: the role of patients’ perspectives about illness and medication in determining self-management behaviour as described by the Common Sense Model. Therefore, understanding physicians’ perspectives about the management of chronic diseases (particularly childhood asthma) may provide an explanation for the reason why these physicians prescribe long-term medication without providing the necessary self-management education and regular follow-up. Furthermore, such perspectives may hamper implementation of patient-centred communication: providing patient-centred care requires a paradigm shift from the traditional medical care most physicians have been trained in.<sup>43</sup> This change from physician-based asthma management to patient-centred care is urgently needed, as discussed in the next section.

## **PATIENT-CENTRED COMMUNICATION: TIME TO CHANGE**

The paucity of randomized controlled trials studying the effect of patient-centred interventions fuels an on-going discussion between believers and sceptics about the effectiveness of patient-centred care. This paucity of evidence from trials, however, is likely to remain for the following two reasons. First, patient-centred care is a complex multifaceted intervention. Clinical trials, mainly designed and suited to study straightforward drug interventions, are difficult to perform for such complex interventions, and their interpretation is fraught with difficulties.<sup>44</sup> Second, documenting effects of patient-centred care on illness outcomes in chronic diseases requires long-term fol-



low-up, which increases the complexity and cost of trials, and reduces the willingness and possibilities of researchers to embark on them. Criticasters of patient-centred care can therefore rely on an on-going ‘absence of evidence’ to support their rejection of the concept. Because of the substantial indirect evidence supporting the adoption of patient-centred care, this attitude appears to be short-sighted. Meanwhile, the disparity between the level of evidence showing the effectiveness of patient-centred care and the worldwide urgent call for patient-centred care is striking. The call for patient-centred care is driven by patient associations, which have developed a strong lobby on governmental institutes and quality-of-care institutes to encourage doctors to adopt patient-centred care.<sup>45,46</sup>

This lobby reflects the almost universal patients’ preferences to collaborate with their doctors.<sup>47,48</sup> The call for patient-centred care is also driven by an ethical and humanistic perspective as patient-centred care is increasingly being viewed as the paradigm of “good quality” care.<sup>49</sup>

Although these humanistic and ethical arguments may already provide sufficient reason to implement patient-centred care, there also is accumulating evidence for a range of chronic conditions showing the benefits of patient-centred communication and care. A large systematic review reported a consistent relationship of patient-centred communication to good adherence.<sup>50</sup> We already discussed how tailored self-management education, based on an assessment of the patient’s and parents’ illness perceptions and medication beliefs, and aimed at modifying these into adherence-promoting constructive beliefs, may improve adherence. Other patient-centred communication strategies may also be effective in improving adherence. These include shared decision making, motivational interviewing, and solution focused therapy.

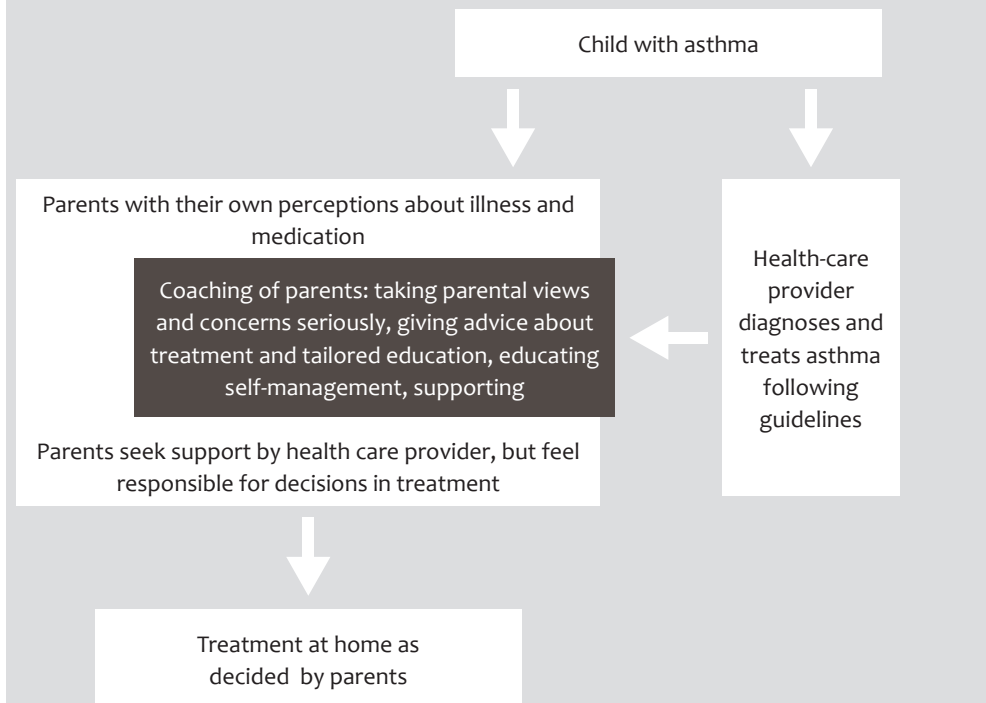
- Shared decision making involves discussing patients’ perspectives during the medical consultation and negotiating towards a mutually agreed treatment plan, taking the patient’s context, goals, and perspectives into account. A recent proof-of-principle study in adults with asthma showed improved adherence in adult patients with asthma involved in shared decision making, as compared to a control group receiving standard guideline-based therapy.<sup>51</sup> Similar improvements in adherence and health outcomes have been noted for shared decision making in several other conditions in adults.<sup>52</sup>
- Motivational interviewing is a patient-focused method of motivating behaviour change, centred on enhancing intrinsic motivation, and on resolving ambivalence about change. Through motivational interviewing, persons are guided to make self-care decisions based on their own personal goals and values. A number of studies reported benefits of this communication strategy regarding self-management behaviour and adherence.<sup>53-55</sup>

- Focusing on individual barriers which may hinder parents to achieve their intended level of adherence can also be a patient-centred communication strategy. Because of the unique individual set of barriers endangering optimal adherence in each case (as described in chapter 7), patient-centred interviewing is needed to detect such barriers. Because a parental lack of motivation and ineffective problem-solving behaviour may underlie the persistence of individual barriers, physicians should address these problems (chapter 7). A study on physicians' communication during follow-up consultations reported a lack of focus on problems and suggested that physician collaborative communication can be most improved in the area of participatory monitoring and problem solving.<sup>56</sup>

### IMPLICATIONS FOR PRACTICE

Childhood asthma care should be patient-centred, taking the reality of parents self-managing their child's asthma into account, and the physician working as a coach. Such patient-centred care is characterized by:

- Information-based and skills-based self-management education
- Discussion of parental (and children's) illness perceptions and medication beliefs
- Tailored self-management education
- Shared decision making
- Exploration of individual barriers to the use of ICS
- Regular follow-up



Taken together, patients' preferences for collaborative care, the solid theoretical framework of the Common Sense Model supporting patient-centred care, the humanistic and ethical perspective that patient-centred care is the desirable paradigm for good quality health care, and the accumulating evidence showing the benefits of such care justify the call for a paradigm shift in health care towards a widespread adoption of patient-centred care.

## IMPLICATIONS FOR RESEARCH

In adherence research, the focus has traditionally been on the patients, driven by the question “why don't patients take medications as prescribed by their physician?” Patient characteristics have been examined as potential determinants of adherence. As confirmed in this study, the strongest patient determinants of adherence are their illness perceptions and medication beliefs. In addition to this finding, this thesis also identified the organization of health care and the approach of the consultation as potentially important determinants of adherence. Future adherence research should therefore not only target the patient, but also the health care provider, driven by the research question ‘How can widespread adoption of patient-centred communication in chronic health care be realized?’. This latter research question can be addressed in different ways, including:

- A qualitative study on the views and preferences of physicians on patient-centred care. What views do physicians have on the optimal organization of health care and on their own consultations? How do they perceive the pros and cons of patient-centred versus doctor-centred consultations? What are the barriers they perceive to implementing patient-centred care? Do they feel sufficiently trained in applying the communication skills needed for patient-centred care? Does this differ between physicians in primary care versus those in hospital-based secondary and tertiary care?
- What approach do patients and parents prefer in health care for children? Do parents of children universally prefer patient-centred care, or does this differ between parents? What are the determinants of such differences, if any, between parents? This can be approached quantitatively and qualitatively.
- How can communication skills for patient-centred care be taught? What is the optimal way of teaching and practicing such communication skills? Is this applicable for all aspects of patient-centred care, including agenda setting, taking patient's views and preferences into account, exploring illness perceptions and medication beliefs, shared decision making, and identifying barriers to adherence? What

implications do these findings have for the teaching of communication skills in graduate and postgraduate medical education?

- What is the difference in time spent on consultations between traditional doctor-centred and patient-centred consultations? What is the result of such consultations in paediatric practice in terms of patient/parent satisfaction, in adherence and in health outcomes?
- What is the long-term cost-effectiveness of patient-centred consultations as compared to regular secondary care?
- In addition, this thesis gives rise to a number of additional novel research areas which will only be described in broad and general terms.
- Is motivational interviewing more effective than regular patient-centred care consultations for the adolescent with a chronic condition and known or suspected poor adherence to maintenance therapy?
- How do illness perceptions and medication beliefs change from the initial consultation in secondary care at referral throughout long-term management and follow-up?
- Which communication strategy is most effective in modifying the patient's and parents' illness perceptions and medication beliefs? Does this differ between different groups of patients?

## CONCLUSIONS

Over the past decade, several systematic reviews reported limited effects of interventions to improve adherence, and a low overall adherence in medical care for paediatric chronic diseases. This thesis, however, describes very high adherence in the large majority of children with asthma in a secondary care practice providing guideline-based comprehensive self-management education and follow-up in a patient-centred fashion. Based on the theoretical framework of the Common Sense Model, we are convinced that the patient-centred tailored self-management education provided to the parents of those children resulted in modification of their medication beliefs, which in turn improved adherence. This justifies a paradigm shift in paediatric chronic disease consultations from a traditional doctor- and disease-centred approach towards patient-centred care, taking the parents' perceptions, beliefs, and preferences into account. This thesis also reported on the reality of health care in daily practice, in which parental perspectives are not acknowledged or discussed in many consultations. Although organisational issues and lack of specific training may play a role in this undesirable state of affairs, physicians' perspectives on the management of chronic disease may be a more important determinant of this lack of attention to patients' ill-

ness perceptions and medication beliefs. Patient-centred communication incorporated in comprehensive asthma care with regular follow-up is a pivotal intervention to improve adherence to medication, as shown by this study, and supported by several other studies. Future studies on adherence should therefore focus on physicians' attitude to patient-centred care.

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# Nederlandse samenvatting

Kinderen met astma die daar regelmatig klachten van hebben, krijgen vaak het advies van een arts om dagelijks medicijnen te gebruiken. Die medicijnen zijn meestal corticosteroïden (net als bijvoorbeeld prednison) en worden ingenomen per inhaler. Deze inhalatiesteroïden hebben een ontstekingsremmend effect op het slijmvlies van de luchtwegen en verminderen de gevoeligheid van de luchtwegen voor prikkels waardoor de klachten van benauwdheid en piepen bij de ademhaling afnemen. Dagelijks gebruik van deze medicijnen, ook als er geen klachten zijn, heeft een goed beschermend effect; uit onderzoek blijkt dat vrijwel alle kinderen die deze medicijnen regelmatig gebruiken nauwelijks last hebben van hun astma. Ernstige bijwerkingen van deze medicijnen komen bijna nooit voor. In het kort is dit het medische model van astma en de behandeling daarvan.

Uit onderzoek blijkt echter dat de meeste kinderen met astma hun medicijnen niet regelmatig gebruiken: er wordt vaak een dosering overgeslagen of medicijnen worden alleen genomen als er klachten zijn. Het advies van de arts om de medicijnen regelmatig te nemen wordt dus niet gevolgd, dat wordt therapieontrouw genoemd. In internationale publicaties is de therapietrouw meestal tussen de 30% en 70%; een percentage dat weergeeft hoeveel van de voorgeschreven pufjes daadwerkelijk wordt genomen. Door therapieontrouw hebben veel kinderen onnodig veel last van hun astma. Lange tijd bestond het beeld dat therapieontrouw vooral voorkwam bij bepaalde groepen van ouders en kinderen. Bijvoorbeeld bij ouders die het advies van de arts niet goed begrepen (mogelijk in relatie met een lager opleidingsniveau) of bij kinderen met milde astmaklachten. Dit is in onderzoek echter onjuist gebleken: therapieontrouw komt in alle lagen van de bevolking voor en is onafhankelijk van de ernst van de ziekte (zo wordt het zelfs ook gevonden bij kankerpatiënten of na een orgaantransplantatie). In de afgelopen jaren is er daarom toenemend aandacht ontstaan voor andere determinanten van therapieontrouw (factoren die samenhangen met therapieontrouw). Geleidelijk aan is daarbij het beeld ontstaan dat het al of niet gebruiken van medicijnen door kinderen met een chronische ziekte een meer of minder bewuste keuze is van hun ouders. Ouders hebben hun eigen opvattingen over astma en over de behandeling er van, en deze opvattingen beïnvloeden hun keuze om het advies van de arts al of niet te volgen. Deze keuze lijkt grotendeels gebaseerd op ‘common sense’, op gezond

(boeren)verstand, en dit onderzoeksmodel van therapietrouw wordt dan ook het “Common Sense Model” genoemd. Ons onderzoek naar therapietrouw bij kinderen van twee tot twaalf jaar met astma heeft als primaire hypothese dat ‘Common Sense’ een grotere invloed heeft op de therapietrouw dan factoren zoals de ernst van het astma of de kennis van ouders over de ziekte. Deze achtergrond van het onderzoek is verder uitgewerkt in hoofdstuk 1.

In dit proefschrift staan verschillende studies beschreven die uitgevoerd zijn om deze hypothese te toetsen. De eerste studie is een focusgroep-onderzoek (groepsinterviews) met ouders waarvan hun kind met astma onder behandeling is bij de huisarts of de kinderarts (hoofdstuk 2). De tweede studie is een observationele studie, waarbij kinderen die van de huisarts of van de kinderarts het advies kregen inhalatiesteroiden te gebruiken gedurende een jaar werden gevolgd. In dat jaar werd de therapietrouw gemeten met behulp van elektronische apparaatjes die op een microchip exact vastlegden wanneer de medicatie gebruikt werd (zogenaamde medicatiloggers), en werd de astmacontrole bijgehouden. Opvattingen van ouders over astma en de medicatie werden vastgelegd met behulp van vragenlijsten. Daarnaast werd uitgebreid informatie verzameld over andere factoren die de therapietrouw zouden kunnen beïnvloeden, zoals de kennis van ouders over het astma, hun zorgen over de gezondheid van hun kind en de waardering van ouders voor de consulten van de arts. De uitkomsten van dit onderzoek zijn beschreven in hoofdstuk 3 tot en met 6. Na afloop van deze follow-up studie werden ouders uit het onderzoek geïnterviewd over het gebruik van de inhalatiesteroiden, zoals dat gedurende een jaar elektronisch was vastgelegd (hoofdstuk 7). Hieronder volgt een korte samenvatting van deze hoofdstukken, waarbij vanwege de overlap in methoden hoofdstuk 3 en 5 zijn samengevoegd.

Het eerste artikel (hoofdstuk 2) beschrijft het focusgroep-onderzoek met ouders. Voor dit onderzoek werd 6 maal een groepsinterview gehouden: 3 met ouders waarvan hun kind door de huisarts werd behandeld en 3 met ouders waarvan hun kind door de kinderarts werd behandeld vanwege astma. De interviews waren gericht op het bespreken van de opvattingen van ouders over astma en het gebruik van inhalatiesteroiden. Er bleken grote verschillen te bestaan tussen ouders uit de huisartsgroep en de kinderartsgroep. In de eerste groep bleken ouders vaak opvattingen over astma en de medicatie te hebben die niet overeenkomen met het medische model van astma en de behandeling. Door deze opvattingen waren veel ouders niet bereid om hun kind dagelijks medicijnen toe te dienen, en werden de inhalatiesteroiden dus onregelmatig gebruikt. Ouders uit de kinderartsgroep hadden opvattingen die veel meer overeenkwamen met het medische model van astma, en dit was voor hen ook de rechtvaardiging om hun kind regelmatig (dagelijks) de voorgeschreven medicatie toe te dienen.

Verder bleek de begeleiding van kinderen met astma door huisartsen vaak beperkt te zijn zonder regelmatige geplande controlebezoeken aan de huisarts. Dit in tegenstelling tot de begeleiding die ouders ontvingen van de kinderarts en de kinderlongverpleegkundige in het ziekenhuis: uitgebreidere informatievoorziening waarbij het beleid werd afgestemd met ouders, gecombineerd met regelmatige geplande controlebezoeken aan de polikliniek.

Dit onderzoek laat zien dat veel ouders bewust een keuze maken of ze het advies van de arts voor dagelijks gebruik van medicatie voor astma al dan niet opvolgen en dat zij zich bij die keuze laten leiden door hun eigen opvattingen over astma en medicatie. Verder toont dit onderzoek dat intensieve begeleiding van kinderen met astma en hun ouders samenhangt met opvattingen die overeenstemmen met het medische model van astma. Deze samenhang suggereert dat opvattingen van ouders over astma en de medicatie te veranderen zijn. Doordat het onderzoek gebaseerd was op de eigen rapportage van een relatief klein aantal ouders, konden er geen algemene conclusies over alle ouders van alle kinderen met astma uit dit onderzoek worden getrokken.

Hoe de uitgebreide reeks van factoren die therapietrouw mogelijk beïnvloeden samenhangt met de therapietrouw zoals die gedurende een jaar elektronisch werd gemeten, is beschreven in hoofdstuk 3 en 5. De primaire hypothese van dit studieproject was dat opvattingen van ouders over astma en de medicatie de grootste invloed hebben op de therapietrouw, een hypothese die gevoed was door de resultaten uit het focusgroep onderzoek uit hoofdstuk 2. Voor dit onderzoek zijn 42 kinderen met astma die door de huisarts werden behandeld en 135 kinderen met astma die door de kinderarts werden behandeld gedurende een jaar gevolgd. De inclusie van kinderen uit de huisartsenpraktijken verliep moeizaam omdat veel kinderen in de huisartspraktijk slechts korte tijd hun medicatie kregen voorgeschreven, waardoor deze groep relatief klein is gebleven (dit is beschreven in hoofdstuk 4).

De eerste opvallende bevinding van dit onderzoek is de hoge mediane therapietrouw in de kinderartsengroep: 84% van de voorgeschreven puffes werd genomen. In de huisartsengroep was dat duidelijk (en statistisch significant) lager: 66%. De mate waarin ouders de noodzaak zagen om dagelijks medicatie te gebruiken en de mate waarin zij zorgen hadden over het dagelijks gebruik van medicatie werd gescoord door middel van vragenlijsten. Bij ouders uit de kinderartsengroep was die score vaker in het voordeel van de noodzaak van medicatie dan bij ouders uit de huisartsengroep (91% versus 75%), hun opvattingen kwamen dus vaker overeen met het medische model van astma en de behandeling. De kinderartsengroep kenmerkte zich door een beperkte spreiding in mate van therapietrouw en in de opvattingen over medicatie; veel ouders geloofden in de noodzaak van medicatie en gaven de medicatie ook regelmatig.

De uitkomsten van dit onderzoek bevestigen de uitkomsten van het focusgroep

onderzoek: therapietrouw is bij de intensievere begeleiding in het ziekenhuis hoger, en dit hangt samen met opvattingen van ouders die beter overeenkomen met het medische model van de behandeling van astma, namelijk dat inhalatiesteroïden nodig zijn om een goede astmacontrole te bereiken. Overigens was de associatie tussen de opvattingen van ouders en therapietrouw binnen de kinderartsengroep slechts zwak vanwege de beperkte spreiding van therapietrouw (de meeste ouders gaven hun kind de medicatie dagelijks zoals voorgeschreven) en de beperkte spreiding in de opvatting dat inhalatiesteroïden nodig zijn (de meeste ouders erkennen de noodzaak er van). In combinatie met de uitkomsten van het focusgroep-onderzoek en omdat een sterke associatie tussen therapietrouw en opvattingen van ouders over de medicatie werd gevonden in de huisartsengroep, is het echter aannemelijk dat het verband tussen opvattingen over medicatiegebruik en therapie(on)trouw wel een oorzakelijke relatie is. Het verschil in opvattingen over astma en het medicatiegebruik daarvoor tussen ouders uit de huisartsengroep en uit de kinderartsengroep veronderstelt dat zulke opvattingen te wijzigen zijn. Kinderen en ouders komen namelijk bij de kinderarts na verwijzing door de huisarts. Waarschijnlijk zijn hun opvattingen op het moment van verwijzing vergelijkbaar met ouders waarvan hun kind nog door de huisarts wordt behandeld. Door de intensieve begeleiding door de kinderarts en de kinderlongverpleegkundige in de vorm van consulten die door ouders als duidelijk meer patiëntgericht worden beoordeeld dan de consulten bij de huisarts, is er in ieder geval volop gelegenheid om met ouders van gedachten te wisselen over hun opvattingen en om gerichte voorlichting te geven. Dat zulke gerichte voorlichting kan leiden tot veranderde opvattingen over astma en medicatie is door andere onderzoekers expliciet aangetoond. Daarmee zijn (gewijzigde) opvattingen van ouders over astma en de behandeling ervan dus niet alleen een belangrijke determinant van therapietrouw, maar ook de verbinding tussen de intensieve begeleiding op de polikliniek en de hoge therapietrouw die wij bij deze patiënten in dit onderzoek vonden.

Deze bevinding heeft belangrijke consequenties. Als er sprake is van therapieontrouw wordt nu vaak de ouder (of de patiënt zelf) gezien als het ‘probleem’. De uitkomsten van dit onderzoek laten echter zien dat artsen een belangrijke rol kunnen hebben in het bereiken van goede therapietrouw, door ouders van kinderen met een chronische ziekte zoals astma voldoende begeleiding aan te bieden. Omdat veel ouders van kinderen met astma deze noodzakelijke begeleiding niet ontvangen, is dit een veelbelovend aangrijpingspunt om de therapietrouw (en daardoor de astmacontrole, zie hoofdstuk 6) bij kinderen met astma te verbeteren.

Omdat huisartsen vaak medicatie voorschrijven aan kinderen met terugkerende luchtwegklachten zonder dat ze daarbij expliciet de diagnose astma bij kinderen stellen, werden voor de inclusie van deze studie kinderen benaderd die in het afgelopen jaar

een recept voor inhalatiesteroïden ontvingen. Gebaseerd op de huisartsenrichtlijnen voor het voorschrijven van inhalatiesteroïden was de verwachting dat deze kinderen allemaal klachten zouden hebben (gehad) die bij astma passen. Tijdens telefonische interviews met de ouders van deze kinderen bleek dit echter niet het geval. Veel kinderen aan wie inhalatiesteroïden waren voorgeschreven hadden klachten die niet kenmerkend zijn voor astma, zoals hardnekkig hoesten of benauwdheid bij inspanning. Meer dan de helft van alle kinderen die we benaderden (en dat waren dus alle kinderen aan wie inhalatiesteroïden in het afgelopen jaar was voorgeschreven) had in de drie maanden voor het telefonisch interview geen inhalatiesteroïden gebruikt, of had deze medicijnen niet dagelijks gebruikt, maar alleen bij klachten. Volgens ouders was dat conform het voorschrift van de huisarts. De kinderen die volgens hun ouders wel dagelijks inhalatiesteroïden kregen werden gedurende een jaar gevolgd. Ook van deze kinderen bleek een gedeelte geen astmaklachten te hebben of de medicatie onregelmatig te gebruiken op advies van de huisarts. In een groepsinterview bevestigden de huisartsen dat zij inhalatiesteroïden laagdrempelig voorschreven aan kinderen met luchtwegklachten anders dan astma en dat zij vaak het advies geven om de medicatie alleen bij klachten te gebruiken. Een aantal redenen lag ten grondslag aan dit voorschrijfgedrag dat dus afwijkt van de huisartsenrichtlijn voor astmabehandeling. Soms schreven de huisartsen inhalatiesteroïden voor om een periode met klachten zonder duidelijke oorzaak te overbruggen, soms was het bedoeld als een start van astmabehandeling. Voor de huisartsen wogen de voordelen van deze praktijk op tegen de nadelen. Toch kregen veel kinderen door dit voorschrijfgedrag inhalatiesteroïden toegediend, soms gedurende langere tijd, terwijl dit volgens de richtlijnen voor astmabehandeling niet nodig en ook niet zinvol was. Aan de andere kant werden de kinderen met astma in de huisartspraktijk vaak niet optimaal behandeld: zij kregen niet het advies om de medicatie dagelijks te gebruiken. Dit onderzoek laat zien dat het onregelmatige gebruik van inhalatiesteroïden bij kinderen zoals dat in veel onderzoek wordt gevonden niet alleen het gevolg is van ouders die adviezen niet opvolgen, maar ook van het voorschrijfgedrag van huisartsen.

Het is waarschijnlijk dat hogere therapietrouw leidt tot betere astmacontrole. In hoofdstuk 6 wordt deze hypothese getoetst bij de kinderen van twee tot zes jaar oud die behandeld worden door de kinderarts. Gedurende het jaar dat de therapietrouw werd gemeten werd de mate van astmacontrole bij deze kinderen met verschillende methoden vastgelegd. Ouders vulden om de drie maanden vragenlijsten in en kinderartsen en kinderlongverpleegkundigen scoorden hun inschatting van de mate van astmacontrole tijdens de controlebezoeken van de deelnemende kinderen aan de polikliniek. Daarnaast werd longfunctieonderzoek verricht. Ondanks de hoge mediane therapietrouw en de beperkte spreiding van de therapietrouw in deze groep kinderen

werd een sterk lineair verband gevonden tussen de therapietrouw en de mate van astmacontrole. Kinderen die meer dan 80% van de voorgeschreven medicatie kregen, hadden de minste klachten en aanvallen van hun astma. Kinderen met lagere therapietrouw hadden vooral aanhoudend milde klachten van hun astma. Voor artsen die kinderen met astma behandelen is het dus belangrijk om bij kinderen met aanhoudende milde klachten aandacht te besteden aan de therapietrouw om ook bij deze kinderen zo goed mogelijke astmacontrole te bereiken.

Ondanks de hoge mediane therapietrouw bij kinderen behandeld door de kinderarts, kregen ook in deze groep sommige kinderen duidelijk minder medicatie dan was voorgeschreven. Om meer duidelijkheid te krijgen over de achtergronden van de lage therapietrouw in sommige gezinnen, ondanks intensieve begeleiding, werden ouders geïnterviewd over de mate van therapietrouw zoals die gedurende een jaar was vastgelegd (hoofdstuk 7). Na interviews met 10 ouders (en kinderen) met een lage therapietrouw werden 10 ouders (en kinderen) met een hoge therapietrouw geïnterviewd. Deze laatste interviews maakten het mogelijk om te bestuderen waarom factoren in het ene gezin wel en in het andere gezin niet tot therapieontrouw leiden.

Drie patronen van therapieontrouw werden geïdentificeerd. Ten eerste, ouders die zeer bewust het advies van de arts niet opvolgden op basis van hun opvattingen over astma en de behandeling. Ten tweede, gezinnen waar regelmatig een dosis werd gemist zonder vooropgezet plan. Dit kwam vooral voor bij ouders die ook andere zorgen aan hun hoofd hadden, zoals problemen met de opvoeding van de kinderen of financiële zorgen. Het derde patroon van therapieontrouw werd gekenmerkt door kinderen die al op jonge leeftijd (vanaf 8 jaar) de volledige verantwoordelijkheid kregen voor het dagelijks nemen van hun medicijnen, zonder toezicht van of controle door de ouders. Deze kinderen namen de medicatie vaak veel minder vaak dan de ouders verwachtten. Dit laatste patroon is een oorzaak van therapieontrouw die nauwelijks bekend is en waar nog weinig onderzoek naar is verricht. Het geeft wel een goed aanknopingspunt voor verbetering van de therapietrouw. Artsen en verpleegkundigen kunnen de verantwoordelijkheid die kinderen aan kunnen bespreken met ouders: kinderen op de basisschoolleeftijd zijn dus nog niet in staat om volledige verantwoordelijkheid te dragen voor het dagelijks gebruik van onderhoudsmedicatie voor een chronische ziekte.

In hoofdstuk 8 worden alle resultaten van het onderzoek bediscussieerd in het licht van actuele wetenschappelijke publicaties over therapietrouw en de zorg voor patiënten met een chronische ziekte. In overeenstemming met deze publicaties laat ons onderzoek zien dat opvattingen over ziekte en medicatie de therapietrouw in sterke mate bepalen. De primaire hypothese van het onderzoek, namelijk dat zulke opvattingen een grotere invloed hebben op de therapietrouw dan factoren zoals de ernst

van het astma of de kennis van ouders over de ziekte, wordt daarmee bevestigd. De uitkomsten van dit onderzoek wijzen erop dat zulke opvattingen kunnen veranderen, wanneer er in voldoende mate en op de juiste manier met ouders wordt gecommuniceerd. Er zijn slechts enkele andere onderzoeken die deze bevinding direct steunen. Wel is er een groot aantal onderzoeken dat laat zien dat patiënten vaker het advies opvolgen van artsen die patiëntgericht communiceren. Een voorbeeld van zulke patiëntgerichte communicatie is Shared Decision Making (gezamenlijke besluitvorming). Hierbij staat het actief inventariseren van de opvattingen van de patiënt over de ziekte en diens wensen over de behandeling centraal, waarbij die opvattingen en wensen worden meegenomen in een gezamenlijk genomen besluit over de behandeling. Voor deze vorm van arts-patiëntcommunicatie is aangetoond dat het de therapietrouw positief beïnvloedt. Ondersteund door deze bevindingen is het aannemelijk dat de hoge therapietrouw zoals die gemeten is in de populatie kinderen die behandeld wordt door de kinderarts samenhangt met de wijze waarop kinderen worden begeleid en de wijze waarop met ouders wordt gecommuniceerd.

Een andere belangrijke constatering van dit onderzoek is dat de astmazorg zoals die door huisartsen wordt gegeven tekortkomingen vertoont. De beperkte begeleiding van kinderen met astma en hun ouders in de huisartsenpraktijk beperkt de mogelijkheden tot een goede afstemming van het behandelbeleid met ouders. Opvattingen van ouders en patiënten komen in de spreekkamer meestal niet aan bod, vaak door (vermeend) tijdgebrek. Er zijn echter ook aanwijzingen dat artsen zich onvoldoende realiseren in welke mate patiënten een bewuste keuze maken om een medicatieadvies te volgen en daarin geleid worden door hun eigen opvattingen. In de opleiding van artsen wordt relatief weinig aandacht besteed aan de communicatie met patiënten met een chronische aandoening. Dat kan een goede verklaring vormen voor de beperkte aandacht in veel spreekkamers voor het perspectief van de patiënt.

Vele onderzoeken tonen een lage therapietrouw voor inhalatiesteroïden bij kinderen met astma. Hierdoor houden veel kinderen onnodig klachten. Uit dit onderzoek, en in overeenstemming met internationale publicaties, blijkt dat de zorg voor kinderen met astma vaak niet aan de richtlijnen voldoet en dat de communicatie met ouders onvoldoende patiëntgericht is. In dit onderzoek vinden wij een ongeëvenaard hoge therapietrouw bij een groep kinderen met astma die intensieve en patiëntgerichte begeleiding ontving op een polikliniek waar kinderartsen en kinderlongverpleegkundigen samen de zorg voor kinderen met astma en hun ouders gestalte geven. Dit onderzoek laat dus zien dat goede therapietrouw haalbaar is voor de meeste kinderen met astma, samen met een goede controle van hun astma. Dit is voor veel meer kinderen met astma haalbaar als zij en hun ouders de juiste intensieve zorg en begeleiding ontvan-



gen. Lange tijd werd vooral naar die ouders gekeken als het ging om therapieontrouw: zij volgden niet het voorschrift van de arts. Dit onderzoek maakt duidelijk dat er ook aandacht moet zijn voor de begeleiding die artsen geven aan ouders van kinderen met astma. Krijgen deze ouders de begeleiding die zij nodig hebben om een goede keuze te maken in de behandeling van hun kind met astma? De medische wereld kan zelf veel doen om de zorg voor kinderen met een chronische ziekte zoals astma te verbeteren.

# Dankwoord

Wat een inspiratie heeft dit promotieproject mij gebracht! Het heeft mijn kijk op de arts-patiënt relatie sterk veranderd, en daarmee ook de wijze waarop ik mijn dagelijks werk doe. Het heeft mij enthousiast gemaakt om zorg aan patiënten met een chronische ziekte te verbeteren. Ik ben ervan overtuigd geraakt dat hierin nog een wereld te winnen is.

“Niet alleen de inhoud van mijn onderzoek was buitengewoon inspirerend, dat geldt zeker ook voor het contact met mijn begeleiders”. De eerste van hen die ik bedank is professor Ad Kaptein. Hij heeft me voortdurend gestimuleerd om te luisteren naar de patiënt en de ouders, hun verhaal te horen. Zijn bevoegenheid en zijn enorme inzet waren een goede motivatie om door te zetten, ook als het minder soepel liep. ‘Doc, doorgaan...’, luidde dan weer de titel van een mailtje. De topografische afstand tussen ons was groot en we hebben elkaar weinig ontmoet. Maar de begeleiding via de mail was van uitstekend niveau. Van grap en grol tijdens lange, saaie bureaudagen tot inspirerende tips en de soms broodnodige steun. Ik denk zelfs dat de topografische afstand onze relatie goed heeft gedaan; door jouw vorm van communicatie vergat ik meestal dat je een (bijna) emeritus-professor uit het keurige Leiden bent. Dat gaf vrijheid in onze correspondentie. Ad, bedankt.

Juist heel dichtbij was professor Paul Brand. Beste Paul, enkele jaren spraken wij elkaar vrijwel elke maandag tijdens de lunch. Afgewisseld met een bezoek bij jou thuis aan de keukentafel of in de tuin. De uitkomsten van het onderzoek waren ook voor jou een eyeopener. Jouw geestdrift voor dit onderzoek, voor de verrassende uitkomsten ervan en voor de implicaties rond de zorg aan kinderen met astma was een enorme stimulans. Door je directe betrokkenheid was je goed op de hoogte van de lastige fasen in het onderzoek; je altijd positieve insteek was opbeurend. Door de vertragingen die het onderzoek opliep, moest het opschrijven van de resultaten in korte tijd plaatsvinden. Dankzij jouw hulp is het gelukt om in vijf maanden tijd vier manuscripten, de ‘introduction’ en ‘general discussion’ te schrijven. Gecorrigeerd in het vliegtuig onderweg naar vakantie of tijdens een congres in het buitenland: ik kreeg mijn stukken altijd in korte tijd terug. Samenwerken met jou is een fenomenale ervaring. Jouw daadkracht

en effectiviteit waren een enorme stimulans om steeds weer een tandje bij te zetten, waardoor sommigen mij inmiddels een workaholic noemen. Bedankt voor alles.

Professor Eric Duiverman was de derde begeleider bij dit onderzoeksproject. Beste Eric, door de rol die je had binnen het onderzoek was ons contact veel minder frequent. Jij was de begeleider die vaak vanuit de coulissen meedeed. Je dacht mee met de ontwikkelingen binnen het onderzoek en probeerde met je nuchtere commentaar op de manuscripten ons enthousiasme in toom te houden. Bedankt voor je adviezen en inzet.

Naast Paul waren vooral Eric de Groot als kinderarts en Lia van Helsdingen en Jacqueline Wolf als kinderlongverpleegkundigen degenen die de astmazorg op de polikliniek kindergeneeskunde van de Isala klinieken realiseerden ten tijde van het onderzoek. Het grootste deel van de onderzochte patiëntenpopulatie was bij hen onder controle. Bedankt voor jullie bijdrage aan het includeren van patiënten en het invullen van vragenlijsten.

Dat het onderzoek ook uitgevoerd kon worden in de eerste lijn heeft een essentiële meerwaarde gehad voor de uitkomsten. Mijn dank aan de huisartsen die hun medewerking gaven is dan ook groot. Het was zeker niet vanzelfsprekend dat jullie ons vanuit de tweede lijn een kijkje gaven in jullie praktijk van kinderastmazorg. Ook toen na de interviews met ouders duidelijk werd dat die zorg misschien wel beter kon, wilden jullie zonder aarzeling meewerken aan een vervolg. Tweemaal hadden we een bespreking over de uitkomsten van dit onderzoek. Uitkomsten die lieten zien hoe anders de benadering is binnen de eerste lijn versus de tweede lijn. Ondanks die grote verschillen lukte het ons om daar op een open en eerlijke manier over te discussiëren. Wat mij betreft is dit een groot compliment aan jullie en een voorbeeld hoe we kunnen samenwerken om tot betere (keten)zorg te komen.

In het ziekenhuis waren natuurlijk veel meer mensen direct en indirect betrokken bij de zorg voor kinderen met astma en daarmee bij het onderzoek. De kinderartsen, het secretariaat, de longfunctieassistenten: doordat iedereen altijd weer een bijdrage wilde leveren, verliep het onderzoek voorspoedig en met weinig frustratie. De sfeer op de Amalia kinderafdeling is goed, dat maakt dat ik daar jaren met veel plezier heb gewerkt. Zowel in de periode dat ik volledig bezig was met onderzoek als de periode dat ik de stages liep voor mijn opleiding tot kinderarts.

Met Hanna beet ik de spits van het onderzoek af: we werkten samen intensief aan het focusgroep onderzoek. Interviews uitwerken is een tijdrovende klus waar jouw hulp

meer dan welkom was. Ook Susanne werkte mee aan een interviewstudie, maar dan juist aan het einde van het onderzoek. Je hebt daar heel wat uren in gestoken. Bijzonder aan dat onderzoek waren de gezamenlijke bezoeken bij ouders thuis, meestal in de avonduren. Wouter, ook jij bedankt voor je bijdrage, niet in het minst voor onze ontspannende tafelvoetbalcompetitie die ik kansloos verloor. Om de uitval van patiënten laag te houden, werden ouders en kinderen soms thuis bezocht. Daarnaast moesten altijd weer de medicatieloggers worden uitgelezen en vragenlijsten afgenomen, ook als ik bezig was met mijn (poli)klinische werkzaamheden. Dat was een tijdrovende klus waar Wouter, Susanne, Cirsten en Wilma mij fantastisch bij hielpen. Zonder jullie hulp was het nooit gelukt om het onderzoek door te laten lopen tijdens de fase dat ik mijn opleiding tot kinderarts hervatte.

En natuurlijk wil ik alle ouders en kinderen bedanken. Door jullie bereidheid mee te werken aan het onderzoek is dit succes behaald. Vele vragenlijsten invullen, extra longfunctie blazen, extra afspraken in het ziekenhuis of thuis: het gebeurde allemaal zonder veel problemen. Over de vanzelfsprekendheid om mee te werken aan dit onderzoek ben ik nog altijd blij verrast.

En dan is het onderzoek af, de manuscripten geschreven en naar de leescommissie verstuurd. Dan gaan plotseling alle verplichtingen rond promoveren de agenda beheersen. Rick, Simen en Rieke, bedankt voor jullie bijdragen aan teksten lezen en redigeren, het opmaken van mijn proefschrift en het ontwikkelen van de door mij zo begeerde website. En Els en Nynke, wat ontzettend leuk dat jullie mijn paranimfen willen zijn. Ik voel me vereerd.

Voor mijn gezin(sleven) was het onderzoek eerder een zegen dan een vloek, of beter eerst een zegen en later een vloek. Door de vrije dag in de week en de flexibiliteit kon ik in de drukke jaren met twee kleine kinderen de zorg goed met je delen, Rieke. Tijdens de laatste loodjes was dat anders, zeker de laatste maanden met de voortzetting van mijn opleiding in het UMCG. Lange werkweken met weinig aandacht voor jou en voor Simon en Hilde. Terwijl jullie zo belangrijk zijn voor mijn plezier in het leven en mij met beide voeten op de grond houden. Zoals Simon mij als 4-jarige al zei tijdens een meningsverschil: “Papa, jij weet ook niet alles”. En zo is het maar net!