

## **Online Depository**

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

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## **Details on methods and results**

*Details on the setting of the Clinic and the characteristics of our comprehensive asthma care.*

This study was performed in the Princess Amalia Children's Clinic in Zwolle, the Netherlands. This outpatient clinic is part of a 1,000-bed general teaching hospital serving a population of 350,000 people in a mixed area of urban and rural communities. After referral from primary care we diagnose and manage children with asthma (including starting maintenance treatment with ICS) according to the Dutch national guidelines on pediatric asthma, which are adapted from international guidelines.[1,2] The follow up of these children is characterized by special attention to building and maintaining a strong partnership with patients and parents. To achieve this, patients are being followed up frequently, both by a pediatric asthma specialist and a dedicated pediatric asthma nurse.[3] During these visits, repeated tailored education about asthma self management is provided, along with an open discussion of parents' perceptions about asthma and its treatment. Correct inhalation technique is trained and checked extensively, and the importance of daily adherence to inhaled corticosteroid treatment is discussed at every visit, ensuring concordance on treatment and its goals between patients/parents and medical team.[4,5]

*Details of putative determinants.* Prior to the start of the study, a list of putative determinants of adherence was defined including demographic and clinical characteristics and the results of the questionnaires used (table S1). These questionnaires were slightly modified to be completed by parents reporting on medication for their 2-6 yr old children. All questionnaires were validated Dutch translations, back-translation into English was performed by independent professional translators; these versions were checked against the original questionnaires and found to be consistent. If necessary authors were asked for permission to

use questionnaires with copyright. Parental illness perceptions were assessed on domains such as consequences, identity and understanding of childhood asthma by the Brief Illness Perception Questionnaire (B-IPQ),[6] perceptions about medication in general and, more specifically, perceptions about the need and concerns of daily use of ICS by the Beliefs about Medicine Questionnaire (BMQ).[7] The BMQ allows not only for analysis of individual item responses, but also yields a balance of parental beliefs about the necessity and parental concerns about ICS. To assess parental satisfaction with effectiveness, side effects, convenience and global satisfaction of daily use of ICS, the Treatment Satisfaction Questionnaire for Medication (TSQM) was used.[8] The I Worry scale was used to score parental worries about their child having asthma and having to use daily ICS.[9] Parental self reported adherence was assessed by the Medication Adherence Report Scale (MARS).[10] In addition, parents completed the Satisfaction with Information about Medicines Scale (SIMS), the Paediatric Asthma Caregiver Quality Of Life questionnaire (PACQOL), and a parental asthma knowledge questionnaire.[11,12]

Asthma control was assessed by parental report using the Asthma Control Questionnaire (ACQ) at the start of the study and after 3 months.[13] In addition, the pediatric asthma specialist rated the patient's degree of asthma control on a visual analogue scale ranging from 0 (worst asthma control possible) to 10 (complete asthma control) at the 3 month follow-up visit to the clinic.[14]

*Details on analysis and results.* Adherence was calculated as follows: the number of inhaled doses as registered by the Smartinhaler® was expressed as a percentage of the number of doses prescribed. For a once-daily dosing regimen, any recorded use of maintenance medication on a single day was considered a correct dose; for a twice daily regimen, each dose had to be given within an interval of 6 hours around the prescribed dosing time (8 AM

and 17 PM). Recorded doses exceeding the number of prescribed doses for the dosing time were censored at 100% of the prescribed dose. The most important reason to do so is that parents may give medication repeatedly when administering the medication failed at first attempt for several reasons (e.g. the child started crying or coughing).

The association of each of these putative determinants to electronically measured adherence to ICS maintenance therapy was assessed in univariate analyses (table S2). Because the distribution of adherence was highly skewed, nonparametric analyses were used throughout. The relationship of adherence to determinants with an ordinal distribution was assessed by Spearman's rank correlation coefficient ( $\rho$ ), and its association to binary determinants with the Mann-Whitney U test. Additional analyses of the relationship between determinants and adherence were performed after adherence was dichotomized as >80% (good adherence) or <80% (poor adherence).[15] We refrained from multivariate analysis because of the exploratory nature of this study, and because of the high degree of potential interaction and multicollinearity between putative determinants. We chose to refrain from adjustments for multiple comparisons because of the exploratory and observational nature of our study.[16]

**Table S1: List of putative determinants of electronically measured adherence**

<b>Determinant</b>	<b>details</b>
<b>clinical and demographic data of children</b>	
Child's age	yrs
Positive specific IgE to common inhalant allergens	% positive
Hospitalisations in year before study	number
Scheduled visits to outpatient clinic in year before study	number
Duration of outpatient clinic asthma care before study (months)	number
Rint baseline	z-score
Rint % change after bronchodilator	% change
FEV <sub>1</sub> baseline	z-score
FEV <sub>1</sub> change after bronchodilator	% change
VAS asthma control by physician	ranging from 0 (worst asthma control possible) to 10 (complete asthma control)
Asthma Control Questionnaire baseline, 6 questions	Mean of six items, Likert-scale 0 (well-controlled asthma) to 6 (not well-controlled asthma)
Asthma Control Questionnaire at 3 months, 6 questions	Mean of six items, Likert-scale 0 to 6
<b>demographic data of parents</b>	
Parental smoking	Mother, father of both parents
Parental diagnosis of asthma	Mother, father of both parents
Educational level mother	Scale ranging from 1 (lowest educational level) to 7 (highest educational level)
Educational level father	Scale ranging from 1 to 7
<b>questionnaires</b>	
Brief Illness Perception Questionnaire, 8 questions	analysis of individual item responses, 11-point Likert-scale

Beliefs about Medicine Questionnaire, specific part, 5 questions about perception of necessity and 5 questions about concerns	mean of necessity and concernscores and need-concern ratio, 5-point Likert-scale
Beliefs about Medicine Questionnaire, general part, 4 questions about perceptions of harm of medicines	Mean of 4 questions, 5-point Likert-scale
Beliefs about Medicine Questionnaire, general part, 4 questions about perceptions of overuse of medicines	Mean of 4 questions, 5-point Likert-scale
Treatment Satisfaction Questionnaire for Medication, 3 questions about effectiveness of daily use of ICS	Sum of 3 questions, 7-point Likert-scale
Treatment Satisfaction Questionnaire for Medication, 3 questions about side effects of daily use of ICS	Sum of 4 questions, 7-point Likert-scale
Treatment Satisfaction Questionnaire for Medication , 3 questions about convenience of daily use of ICS	Sum of 3 questions, 7-point Likert-scale
Treatment Satisfaction Questionnaire for Medication , 3 questions about global satisfaction of daily use of ICS	Sum of 3 questions, 7-point Likert-scale
I Worry scale, 11 questions	Sum of 11 questions, 4-point Likert-scale
Medication Adherence Report Scale, 5 questions	Sum of 5 questions, 5-point Likert-scale
Satisfaction with Information about Medicines Scale, subscale action and usage, 9 questions	Sum of scores, score 1 = satisfied, score 0 = not satisfied,
Satisfaction with Information about Medicines Scale, subscale potential problems of medication, 6 questions	Sum of scores, score 1 = satisfied, score 0 = not satisfied,
Paediatric Asthma Caregiver Quality Of Life questionnaire, 13 questions	Mean of 13 questions, 7-point Likert-scale
parental asthma knowledge questionnaire, 7 questions	Yes, no or I don't know. Number of good answers

Ig: immunoglobulin; Rint: respiratory resistance by the interrupter technique; FEV<sub>1</sub>: forced expiratory volume in one second; FEV<sub>1</sub><sup>1</sup>-change: difference in forced expiratory volume in one second before and after ventolin; VAS: visual analogue scale[13]

**Table S2: Putative determinants and association with electronically measured adherence over 3-month period**

<b>Determinant</b>	<b>Rank correlation coefficient</b>	<b>comparison between children with high (&gt;80%) and low adherence (&lt;80% of prescribed dosages taken)</b>
<b>clinical and demographic data of children</b>		
Child's age	$\rho = -0.06$ (p=0.563)	p=0.214
Positive specific IgE to common inhalant allergens	$Z^{\#} = 0,00$ (p=0,997)	p=0,673
Hospitalisations in year before study	$\rho = 0.00$ (p=0.981)	p=0.824
Scheduled visits to outpatient clinic in year before study	$\rho = 0.06$ (p=0.561)	p=0.345
Duration of outpatient clinic asthma care before study (months)	$\rho = -0.13$ (p=0.213)	p=0.392
Rint baseline (n=33)	$\rho = -0.33$ (p=0.060)*	p=0.045**
Rint % change after bronchodilator (n=33)	$\rho = 0.41$ (p=0.016)**	p=0.006**
FEV <sub>1</sub> baseline (n=33)	$\rho = -0.18$ (p=0.322)	p=0.752
FEV <sub>1</sub> change after bronchodilator (n=33)	$\rho = -0.33$ (p=0.069)*	p=0.085*
VAS asthma control by physician (n=78)	$\rho = 0.26$ (p=0.028)**	p=0.009**
Asthma Control Questionnaire baseline, 6 questions	$\rho = -0.14$ (p=0.21)	p=0.636
Asthma Control Questionnaire at 3 months, 6 questions (n=78)	$\rho = -0.19$ (p=0.105)	p=0.036**
<b>demographic data of parents</b>		
Parental smoking	$Z^{\#} = -0.95$ (p=0,341)	p= 0,876
Parental diagnosis of asthma	$Z^{\#} = -1.37$ (p=0,170)	p= 0.075*
Educational level mother	$\rho = 0.16$ (p=0.142)	p=0.012**
Educational level father	$\rho = 0.06$ (p=0.570)	p=0.173

<b>questionnaires</b>		
<i>Brief Illness Perception Questionnaire (B-IPQ), 8 questions</i>		
B-IPQ: How much does your child's illness affect his/her life? (consequences)	$\rho = 0.00$ (p=0.969)	p=0.870
B-IPQ: How long do you think your child's illness will continue? (timeline)	$\rho = -0.09$ (p=0.425)	p=0.289
B-IPQ: How much control do you feel you have over your child's illness? (personal control)	$\rho = 0.11$ (p=0.319)	p=0.760
B-IPQ: How much do you think your child's treatment can help his/her illness? (treatment control)	$\rho = 0.11$ (p=0.294)	p=0.526
B-IPQ: How much does your child experience symptoms from his/her illness? (identity)	$\rho = -0.05$ (p=0.663)	p=0.598
B-IPQ: How concerned are you about your child's illness? (concern)	$\rho = 0.00$ (p=0.970)	p=0.835
B-IPQ: How well do you feel you understand your child's illness? (understanding)	$\rho = -0.08$ (p=0.440)	p=0.260
B-IPQ: How much does your child's illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?) (emotional response)	$\rho = 0.13$ (p=0.203)	p=0.961
<i>Beliefs about Medicine Questionnaire, specific part, (BMQ-specific): 10 questions</i>		
BMQ-necessity	$\rho = 0.221$ (p=0.035)**	p=0.299
BMQ-concerns	$\rho = -0.007$ (p=0.949)	p=0.368
BMQ need-concern ratio	$\rho = 0.09$ (p=0.414)	p=0.394
Beliefs about Medicine Questionnaire, general part		
4 questions about perceptions of overuse	$\rho = 0.181$ (p=0.082)*	p=0.418
4 questions about perceptions of harm	$\rho = 0.233$ (p=0.025)**	p=0.253



Treatment Satisfaction Questionnaire for Medication, 3 questions about effectiveness of daily use of ICS	$\rho = -0.10$ (p=0.342)	p=0.633
Treatment Satisfaction Questionnaire for Medication, 3 questions about side effects of daily use of ICS	$\rho = -0.01$ (p=0,963)	p=0.838
Treatment Satisfaction Questionnaire for Medication , 3 questions about convenience of daily use of ICS	$\rho = -0.25$ (p=0.020)**	p=0.212
Treatment Satisfaction Questionnaire for Medication , 3 questions about global satisfaction of daily use of ICS	$\rho = -0.19$ (p=0.067)**	p=0.522
I Worry scale, 11 questions	$\rho = -0.05$ (p=0.617)	p=0.836
Medication Adherence Report Scale, 5 questions	$\rho = 0.53$ (p<0.001)**	p=0.001**
Satisfaction with Information about Medicines Scale, subscale action and usage	$\rho = -0.06$ (p=0.564)	p=0,107
Satisfaction with Information about Medicines Scale, subscale potential problems of medication	$\rho = -0.08$ (p=0.482)	p=0.126
Paediatric Asthma Caregiver Quality Of Life questionnaire, 13 questions	$\rho = 0.15$ (p=0.162)	p=0.124
parental asthma knowledge questionnaire, 7 questions	$\rho = 0.00$ (p=0.996)	p=0.833

\*\* = p <0.05; \* = p<0.1; # = binary data; Ig: immunoglobulin; Rint: respiratory resistance by the interrupter technique; FEV<sub>1</sub>: forced expiratory volume in one second; FEV<sub>1</sub><sup>1</sup>-change: difference in forced expiratory volume in one second before and after ventolin; VAS: visual analogue scale[13];

## Reference List

1. Global Initiative for Asthma. Global Strategy for asthma management and prevention. 2010. Downloaded from [www.ginasthma.org](http://www.ginasthma.org). Date last accessed Sept 12, 2011.
2. Bindels PJE, van der Wouden JC, Ponsioen BP, Brand PLP, Salomé PL, van Hensbergen W, et al. NHG-standaard Astma bij kinderen. Tweede herziening. *Huisarts Wetensch* 41:130-143,2006 (article in Dutch)
3. Kamps AW, Brand PL, Kimpen JL, Maille AR, Overgoor-van de Groes AW, van Helsdingen-Peek LC, Roorda RJ. Outpatient management of childhood asthma by paediatrician or asthma nurse: randomised controlled study with one year follow up. *Thorax*. 2003;58:968-973.
4. Kamps AW, Brand PL, Roorda RJ. Determinants of correct inhalation technique in children attending a hospital-based asthma clinic. *Acta Paediatr*. 2002;91:159-163.
5. Brouwer AF, Brand PL. Asthma education and monitoring: what has been shown to work. *Paediatr Respir Rev*. 2008;9:193-199.
6. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res*. 2006;60:631-637.
7. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*. 1999;14:1-24.
8. Atkinson MJ, Sinha A, Hass SL, Colman SS, Kumar RN, Brod M, Rowland CR. Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. *Health Qual Life Outcomes*. 2004;2:12.

9. DeVet KA, Ireys HT. Psychometric properties of the maternal worry scale for children with chronic illness. *J Pediatr Psychol.* 1998;23:257-266.
10. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res.* 1999;47:555-567.
11. Horne R, Hankins M, Jenkins R. The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research. *Qual Health Care.* 2001;10:135-140.
12. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res.* 1996;5:35-46.
13. Juniper EF, Bousquet J, Abetz L, Bateman ED. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respir Med.* 2006;100:616-621.
14. Hammer SC, Robroeks CM, van RC, Heynens J, Droog R, Jobsis Q, Hendriks HJ, Dompeling E. Actual asthma control in a paediatric outpatient clinic population: do patients perceive their actual level of control? *Pediatr Allergy Immunol.* 2008;19:626-633.
15. Lasmar L, Camargos P, Champs NS, Fonseca MT, Fontes MJ, Ibiapina C, Alvim C, Moura JA. Adherence rate to inhaled corticosteroids and their impact on asthma control. *Allergy.* 2009;64:784-789
16. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ.* 1998;316:1236