



# Factors associated with medication adherence in school-aged children with asthma

Amy H.Y. Chan<sup>1</sup>, Alistair W. Stewart<sup>2</sup>, Juliet M. Foster<sup>3</sup>, Edwin A. Mitchell<sup>4</sup>, Carlos A. Camargo Jr<sup>5</sup> and Jeff Harrison<sup>1</sup>

**Affiliations:** <sup>1</sup>School of Pharmacy, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand. <sup>2</sup>Epidemiology & Biostatistics, School of Population Health, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand. <sup>3</sup>Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia. <sup>4</sup>Dept of Paediatrics: Child and Youth Health, School of Medicine, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand. <sup>5</sup>Dept of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA.

**Correspondence:** Amy H.Y. Chan, School of Pharmacy, Faculty of Medical and Health Sciences, The University of Auckland, Grafton, Auckland 1023, New Zealand. E-mail: a.chan@auckland.ac.nz

**ABSTRACT** Adherence to preventive asthma treatment is poor, particularly in children, yet the factors associated with adherence in this age group are not well understood.

Adherence was monitored electronically over 6 months in school-aged children who attended a regional emergency department in New Zealand for an asthma exacerbation and were prescribed twice-daily inhaled corticosteroids. Participants completed questionnaires including assessment of family demographics, asthma responsibility and learning style. Multivariable analysis of factors associated with adherence was conducted.

101 children (mean (range) age 8.9 (6–15) years, 51% male) participated. Median (interquartile range) preventer adherence was 30% (17–48%) of prescribed. Four explanatory factors were identified: female sex (+12% adherence), Asian ethnicity (+19% adherence), living in a smaller household (–3.0% adherence per person in the household), and younger age at diagnosis (+2.7% for every younger year of diagnosis) (all  $p < 0.02$ ).

In school-aged children attending the emergency department for asthma, males and non-Asian ethnic groups were at high risk for poor inhaled corticosteroid adherence and may benefit most from intervention. Four factors explained a small proportion of adherence behaviour indicating the difficulty in identifying adherence barriers. Further research is recommended in other similar populations.



@ERSpublications

**Girls, children of Asian ethnicity, small household size and younger diagnosis age have better adherence to asthma** <http://ow.ly/Z1y6Q>

Received: Nov 16 2015 | Accepted after revision: Feb 28 2016

Clinical trial: This trial was registered with the Australian New Zealand Clinical Trials Registry (number ACTRN12613001353785).

**Support statement:** This study was funded by the Health Research Council of New Zealand (a government funding organisation) and Cure Kids (a charitable organisation that funds child health research). Electronic monitoring devices were provided by Nexus 6 Ltd (Auckland, New Zealand). Nexus 6 Ltd had no role in the study design, data collection, analysis, interpretation or writing of this report. Investigators gave feedback to the manufacturer about device functions; the manufacturer had no involvement in any aspect of the study. Funding information for this article has been deposited with FundRef.

**Conflict of interest:** Disclosures can be found alongside this article at [openres.ersjournals.com](http://openres.ersjournals.com)

Copyright ©ERS 2016. This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0.



## Introduction

Asthma is one of the most common chronic conditions in childhood [1]. Adherence with preventive medication remains poor in this age group ( $\leq 16$  years of age) [2, 3]. Poor adherence with inhaled corticosteroids is associated with morbidity [4] and mortality [5]. Interventions to improve adherence have shown benefits on adherence; however, effects are inconsistent, even when using similar strategies [6]. In order to develop effective childhood interventions it is important to investigate the unique adherence barriers children face [7], as these are different to adults [4, 7]. There are few studies in children that aim to understand these barriers, and even fewer interventional studies which aim to improve adherence in children [6, 8]. Previous research investigating adherence barriers in childhood have used inconsistent methodology, with data on adherence factors being collected from either the child, a proxy (e.g. parent) or both. Commonly used adherence measures, such as self-reported or pharmacy claims data, are subject to bias [3, 9]. Electronic monitoring provides the most objective measure of adherence monitoring [3, 8]; however, only a few studies have used electronic monitoring to provide adherence data to investigate adherence barriers [4, 10–13]. Of the studies that have used electronic monitoring, these have tended to focus on a narrow set of adherence barriers, such as psychological factors [4, 10, 12] or asthma knowledge [11], or used data collected over only a short duration [13]. MORTON *et al.* [3] recently reviewed the literature surrounding adherence in childhood asthma. The authors reported a paucity of studies investigating adherence barriers in children, and that future studies investigating adherence in children with asthma should use electronically monitored adherence data. Therefore, there is a need to examine a range of adherence barriers unique to children using objective adherence data.

Learning style is one adherence factor that has not been previously examined. Learning style has been linked with a patient's understanding of health information and subsequent medication taking behaviours [14] and responses to interventions [15]. Although there is no current literature examining this relationship, learning style may influence adherence. For example, individuals with an aural learning style may benefit more from an auditory intervention such as reminders, than those with alternative learning styles.

We previously conducted a randomised controlled trial investigating the effects of audio-visual reminders on medication adherence and asthma outcomes in children with asthma [16]. The present study uses the objectively measured adherence data from the randomised controlled trial to: 1) identify the adherence barriers unique to children, particularly in those at high risk of non-adherence; and 2) examine the relative importance of these factors for non-adherence, including the novel concept of learning style as a factor associated with adherence.

## Material and methods

### *Study subjects and design*

The randomised controlled trial investigated the effect of a reminder on adherence to preventer treatment and asthma outcomes, as described previously [16]. Briefly, 220 children between 6 and 15 years of age were recruited from the regional emergency department in Auckland, New Zealand. Inclusion criteria were: current diagnosis of asthma; current treatment or those started on treatment at the emergency department with a twice-daily inhaled corticosteroid; no comorbid congenital heart disease, chronic lung disease (other than asthma) or a severe chronic medical condition leading to increased morbidity; and residence inside the Auckland area.

Patients were enrolled after a minimum of 4 weeks had elapsed since hospital attendance, and were followed prospectively for 6 months, with 2-monthly follow-up visits by study investigators. Patients were randomly allocated to the intervention ( $n=110$ ) or control ( $n=110$ ) group. All received an electronic monitoring device for use with their preventer inhaler. The intervention group had the reminder function enabled; this was disabled in the control group. Information on asthma control was collected at each visit and at the end of the study participants and their caregiver completed a series of questionnaires to assess variables associated with adherence. Verbal and written informed consent was obtained from the child's parent or caregiver, and ethics approval was received from the New Zealand Northern Y Regional Ethics Committee (NTY/08/12/116) and District Health Boards. The trial was registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12613001353785.

### *Adherence measurement*

Inhaled corticosteroid adherence was objectively measured by an electronic monitoring device (Smart Track; Nexus 6 Ltd, Auckland, New Zealand), which recorded date, time and number of doses taken. An on-board screen displayed the date and time of the last dose. Participants were unaware of the device adherence monitoring function. This covert monitoring method followed published ethical guidelines as discussed previously by RAND and SEVICK [17], and was accordingly approved by the regional ethics committee. At the end of the study, participants and their general practitioner, or other asthma healthcare

provider, were offered access to the study results. Adherence was defined as median percentage of the daily prescribed dose taken.

### ***Analysis of factors associated with adherence***

Caregivers (parent or guardian) of participants completed self-reported questions on demographics and the primary caregiver's highest educational qualification (none (did not finish secondary school), secondary, tertiary or postgraduate). Participant ethnicity was obtained from their New Zealand National Health Index number. Deprivation was assessed using the NZDep2006 Deprivation Index (1=least deprived, 10=most deprived area) of the area the participant lived in [18]. Caregivers self-reported household size (number of people usually living in the household) and family status (single/divorced/separated/widowed/married/*de facto* (cohabitating)/extended family or whanau (Māori concept of an extended family or community of families living together)). Information on the caregivers' experience of the health system and healthcare access was collected using the following questions (scored yes/no): "Do you feel you can discuss concerns with the health professional who looks after the child's asthma?"; "Have you ever delayed or avoided picking up medications due to cost?"; "Have you ever delayed or avoided seeing the doctor due to cost?"; "Is your doctor easy to access?" and "Is your local pharmacy easy to access?".

Age at diagnosis was obtained by caregiver self-report. Asthma control was measured using two validated questionnaires: the childhood Asthma Control Test (0=worst control, 27=best control) [19] completed by the child and caregiver, and the Asthma Morbidity Score [20] (17=maximum morbidity, 4=lowest morbidity) completed by the caregiver. Caregivers answered a question about side-effects (scored yes/no): "Does the child complain of, or have, any side-effects from their medications?". Caregivers gave information about the type of healthcare professional who followed up their child's asthma (in addition to the 2-monthly investigator-initiated visits), by choosing one or more of the following options: asthma nurse, specialist, general physician (family doctor), no usual care follow-up or other. Asthma responsibility was evaluated using the 10-item Asthma Responsibility Questionnaire [21] completed by the caregiver. This assesses how responsibility is shared for 10 asthma management tasks. Each item is scored from 1 (parent is completely responsible) to 5 (child is completely responsible); total score 10=maximum parent responsibility, 50=maximum child responsibility. The child's asthma knowledge was assessed using the child-reported 24-item questionnaire (0=worst knowledge, 26=best knowledge) validated for primary school-aged children [22].

Children completed the Visual Aural Read/Write Kinaesthetic (VARK) Learning Styles Inventory for Younger People [23], which identified each participant's learning style preference (visual, aural, reading/writing and kinaesthetic, or various combinations of these) based on the standard scoring system [24]. As this questionnaire was for children aged  $\geq 12$  years, the language was modified for the reading skills of our population of 6–15 year olds. Results were categorised into two groups for analysis: those with an aural learning style preference (aural group) *versus* no aural learning style preference (non-aural group).

### ***Statistical analysis***

Descriptive statistics were used to describe the study population. All statistical tests were performed at the 0.05 level of significance (two-tailed) using SPSS Statistics (version 22; IBM, Armonk, NY, USA) or SAS (version 9.3; SAS Institute, Cary, NC, USA).

### ***Factors associated with adherence***

#### *Unadjusted analysis*

To avoid interference from the intervention, only data from the control group of the trial was used as the analytical cohort to analyse factors associated with adherence. Unadjusted analyses on 20 variables were conducted in this analytical cohort using a general linear model.

#### *All possible subsets regression*

To determine the factors associated with adherence, an all possible subsets regression was conducted. This multivariable regression technique was chosen over the traditional stepwise regression as it tests all possible subsets of potential variables. This allows models that have similar predictive value to be identified and compared, rather than selecting just one model. Binary variables with low numbers in one outcome group, *i.e.* <25% of participants in one outcome group, were not included in the multivariable regression. Participants with complete data across all remaining variables were used for the multivariable analysis. The remaining variables were included in the model and multiple subsets of variables were generated, ranging from single variable models to models using all remaining variables. By examining the five best models at each level, alternative variable combinations were assessed, including whether the addition of other variables to the model led to a masking effect. The model accounting for the greatest variance (maximum  $R^2$ ), whilst still consisting of only significant ( $p < 0.05$ ) variables, was selected.

TABLE 1 Characteristics of 101<sup>#</sup> participants in the analytical cohort and unadjusted analyses of 20 factors associated with adherence

Variable	Participants	Effect size	p-value
<b>Age years</b>	8.9±2.7	-1.5% [95% CI=-3.2-0.2%] per year	0.09
<b>Sex</b>			
Male	52	26 (15-43)	0.05
Female	49	40 (19-60)	
<b>Qualification of primary caregiver</b>			
None	8	36 (11-42)	0.81
Secondary school	22	28 (15-53)	
Tertiary	45	26 (12-47)	
Postgraduate	22	42 (21-51)	
Missing	4		
<b>Ethnicity</b>			
Māori	10	19 (13-44)	0.002
European	39	26 (17-43)	
Pacific Peoples	20	28 (13-40)	
Middle Eastern/Latin American/African	4	35 (5-68)	
Asian	19	47 (30-83)	
Other	9	31 (21-46)	
<b>Deprivation index<sup>¶</sup></b>	6.0±2.7	+0.002% [95% CI=-1.7-1.7%] per deprivation scale	0.99
<b>People in household</b>	4.8±1.9; 98 <sup>#</sup>	-3.4% [95% CI=-5.8--0.1%] per person added to household	0.005
<b>Family status</b>			
Single <sup>†</sup>	35	26 (15-47)	0.39
Not single <sup>§</sup>	65	32 (18-49)	
Missing	1		
<b>Able to discuss concerns with the healthcare professional looking after the child</b>			
No	8	24 (6-49)	0.68
Yes	92	31 (17-48)	
Missing	1		
<b>Delayed picking up medications due to cost</b>			
No	78	31 (16-48)	0.87
Yes	21	26 (16-49)	
Missing	2		
<b>Delayed seeing the doctor due to cost</b>			
No	69	31 (16-54)	0.28
Yes	30	28 (16-46)	
Missing	2		
<b>Easy access to doctor</b>			
No	10	37 (18-52)	0.91
Yes	90	30 (17-48)	
Missing	1		
<b>Easy access to pharmacy</b>			
No	2	20 (7- -)	0.37
Yes	99	30 (17-48)	
<b>Age at asthma diagnosis years</b>	3.3±2.3	-1.7% [95% CI=-3.7-0.3%] per year	0.09
<b>Childhood Asthma Control Test</b>	18.8±4.2; 100 <sup>#</sup>	+0.9% [95% CI=-0.2-2.0%] per 1 point on the Childhood Asthma Control Test	0.11
<b>Asthma Morbidity Score</b>	9.2±2.6; 100 <sup>#</sup>	-0.3% [95% CI=-2.1-1.5%] per 1 point on the Asthma Morbidity Score	0.73
<b>Medication side-effects</b>			
No	91	29 (17-48)	0.84
Yes	10	33 (11-46)	
<b>Healthcare provider involved in routine follow-up asthma care</b>			
None (no follow-up)	2	72 (60- -)	0.003
General practitioner	74	26 (12-43)	
Specialist	5	31 (23-61)	
Asthma nurse	15	51 (15-85)	
Multiple providers	5	46 (26-61)	

Continued

TABLE 1 Continued

Variable	Participants	Effect size	p-value
<b>Asthma Responsibility Questionnaire</b>	23.7±8.1	−0.2% (95% CI−0.7–0.4%) per 1 point of Asthma Responsibility Questionnaire	0.53
<b>Asthma Knowledge Test</b>	19.1±2.7	+0.7% (95% CI−1.0–2.4%) per 1 point of Asthma Knowledge Test	0.42
<b>Learning styles</b>			
Aural	64	29 (17–48)	0.76
Non-aural	30	30 (14–49)	
Missing	7		

Data are presented as mean±SD, n or median (interquartile range), unless otherwise stated. Bold data indicates statistical significance. #: data do not total 101 for some parameters due to missing data from participants who did not completed the relevant questionnaire(s). Median (interquartile range) adherence for the total sample (n=101) was 30% (17–48%); ¶: based on the NZDep2006 deprivation index (1=least deprived, 10=most deprived). This is an indicator of socioeconomic deprivation of the area where the individual resides. Scores are derived from census data on income, home ownership, employment, qualifications, family structure, housing, access to transport and communications; \*: single parent/divorced/separated /widowed/single; §: *de facto*/extended whanau/married.

Data were then analysed using an alternative model as a sensitivity analysis by performing the all subsets regression with the variables that had missing data removed (rather than removal of participants with missing data).

#### *Effect of aural learning styles*

Analysis of the effect of aural learning styles on adherence was conducted using a general linear model. Data from both the intervention and control groups were used as participants with an aural learning style may not only be more responsive to an auditory adherence intervention, but may also be more responsive to adherence advice from health providers, which is often delivered verbally.

## Results

Of the 110 participants forming the analytical cohort, nine did not complete the questionnaires, leaving 101 for analysis. Overall adherence was low (median (interquartile range) adherence 30% (17–48%)). Table 1 shows the characteristics of the analytical cohort (n=101) and describes the unadjusted analyses of factors associated with adherence.

#### *Unadjusted analyses of factors associated with adherence*

Only three out of 20 variables examined were significantly associated with adherence to preventive treatment (table 1). These were ethnicity (Asian ethnicity most adherent), living with a lower number of people in the household, and type of healthcare provider involved in asthma follow-up (those with no asthma follow-up by their own healthcare provider had better adherence, though the outcome group only had two participants). Younger age, female sex and a younger age at diagnosis were of borderline significance.

#### *Multivariable analysis of factors associated with adherence*

The following variables, which had very low numbers in one outcome group compared to the other, were not included in the analysis: whether or not the caregiver could discuss concerns with their asthma healthcare provider; whether or not the caregiver had ever delayed picking up medicines due to cost; whether or not the caregiver had easy access to the doctor or pharmacy; presence or absence of medication adverse effects in the child; and lack of follow-up for the child's asthma by their own healthcare provider. After removal of these variables, 87 of the 101 participants in the analytical cohort had complete data across all variables and were included in the multivariable analysis.

The all subsets regression selected a subset of four factors that together explained 30% of the variance in objective adherence ( $R^2=0.33$ ; adjusted  $R^2=0.30$ ) (table 2). The addition of all the other predictor variables only accounted for an additional 14% in variance ( $R^2=0.47$ ; adjusted  $R^2=0.29$ ) and included variables that were not statistically significant. The multivariable analysis found those of Asian ethnicity, female sex, living with a lower number of people in the household and having a younger age at diagnosis were more likely to adhere to treatment. Lack of asthma follow-up by their own healthcare provider was also significant, but as there were only two participants who did not have follow-up this was not included in the model (median adherence 72%) (table 1). These two participants had high adherence. There was no

TABLE 2 Multivariable regression analysis with objective adherence as independent variable<sup>#</sup>

Variable	Effect size	p-value
<b>Sex</b>	12±4%	0.005
<b>Asian ethnicity</b>	19±5%	<0.001
<b>People in the household</b>	-3.0±1.0% per person	0.01
<b>Age at asthma diagnosis years</b>	-2.7±0.9% per year	0.004

Data are presented as change±SE. <sup>#</sup>: n=87.

indication that any variables were masked by the presence of other variables. The sensitivity analysis produced very similar results confirming the results of the all subsets regression described above.

#### *Effect of aural learning styles*

There was no relationship between aural learning style and adherence in either the control (analytical cohort for this study) or in the intervention (reminder) group (aural 29% versus non-aural 30% (p=0.76) and aural 85% versus non-aural 88% (p=0.34), respectively).

## Discussion

This study investigated factors associated with adherence in children presenting to a regional emergency department with an asthma exacerbation. Electronically monitored adherence was poor with median adherence being 30%, a rate similar to other studies in children at high risk of non-adherence [25–27] but lower than the average reported adherence from studies using electronic monitoring and when compared to other developed Western countries [3, 8]. We examined a number of factors that have previously been associated with adherence, such as ethnicity [13, 28] and asthma knowledge [10], as well as factors not previously investigated, such as learning style. Of the variables examined in this study, only a few were significantly associated with adherence.

Ethnicity had a strong association with adherence, with Asian participants having the highest overall adherence (47%). The reason for this is unclear. There is little literature available on adherence for ethnic groups in New Zealand beyond Māori, Pacific and European populations. Education studies in Australia show that Asian students are more compliant with orders from teachers than other ethnic groups [29] due to respect and perceived dominance of the teacher [30]. The healthcare provider–patient relationship may be associated with a similar respectful or submissive response, which may enhance adherence. Māori children had the poorest adherence (median adherence 19%), followed closely by New Zealand European (26%) and Pacific peoples (28%). From studies in mild-to-moderate asthmatics, Māori and Pacific children show poorer asthma control than other ethnic groups [31] due to under treatment and poor adherence with preventive treatment [31, 32]. Therefore, the ethnic differences in our study were unexpected, as although adherence rates for New Zealand Europeans were higher than Māori children, they were lower than that of other minority ethnic groups. The participants in our study attended the emergency department for asthma and therefore represent those with the poorest asthma control and adherence [27]. This suggests that the effect of ethnicity may be different in those with poorly controlled asthma and at high risk of non-adherence, but more research is needed to confirm this. We note that the adherence rate in our population of high-risk children was particularly low when compared to populations recruited from outpatient clinics [12, 33–37], and more similar to those recruited from tertiary centres or hospitals [38]. Indeed, in adults, KRISHNAN *et al.* [39] reported a drop in inhaled corticosteroid use to ~50% within a week of hospital discharge after an asthma exacerbation. This highlights the potential vulnerability of patients presenting to tertiary care settings and the importance of considering the contribution of this as a potential marker of poor adherence. The high-risk nature of a population presenting to the emergency department with asthma may override the usual effects of other adherence determinants, such as ethnicity, as seen in our study.

Female sex was significantly associated with better adherence in our study. The relationship between sex and adherence is inconsistent in the literature, with many studies showing no association [9, 40, 41]. Only one study has reported an association between female sex and higher adherence in adult asthma [42]. In other chronic conditions, female sex has been linked with poorer adherence in adolescents [43]. Mental health and coping strategies may mediate the relationship between sex and adherence [43], but we did not measure psychological factors.

No clear relationship was found between socioeconomic status, determined by NZDep scores, and adherence. Some studies have reported a lack of correlation between adherence and general socioeconomic status, family income or qualifications of the primary caregiver [35, 44], although others report low

adherence rates in those with poor socioeconomic status [3]. Compared to studies that report higher overall adherence, the population in our study did incline towards higher deprivation scores (mean deprivation 6 out of 10). We found a significant relationship between household size and adherence, a factor seldom studied in asthma. KYNGÅS [45] found that adherence improved with increasing number of siblings and similarly LIEU *et al.* [46] reported better adherence in larger families. Our study found the opposite effect, with larger household size associated with poorer adherence. It is possible that larger families present more competing demands, thus limiting the time available to manage a child's asthma [47] and increasing forgetfulness, a key reason for non-adherence in childhood asthma [48]. This negative effect of family size on adherence may be more pronounced in our study as over half of the participants were aged <8 years of age. Previous studies have demonstrated that younger children have the majority of their medications managed by their parents [4, 47, 49], which may contribute to poorer adherence with increased household size. This is also supported by the negative relationship seen between asthma responsibility scores and adherence, where adherence decreased with increasing child responsibility for their own asthma management, though the relationship did not reach statistical significance.

The relationship between age at diagnosis and adherence is unclear; the few studies investigating this relationship have not found any association [40, 41]. Our study found age at diagnosis was a significant factor, with a reduction in adherence of 3% per increasing year of age at diagnosis. There was a corresponding nonsignificant trend between age of the child and adherence, with adherence being worse in older children, similar to previous findings [2, 4, 44, 45, 50]. This may, in part, explain the association between age of diagnosis and adherence. The association between increased age and worsened adherence might also explain the overall low adherence seen in this population. Most previous studies that have reported higher adherence have included much younger age range, from as young as 15 months [3]. Disease duration may play a role as those with a younger age of onset have more opportunity for habit formation for medication adherence [51]. Conditioning may lead children or their parents to believe that asthma is a long-term condition requiring long-term preventive treatment and, as a result, lead to better adherence. Indeed, adherence is higher in those that believe asthma is a long-lasting condition [42].

This is the first study investigating the impact of learning style on adherence. A link between the two is plausible given that learning style is associated with behaviour [14, 15], but no association was found in either the group receiving the auditory intervention or control. This may be due to the difficulties in characterising learning styles in children as younger children tend to have multimodal learning styles rather than a single learning modality [23]. The lack of a validated tool for assessing learning style in the younger age groups in our study may have also limited the accuracy of determining the child's learning style. Although a relationship between learning styles and adherence was not found, there is a possibility that interventions tailored to an individual's learning style may be more successful. The literature supports interventions that are personalised to an individual [3, 8]; future research should investigate the usefulness of incorporating learning style into the intervention tailoring process.

Of the factors that were investigated, only four were found to be significantly associated with adherence. However, these factors still only explained 30% of the variance seen in adherence. Although a wide range of adherence determinants were examined, we did not investigate the effect of illness perceptions [52–57] or medication beliefs [12, 50, 58–62], which are thought to be more powerful determinants of adherence [57] than sociodemographic and clinical factors in adults. In children, the review by DROTAR and BONNER [63] of studies investigating the factors associated with adherence in children reports that parental and, to a lesser extent, child beliefs demonstrate significant relationships with adherence. Medication beliefs and illness perceptions were not measured in our study but future research should include them in order to develop a clearer understanding of the extent to which these may explain adherence behaviour in children with poorly controlled asthma and to investigate how these may interact with the adherence determinants identified in our study.

The generalisability of our study results may be limited by data collection in a single centre and country. Nevertheless, our study population were representative of the total population presenting to the emergency department with asthma, as described previously [16], and included a wide range of ethnic and socioeconomic groups. Due to missing data we excluded 14 participants from the multivariable analysis, which could have led to selection bias. However, bias as a result of this exclusion is unlikely as our sensitivity analysis, where variables with missing data were excluded rather than participants, showed similar results. Questionnaires were administered in the presence of research personnel, which may have affected the reliability of the data collected. A small number of participants chose not to complete some questions, but the numbers with missing data were low and unlikely to affect our results. The application of these findings to the design of adherence interventions may be limited, as the adherence determinants identified were largely non-modifiable. Nevertheless, our findings add important information to the literature on factors that contribute to poor adherence in children, particularly in those with poorly controlled asthma. As the factors identified from our study are easily quantifiable, they may be used to

help prioritise those at greatest need for intervention. Our work sets a platform for further research into how potentially modifiable adherence determinants, such as medication beliefs, may be related to non-modifiable factors such as ethnicity or duration/experience in managing asthma, and how these non-modifiable factors may serve as proxies for identifying those who are most at risk of poor adherence.

In summary, female sex, Asian ethnicity, smaller household size and younger age at diagnosis were strongly associated with better preventive medication adherence in children with poorly controlled asthma presenting to a regional emergency department. These factors explained only 30% of the variation in adherence, highlighting the difficulty of identifying adherence barriers in this age group. There was no association between adherence and learning styles. Further research in other emergency department populations is needed. Given the combination of poor adherence and high risk for life-threatening asthma in children presenting to the emergency department, there is an urgent need to identify the specific adherence barriers and develop effective interventions for this population of children.

### Acknowledgements

We would like to thank Maye Hamed, Elizabeth Garrett and Sherron Kneebone (Dept of Paediatrics, Faculty of Medical and Health Sciences, The University of Auckland, Auckland, New Zealand) who were involved in data collection; Auckland and Waitemata District Health Board emergency department staff for assistance with organisation of the trial; and the study participants and their families for their involvement in the study.

### References

- Lai C, Beasley R, Crane J, *et al.* Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax* 2009; 64: 476–483.
- Jonasson G, Carlsen KC, Mowinckel P. Asthma drug adherence in a long term clinical trial. *Arch Dis Child* 2000; 83: 330–333.
- Morton RW, Everard ML, Elphick HE. Adherence in childhood asthma: the elephant in the room. *Arch Dis Child* 2014; 99: 949–953.
- McQuaid EL, Kopel SJ, Klein RB, *et al.* Medication adherence in pediatric asthma: reasoning, responsibility, and behaviour. *J Pediatr Psychol* 2003; 28: 323–333.
- Suissa S, Ernst P, Benayoun S, *et al.* Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med* 2000; 343: 332–336.
- Dean AJ, Walters J, Hall A. A systematic review of interventions to enhance medication adherence in children and adolescents with chronic illness. *Arch Dis Child* 2010; 95: 717–723.
- Graves MM, Adams CD, Portnoy JM. Adherence in young children with asthma. *Curr Opin Allergy Clin Immunol* 2006; 6: 124–127.
- Klok T, Kaptein AA, Brand PL. Non-adherence in children with asthma reviewed: the need for improvement of asthma care and medical education. *Pediatr Allergy Immunol* 2015; 26: 197–205.
- van Dellen QM, Stronks K, Bindels PJE, *et al.* Adherence to inhaled corticosteroids in children with asthma and their parents. *Respir Med* 2008; 102: 755–763.
- Bender B, Milgrom H, Rand C, *et al.* Psychological factors associated with medication non-adherence in asthmatic children. *J Asthma* 1998; 35: 347–353.
- Ho J, Bender BG, Gavin LA, *et al.* Relations among asthma knowledge, treatment adherence, and outcome. *J Allergy Clin Immunol* 2003; 111: 498–502.
- Klok T, Kaptein AA, Duiverman EJ, *et al.* High inhaled corticosteroids adherence in childhood asthma: the role of medication beliefs. *Eur Respir J* 2012; 40: 1149–1155.
- Vasbinder E, Dahhan N, Wolf B, *et al.* The association of ethnicity with electronically measured adherence to inhaled corticosteroids in children. *Eur J Clin Pharmacol* 2013; 69: 683–690.
- Giuse NB, Koonce TY, Storrow AB, *et al.* Using health literacy and learning style preferences to optimize the delivery of health information. *J Health Commun* 2012; 17: 122–140.
- Boyde M, Tuckett A, Peters R, *et al.* Learning style and learning needs of heart failure patients (The Need2Know-HF patient study). *Eur J Cardiovasc Nurs* 2009; 8: 316–322.
- Chan AHY, Stewart AW, Harrison J, *et al.* The effect of an electronic monitoring device with audiovisual reminder function on adherence to inhaled corticosteroids and school attendance in children with asthma: a randomised controlled trial. *Lancet Respir Med* 2015; 3: 210–219.
- Rand CS, Sevick MA. Ethics in adherence promotion and monitoring. *Control Clin Trials* 2000; 21: Suppl. 2, S241–S257.
- Salmond C, Crampton P, Atkinson J. NZDep2006 Index of Deprivation. Wellington, Dept of Public Health, University of Otago, 2007.
- Liu A, Zeiger R, Sorkness C, *et al.* Development and cross-sectional validation of the Childhood Asthma Control Test. *J Allergy Clin Immunol* 2007; 119: 817–825.
- Mitchell E, Stewart A, Rea H, *et al.* Measuring morbidity from asthma in children. *N Z Med J* 1997; 110: 3–6.
- McQuaid EL, Penza-Clyve SM, Nassau JH, *et al.* The Asthma Responsibility Questionnaire: patterns of family responsibility for asthma management. *Child Health Care* 2001; 30: 183–199.
- Al-Motlaq M, Sellick K. Development and validation of an asthma knowledge test for children 8–10 years of age. *Child Care Health Dev* 2011; 37: 123–128.
- Teaching and learning styles: VARK strategies. Fleming ND, ed. 1st Edn. Christchurch, N.D. Fleming, 2001.
- Fleming ND. The 2009 VARK Scoring Trial. <http://vark-learn.com/wp-content/uploads/2014/08/scoring-trial.pdf> Date last updated: May 2009. Date last accessed: March 20, 2016.
- Rohan J, Drotar D, McNally K, *et al.* Adherence to pediatric asthma treatment in economically disadvantaged African-American children and adolescents: an application of growth curve analysis. *J Pediatr Psychol* 2010; 35: 394–404.



- 26 Bartlett SJ, Lukk P, Butz A, *et al.* Enhancing medication adherence among inner-city children with asthma: results from pilot studies. *J Asthma* 2002; 39: 47–54.
- 27 Camargo CA Jr, Ramachandran S, Ryskina KL, *et al.* Association between common asthma therapies and recurrent asthma exacerbations in children enrolled in a state Medicaid plan. *Am J Health Syst Pharmacy* 2007; 64: 1054–1061.
- 28 Apter AJ, Reisine ST, Affleck G, *et al.* Adherence with twice-daily dosing of inhaled steroids. Socioeconomic and health-belief differences. *Am J Respir Crit Care Med* 1998; 157: 1810–1817.
- 29 Baumgart N, Halse C. Approaches to learning across cultures: the role of assessment. *Assessment in Education* 1999; 6: 321–339.
- 30 Lu J, Chin KL, Yao J, *et al.* Cross-cultural education: learning methodology and behaviour analysis for Asian students in IT field of Australian universities. 12th Australasian Computing Education Conference 2010; 103: 117–126.
- 31 Mitchell EA. Racial inequalities in childhood asthma. *Soc Sci Med* 1991; 32: 831–836.
- 32 Pilcher J, Patel M, Smith A, *et al.* Combination budesonide/formoterol inhaler as maintenance and reliever therapy in Māori with asthma. *Respirology* 2014; 19: 842–851.
- 33 Gibson N, Ferguson A, Aitchison T, *et al.* Compliance with inhaled asthma medication in preschool children. *Thorax* 1995; 50: 1274–1279.
- 34 Burgess SW, Sly PD, Devadason SG. Providing feedback on adherence increases use of preventive medication by asthmatic children. *J Asthma* 2010; 47: 198–201.
- 35 Burgess SW, Sly PD, Morawska A, *et al.* Assessing adherence and factors associated with adherence in young children with asthma. *Respirology* 2008; 13: 559–563.
- 36 Nikander K, Turpeinen M, Pelkonen AS, *et al.* True adherence with the Turbuhaler in young children with asthma. *Arch Dis Child* 2010; 96: 168–173.
- 37 O'Connor SL, Bender BG, Gavin-Devitt LA, *et al.* Measuring adherence with the Doser CT in children with asthma. *J Asthma* 2004; 41: 663–670.
- 38 McNally KA, Rohan J, Schluchter M, *et al.* Adherence to combined montelukast and fluticasone treatment in economically disadvantaged African American youth with asthma. *J Asthma* 2009; 46: 921–927.
- 39 Krishnan J, Riekert K, McCoy J, *et al.* Corticosteroid use after hospital discharge among high-risk adults with asthma. *Am J Respir Crit Care Med* 2004; 170: 1281–1285.
- 40 Apter AJ, Boston RC, George M, *et al.* Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol* 2003; 111: 1219–1226.
- 41 Berg CJ, Rapoff MA, Snyder CR, *et al.* The relationship of children's hope to pediatric asthma treatment adherence. *J Posit Psychol* 2007; 2: 176–184.
- 42 Jessop DC, Rutter DR. Adherence to asthma medication: the role of illness representations. *Psychol Health* 2003; 18: 595–612.
- 43 Korbel CD, Wiebe DJ, Berg CA, *et al.* Gender differences in adherence to type 1 diabetes management across adolescence: the mediating role of depression. *Child Health Care* 2007; 36: 83–98.
- 44 Bender B, Wamboldt FS, O'Connor SL, *et al.* Measurement of children's asthma medication adherence by self report, mother report, canister weight, and Doser CT. *Ann Allergy Asthma Immunol* 2000; 85: 416–421.
- 45 Kyngäs HA. Compliance of adolescents with asthma. *Nurs Health Sci* 1999; 1: 195–202.
- 46 Lieu TA, Lozano P, Finkelstein JA, *et al.* Racial/ethnic variation in asthma status and management practices among children in managed Medicaid. *Pediatrics* 2002; 109: 857–865.
- 47 Adams CD, Dreyer ML, Dinakar C, *et al.* Pediatric asthma: a look at adherence from the patient and family perspective. *Curr Allergy Asthma Rep* 2004; 4: 425–432.
- 48 Penza-Clyve SM, Mansell C, McQuaid EL. Why don't children take their asthma medications? A qualitative analysis of children's perspectives on adherence. *J Asthma* 2004; 41: 189–197.
- 49 Orrell-Valente JK, Jarlsberg LG, Hill LG, *et al.* At what age do children start taking daily asthma medicines on their own? *Pediatrics* 2008; 122: e1186–e1192.
- 50 Koster ES, Raaijmakers JAM, Vijverberg SJH, *et al.* Inhaled corticosteroid adherence in paediatric patients: the PACMAN cohort study. *Pharmacoepidem Drug Safe* 2011; 20: 1064–1072.
- 51 Reach G. Role of habit in adherence to medical treatment. *Diabet Med* 2005; 22: 415–420.
- 52 Kaptein AA, Klok T, Moss-Morris R, *et al.* Illness perceptions: impact on self-management and control in asthma. *Curr Opin Allergy Clin Immunol* 2010; 10: 194–199.
- 53 Spurrier N, Sawyer M, Staugas R, *et al.* Association between parental perception of children's vulnerability to illness and management of children's asthma. *Pediatr Pulmonol* 2000; 29: 88–93.
- 54 Bokhour BG, Cohn ES, Cortes DE, *et al.* Patterns of concordance and non-concordance with clinician recommendations and parents' explanatory models in children with asthma. *Patient Educ Counsel* 2008; 70: 376–385.
- 55 Yoos HL, Kitzman H, Henderson C, *et al.* The impact of the parental illness representation on disease management in childhood asthma. *Nurs Res* 2007; 56: 167–174.
- 56 Kaptein AA, Hughes BM, Scharloo M, *et al.* Illness perceptions about asthma are determinants of outcome. *J Asthma* 2008; 45: 459–464.
- 57 Horne R, Weinman J. Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication. *Psychol Health* 2002; 17: 17–32.
- 58 Desai M, Oppenheimer JJ. Medication adherence in the asthmatic child and adolescent. *Curr Allergy Asthma Rep* 2011; 11: 454–464.
- 59 Adams S, Pill R, Jones A. Medication, chronic illness and identity: the perspective of people with asthma. *Soc Sci Med* 1997; 45: 189–201.
- 60 Weinstein AG. The potential of asthma adherence management to enhance asthma guidelines. *Ann Allergy Asthma Immunol* 2011; 106: 283–291.
- 61 Menckeborg TT, Bouvy ML, Bracke M, *et al.* Beliefs about medicines predict refill adherence to inhaled corticosteroids. *J Psychosom Res* 2008; 64: 47–54.
- 62 Conn KM, Halterman JS, Lynch K, *et al.* The impact of parents' medication beliefs on asthma management. *Pediatrics* 2007; 120: e521–e526.
- 63 Drotar D, Bonner MS. Influences on adherence to pediatric asthma treatment: a review of correlates and predictors. *J Dev Behav Pediatr* 2009; 30: 574–582.