

ORIGINAL ARTICLE

Prescription patterns of inhaled corticosteroids for preschool children – A Norwegian register study

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Abstract

Background: Although guidelines for treatment of wheeze and asthma in preschool children are available, symptoms are overlapping and it may be difficult to decide which children should be given inhaled corticosteroids (ICS). Previous studies suggest an inappropriate prescription pattern of ICS in this age group. We studied time trends of ICS use in preschool children in Norway during 2004–2013 by age, gender and physician specialty, and the persistence of ICS use during preschool years.

Methods: Data were drawn from the Norwegian Prescription Database. The study population consisted of children ≤ 5 years who were prescribed ICS (alone or in combination) during 2004–2013.

Results: The one-year prevalence of ICS use was generally high, and increased from 2004 to 2010, but decreased thereafter. The prevalence was highest in 2-year-olds (boys 12.9% and girls 9.3% in 2010) and declined by age, and higher among boys in all ages. 40–50% of ICS users received only one prescription per year. The share of children with persistent use of ICS over several preschool years was low, irrespective of the age at the first prescription. The majority of prescriptions were given by general practitioners, increasing during the study period.

Conclusions: The prevalence of ICS prescription for preschool children was high, but with low persistence, suggesting that ICS are frequently given for intermittent asthma-like symptoms. Asthma guidelines suggest a restrictive use of ICS during the first years of life, and the results may call for actions to better implement these guidelines.

Episodic or chronic wheezing is common in preschool children, especially during the first 3 years of life (1–3). Such symptoms may be early signs of asthma, but are for most children transient during early childhood (4, 5). Consensus reports have different approaches to when recurrent wheezing should be defined as asthma (1–3). However, it is a common understanding that preschool wheezing or asthma represents a spectrum of heterogeneous conditions (4, 5).

Inhaled corticosteroids (ICS) are the cornerstone of treatment for established asthma for school-aged children, with a well-documented effect and a low frequency of side effects (1, 2, 4, 6). ICS may also prevent asthma symptoms or exacerbations in preschool children, although the effect in this age group is less documented, particularly for children younger than 3 years of age (7–9). Differences in pathophysiology may highly influence the effect of ICS in

these children, but no strict criteria for which preschool children should be treated with ICS have been established (9).

A restrictive use of ICS in preschool children may be advocated by the risk of side effects. ICS potentially have a higher potency for systemic side effects in early years, during an age with extensive total body and lung growth (4, 7, 10). High doses of ICS have been shown to affect linear growth in preschool children (7), and growth deficit may last into adulthood (11). Even intermittent use of ICS in preschool children may affect growth (12), and regular use of ICS during preschool age is also associated with a reduced bone density in adolescence (13).

Most international consensus recommend restrictive use of ICS during the first years of life, especially for the first 2 years (6). However, preschool children are frequently given ICS without

being diagnosed with asthma or being diagnosed with asthma later in childhood (14–16), few of those who are prescribed ICS very early in life receive ICS later in childhood (17–19), and short courses of ICS are frequently given for lower airway infections (20, 21). The variation between general practitioners in how frequent they prescribe ICS is significantly higher for preschool children compared to older children (22, 23).

Studies of prescription patterns may be a basis for considering the implementation of guidelines and safety measures. Since 2004, the Norwegian Prescription Database (NorPD) has registered electronic data on all prescriptions filled at pharmacies in Norway (24). The aim of this study was to describe the prescribing of ICS to preschool children in Norway, with focus on time trends, longitudinal prescription patterns and the specialty of physicians prescribing ICS in this age group.

Methods

The Norwegian prescription database

Data were retrieved from the NorPD which covers the entire population of Norway. From 1 January 2004, all Norwegian pharmacies have been obliged to send electronic data to NorPD on all dispensed drugs (irrespective of reimbursement status) to patients in ambulatory care (24). Medications are classified according to the Anatomical Therapeutic Chemical (ATC) classification system (25).

A unique personal identity number assigned to every Norwegian citizen was the key to identify the drug dispensed to the individual child. The following data from NorPD were retrieved for this study: personal identity number (encrypted), gender, age, date of dispensing the drug, ATC code, reimbursement code, identity number of prescriber (encrypted) and prescriber specialty.

All Norwegian citizens have unrestricted access to the national tax-supported public health service. There is no copayment on reimbursed drugs for children. General reimbursement of drugs is basically a 'positive list' system based on a list of diseases or conditions for which specified drugs can be reimbursed. Reimbursement should only be granted if the patient has a chronic condition in which long-term drug treatment is needed (>3 months of regular or intermittent treatment during a year). The physician writes a specific code (ICD-10 or ICPC-2) on prescriptions deemed eligible for reimbursement due to asthma, which is recorded in NorPD. Each dispensing from the pharmacy is limited to the amount needed for 3-month use; consequently, regular use requires several dispensings during 1 year.

Study population

The prescribing of ICS during 2004–2013 was studied in the Norwegian population aged 0–5 years (approximately 345,000 children in 2013). Medications included were ICS prescribed and dispensed as a single component inhaler or as a fixed combination inhaler with long-acting β_2 -agonists (ATC codes R03BA and R03AK).

Definitions

A prescription: one dispensing of ICS from a pharmacy. *Prevalence*: estimated as the number of individuals who filled at least one prescription of ICS at the pharmacy in a calendar year. The denominator was gender- and age-specific figures for the midyear Norwegian population in each year retrieved from Statistics Norway. *Incidence* (new users): individuals who filled at least one prescription in a given year and who had not filled any prescriptions during the past years from birth. The denominator was the gender- and age-specific figures for the Norwegian population 1 January in each year, minus those of the same age group who had filled ICS prescriptions during the past years of life. *Prescriber specialty*: the share of all patients who received ICS during 1 year from each specialty category was examined. Specialties were grouped into four categories, and patients who received ICS from more than one specialty during 1 year were counted in the highest hierarchical category: (i) paediatric specialist, (ii) general practitioner specialist, (iii) other specialty, and (iv) no specialty. Category 4 includes physicians who are under training for a specialty. *Longitudinal pattern of prescription*: the age of filling the first prescription of ICS (A0) was recorded for all children. These children were then followed up for 5 years after their initial prescription by one-year age increments to examine filling of prescriptions. *One-year user*: children who only filled prescriptions at the initiation age (A0). *Persistent users*: children who filled at least one prescription in each of the following years after A0. Once persistent users did not fill a prescription in one age class (i.e. were non-persistent), they were considered as either *intermittent users* (filling one or more prescriptions the given year) or *intermittent non-users* (no prescription the given year) for the rest of the follow-up.

Statistics

Prevalence and incidence were expressed as percentage for the different age groups. The actual numbers of users and non-users of ICS were seen as a binomial event, and differences were analysed by logistic regression with year as a continuous variable when analysing time trends. Comparison of categorical data was performed by the chi-square test. Analyses were carried out by SPSS 22.0 and Stata 13, and a p-value of < 0.05 was considered as significant.

Results

Total and annual prescriptions of ICS

For the years 2004–2013, a total of 587,447 prescriptions (62% boys) were filled for 117,008 children 0–5 years old (60% boys). Fig. 1a and b shows the one-year prevalence of boys and girls of different age groups who filled at least one prescription of ICS during the study period. For all age groups and both genders, there was an increasing prevalence from 2004 to 2010 ($p_{\text{trend}} < 0.001$ for all) and a decreasing prevalence from 2010 to 2013 ($p_{\text{trend}} < 0.001$ for ages 0–3 years and $p_{\text{trend}} < 0.05$ for ages 4–5 years). The highest prevalence for both genders was seen in

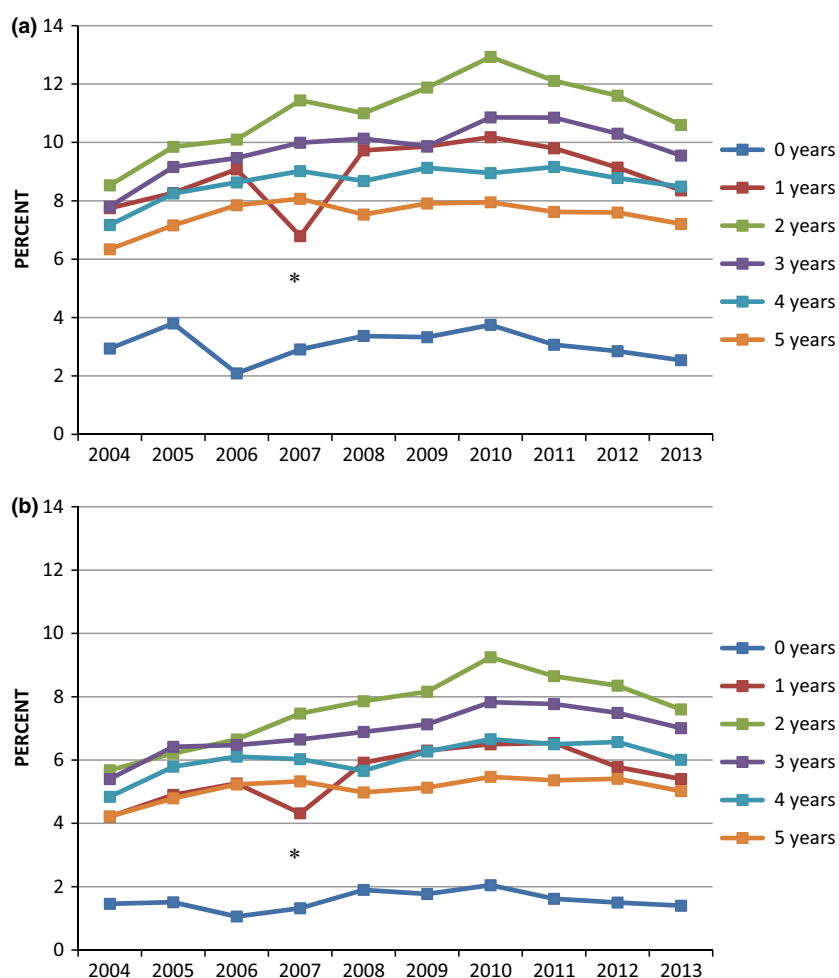


Figure 1 (a) boys and (b) girls. Percentage of children per year of age in Norway receiving at least one prescription of inhaled corticosteroids during 2004–2013. *There was an unproportional high number of prescriptions with missing personal identity number in 2006 for 0-year-olds and in 2007 for 0- and 1-year-olds, and these prevalence figures are therefore not comparable.

children 2 years old, increasing from 8.5% in 2004 to 12.9% in 2010 in boys and from 5.7% to 9.3% in girls. Thereafter, there was a decline to 10.6% for boys and 7.6% for girls in 2013 (Fig. 1a,b) ($p_{\text{trend}} < 0.001$ for all). For all years and age groups, the prescription prevalence was higher in boys than in girls ($p < 0.001$ for all).

Incidence (new users)

Figure 2 shows the incidence for 2013 for boys and girls by the age at which they received their first prescription ever of ICS. Except for children younger than 1 year, there was a decreasing incidence by age ($p < 0.001$ for both genders).

Number of prescriptions per year

Figure 3 shows the numbers of prescriptions filled during 2013 by age groups and for both genders together. For all age groups, one prescription per year was most common. The number of prescriptions per year showed substantial similarity between boys and girls for all age groups (data not shown).

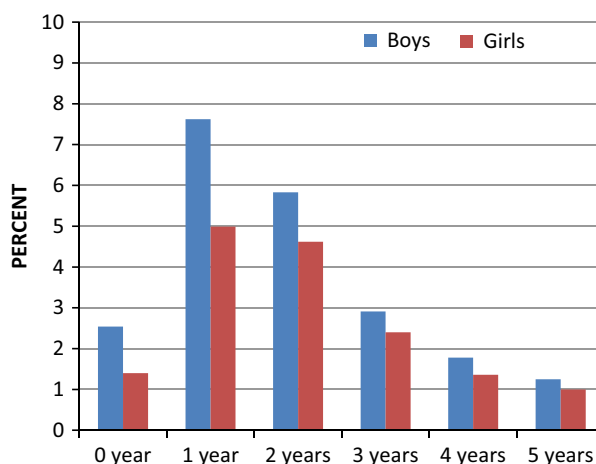


Figure 2 Incidence (new users) of boys and girls in different age groups who were redeemed at least one prescription of inhaled corticosteroids (ICS) during 2013, and were not prescribed ICS before since birth.

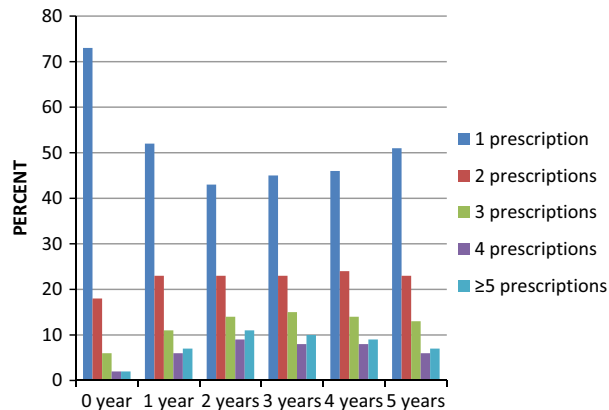


Figure 3 The share by age groups who redeemed different numbers of prescriptions during 2013 for both genders together.

Longitudinal prescription pattern

Table 1 shows the number of children born in 2004 who filled the first prescription of ICS at different ages, and the share who also filled a prescription each of the following years. Use of ICS only the first year (one-year user) was more common for those initiating ICS at an older age than those initiating ICS during first year of life. Regardless of age at initiation of ICS, few children were persistently using ICS in all the 5 years of follow-up (9–18%). A minor share of children were intermittent users during follow-up (approximately 10% each year), having one or several years without filling ICS prescriptions. A similar analysis from children born in 2005 and 2008 essentially gave the same results (data not shown).

Table 2 shows the number of children born in 2004 who filled a prescription for ICS at different age groups, and the age

Table 1 The number of children born in 2004 who filled the first prescription of inhaled corticosteroids at different ages, and the share who also filled a prescription each of the following years

Age A0 (years) when filling the first ICS prescription	Type of ICS user at age A0 + X years of follow-up*	Number of users (N) filling first prescription at age A0 and the share (%) filling prescription at age A0 + X of follow-up														
		Boys	N	1	2	3	4	5	Girls	N	1	2	3	4	5	
1	One-year user		1400	21	21	21	21	21		686	26	26	26	26	26	
	Persistent user			68	49	34	24	18			63	45	31	20	16	
	Intermittent user			0	7	9	11	12			0	7	10	10	12	
	Intermittent non-user			11	23	36	45	49			11	22	32	43	46	
2	One-year user		1952	28	28	28	28	28		1296	32	32	32	32	32	
	Persistent user			62	41	28	21	15			59	37	25	18	13	
	Intermittent user			0	5	9	11	10			0	6	9	9	8	
	Intermittent non-user			9	25	34	40	46			9	25	33	40	46	
3	One-year user		1100	29	29	29	29	29		851	35	35	35	35	35	
	Persistent user			59	40	29	20	14			54	34	24	16	11	
	Intermittent user			0	8	11	11	13			0	7	11	9	11	
	Intermittent non-user			12	23	31	40	43			10	24	31	40	42	
4	One-year user		598	33	33	33	33	33		473	37	37	37	37	37	
	Persistent user			53	38	26	19	14			52	34	21	13	9	
	Intermittent user			0	8	11	13	13			0	8	11	11	12	
	Intermittent non-user			14	21	31	35	40			11	21	31	38	42	
5	One-year user		414	n.e.	n.e.	n.e.	n.e.	n.e.		278	n.e.	n.e.	n.e.	n.e.	n.e.	
	Persistent user			52	35	24	16	n.e.			49	27	19	11	n.e.	
	Intermittent user			0	9	12	17	n.e.			0	7	13	12	n.e.	
	Intermittent non-user			n.e.	n.e.	n.e.	n.e.	n.e.			n.e.	n.e.	n.e.	n.e.	n.e.	

One-year user: only filled prescription at age A0.

Persistent user: filled prescription in each year of follow-up up to age A0 + X.

Intermittent user: non-persistent user during follow-up filling prescription at age A0 + X.

Intermittent non-user: non-persistent user during follow-up and not filling prescription at age A0 + X.

n.e.: not able to estimate due to lack of follow-up years (data ends in 2013).

*If a child did not fill a prescription in 1 year, the child is moved to intermittent non-user group and may subsequently move to the intermittent user group.

Table 2 The number of children born in 2004 filling a prescription for inhaled corticosteroids (ICS) at different ages, and the age when they filled their first prescription of ICS (x-column)

Numbers of children filling prescriptions for ICS at different ages (A)		Age (A) filling the first prescription for ICS (A minus X years)				
A	N	A-0	A-1	A-2	A-3	A-4
Boys						
1	1400	100%	n.a.	n.a.	n.a.	n.a.
2	2905	67%	33%	n.a.	n.a.	n.a.
3	3105	35%	39%	25%	n.a.	n.a.
4	2753	22%	24%	33%	22%	n.a.
5	2466	17%	13%	21%	30%	19%
Girls						
1	686	100%	n.a.	n.a.	n.a.	n.a.
2	1725	75%	25%	n.a.	n.a.	n.a.
3	1970	43%	39%	18%	n.a.	n.a.
4	1774	27%	26%	31%	16%	n.a.
5	1533	18%	16%	23%	29%	14%

n.a.: data not available.

when they filled their *first* prescription for ICS. A high share of children in the oldest age groups also received ICS during previous years, but the results in Table 1 indicate that this pattern was intermittent.

Table 3 shows the number of children born in 2004 who filled a prescription for ICS at different age groups, and the share who also filled a prescription each of the previous years. Few children were prescribed ICS continuously for more than 2 or 3 years.

Prescription by specialty

For 2013, 54.224 ICS prescriptions from 6.048 physicians were filled. Thirty per cent of children received ICS from paediatric specialists, 11% from GPs with specialty, 4% from other specialties, while 55% received ICS from non-specialists only. This pattern was consistent for all age groups and for both genders (data not shown). Eighty-five per cent of the non-specialists exclusively used ICPC codes on prescriptions, indicating that this group mainly works as GPs. A higher share of children received ICS from paediatric specialist in 2004 than in 2013 (39% vs. 30%; $p < 0.001$), and fewer received ICS from non-specialists only (33% vs. 55%; $p < 0.001$).

Discussion

The prescription of ICS to preschool children in Norway has increased from 2004 to 2010 and decreased thereafter until 2013. The highest prevalence of prescription was among children 2 years of age and higher for boys in all preschool ages. The majority of children received only one prescription during 1 year irrespective of age. The incidence decreased by

Table 3 The number of children born in 2004 who at different ages filled a prescription of inhaled corticosteroids, and the percentage who filled a prescription each of the previous years

All children with prescription at different ages (A)		Age (A) filled prescription for ICS (A minus X years)			
A	N	A-1	A-2	A-3	A-4
Boys					
1	1400	n.a.	n.a.	n.a.	n.a.
2	2905	33%	n.a.	n.a.	n.a.
3	3105	61%	22%	n.a.	n.a.
4	2753	71%	46%	17%	n.a.
5	2466	71%	55%	36%	14%
Girls					
1	686	n.a.	n.a.	n.a.	n.a.
2	1725	25%	n.a.	n.a.	n.a.
3	1970	54%	16%	n.a.	n.a.
4	1774	67%	39%	12%	n.a.
5	1533	69%	50%	31%	9%

n.a.: not available.

increasing age, and few children were dispensed ICS regularly through several of the preschool years. A minority of children was prescribed ICS by a paediatric specialist.

Few nationwide studies have explored the rate of prescription of ICS in preschool children, and studies may differ regarding age distribution and type of data reported, which hamper comparisons between studies. In a study from Italy, UK and the Netherlands for the years 2000–2005, a substantial difference in prescription patterns of asthma drugs was shown (16). The prescription of ICS to preschool children was high in Italy, reaching about 20% in children aged 2–4 years, whereas the level in UK and the Netherlands was about 5% for this age group. An overuse of ICS in Italy and a possible underuse in UK and the Netherlands were suggested. Also, a north–south gradient in Europe regarding both morbidity and ICS prescription was suggested (16), which seems contradicted by our results.

In two British studies, the share of children aged 0–4 years receiving ICS increased from 1.0% in 1992 to 4.8% in 1998 and then decreased to 1.6% in 2005–2006 (26, 27). For the same age group, the numbers from Norway extracted from the present study were 6% in 2004, increasing to 8.8% in 2010. The prevalence of prescription of ICS in children 0–4.5 years in Sweden was in 2008 found to be 3.9% in boys and 2.6% in girls (28). In one of the British studies, the prescription rate for ICS was significantly higher in children aged 5–11 years compared to children 0–4 years, opposite to what is found in Norway and Italy (16, 29). Together, this shows that the prescription of ICS during preschool years is especially high in Norway compared to UK and the Netherlands and also higher than in Sweden. The observed decline in the proportion of children receiving ICS during early years of life is observed many years later in

Norway compared to the UK. The reason for the recent decline in prescribing is not known, but awareness of an inappropriate practice of prescribing may partly explain this change.

Less than half of the children were prescribed ICS during the preschool age, were prescribed ICS more than two consecutive years and less than a third for three consecutive years (Tables 1 and 3). For all age groups, more than 40% of the children redeemed only one prescription of ICS during 1 year (Fig. 3). Consequently, a high proportion of children were dispensed ICS only once during the whole preschool age. For children given their first prescription during the first 2 years of life, only 10–15% received ICS at least once per year until the age of 5 and 6 years. Furthermore, few children in the oldest age groups received ICS for more than one or two consecutive years (Table 1), and few of the children who received ICS during the fifth and sixth year of life received the first prescription during the first few years of life (Table 2).

Surprisingly, a transient pattern of filling prescriptions was found also after 3 years of age when wheezing episodes are more likely to be asthma (6). A possible reason may be that a high number of preschool children are given ICS for single episodes (wheezing or lower airway infections) or for transient symptoms that are more persistent in the youngest age groups, but not persisting into the late preschool years. This pattern has been shown in other studies, demonstrated by the coprescribing of ICS and antibiotics also in children (21), and the pattern of prescribing short courses of ICS to children with various respiratory symptoms (20). The low persistence of prescribing ICS, and a discrepancy between prescribing ICS and the diagnosis of asthma, seems to be consistent for several age groups, including adults (14, 15, 17, 29, 30). However, in a Dutch study, a higher persistence of prescribing asthma medication at the age of six was seen for children starting treatment at the age of 2 or 3 years, compared to those starting during the first year of life (17), which was not observed in our data.

Early childhood wheezing is highly heterogeneous, and no indexes are able to predict with high specificity and sensitivity

which children with asthma could benefit from anti-asthmatic treatment (4). Consequently, consensus recommends a trial treatment with ICS to evaluate treatment response and to support or weaken the diagnosis of asthma (1, 2, 6). This approach could partly explain a high prescribing rate during the first years of life and the non-persistent pattern of prescription in this age group. However, the non-persistent pattern of prescription was seen in all age groups. Our results may be in agreement with other studies suggesting an inappropriate use of ICS for other conditions than chronic asthma during childhood (21).

Two-thirds of prescriptions were given outside hospital or by a non-paediatrician. In Norway, most children first visit a GP and may be further referred to a paediatrician. Our results do not show whether the prescription pattern differs between GPs and paediatricians regarding the persistence of prescription through years. However, the increasing prevalence of ICS prescribing coincides with an increasing share of prescriptions being given by a GP. Studies from other countries have shown that GPs may have an inappropriate prescribing pattern (17, 21), and as the majority of prescriptions in Norway are prescribed by GPs, our results support this.

Together with the results from other countries, our results show a wide variation in the pattern of ICS prescribing to preschool children in Europe, with a possible overuse and inappropriate prescription. We share the same guidelines (2), so the large differences in prescribing may at least partly be due to different implementation of these guidelines. This may be attributable to the uncertainty regarding the asthma diagnosis and phenotypes in preschool children. Nevertheless, this calls for actions for a better implementation of guidelines, especially for general practitioners, to ensure a safe and cost-effective treatment for preschool children.

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References

- Papadopoulos NG, Arakawa H, Carlsen KH, et al. International consensus on (ICON) pediatric asthma. *Allergy* 2012; **67**: 976–97.
- Pedersen SE, Hurd SS, Lemanske RF Jr, et al. Global strategy for the diagnosis and management of asthma in children 5 years and younger. *Pediatr Pulmonol* 2011; **46**: 1–17.
- Brand PL, Caudri D, Eber E, et al. Classification and pharmacological treatment of preschool wheezing: changes since 2008. *Eur Respir J* 2014; **43**: 1172–7.
- Bacharier LB, Guilbert TW. Diagnosis and management of early asthma in preschool-aged children. *J Allergy Clin Immunol* 2012; **130**: 287–96.
- Stein RT, Martinez FD. Asthma phenotypes in childhood: lessons from an epidemiological approach. *Paediatr Respir Rev* 2004; **5**: 155–61.
- Brand PL, Baraldi E, Bisgaard H, et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J* 2008; **32**: 1096–110.
- Guilbert TW, Mauger DT, Allen DB, et al. Growth of preschool children at high risk for asthma 2 years after discontinuation of fluticasone. *J Allergy Clin Immunol* 2011; **128**: 956–63.
- Castro-Rodriguez JA, Rodrigo GJ. Efficacy of inhaled corticosteroids in infants and preschoolers with recurrent wheezing and asthma: a systematic review with meta-analysis. *Pediatrics* 2009; **123**: e519–25.
- Esposito S, Principi N. Pharmacological approach to wheezing in preschool children. *Expert Opin Pharmacother* 2014; **15**: 943–52.
- Garcia-Marcos L, Ros-Lucas JA, Sanchez-Solis M. Inhaled corticosteroids in asthmatic children: are they as safe in infants and preschoolers as in older children? A review *Curr Drug Saf* 2008; **3**: 35–45.
- Kelly HW, Sternberg AL, Lescher R, et al. Effect of inhaled glucocorticoids in childhood on adult height. *N Engl J Med* 2012; **367**: 904–12.
- Ducharme FM, Lemire C, Noya FJ, et al. Preemptive use of high-dose fluticasone for

- virus-induced wheezing in young children. *N Engl J Med* 2009; **360**: 339–53.
13. Sidoroff VH, Ylinen MK, Kroger LM, Kroger HP, Korppi MO. Inhaled corticosteroids and bone mineral density at school age: a follow-up study after early childhood wheezing. *Pediatr Pulmonol* 2013; **50**: 1–7.
 14. Zuidgeest MG, van Dijk L, Smit HA, et al. Prescription of respiratory medication without an asthma diagnosis in children: a population based study. *BMC Health Serv Res* 2008; **8**: 16.
 15. Ingemansson M, Wettermark B, Jonsson EW, et al. Adherence to guidelines for drug treatment of asthma in children: potential for improvement in Swedish primary care. *Qual Prim Care* 2012; **20**: 131–9.
 16. Sen EF, Verhamme KM, Neubert A, et al. Assessment of pediatric asthma drug use in three European countries; a TEDDY study. *Eur J Pediatr* 2011; **170**: 81–92.
 17. Schokker S, Groenhof F, van der Veen WJ, van der Molen T. Prescribing of asthma medication in primary care for children aged under 10. *Prim Care Respir J* 2010; **19**: 28–34.
 18. Zuidgeest MG, Smit HA, Bracke M, et al. Persistence of asthma medication use in preschool children. *Respir Med* 2008; **102**: 1446–51.
 19. Koster ES, Wijga AH, Zuidgeest MG, et al. Patterns of asthma medication use: early asthma therapy initiation and asthma outcomes at age 8. *Pharmacoepidemiol Drug Saf* 2010; **19**: 991–9.
 20. Klok T, Kaptein AA, Duiverman E, Oldenhof FS, Brand PL. General practitioners' prescribing behaviour as a determinant of poor persistence with inhaled corticosteroids in children with respiratory symptoms: mixed methods study. *BMJ Open* 2013; **3**: e002310. doi:10.1136/bmjopen-2012-002310.
 21. Poulos LM, Ampon RD, Marks GB, Reddel HK. Inappropriate prescribing of inhaled corticosteroids: are they being prescribed for respiratory tract infections? A retrospective cohort study. *Prim Care Respir J* 2013; **22**: 201–8.
 22. Zuidgeest MG, van Dijk L, Spreeuwenberg P, et al. What drives prescribing of asthma medication to children? A multilevel population-based study. *Ann Fam Med* 2009; **7**: 32–40.
 23. Uijen JH, van der Wouden JC, Schellevis FG, et al. Asthma prescription patterns for children: can GPs do better? *Eur J Gen Pract* 2011; **17**: 109–15.
 24. Furu K, Wettermark B, Andersen M, et al. The Nordic countries as a cohort for pharmacoepidemiological research. *Basic Clin Pharmacol Toxicol* 2010; **106**: 86–94.
 25. WHO Collaborating Centre for Drug Statistics Methodology. *Guidelines for ATC Classification and DDD Assignment*. Oslo: WHO, 2013.
 26. Turner S, Thomas M, von Ziegenweidt J, Price D. Prescribing trends in asthma: a longitudinal observational study. *Arch Dis Child* 2009; **94**: 16–22.
 27. Elkout H, Helms PJ, Simpson CR, McLay JS. Changes in primary care prescribing patterns for paediatric asthma: a prescribing database analysis. *Arch Dis Child* 2012; **97**: 521–5.
 28. Ortvist AK, Lundholm C, Wettermark B, et al. Validation of asthma and eczema in population-based Swedish drug and patient registers. *Pharmacoepidemiol Drug Saf* 2013; **22**: 850–60.
 29. Karlstad O, Nafstad P, Tverdal A, Skurtveit S, Furu K. Prevalence, incidence and persistence of anti-asthma medication use in 2- to 29-year-olds: a nationwide prescription study. *Eur J Clin Pharmacol* 2010; **66**: 399–406.
 30. Weidinger P, Nilsson JL, Lindblad U. Medication prescribing for asthma and COPD: a register-based cross-sectional study in Swedish primary care. *BMC Fam Pract* 2014; **15**: 54.