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Variations in Pediatric Asthma Hospitalization Rates and Costs Between and Within Nordic Countries*

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Background: **We assessed variations in hospitalization parameters and costs among asthmatic children in four Nordic countries by geographic location and age groups.**
Methods: **Cross-sectional, county-level aggregate data on asthma-related hospitalizations in 1999, obtained from public national databases for children < 15 years old from Denmark, Sweden, Norway, and Finland, together with country-specific asthma management cost were used to estimate the incidence of first hospital admission (per 1,000), length of hospital stay (LOS), and hospitalization cost. Longitudinal patient-specific data from 1998/1999 were used to calculate the relative hazard of readmission (RHR) using a multivariate Cox proportional hazards model.**
Results: **Nordic incidence of first hospital admission in 1999 was 2.17 per 1,000 children, readmission was noted in 16% of the patients, mean LOS was 2.64 days, and total hospitalization cost was almost $14 million. Hospitalization incidence, RHR, and costs were significantly higher in children < 5 years old compared with school children 6 to 14 years old. Hospital LOS, incidence of first hospital admission, and cost per child were the highest in Denmark, though RHR did not differ significantly from Sweden.**
Conclusions: **Large variations in all parameters were observed between and within countries. Given the similarities among the four countries studied, these results may, among other reasons, indicate different efficiencies of the various asthma management plans between and within them. The presented measures of hospitalization patterns could prove to be valuable quality-of-care measures to guide further improvements in asthma management.**
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Key words: asthma; asthma management; child; hospitalization; quality of care

Abbreviations: DRG = diagnosis related group; ICD = *International Classification of Diseases*; LOS = length of hospital stay; RHR = relative hazard of readmission

One of the main goals of long-term asthma management is to avoid asthma-related hospital admissions, which remain the second most common cause of hospitalizations in children.[1–3] In addition, hospitalization costs account for 46 to 74% of the total direct cost of asthma management in the United States and Europe.[4–8] Significant reductions in hospitalization and readmission rates have been reported during the recent decade from Denmark,[9] and also from local regions within other Nordic countries.[10,11] However, a large proportion of children is still hospitalized each year despite extensive educational programs and use of preventive drugs, and the rate of variation within and between national health-care systems remains unknown.[2] Denmark,

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Sweden, Norway, and Finland are relatively homogeneous in terms of culture, sociodemographic characteristics, and access to publicly funded care. Validated nationwide inpatient registries, based on the *International Classification of Diseases* (ICD), *10th Revision*, and used for prospective hospital financing and policy development, also are available throughout the region, creating a favorable setting for clinical and health-services research.

The objective of this study was to assess variations in asthma-related hospitalization patterns between and within Nordic counties, as well as between age groups. Incidence of first hospital admissions, length of hospital stay (LOS), hospitalization costs, and relative hazard of readmission (RHR) were used to reflect the patterns of hospitalization. Such measures may be useful to evaluate and guide improvement in quality of care and asthma management plans, which have previously been shown, together with other factors, shown to significantly impact the rate of asthma-related hospital admissions.[2–4,7,12]

Materials and Methods

The study was designed as a 12-month retrospective database analysis on a regional, national, and overall Nordic level assessing inpatient resource use in Denmark, Sweden, Norway, and Finland in 1999. Two types of data on asthma-related hospitalizations were obtained from publicly available national inpatient registries (Danish National Board of Health and Welfare, Norwegian Patient Register, Finnish National Research and Development Centre for Health and Welfare, and Swedish National Board of Health and Welfare) for children < 15 years old. The first source included data on county-level aggregate inpatient services use according to gender and three age groups (< 2 years [infants], 2 to 5 years [young children], and 6 to 14 years [schoolchildren]) from Denmark, Sweden, Norway, and Finland. Variables requested from these validated databases, which routinely collect inpatient resource use (via ICD codes recorded by doctors) from all hospitals nationwide and link it to patient identifying numbers and sociodemographic characteristics, were the number of children hospitalized, the number of hospital admissions (hospital episodes), and bed days incurred. Populations included children whose primary reason for admission was asthma related as defined through ICD, 10th Revision codes. These included J45.0 (mainly allergic asthma), J45.1 (nonallergic asthma), J45.8 (mixed asthma), J45.9 (unspecified asthma), and J46.x (acute severe asthma). A second (longitudinal) source of data were patient-specific hospitalizations for asthma in 1998 and 1999 obtained from Sweden, Denmark (ICD 10th Revision), and Norway (ICD, Ninth Revision in 1998, ICD, 10th Revision in 1999), including the following variables: date of hospital admission, gender, age at first hospital admission, county of residence, and county of the hospital. Data in national inpatient registries are periodically checked for quality of diagnostic codes and identifying numbers for patients.

Data sources on cost per asthma episode were obtained from the Ministries of Health in respective countries, which routinely collect data for prospective budgeting purposes. The total number of children living in each county and country was obtained from the national statistical institutes for 1999, where centralized population census serves as a data collection tool. Counties were first classified into either urban or rural, according to the population density and presence of major urban centers, and later grouped into geographic regions.

The following calculations were based on aggregate inpatient data provided by national inpatient registries. The age group-specific incidence of first hospital admissions in 1999 was calculated for each region and country by dividing the total number of first hospitalizations in 1999 with the number of children living in the respective areas standardized per 1,000. The average LOS per hospitalization was estimated by dividing the total number of bed days with the total number of hospital episodes in each region and country. χ^2 proportional tests were carried out in order to assess possible association between LOS > 2 days and gender, age groups, and location (urban/rural). The cutoff was selected according to the mean LOS in the Nordic region, rounded to the whole number due to the discrete nature of the variable.

The total annual hospitalization cost for each region and age group was calculated by multiplying the total number of bed days with a unit cost per bed day. To estimate the latter in each country, we obtained asthma-related hospitalization cost and average LOS for patients hospitalized under the diagnosis related group (DRG)-98 (asthma and bronchitis in patients < 18 years old) for 1999. The unit cost per bed day was then calculated by dividing total DRG-98 hospitalization cost by average LOS for the DRG. All currency conversions were based on the purchase power parity exchange rate in 1999. Any differences in resource utilization found among the care-seeking populations across countries were definitive and did not require further statistical inference in order to draw conclusions, as we were working with the entire pediatric population with asthma and not samples.

The longitudinal, patient-specific data from Sweden, Denmark, and Norway were used to assess the RHR, defined as a separate admission to the hospital > 1 week after the first asthma discharge during the study period. At least 7 days between the hospitalizations were required in order to ensure that the second hospitalization was a consequence of a new exacerbation and not administrative transfer/shifting between departments (*eg*, emergency department to pediatrics) during the same episode. *Ex ante* sensitivity analysis revealed no significant differences in rate of rehospitalization when required gap was varied between 1 day and 7 days. The Cox proportional hazards model was used to estimate the RHR between age groups, regions and countries, controlling for asthma type (based on ICD, 10th Revision) and gender. The response variable was the length of time between subsequent hospitalizations during a 2-year period. Cox modeling is a semiparametric method, which uses the data on patients whose event of interest has occurred (*eg*, second hospitalization in a given time period), and also on patients who did not experience the event of interest (censored patients). It accounts for the timing of the outcome variable, such as second hospitalization in our example, vs regular nonlinear multivariate models, which only account for whether the event of interest occurred or not.

Results

Among 4,437,254 children < 15 years old in the four Nordic countries in 1999, 9,635 children (0.22%) were hospitalized due to asthma at least once during 1999, with a total of 11,484 hospital admissions and 30,264 bed days. Among previously hospitalized children, 15.7% were readmitted within the 2-year period. Mean LOS for Nordic children

< 15 years of age was 2.64 days in 1999. The total annual costs of asthma-related hospitalizations were \$4.9 million, \$3.6 million, \$3.7 million, and \$1.9 million in Denmark, Finland, Sweden, and Norway, respectively. Overall cost per bed day was estimated as \$456 in US dollars (\$1 = 8.58 Danish krona) in Denmark, \$498 in US dollars (\$1 = 9.78 Swedish krona) in Sweden, \$581 in US dollars (\$1 = 6.15 Finnish marks) in Finland, and \$304 in US dollars (\$1 = 9.49 Norwegian krona) in Norway.

The incidence of first hospital admissions, LOS, hospitalization cost, and RHR are given by geographic location in Table 1. Large variations in these measures of hospitalization patterns were observed between and within the countries. χ^2 tests showed no consistent pattern in LOS regarding rural vs urban areas nor gender. Denmark presented with the highest figures regardless of the measure, apart from the nonsignificantly higher RHR in Sweden. (Table 1).

The youngest children (< 2 years) were the highest users of health-care resources due to more common first admissions as well as readmissions (Table 2). However, schoolchildren in Denmark and Finland were 2 times and 1.4 times more likely ($p < 0.0001$) to have longer LOS, respectively, than children aged ≤ 5 years. Overall on the Nordic level, the youngest children (< 2 years) consumed approximately 8.5 times more *per capita* for inpatient health care due to asthma compared to school children, and 2 to 5 year olds consumed approximately 2.8 times more than school children.

Discussion

This is the first study to compare asthma-related hospitalization patterns between and within Nordic countries. We found marked variations in the rate of asthma-related hospitalizations, LOS, and cost, both between and within countries. There was no consistent difference in terms of utilization between rural

Table 1—*Hospitalization Parameters and Costs in Nordic Children Below 15 Years of Age*

Country	Regions	Incidence of First Admissions per 1,000 Children†	Relative Hazard of Readmission‡	Length of Hospital Stay (days)§	Hospitalization Cost per 1,000 Children (US \$)§
Denmark*	**Total**	**2.8**	**1.18 [1.06–1.32] ‖**	**3.31**	**4,991**
	Funen	3.21	1.50 [1.18–1.91] ‖	5.45	9,922
	Jutland	3.06	0.97 [0.82–1.15]	2.88	4,742
	Zealand	2.4	1-reference group	3.30	4,287
Sweden	**Total**	**1.8**	**1.24 [1.11–1.38] ‖**	**2.16**	**2,219**
	Södra	1.58	0.97 [0.77–1.22]	2.73	2,550
	Uppsala-Örebro	1.83	1.19 [0.97–1.47] ¶	1.96	2,119
	Västra	2.10	1.13 [0.92–1.41]	2.13	2,623
	Sydöstra	1.82	1.10 [0.86–1.42]	2.13	2,224
	Stockholm-Gotland	1.73	1-reference group	2.09	2,075
	Norra	1.38	1.04 [0.78–1.40]	1.79	1,392
Norway	**Total**	**2.3**	**1-reference group**	**2.64**	**2,134**
	East-Oslo	2.20	1-reference group	2.61	2,013
	South	2.34	1.12 [0.87–1.44]	3.18	2,657
	West	2.82	1.38 [1.10–1.71] ‖	2.38	2,452
	Mid	1.90	1.06 [0.79–1.42]	2.73	1,800
	North	1.77	0.95 [0.64–1.40]	2.25	1,355
Finland#	**Total**	**2.2**		**2.42**	**3,836**
	Helsinki	1.88		2.45	3,374
	Turku	1.58		2.34	2,605
	Tampere	1.69		2.85	3,483
	Kuopio	3.93		2.03	6,295
	Oulu	2.04		2.77	3,799

*Two Danish regions (Lolland-Falster, Bornholms) are not presented in Table 1 but were considered in all nationwide calculations. Relative hazards were not significantly different from Zealand for these two regions.

†Incidence of first admissions in year 1999.

‡Relative hazard ratios were based on patient-specific data from 1998/1999 in Denmark, Sweden, and Norway. Data for Finland were not available. Relative hazard ratios at the country level compare Denmark and Sweden to Norway. Within country level compares all regions to the region with capital city. Confidence interval of 95% is presented.

§Based on county-level aggregate data in 1999.

‖Denotes statistically significant difference from reference location at 0.01.

¶Denotes statistically significant difference from reference location at 0.1.

#Relative hazard of readmission data for Finland are not available.

Table 2—*Hospitalization Parameters and Costs in Nordic Region by Age Group*

Age (yr)	Incidence of First Admissions per 1,000 Children*	Relative Hazard of Readmission†	Length of Hospital Stay (days)‡	Hospitalization Cost per 1,000 Children (US $)‡
< 2	7.13	1.57 [1.38–1.79]§	2.73	11,140
2–5	3.09	1.38 [1.20–1.57]§	2.21	3,660
6–14	0.77	1-reference group	3.24	1,310

*Incidence of first admissions in year 1999.

†Relative hazard ratios were based on patient-specific data from Denmark, Sweden, and Norway in 1998/1999. Data from Finland were not available. Confidence interval of 95% is presented.

‡Based on county-level aggregate data in 1999.

§Denotes statistically significant difference from reference group at 0.01.

and urban areas, or gender. Denmark incurred the highest incidence of first hospital admissions as well as cost per capita, with large variations within the country, while Sweden incurred the highest RHR numerically, though not statistically different from RHR in Denmark. Variations were also observed with respect to age group. Children < 2 years old had the highest hospitalization rates, cost *per capita*, and RHR readmission. Children < 5 years of age consumed 75% of the total pediatric inpatient resources for asthma management in the Nordic region.

Hospitalization rates may reflect reliance on hospitalization for asthma management and/or a lower level of asthma control in the primary care setting. Lack of disease control at the primary care level often results in higher hospital utilization.[2–4,7,12] We previously introduced readmission rate as a measure of the efficiency of asthma management in the secondary care setting.[9] Once the child has been hospitalized, it is largely a failure of the secondary care if readmission for asthma is needed. Hospital LOS also may reflect the efficiency of hospital-based asthma management. In this study, LOS showed geographic variations in concordance with the differences in hospital admission rates and RHR, which supports the validity of these measures.

Hospitalization rates, RHR, and cost were higher among younger children, which is consistent with other studies[10,11,13] that reported higher resource utilization among younger patients. Our findings suggest that the hospitalization rate among children < 2 years old was 2.3 times higher than for 2- to 5-year-olds, which was four times higher than for children aged 6 to 14 years. This is partly a consequence of the disease prevalence and onset, but also may be a reflection of the disease management at the primary level. Asthma has an early onset, usually with symptoms of low specificity. In addition, the management of very young asthmatic children lacks the evidence base and consensus available for management of older children. These factors may have caused the observed greater resource use among younger children. To exclude the possibility that younger children were experiencing more severe asthma on average, we examined the proportion of children by age group and country, admitted according to specific ICD codes adjusted for severity (J46.x). This subanalysis revealed that a smaller proportion of younger children actually had severe asthma at hospital admission in all countries. Children who were admitted due to any other asthma-related diagnosis not described with ICD codes J45.x and J46.x were not included in our study, and therefore those diagnoses (*eg*, bronchiolitis, wheezing bronchitis) could not account for hospitalizations in our population.

Large regional variations in hospitalization patterns found in this study are surprising in view of the sociodemographic, health status, and health-care system similarities among the four Nordic countries. Indicators like gross domestic product, percentage of gross domestic product spent on health care, public spending for health care per inhabitant, proportion of urban population, infant mortality rate, life expectancy at birth, and the number of physicians per 100,000 inhabitants, are very similar for the Nordic countries.[14,15] In addition, asthma-specific mortality rates and access to specialist care as approximated by the presence of pediatric departments do not vary substantially.[16–18] The prevalence of asthma in children also has been shown to be similar between countries, as well as between regions within Norway[19] and Sweden.[20] Our data indicate that according to the ICD coding system, the proportion of children with severe asthma at hospital admission is similar among the four countries studied. Finally, the association between poverty and asthma severity is inconsistent.[21] Even if evidence was pointing into any particular direction, due to similar distribution of sociodemographic and clinical characteristics of the asthmatic children in Nordic countries, we have no reason to believe that these characteristics could have been unequally distributed between regions

and countries, and therefore a possible explanation for unequal distribution of hospitalizations and secondary care demand in general.

Therefore, our findings may indicate differences in diagnosis and the efficiency of asthma management plans between the regions and countries, and some evidence already confirmed differences in diagnosis of pediatric asthma among regions within Finland.[22] Previous research into asthma-related hospital admissions among children identified at least eight preventable factors associated with hospital admission.[2] Among those, "failure to use asthma crisis management plan," and "inappropriate preventive treatment," ranked as first and third most commonly reported for patients admitted. The "management plan" was only established for 49% of the children, and among those only 9% followed it at the time of need.[2] Therefore, it appears that there is room for improvement in terms of appropriate preventive treatment as well as development of individual crisis management plans for patients at the provider side, as well as in terms of patient education. Among other factors, the "low level of asthma knowledge," partly responsibility of the patients as well as health-care providers, ranked second, and "compliance" ranked fourth. These findings support the notion that pediatric asthma-related hospital admissions are in part a consequence of variations in asthma management at primary care level, which has been previously established for adults.[2-4,7,12] Analyses of small area variations have been successfully used in other disease areas to identify opportunities for improvement in disease management at a population level.[23,24] For example, Ashton et al[25] found substantial geographic variation in the hospital and outpatient use for COPD and seven other chronic diseases in the US Veterans Affairs health-care system.

Several limitations are present in this study. For many reasons, administrative databases routinely include incomplete and biased data that can significantly influence the numerators and denominators used in the analyses. In order to ensure homogeneity of the data sources, our study used the nationwide inpatient registries, which are established in each country included in this article by the ministry of health (government institutes). Due to the nature of the health systems in these countries as well as in Europe in general ("universal" health-care systems), uniform systems of delivery, financing, and tracking of health care within the countries are in place. Therefore, the nature of the data collection within each country is homogeneous, though there may well be differences between the countries. To avoid the latter, four countries were selected that share common history as well as development of the health-care systems within Europe. Data reported from the hospitals to the inpatient registries use the common coding system (ICD). Coding in all four countries is performed by treating physicians on a per-patient/individual basis using a unique patient identifying number. Due to the similarities in the training of medical personnel in Nordic region, we would not expect differential coding between countries, and even less so within the countries. In addition, no financial incentives exist in any of the systems included to code patients differentially (*eg*, as more severe). Financing in most county councils is based on DRGs, which creates incentives for having systems in place that generate complete and accurate records of hospitalizations. The risk for bias toward more expensive DRGs is low, however, since the salaries of physicians (who record the ICD codes that the DRGs are based on) are not affected by the DRGs. Data quality is periodically checked by the institutes creating inpatient registries, and is reported to be $> 99\%$ reliable with respect to diagnoses and patient identification numbers.[26]

We relied on existing data on hospital resource use that did not have objective outcome measures such as lung function and disease history. Therefore, we could not compare severity of the underlying asthma among different populations. We were only able to establish severity of the current asthma episode. To approximate the latter, we used the ICD coding system. We based our comparisons within and between countries on the assumption that the diagnosis of asthma as a cause of hospital admission through ICD coding is reliable within this geographic area. Since ICD coding is not used for direct billing purposes in Europe as it is in the United States, we would not expect adverse behavior with respect to coding. Even if evidence of such behavior existed, there is no reason to believe it would be adversely distributed, which means substantial differences among the four Nordic countries are not to be expected. Physicians who code patients with respect to ICD system receive salaries independently of the ICD codes reported. Evidence also suggests that when classifying severity, which is based on pathophysiology of the disease as well as medication use,[1] patients may be falsely assessed with respect to asthma severity level on the part of physicians. Some of the patients might fall into a higher severity category, based on their underlying pathophysiology, but were well controlled at the time of assessment and were, therefore, "upgraded" to a milder asthma category. This illustrates how assessment of severity level is inextricably confounded with level of control.[27] Hence, underlying asthma severity assessment may be problematic in itself. In addition, the specificity of the asthma diagnosis is probably low, partic-

ularly in the younger children. This may bias the comparison of hospitalization data among age groups, though the tendency is likely to underdiagnose asthma in young children, which would suggest that the relative burden of asthma hospitalization is even greater in young children. Lack of specificity of diagnosis is unlikely to significantly affect comparisons between regions and countries.

In conclusion, large variations found in this study may indicate significant differences in the efficiency of management plans in the primary and secondary care settings for children with asthma throughout the four Nordic countries. Education and disease management programs may be needed to reduce the variations in hospital resource use and to improve patient care. The measures applied in our study may be used to monitor the effect of such interventions in management plans. It may prove valuable to establish national and international databases to monitor asthma hospitalization rates, readmission rates, and LOS as a tool to evaluate improvements in asthma management.

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make up the health system must be better served by knowledge from various sources. If this is achieved, progress can be made in overcoming the seven ubiquitous health-care problems: errors and mistakes, poor quality health care, waste, unknowing variations in policy and practice, poor experience by patients, overenthusiastic adoption of interventions of low value, and failure to get new evidence into practice. These problems are shared by countries in both the developed and developing worlds—overcoming them will be as critical for achieving the Millennium Development Goals in the developing world as it will be for tackling the myriad health problems facing more developed economies. Ultimately, the 15th grand challenge will work synergistically with those stated previously to advance global health and health equity.

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Long-acting β_2 agonists and paediatric asthma

The US Food and Drug Administration's (FDA) Pulmonary and Allergy Drugs Advisory Committee recently strengthened the warning on all long-acting β_2 agonists.[1] This action was based on a number of pharmaceutical company initiated post marketing studies including the SMART study[1,2] in adults showing a 1·71 (95% CI 1·01–2·89) total relative risk of asthma death or life-threatening experience with use of salmeterol compared with placebo. This RR rose to 4·9 (95% CI 1·68–14·45) in African-Americans.[1,2] SMART is the only study powered for such outcomes, although smaller studies have reported the same increase in exacerbation rates in children and adults.[4,5] The Canadian health body also warns of the possible increased risk of asthma-related deaths associated with the use of long-acting β_2 agonists. We are still waiting for a reaction from the European Medicines Agency (EMEA).

Neither the FDA nor EMEA have as yet addressed the insufficient paediatric evidence-base. Two reviews, which analysed available studies in children and adolescents under 17 years old, have drawn attention to the twin lacunae in the paediatric evidence-base for long-acting β_2 agonists: the absence of evidence of a bronchodilator effect with regular use;[3] and the absence of evidence that long-acting β_2 agonists offer protection against exacerbations of asthma.[4] The available studies not only fail to show a protective effect of long-acting β_2 agonists, but also suggest that asthma exacerbations are increased in some groups of patients taking such drugs regularly, even when used as add-on to inhaled corticosteroids. In three studies where the numbers of hospital admissions for asthma were available, the number of hospital admissions in children between 4 years and 17 years old on regular long-acting β_2 agonist therapy was significantly raised, with a relative risk of 3–22.[4,5]

However, children with asthma are rapidly being switched from inhaled corticosteroids to fixed combination therapy with inhaled corticosteroids plus long-acting β_2 agonists, as in the *Danish Medicines Registry*,[6] which reflects family practitioners' prescription practice. This shows a rapid decline in fluticasone use with a mirrored increase in fixed combination therapy with fluticasone plus salmeterol now constituting more than half of all children with asthma treated with inhaled corticosteroid, even though family practitioners typically manage patients with intermittent or mild asthma. (figure). The other combination therapy (budesonide plus formoterol) shows a similar exponential increase in this patient segment. It is puzzling to consider what drives such rapid change in therapy in the face of ambiguous evidence.

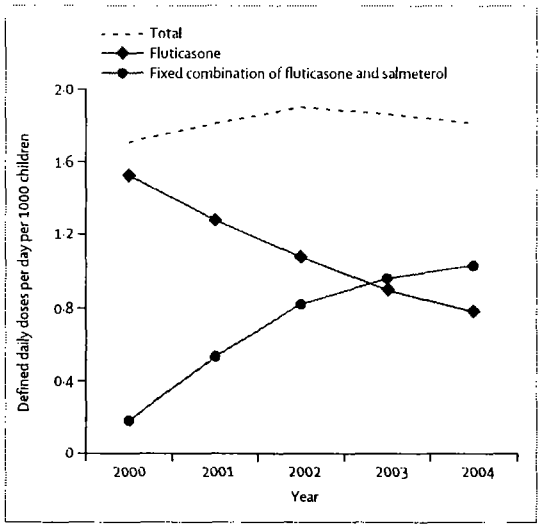

Figure: **Prescriptions filled (defined daily doses) standardised for catchment population aged 5–14 years in Denmark.[6]**
Only prescriptions by primary-care physicians. Data accessed August 24, 2005 on http://www.medstat.dk.

The pivotal issue here is not that children should never use long-acting β_2 agonists, but how they should be used. An abundance of evidence shows that long-acting β_2 agonists provide effective bronchodilation and bronchoprotection when used as an intermittent single-dose treatment for asthma for children.[3] Also, regular long-acting β_2-agonist therapy is probably useful in a subgroup of asthmatic children. But, there is no evidence to support the use of long-acting β_2 agonists as standard add-on treatment in paediatric asthma when asthma is not adequately controlled on inhaled corticosteroids, as recommended in international guidelines.[7] Similarly, *The British National Formulary for Children* (*BNFC*) recommends the use of long-acting β_2 agonists as an add-on therapy to inhaled corticosteroids if asthma is not controlled with occasional relief bronchodilators or regular standard dose inhaled corticosteroids plus inhaled short-acting β_2 agonist (although the *BNFC* does stress that long-acting β_2 agonists should be discontinued if there is no response).[8] These recommendations are not based on evidence in children, but largely based on extrapolation from studies in adults (over 18 years old) or other existing guidelines rather than review of the specific evidence in children. Likewise, product labelling for paediatrics is granted on the basis of results from studies in adults, assuming the disease is similar in children and adults, and only requesting comparable pharmacokinetics and safety.

Asthma is not the same in adults and children, therefore we cannot rely on an inherited model. Separate documentation is needed for paediatric asthma. Several recent policy initiatives from the FDA and the European Commission highlight the importance of having separate clinical data for adult and paediatric populations.[9–11] The European Commission has expressed grave concerns that more than half the drugs prescribed for children are given on the basis of data from studies in adults.[11–14] It acknowledges that without specific paediatric studies, children may be exposed to unwanted side-effects or be under-treated: "This is a vulnerable group with developmental, physiological and psychological differences from adults, which makes age and development related research of medicines particularly important".[11]

However, there is a gap between the official stance on paediatric studies and actions. The objectives sit uncomfortably with the fact that drugs such as long-acting β_2 agonists continue to be labelled for standard treatment of children when the paediatric evidence-base does not support this position.

For too long we have accepted that instead of rooting our decisions on results gathered from a paediatric population, we base our choices on data from adult studies. Instead, it would be judicious to revisit the positioning of long-acting β_2 agonists as a routinely used add-on treatment in children with asthma, in line with the available paediatric evidence-base.

The Lancet has editorialised that the FDA's experience with the Pediatric Exclusivity clause and the Pediatric Rule shows that without legislation, companies will not voluntarily undertake paediatric trials.[15] Therefore, the FDA and European Commission should make strong recommendations bound up in legislation to ensure that the place of both new and currently marketed drugs in paediatric medicine is closely scrutinised. Meanwhile, it is the responsibility of clinicians to critically appraise the evidence-base on which we decide the management of asthma in children, and challenge the absence of paediatric data, so that appropriate studies can be done to reveal the optimum position of long-acting β_2 agonists in paediatric asthma management. In addition, it is appropriate that

physicians, parents of patients, and patients are made aware of this lack of evidence.

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HB has been a consultant to, paid lecturer for, and holds sponsored grants from, Aerocrine, AstraZeneca, Altana, GSK, and Merck. He does not hold stock or options in any pharmaceutical company in the respiratory field. He holds a worldwide patent (WO 92/04066) for a spacer for dry-powder inhalation. The patent was never commercialised and will expire in 2006; he had to file such a patent as a condition of his employment. SS has served as a consultant and member of an advisory board for GSK, AstraZeneca, and Aventis for the past three years, and for Merck for the past two years. He has received research funds for clinical trial performance from AstraZeneca and Ross. He has no stock ownership or commercial royalties in any of these companies.

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