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Parental questionnaires provided reliable data on childhood asthma compared with national registers

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Abstract

Background: Much of our knowledge of childhood asthma comes from questionnaire-based studies. Our main aim was to assess the agreement between parentalreported data at 12 years of age and data from two national Swedish registers.

Methods: Data were obtained from the prospective, longitudinal, population-based Children of Western Sweden cohort, which focused on children born in 2003. The parents answered questionnaires at six months and one, four, eight and 12 years of age. Personal identity numbers linked 3634 children to the Swedish Prescribed Drug Register (SPDR) and the National Patient Register (NPR).

Results: At 12 years of age, there was substantial overall agreement between the asthma medication reported by the parents in the questionnaire and the SPDR for any asthma medication (94.8%, kappa 0.71) and maintenance treatment (95.3%, kappa 0.68). In contrast, the agreement between the outpatient asthma diagnoses in the NPR and the questionnaire-based asthma was 30.5% and it was 32.8% between the NPR and the dispensed asthma medication in the SPDR. Hospitalization was rare for obstructive diseases after early childhood, and 38.2% of the 12-year-old children only received a short-acting beta agonist, with no maintenance treatment.

Conclusion: There was good agreement between the questionnaire-based data on asthma medication and the national drug register, but the National Patient Register provided incomplete information on asthma diagnoses, probably because it did not include primary care diagnoses. The results show that well-constructed parental questionnaires can provide reliable data on childhood asthma.

KEYWORDS

agreement study, asthma, asthma medication use, childhood, diagnosis, healthcare register, hospitalization, medication, outpatient care, parental questionnaire

1 | INTRODUCTION

Asthma is one of the most common chronic diseases in childhood, and it is largely controlled with effective medication. Much of our knowledge on the prevalence of childhood asthma, the risk factors

and the natural course of the disease has come from epidemiologic questionnaire-based studies.

Our research group has been studying asthma, and the early risk factors for asthma, in a cohort of children born in 2003, were based on parental questionnaires. Some studies have reported

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good agreement between asthma questionnaires and health register data, 1,2,3 but others have questioned the validity of questionnaire-based results. 4,5 It can be argued that patient registers can provide information that questionnaires cannot and vice versa. However, it is also important to investigate disagreements between different types of data to understand their limitations and how they can complement each other.

National registers that provide information on drugs, healthcare visits and hospitalization are now available in, for example, the Nordic countries, ^{6,7,8} including Sweden. For example, the Swedish Prescribed Drug Register (SPDR) has provided population-based data on all prescribed drugs dispensed to the country's residents since 2005. ⁹ Sweden also has a National Patient Register (NPR), established in 1964, which contains information on all inpatient care in Sweden and some outpatient care visits. ¹⁰ It is possible to combine, and compare, questionnaire data gathered from a cohort and data from these national registers by using the Swedish personal identity numbers that are issued to all residents.

In a large prospective, longitudinal follow-up study, we have previously reported a prevalence of asthma medication of 8.7%, and current asthma of 6.4% at 12 years, based on parental questionnaire data. We now have new register-based asthma data from the SPDR and NPR in the same cohort, providing an opportunity to compare register data with questionnaire data in the same individuals over time.

The main aim of this study was to compare the question-naire-based asthma data we had gathered and the register-based data on dispensed asthma medication, hospitalization and outpatient visits. We focused on the results at 12 years of age. In addition, we wanted to explore how the information on asthma from the SPDR and the NPR might differ and therefore compare the register-based data on dispensed asthma medication from the SPDR with outpatient visits for asthma from the NPR. A second aim was to examine the pattern of dispensed asthma medication, hospitalizations and asthma outpatient visits during childhood.

2 | METHODS

2.1 | Participants and study population

Data were obtained from a prospective, longitudinal, population-based cohort study of children born in Sweden in 2003, the Children of Western Sweden cohort. The initial cohort was based on a randomly selected 50% sample of the children born in the region that year and 5654 of the 8176 families who were approached agreed to take part. Postal questionnaires were carried out when the cohort was six months and one, four, eight and 12 years of age. Details of the questionnaires, response rates and patient characteristics have previously been published. 11,12,13,14

A flow chart of participation and response rate in the study from infancy to 12 years of age is shown in Figure 1. Of the participants at eight years of age, 90% also took part at 12 years of age, 3637 of 4051.

Key message

Much of our knowledge of childhood asthma comes from questionnaire-based studies. This study showed good agreement between questionnaire-based data on asthma medication and the national drug register. We conclude that well-constructed parental questionnaires can provide reliable data on childhood asthma prevalence and asthma medication.

2.2 | Study design and data sources

We were able to confirm the personal identity numbers for 3634 of the 3637 children, and we requested their information from the SPDR and NPR. In Sweden, counties are obliged to report physician visits from included units to NPR and the coverage is high, almost 100% during the last years, steadily rising from 2005 when the coverage was around $70\%.^{10,15}$ The collection process regarding the SPDR data is automatic from the pharmacies and the coverage close to $100\%.^{16}$

The SPDR data contained information on dispensed medication, namely the Anatomical Therapeutic Chemical (ATC) codes, date, age and sex of the patient. The NPR contained information on the International Classification of Diseases, Tenth Revision (ICD-10) codes for both main diagnosis and secondary diagnosis for all inpatient care and some specialist outpatient visits. Primary care is not included in the NPR. The Swedish personal identity numbers made it possible to link the questionnaire data to data from the SPDR and NPR. The SPDR was created in 2005 when our cohort was two years old. We received data from the SPDR 2005-2016 covering age two until 13 years. We received data from the NPR 2003-2015 ranging from birth until 12 years of age.

2.3 Definitions used for the register-based data

The following definitions of asthma medication at 11-13 years of age were based on the SPDR and referred to at least one medication of the type specified, dispensed at 11-13 years of age. The medication was inhaled corticosteroids (ICS), long-acting beta-2 agonists (LABA), leukotriene receptor antagonists (LTRA) and short-acting beta-2 agonists (SABA). ICS treatment was covered by the ATC codes R03BA (ICS) or R03AK (ICS and LABA). Maintenance treatment was codes R03BA (ICS), R03DC03 (LTRA), R03AK (ICS and LABA) or R03AC12/13 (LABA). Any asthma medication was ATC codes R03AC02/03 (inhaled SABA), R03AC12/13 (LABA), R03BA (ICS), R03DC03 (LTRA) or R03AK (ICS and LABA). The time span of 11-13 years was chosen to include all children who were on asthma medication at age 12 years, and since there sometimes is more than one year between the prescription dates, we found it important to use a wider time span.

Three definitions were based on the NPR. Obstructive bronchitis/bronchiolitis was at least one inpatient ICD-10 code of J20 or J21.

Recruitment 6 mo Invited = 8176 Entered the study=5654 Participation 1 yr Participated 4987 (87%) Participation 4.5 yr Participated 4496 (79%) Participation 8 yr Participated 4051 (72%) Participation 12 yr Participated 3637 (64%)

FIGURE 1 A flow chart of participation and response rate in the study from infancy to 12 y of age

Asthma was at least one inpatient main diagnosis or outpatient (main or secondary) diagnosis of ICD-10 code of J45. Obstructive disease was at least one inpatient ICD-10 code of J20, J21 or J45. We chose a time span of the first two years of life regarding the NPR inpatient data to include relevant inpatient data suggestive of an asthma diagnosis in early life.

The time span of 11-12 years regarding the NPR outpatient data was chosen to include all children who were to be found with asthma at 12 years, and since there sometimes is more than one year between the physician visits, we found it important to use a wider time span.

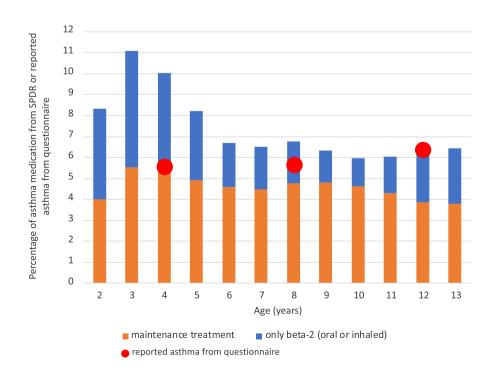
2.4 | Definitions used for the questionnairebased data

At one year of age, any wheeze was any parent-reported wheeze during the first year of life and recurrent wheeze was at least three episodes. Doctor-diagnosed asthma was defined as parental-reported, doctor-diagnosed asthma during the first year. In Figures 2, 4 and 5, asthma at one and four years of age was defined as recurrent wheeze with at least three episodes during the last year. At 12 years of age, current asthma was defined as parental-reported, ever doctor-diagnosed asthma and either current asthma medication or current symptoms during the last 12 months. Asthma medication was defined as any reported asthma maintenance treatment or inhaled SABA. Asthma maintenance treatment was defined as reported treatment with ICS and/or LABA and/or LTRA. The questions used to generate these data are shown in Appendix S1.

2.5 | Statistical analysis

The chi-square test and chi-square for trend were used to compare the prevalence of asthma/asthma medication from questionnaire with the corresponding variables from SPDR and NPR.

FIGURE 2 Dispensed asthma medication from 2 to 13 y of age for the 3634 children covered by the responses to the 12-year questionnaire. Data on maintenance treatment or just beta-2 agonists were retrieved from the Swedish drug register. Maintenance treatment was dispensed inhaled corticosteroids, leukotriene receptor antagonists or long-acting beta agonists. Beta-2 only means dispensed treatment with a beta-2 agonist, but no other asthma medication. The red dots show the percentage of questionnaires that reported asthma at four, eight and 12 y of age



Questionnaire	Register	Overall agreement	Kappa statistics (95% CI)	Strength of agreement
Any asthma medication	Any asthma medication	94.8%	0.71 (0.67-0.75)	Substantial
Any asthma medication	Maintenance treatment	95.3%	0.68 (0.64-0.72)	Substantial
Current asthma	Maintenance treatment	96.0%	0.68 (0.63-0.73)	Substantial

TABLE 1 Agreement at 12 y of age between the questionnaire data and the drug register data

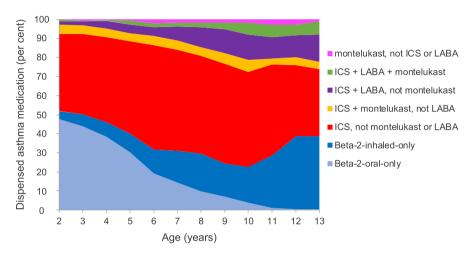


FIGURE 3 The changing pattern of asthma medication from 2 to 13 y of age, based on the various kinds of dispensed asthma medication to the children in the 12-year-old cohort, according to the Swedish drug register. The y-axis (percentage) represents the medication dispensed at each age. The total number of children who received medication was as follows: age 2 y, 303; age 3, 403; age 4, 364; age 5, 298; age 6, 243; age 7, 236; age 8, 246; age 9, 229; age 10, 217; age 11, 219; age 12, 223; and age 13, 234. ICS is inhaled corticosteroids, LTRA is leukotriene receptor antagonists, LABA is long-acting beta agonists, and beta-2 is dispensed treatment with a beta-2 agonist and no other asthma medication

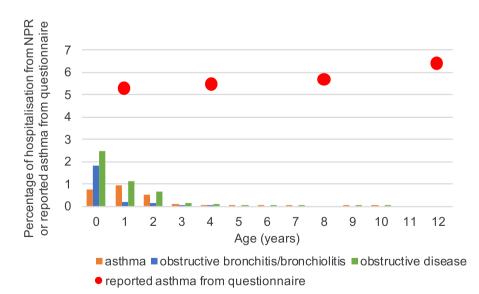


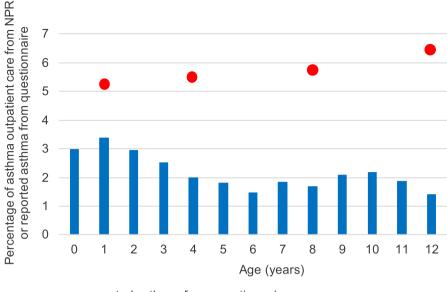
FIGURE 4 Register-based inpatient care for obstructive disease. It shows the percentage of the 3634 children in the National Patient Register who received inpatient treatment for the main ICD-10 diagnoses of bronchitis/bronchiolitis (J20, J21), asthma (J45) and obstructive disease (J20, J21, J45) for each year from 0 to 12 y of age. The red dots show the percentage of questionnaire-reported asthma at one, four, eight and 12 y

The agreement between the questionnaire data and the SPDR data was calculated using Cohen's kappa with 95% confidence intervals (95% CIs). Cohen's kappa measures agreement beyond what would be expected by pure randomness. The calculations were unprejudiced, which means that neither the register data nor the questionnaire data were considered the gold standard. Cohen's

kappa was calculated using the formula kappa = $(P_o - P_e) / (1 - P_e)$, where P_o was the relative observed agreement among the raters, and P_e was the hypothetical probability of chance agreement. A kappa value of more than 0.8 was characterized as almost perfect agreement, 0.61 to 0.80 was considered substantial agreement, 0.41-0.60 was considered moderate agreement, 0.21-0.40 was

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FIGURE 5 Register-based outpatient care for asthma. It shows the percentage of 3634 children in the National Patient Register who received a main or secondary ICD-10 diagnosis of asthma (J45) for each year from 0 to 12 y of age. The red dots show the percentage of questionnaire-reported asthma at one, four, eight and 12 y



- reported asthma, from questionnaire
- asthma outpatient care, from register

considered fair agreement, and 0.01-0.2 was considered slight agreement.

IBM SPSS Statistics version 23.0 (IBM Corp, Armonk, NY, USA) was used for the statistical calculations.

2.6 | Ethical approval

The study was approved by the Ethics Committee of the University of Gothenburg (diary number 846-14). The postal questionnaires included a thorough description letter on the study rational approved by the ethical committee where it was clearly stated that by completing the questionnaire and responding, they gave their informed consent to be included in the study.

3 | RESULTS

Case numbers and prevalence of each relevant variable from questionnaire, SPDR and NPR at 1 year and 4, 8 and 12 years can be seen in Appendix S2.

3.1 | Comparison between the SPDR and the questionnaire

According to the SPDR, 262 of 3634 (7.2%) were dispensed any asthma medication at 11-13 years of age.

As shown in Table 1, the overall agreement (according to the criteria established by Landis and Koch) ¹⁸ was substantial for questionnaire-based data on asthma medication and SPDR data on any asthma medication and for maintenance treatment.

Of the 233 children with reported current asthma at 12 years of age, 213 (91.4%) were dispensed any asthma medication at 11-13 years of age, according to the SPDR data.

The overall agreement was substantial for current asthma from the questionnaire and SPDR data on maintenance treatment (Table 1).

3.2 | Pattern of dispensed asthma medication in the SPDR

According to the SPDR data, 1085 of 3634 (29.9%) cohort received asthma medication at least once between 2 and 13 years of age. The changing pattern of asthma medication during childhood is shown in Figures 2 and 3. SABA as the only dispensed asthma medication was found in a large proportion of younger children before decreasing. However, after 10 years of age we noticed an increase regarding SABA as the only dispensed asthma medication, 100 of 262 (38.2%) children in our study who were dispensed asthma medication at 11-13 years of age received inhaled SABA only. Having ICS as the only maintenance asthma treatment remained rather stable during childhood. At 11-13 years of age, 98 of 262 (37.4%) children who were dispensed asthma medication received ICS as maintenance treatment and an additional 45 of 262 (17.2%) received a combination of ICS and LABA. LABA was never dispensed as a single treatment (Figure 3).

3.3 | Patterns of inpatient care in the NPR and comparison between inpatient care in the NPR and the questionnaire

Hospitalization due to asthma or other obstructive diseases was most frequent during the first year of life and very rare after the age of two years. Inpatient treatment for obstructive disease according to data from the NPR from age 0 to 12 years is shown in Figure 4.

According to the NPR, 123 of 3634 (3.4%) children in our study received inpatient treatment due to obstructive diseases during the first two years of life. Out of the 123 children, we had relevant questionnaire data from 112 in the one-year questionnaire. Of these, 83 of 112 (74.1%) had reported any wheeze, 36 of 112 (32.1%) recurrent wheeze and 25 of 112 (22.3%) doctor-diagnosed asthma in the questionnaire at one year of age (*P* for trend < .01).

In the questionnaire, 661 children were reported with any wheeze, 173 with recurrent wheeze and 69 with doctor-diagnosed asthma at one year of age. Of the children with reported any wheeze, 83 of 661 (12.6%) received inpatient treatment due to obstructive disease during the first two years of life according to the NPR. In comparison, 36 of 173 (20.8%) children with recurrent wheeze at one year of age and 25 of 69 (36.2%) children with doctor-diagnosed asthma received inpatient treatment during the first two years of life according to the NPR (P for trend < .01).

When the children were 12 years old, the parents of six children reported that they had been hospitalized for asthma, but that was not confirmed by the NPR data.

3.4 | Pattern of outpatient care in the NPR and comparisons between outpatient care in the NPR and the questionnaire

Outpatient care visits due to asthma recorded in NPR peaked during the first three years of life. Thereafter, the numbers decreased and remained at a lower level up to 12 years of age (Figure 5).

At 11-12 years, 91 of 3634 (2.5%) children received an outpatient asthma diagnosis in the NPR. This can be compared with data from the SPDR, 262 of 3634 (7.2%) were dispensed with any asthma medication at the age of 11-13 years. Of the 91 children who received an outpatient diagnosis of asthma in the NPR, 71 (78%) were also identified in the questionnaire as having current asthma. In addition, 86 of 91 (94.5%) children identified in the NPR were dispensed with any asthma medication at the age of 11-13 years, according to SPDR.

The NPR included outpatient diagnoses for 71 of 233 (30.5%) children with current asthma in the questionnaire at 12 years of age and 86 of 262 (32.8%) children dispensed with any asthma medication at 11-13 years of age according to the SPDR.

4 | DISCUSSION

The main finding of this study was the good agreement between the questionnaire data that was provided by the parents when their children were 12 years old and the data obtained on asthma medication from the national Swedish drug register. In contrast, the National Patient Register, which does not include primary care data, was incomplete with regard to asthma diagnoses. As expected, hospitalizations for obstructive disease were very rare after early childhood.

Studies based on questionnaires are often low cost and time-efficient, and they can allow much larger samples than clinical data collections. However, the validity of questionnaire-based results has been questioned. The good agreement that we found between our questionnaire-based data and the asthma drug register data suggests that our questionnaire data were reliable when it came to estimating asthma prevalence and asthma medication. Besults from previous studies support this conclusion. Based on our results, we can argue that parental reports of asthma medication and diagnosis have high validity with regard to agreement with register-based dispensed asthma medication. However, parents may struggle to remember the names or types of asthma medication and the register-based data therefore complement the questionnaires.

Our study confirmed that hospitalization due to asthma or other obstructive diseases mostly occurred during the first years of life and was uncommon after that. During the first year of life, hospitalization for obstructive bronchitis or bronchiolitis dominated. Thereafter, the diagnosis of asthma became more common (Figure 4). This pattern of asthma hospitalization during childhood has been shown in previous studies, which suggests that the register-based data on inpatient care for asthma in the NPR had good validity. ^{19,20}

However, the outpatient data in the NPR did not reflect the prevalence of asthma that we saw in the SPDR dispensing data or the questionnaires that were completed by parents. At 12 years of age, parents reported that current asthma was 6.4% in the questionnaires, and according to the SPDR, 7.2% received asthma medication at 11-13 years of age. These data were in line with national and international studies of asthma prevalence at 12 years of age, which reported that the prevalence was around 8%-10%. 21,22,23 The corresponding prevalence of asthma in the outpatient NPR was as low as 2.5%, which indicated that a lot of asthmatic children were missing in that section of the register. The reason for the discrepancy was probably that many asthmatic children are cared for in primary care in Sweden. Because primary care is not covered in the outpatient NPR, these children are not recorded. It is important to be aware of this lack of data in the NPR. Our findings show that the NPR cannot be regarded as a population-based register for asthma outpatient care and that outpatient data on asthma must be treated with caution.

Our study also examined the pattern of dispensed asthma medication during childhood. As expected, the vast majority of younger children received either just SABA as controller treatment or a combination of SABA and ICS or LTRA as maintenance treatment. Most of the children received maintenance treatment with ICS, which is the recommended treatment in Sweden, and not LTRA, which is normally used as an alternative.²⁴ This result was in line with other studies.²⁵

Maintenance treatment with ICS or LTRA, combined with LABA, became more common with increasing age in our cohort,

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and this was in line with other studies.²⁶ Despite this, we found that 38.2% of our cohort only received SABA at 11-13 years of age and this suggests that clinicians were under prescribing maintenance treatment to this age group.

4.1 | Strengths and limitations

The strengths of this prospective follow-up study included the large size of the birth cohort, the high response rate at 12 years of age and the fact that we combined questionnaire data with data from the national Swedish drug register. The questionnaires were based on validated, well-known questions that were used by two major paediatric studies, the International Study of Asthma and Allergies in Childhood (ISAAC) ²⁷ and the Children Allergy Milieu Stockholm Epidemiology (BAMSE) study. ²⁸

The limitations were that we do not know to what extent the collected medication was taken. However, this did not pose any problems when we focused on the agreement between the questionnaire and register data. There were also some content and age mismatches between the data in the registers and our questionnaire data. The SPDR was only established two years into our study, in 2005.

In conclusion, we found good agreement between our questionnaire data and drug register data, suggesting that using our questionnaire data was a reliable way of estimating asthma prevalence and asthma medication. However, the national outpatient register was incomplete, possibly because the data on children treated by primary care practitioners were not covered by the register. The fact that well-constructed parental questionnaires on asthma provide reliable results is good news for countries that do not record asthma medication and prevalence on a country-wide basis.

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CONFLICT OF INTEREST

The authors have no conflicts of interests to declare.

AUTHOR CONTRIBUTION

Frida Strömberg Celind: Formal analysis (lead); Methodology (equal); Project administration (equal); Writing-original draft (lead); Writing-review & editing (equal). Styliana Vasileiadou: Formal analysis (supporting); Writing-review & editing (supporting). Emma Goksör: Formal analysis (supporting); Funding acquisition (lead); Methodology (equal); Project administration (equal); Supervision (lead); Writing-original draft (supporting); Writing-review & editing (equal).

PEER REVIEW

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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