# Sleep in Children with Asthma: Results of the PIAMA Study

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### Abstract

Children with asthma are thought to have impaired sleep quality and quantity. In this study we investigated which of many sleep aspects are associated with asthma.

The sample consisted of 2529 children (11 years) who participated in the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. Parents reported about asthma symptoms (wheezing, dyspnea, prescription of inhaled corticosteroids, asthma diagnosis) and children reported about different aspects of sleep (bedtime, rise time, sleep quality, daytime sleepiness/tiredness). Results were analysed with (logistic) regression analysis.

Children with frequent asthma symptoms significantly more often reported that they felt sleepy or tired during the day (34.4% experienced daytime sleepiness/tiredness at least once a week) than children without asthma symptoms (22.2%), and children with infrequent asthma symptoms (21.9%). This association was not confounded by gender, age of the child, parental educational level, or smoking inside the house; nor was the effect modified by gender. There were no associations between asthma and bedtime, time spent in bed or sleep quality.

Children with frequent asthma symptoms more often experienced daytime sleepiness/tiredness than children with infrequent or no asthma symptoms. Children with asthma did otherwise not differ much from children without asthma with regard to sleep.

Keywords: childhood asthma, daytime sleepiness/tiredness, dyspnea, wheezing

## Introduction

Asthma is a chronic inflammatory airway disease and is considered the most prevalent chronic respiratory disorder in childhood [1]. Asthma seems a risk factor for disturbed sleep: asthma symptoms often worsen at night [2] and can cause sleep disruptions [1]. Sleep problems in turn have negative consequences for health [3], behaviour [4], cognitive functioning and school performance [5, 6]. Since children with asthma generally show more behavioural problems than children without asthma [7] it is important to gain more insight into sleep in childhood asthma.

Research on sleep in children with asthma has yielded contradictory results. On the one hand, several studies have shown that children with asthma more often wake up in the night [1, 8-11] and have worse sleep quality than healthy children [1, 8-10, 12]. On the other hand, some other studies did not find that children with asthma have lower sleep quality or more disrupted sleep [13, 14]. Asthma does not seem to influence sleep latency or sleep duration [8-10, 12, 14]. However, asthma appears consistently related to sleepiness or tiredness in children [1, 8, 9, 12, 15]. This may have important bearings on daytime activities and cognitive performance and hence school achievements [16].

In addition, it was found that *persistent* wheezing [17], more *severe* asthma [12, 16, 18] and *uncontrolled* asthma [19] associate with worse sleep. These findings may partly explain the contradictory results described above. It is possible that well-controlled asthma does not affect sleep, but sleep is negatively affected in case of more serious symptoms or uncontrolled asthma. As most studies only investigated one or a few sleep aspects (most often nighttime awakenings) and used different definitions of asthma, it is difficult to draw firm conclusions about whether asthma affects sleep.

In the present study we investigated sleep in different groups of children with asthma, based on the frequency of their symptoms. To investigate the most essential aspects of sleep, we examined bedtime, a prominent feature of sleep in children. Secondly, we investigated time spent in bed as indicator of sleep duration and sleep latency, frequency of nocturnal awakenings, sleep latency after nocturnal awakenings and feeling fit at rise time as indicators of sleep quality. Sleep duration and sleep quality are considered two different sleep domains [20]. Finally, we assessed daytime sleepiness/tiredness as one of the consequences of insufficient sleep duration and/or unsatisfying sleep quality. By using these different asthma phenotypes and investigating several sleep aspects in the same individuals, we aim to clarify the contradictory results that are found in the literature on the relation between childhood asthma and sleep.

The research questions we aim to answer are the following: (1) Are there differences in sleep between children with and without asthma? (2) Are there differences in sleep between children with frequent and infrequent asthma symptoms?

### Method

# Study design and study population

The study population consisted of children born in 1996–1997 who participated in the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study. A detailed description of the study design has previously been published [21]. Briefly, pregnant women were recruited from the general population by means of a validated screening questionnaire on maternal allergy [22], distributed to the women when visiting a prenatal clinic in the Netherlands. On the basis of this screening, 7862 women (2779 allergic mothers and 5083 non-allergic mothers) were invited to participate in the study. Approximately 50% of the invited pregnant women (n=4146) agreed for participation. In case of multiple births, only one of the children was included in the study. After birth, the baseline study population consisted of 3963 children. Questionnaires were sent to the participating parents during pregnancy, at 3 months, yearly from age 1 to 8 years, and at 11 years of age, around the child's birthday. At the age of 11, questionnaires were also completed by the children themselves. The present study reports about the 11-year questionnaires completed by parents and children and includes data on 2529 children for whom data on both asthma and sleep were available.

The study protocol was approved by the medical ethics committees of the participating research institutes, and all parents gave written informed consent.

### Measures

*Asthma*. In all questionnaires from age 1 onwards, the parents were asked to report whether the child had an episode of wheezing, an episode of dyspnea, or a prescription of inhaled corticosteroids for respiratory or lung problems in the last 12 months. In addition, parents were asked about the frequencies in which attacks of wheezing or dyspnea occurred. Additional questions were whether the child was ever diagnosed with asthma by a doctor and whether the child had asthma in the previous 12 months. Based on these questions, the following variables were defined and used in the present study:

*Asthma symptoms*: parents reported that their child had one or more attacks of wheezing and/or one or more attacks of dyspnea and/or a prescription of inhaled corticosteroids for respiratory or lung problems by a medical doctor in the last 12 months. If parents reported no wheeze, no dyspnea and no prescription of inhaled corticosteroids the child was defined as having no asthma symptoms. The group of children with asthma symptoms can be divided into children with frequent asthma symptoms and children with infrequent asthma symptoms:

*Frequent asthma symptoms*: parents reported that their child had 4 or more attacks of wheezing and/or 4 or more attacks of dyspnea in the last 12 months.

*Infrequent asthma symptoms*: parental report of asthma symptoms, but no frequent symptoms reported.

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*Diagnosed asthma*: if parents reported that their child was ever diagnosed with asthma by a doctor and reported that their child had asthma in the last 12 months.

*Sleep.* Children reported on bedtimes and rise times at both school and non-school days; sleep latency (how long it takes to fall asleep after lights off), frequency of nocturnal awakenings, sleep latency after nocturnal awakenings, feeling fit at rise time (measures of sleep quality); and daytime sleepiness/tiredness ("Do you feel tired or sleepy during the day?"). Based on children's report of their bedtimes and rise times their time spent in bed was calculated.

*Confounding factors.* The following variables were tested for possible confounding influences: gender of the child, age of the child (exact age at the time that the questionnaire was completed), educational level of parents (highest attained educational level for mother and father separately), and smoking inside the house. The last two variables were considered indicators of life style that might affect asthma and sleep [23-26].

# Statistical analysis

Analyses were conducted with SPSS (version 17). To investigate the associations between asthma and sleep, regression analyses were conducted with the different sleep items as dependent variables and binary indicators of asthma symptoms, frequent asthma symptoms, or diagnosed asthma (defined according to the descriptions above) as independent variables. For the dependent variable with two response categories (feeling fit at rise time) logistic regression analyses was used, for dependent variables with three and five response categories (sleep latency, frequency of nocturnal awakenings, sleep latency after nocturnal awakenings, daytime sleepiness/tiredness) ordinal regression analyses were conducted, and for the dependent variables with nine (bedtimes) or more (time spent in bed) response categories regular linear regression analyses were conducted.

The influence of possible confounding variables was investigated by adding these as a covariate to the regression models. If after addition of the covariate the regression coefficient of asthma changed with 10% or more for several of the sleep outcomes, the covariate was considered a confounder.

To investigate whether the association between asthma and sleep differed for boys and girls, interaction effects between gender and asthma on the different sleep characteristics were examined. A significant interaction effect would indicate that the relation between asthma and sleep was modified by gender (i.e., the relation between asthma and sleep is different for boys and girls).

### Results

At 11 years of age, 116 children (4.6%) wheezed in the last year, 243 children (9.6%) had dyspnea, and 169 children (6.7%) had a prescription of inhaled corticosteroids. There were 317 children (12.6%) with asthma symptoms, of which 97 (3.9%) had frequent symptoms and 220 (8.7%) had infrequent symptoms.100 children (4.0%) had diagnosed asthma (see Table 1).

# (Table 1 here)

# Differences in sleep between children with and without asthma

The mean time at which children went to bed and the mean time they spent in bed (difference between rise time and the time the lights were turned off) were not significantly different for children with asthma symptoms, children with frequent asthma symptoms (both compared to children without symptoms), or children with diagnosed asthma (compared to children who do not meet the criteria for diagnosed asthma). When examining the results for daytime sleepiness/tiredness and sleep quality, a significant association was found only between children with frequent asthma symptoms and without symptoms on daytime sleepiness/tiredness. Children with frequent asthma symptoms significantly more often reported that they felt sleepy or tired during the day than children without asthma symptoms (see Table 2). There was a trend in the same direction for children with asthma symptoms (frequent and infrequent symptoms taken together) and children with diagnosed asthma. Children with asthma symptoms more often felt sleepy or tired during the day than children without asthma symptoms (of the children with asthma symptoms 25.7% experienced daytime sleepiness/tiredness at least once a week versus 22.2% of children without symptoms). Children with diagnosed asthma more often indicated that they felt sleepy or tired during the day when compared to children who do not meet the criteria for diagnosed asthma (30.0% versus 22.4% of children in the respective groups experienced daytime sleepiness/tiredness at least once a week), yet these associations did not reach significance (p = 0.06 and p = 0.11, data not shown). Only results of the analysis comparing children with frequent asthma symptoms and children without symptoms are reported in the table.

Addition of gender, age of the child, educational levels of parents, and smoking inside the house as covariates to the regression models changed the effect estimates for the associations with several of the sleep characteristics, but had little influence on the association between frequent asthma symptoms and daytime sleepiness/tiredness. In Table 2 the results of both the crude and the adjusted analyses are shown. Next, we investigated interaction effects between asthma and gender to determine whether the associations between asthma and sleep differed for boys and girls. As no significant interaction effects were found, it appears that the relation between asthma and sleep is not modified by gender.

# Differences in sleep between children with frequent and infrequent asthma symptoms

Ordinal regression analysis showed a significant effect on daytime sleepiness/tiredness when comparing children with frequent and with infrequent asthma symptoms (Table 2). Children with frequent asthma symptoms significantly more often reported to feel sleepy or tired during the day than children with infrequent asthma symptoms. There were no significant associations between frequent asthma symptoms as compared to infrequent asthma symptoms and other sleep outcomes.

### (Table 2 here)

#### Discussion

Children with frequent asthma symptoms experienced more daytime sleepiness/tiredness than children without asthma symptoms and children with infrequent asthma symptoms. This association was not confounded by gender, age, educational level of parents, or smoking inside the house, and was not modified by gender. There were no associations between asthma and bedtime, time spent in bed or sleep quality.

Nocturnal awakening frequently occurs in asthma [1, 8-11, 16]. However, no effect of asthma on nocturnal awakenings was found in our study. We did find that 46.9% of the children with frequent asthma symptoms sometimes had nocturnal awakenings and 5.2% (almost) always experienced awakenings during the night. However, our results showed that nocturnal awakenings also occurred in children without asthma symptoms and the difference between these groups was not statistically significant. It might be that the question on nocturnal awakenings was not sensitive enough to find an effect, as children could only choose from three response categories ((almost) never, sometimes, (almost) every night).

Since we did not find differences on any of the other sleep variables, we cannot give a straightforward interpretation for the finding of increased daytime sleepiness/tiredness in children with frequent asthma symptoms compared to children with infrequent or without asthma symptoms. However, it could be that children with frequent asthma symptoms are more sleepy or tired during the day, partly because they have worse sleep quality (they do have lower scores on most indicators of sleep quality, although not significantly worse), and partly because normal daytime activities are more tiring for them due to their asthma

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complaints. In addition, children with frequent asthma symptoms might become more sleepy or tired during the day than other children not only because of their asthma complaints, but also because of possible emotional/behavioural problems, which are more pronounced in children with asthma [7].

We found significant associations between asthma and sleep only to be present in children with frequent asthma symptoms. This result is in accordance with earlier studies that also found a relation between severity of asthma and the extent to which sleep was impaired [12, 16-19]. This indicates that only when asthma is not well controlled, an impact on sleep is evident.

A possible explanation for the fact that we did not find associations between diagnosed asthma and any of the sleep characteristics could be that 77.0% of the children with diagnosed asthma had a prescription of inhaled corticosteroids, which has likely reduced nocturnal symptoms [27, 28]. Almost half (48%) of the children with diagnosed asthma only had infrequent symptoms. Although also 56.7% of all children with frequent asthma symptoms had a prescription of inhaled corticosteroids, still *all* children in this group had 4 or more attacks of dyspnea and/or 4 or more attacks of wheezing in the last 12 months. Thus, this group does not include children who are symptom free because of their treatment. That only about half of the children in the group with diagnosed asthma had frequent symptoms is likely to be the result of adequate treatment and may also explain why we observed no associations between diagnosed asthma and sleep.

In our study parents reported about asthma symptoms and children reported about their sleep. We used questionnaires to measure sleep, which enabled us to assess a wide range of different aspects of sleep, including factors like 'feeling fit at rise time' and 'daytime sleepiness/tiredness'. On the other hand, we cannot exclude the possibility that self-report may have resulted in some misclassification of for example sleep duration. Use of objective

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measures (e.g., actigraphy) in addition to subjective measures might have been useful to support the findings. However, although actigraphy data are reported to be reliable and valid, they appear to have a low specificity in detecting wakefulness within sleep periods [29]. Although it is suggested that parents might underestimate sleep problems of their children [30], there are studies that did find relationships between asthma and sleep using parent report (e.g., [8]). Therefore, it would be advisable to include parental and child report about sleep in one study, to enable comparison of results.

Our study contributes to the field as it offers a careful consideration on the association between asthma (using different phenotypes) and important sleep characteristics in a large sample of children. The results of this study provide support for the idea described in the introduction that the severity or frequency of symptoms is an important factor influencing the relation between asthma and sleep.

# Conclusion

Our study found a difference in daytime sleepiness/tiredness between children with frequent asthma symptoms and children with infrequent symptoms or without symptoms. No differences on bedtime, time spent in bed or sleep quality were found. It can be concluded that children with asthma do not differ much from children without asthma with regard to sleep. However, we recommend physicians to pay attention to sleep in children with frequent asthma symptoms, considering the negative effects of daytime sleepiness/tiredness on behaviour, mood, cognitive functioning and school achievements of these children [3-6].

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| General characteristics                                   | M (SD)            |
|---|-------------------|
| Age (years)   | 11.4 (0.3)        |
|   | N (%)             |
| Boys  | 1286 (50.9)       |
| Asthma symptoms   | 317 (12.6)        |
| Frequent asthma symptoms                                  | 97 (3.9)          |
| Infrequent asthma symptoms                                | 220 (8.7)         |
| Diagnosed asthma (including asthma in previous 12 months) | 100 (4.0)         |
| No asthma symptoms  | 2202 (87.4)       |
| Specific aspects of asthma                                | N (%)             |
| Wheezing (in last year)                                   | 116 (4.6)         |
| Dyspnea (in last year)                                    | 243 (9.6)         |
| Corticosteroids   | 169 (6.7)         |
| Ever diagnosed with asthma                                | 288 (11.4)        |
| Sleep   | M (SD)            |
| Bedtime school day (hh:mm)                                | 20:43 (27.4 min.) |
| Bedtime not school day (hh:mm)                            | 21:41 (39.7 min.) |
| Time in bed school day (hh:mm)                            | 10:06 (39.2 min.) |
| Time in bed non-school day (hh:mm)                        | 11:23 (55.0 min.) |
| Sleep latency   | N (%)             |
| Fall asleep immediately                                   | 619 (24.5)        |
| Stay awake for a while                                    | 1509 (59.8)       |
| Takes a long time to fall asleep                          | 394 (15.6)        |
| Nocturnal awakenings                                      |                   |
| (Almost) never  | 1324 (52.5)       |
| Sometimes   | 1090 (43.2)       |
| (Almost) every night                                      | 110 (4.4)         |
| Sleep latency after nocturnal awakenings                  |                   |
| Mostly fall asleep immediately                            | 615 (51.3)        |
| Mostly awake for a while                                  | 488 (40.7)        |
| Mostly takes a long time to fall asleep                   | 96 (8.0)          |
| Feeling fit at rise time school day                       |                   |
| Yes   | 2061 (82.0)       |
| No  | 452 (18.0)        |
| Daytime sleepiness/tiredness                              |                   |
| (Almost) never  | 1069 (42.4)       |
| < 1/week  | 880 (34.9)        |
| $\pm 1/week$  | 282 (11.2)        |
| $\pm 2$ /week   | 165 (6.5)         |
| > 3/week  | 124 (4 9)         |

Table 1 Description of the study population (N = 2529)

| -symptoms)                               |              |             |                 |               |               |          |
|--|--------------|-------------|-----------------|---------------|---------------|----------|
|  | No asthma    | Infrequent  | Frequent asthma | β (95% CI)    | β (95% CI)    | $p^{**}$ |
|  | Symptoms     | asthma      | symptoms        |               | (confounders  |          |
|  | (N = 2202)   | symptoms    | (N = 97)        |               | included)     |          |
|  |              | (N = 220)   |                 |               |               |          |
| Bedtime school days hh:mm (sd)           | 20:44        | 20:42       | 20:42           | -1.22         | -1.60         | 0.57     |
|  | (27.4 min.)  | (27.3 min.) | (27.7 min.)     | (-6.80;4.36)  | (-7.13;3.92)  |          |
| Bedtime non-school days hh:mm (sd)       | 21:42        | 21:39       | 21:40           | -1.34         | -0.81         | 0.84     |
|  | (39.8 min.)  | (37.0 min.) | (44.0 min.)     | (-9.53;6.84)  | (-8.88;7.26)  |          |
| Time in bed school days hh:mm (sd)       | 10:06        | 10:03       | 10:08           | 1.20          | 2.27          | 0.57     |
|  | (38.9 min.)  | (45.0 min.) | (33.1 min.)     | (-6.66;9.06)  | (-5.54;10.07) |          |
| Time in bed non-school days hh:mm (sd)   | 11:23        | 11:17       | 11:29           | 6.16          | 8.64          | 0.12     |
|  | (55.1 min.)  | (54.9 min.) | (54.5 min.)     | (-5.04;17.36) | (-2.28;19.56) |          |
| Sleep latency                            |              |             |                 |               |               |          |
| Fall asleep immediately                  | 540 (24.6%)  | 58 (26.5%)  | 20 (20.6%)      | 0.26          | 0.28          | 0.18     |
| Stay awake for a while                   | 1318 (60.0%) | 127 (58.0%) | 58 (59.8%)      | (-0.15;0.66)  | (-0.13;0.68)  |          |
| Takes a long time to fall asleep         | 338 (15.4%)  | 34 (15.5%)  | 19 (19.6%)      |               |               |          |
| Nocturnal awakenings                     |              |             |                 |               |               |          |
| (Almost) never                           | 1168 (53.1%) | 105 (47.9%) | 46 (47.9%)      | 0.21          | 0.25          | 0.23     |
| Sometimes                                | 940 (42.7%)  | 101 (46.1%) | 45 (46.9%)      | (-0.19;0.61)  | (-0.15;0.65)  |          |
| (Almost) every night                     | 91 (4.1%)    | 13 (5.9%)   | 5 (5.2%)        |               |               |          |
| Sleep latency after nocturnal awakenings |              |             |                 |               |               |          |
| Mostly fall asleep immediately           | 536 (52.0%)  | 56 (49.1%)  | 21 (42.0%)      | 0.35          | 0.35          | 0.21     |
| Mostly awake for a while                 | 416 (40.4%)  | 45 (39.5%)  | 25 (50.0%)      | (-0.20;0.89)  | (-0.20;0.90)  |          |
| Mostly takes a long time to fall asleep  | 78 (7.6%)    | 13 (11.4%)  | 4 (8.0%)        |               |               |          |
| Feeling fit at rise time school day      |              |             |                 |               |               |          |
| Yes                                      | 1803 (82.3%) | 171 (78.1%) | 78 (83.0%)      | 1.05*         | 1.00*         | > 0.99   |
| No                                       | 387 (17.7%)  | 48 (21.9%)  | 16 (17.0%)      | (0.60; 1.81)  | (0.58; 1.73)  |          |
| Daytime sleepiness/tiredness             |              |             |                 |               |               |          |
| (Almost) never                           | 943 (43.0%)  | 92 (42.0%)  | 28 (29.2%)      | 0.58          | 0.63          | < 0.01   |
| < 1/week                                 | 764 (34.8%)  | 79 (36.1%)  | 35 (36.5%)      | (0.21; 0.95)  | (0.26; 1.00)  |          |
| $\pm 1/\text{week}$                      | 244 (11.1%)  | 20 (9.1%)   | 17 (17.7%)      |               |               |          |
| $\pm 2$ /week                            | 140 (6.4%)   | 16 (7.3%)   | 9 (9.4%)        |               |               |          |
| $\geq$ 3/week                            | 104 (4.7%)   | 12 (5.5%)   | 7 (7.3%)        |               |               |          |

Table 2 Effects of asthma on sleep characteristics (regression coefficients are shown for children with frequent asthma symptoms compared to children without asthma symptoms)

For sleep latency, nocturnal awakenings, sleep latency after nocturnal awakenings, and daytime sleepiness/tiredness the results of ordinal regression analyses are reported.  $\beta$ =unstandardized regression coefficient; 95% CI = 95% Confidence Interval. \*The odds ratio is reported here. \*\**p* reported for the models with inclusion of the confounders.