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Original Article

Potential determinants during ‘the first 1000 days of life’ of sleep problems in school-aged children

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A B S T R A C T

Study objectives: Early life determinants of sleep problems are mostly unknown. The first 1000 days of life (ie, the time between conception and a child's second birthday) is a period where the foundations for optimum health, growth and neurodevelopment are established. The aim of this explorative study is to identify potential early life determinants of sleep problems at age 7–8 years.
Methods: Data from the Amsterdam Born Children and their Development cohort study ($n = 2746$) were analyzed. Sleep problems at age 7–8 years were reported by the caregiver in the ‘Child Sleep Habits Questionnaire’. A higher total score indicates more sleep problems. After multiple imputation ($n = 20$), we studied multivariable associations between all potential determinants and sleep problems using regression analysis.
Results: A higher pre-pregnancy body mass index (BMI) was associated with more sleep problems at age 7–8 years [β 0.12 (95% CI 0.05, 0.18)]. Children of mothers with symptoms of anxiety during pregnancy [β 0.06 (95% CI 0.03, 0.09)] and infancy period [β 0.04 (95% CI 0.00, 0.07)] had more sleep problems. Children of mothers drinking ≥1 glass of alcohol a day around 14 weeks of gestation had a 2 points higher sleep problem score [β 2.55 (95% CI 0.21, 4.89)] and children of mothers smoking ≥1 cigarette per day in that period had a one point higher score [β 1.07 (95% CI 0.10, 2.03)]. Infants with relative weight loss (delta BMI-SD) had a higher sleep problem score during childhood [β −0.32 (95%CI -0.60, −0.04)].
Conclusions: We identified several potential determinants during pregnancy and infancy associated with childhood sleeping problems. We encourage further research into these and other potential determinants to replicate results and to identify underlying mechanisms.

1. Introduction

Sleep related problems are common among children, with prevalence rates reported up to 40% [1–7]. Childhood sleep problems are associated with negative physical, emotional, behavioral and cognitive outcomes during childhood and later life, such as an increased risk of obesity, more symptoms of anxiety and depression and lower IQ scores [8–12].

The first 1000 days of life (ie, the time between conception and a child's second birthday) is a period where the foundations for optimum health, growth and neurodevelopment are established [13,14]. During this period, neuronal and hormonal maturation play an important role in the development of normal sleep behavior and patterns [15–17]. Hormonal changes due to the environment of the fetus and infant might have long-term consequences on sleep during lifetime. Currently, few studies exist on the topic of early life origins of sleep problems. These studies observed an association between potential determinants within the first 1000 days and

Abbreviations: ABCD study, Amsterdam Born Children and their development study; CES-D, Center for Epidemiologic Studies Depression; STAI, State-Trait Anxiety Inventory; CSHQ, Child Sleep Habits Questionnaire; MFI, Multidimensional Fatigue Inventory.

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childhood sleep problems (eg, nicotine exposure during pregnancy; parental emotional availability; and gestational age) [18–23]. The most recent study by Fatima et al., found that girls had more trouble sleeping but less nightmares at age 14 years than boys. Nightmares were also associated with maternal smoking and poor dyadic adjustment during late pregnancy, premature birth and short or no breastfeeding [24]. Potential determinants, not specific for the first 1000 days, that have been associated with sleep problems in school-aged children are lifestyle and health determinants (eg, excessive screen use; difficult temperament; poor health; and affective disorders) [23,25–27].

The aim of this study was to investigate potential determinants during the first 1000 days that are associated with higher sleep problem scores in school-aged children within a large prospective cohort study: the Amsterdam Born Children and their development (ABCD) study. Hereby we aimed to replicate previously observed associations with sleep, but also explore whether factors, within the first 1000 days of life, that are associated with cognitive development are also associated with sleep in school-aged children [28,29]. This study will provide explorative information about potential determinants that could be used as focus areas for the development of effective strategies during the first 1000 days of life, to prevent sleep problems in later life.

2. Methods

2.1. Design and study population

The data was retrieved from the ABCD study (www.abcd-study.nl). This is a large multi-ethnic prospective cohort study in the city of Amsterdam, the Netherlands. The main goal of the ABCD study is to examine and determine factors in early life (during pregnancy and infancy) that might explain subsequent differences in children's health. In depth details of this study can be found elsewhere [30]. Between January 2003 and March 2004 all pregnant women living in Amsterdam were invited to participate in the ABCD study during their first antenatal visit to an obstetric caregiver. We only included children with complete information about sleep problems. Multiples, stillbirths and children with congenital abnormalities were excluded.

Approval of the study was obtained from the Central Committee on Research Involving Human Subjects in The Netherlands, the medical ethics review committees of the participating hospitals and from the Registration Committee of the Municipality of Amsterdam.

2.2. Sleep problems

Sleep problems were measured when the child was seven to eight years old by the Child Sleep Habits Questionnaire (CSHQ) completed by the mother or primary caregiver. The CSHQ is a 33-item questionnaire developed as a sleep screening tool for caregivers of school-aged children [31,32]. The responder was asked to report their child's average sleep behavior during the last typical week. The CSHQ includes eight subscales: sleep-onset delay, sleep duration, night wakening, parasomnias, daytime sleepiness, bedtime resistance, sleep anxiety and sleep disordered breathing. Items were rated on a 3-point scale; usually (5–7 times a week), sometimes (2–4 times a week), and rarely (0–1 time a week). A higher CSHQ score indicates more sleep problems on a continuous scale. We examined internal consistency of the CSHQ total sum score and each subscale separately by calculating correlations between items using a Cronbach's alpha. The total CSHQ sum score had an adequate internal consistency ($\alpha = 0.76$). In order to describe the differences in potential determinants between children without and with sleep problems, we created a binary outcome with a cut-off at the 90th percentile. Average sleep duration at night and daytime per 24 h was calculated by the parents and reported in hours and minutes per 24 h.

2.3. Potential determinants

Potential determinants were all factors influencing the child during the first 1000 days based on prior research on childhood sleep or cognitive development, as sleep problems in childhood are seen as a cognitive function or often closely related to cognitive functioning [18–24,33]. Information about the potential determinants was derived from the ABCD-study questionnaires; the Dutch Youth Health Care health records; pregnancy health records; and Perined (Dutch institute for registration concerning birth care). Mothers filled out the pregnancy questionnaire around 14 weeks of gestation, as they were invited after their first antenatal clinical visit in the first trimester. Most information about infancy was self-reported in the infancy questionnaire at age three months. Potential determinants are categorized into four categories (pregnancy; birth outcomes; infancy; and context) based on chronological order for theoretical understanding; to check correlation within each category; and for regression analysis per category.

2.3.1. Pregnancy

Pre-pregnancy body mass index (BMI, kg/m^2) was computed from pre-pregnancy weight and height. Substance use was assessed as: alcohol use during pregnancy (<1 glass a day vs. ≥1 glass a day); smoking during pregnancy (<1 cigarette a day vs. ≥1 cigarette a day); drug use during pregnancy (cannabis (no, yes); cocaine (no, yes); xtc or speed (no, yes)); medicine use during pregnancy (painkillers (no, yes); sedatives or sleep medication (no, yes); antidepressants (no, yes)). Caffeine use during pregnancy (mg a day) was computed from the number of drinks including coffee, tea and caffeinated soft drinks. Maternal psychological wellbeing during early pregnancy was assessed on the domains of depression; anxiety and fatigue using the following questionnaires: Center for Epidemiologic Studies Depression (CES-D, depression symptoms score); the State-Trait Anxiety Inventory (STAI, anxiety symptoms score); and the Multidimensional Inventory for Fatigue (MFI, fatigue symptoms score) [34–36]. A higher score on these questionnaires indicates more problems. Maternal sleep/resting duration (hours a day) during pregnancy was part of the MFI. We created a binary variable for gestational diabetes [37] (pre-existent or gestational (yes/no)) from pregnancy records.

2.3.2. Birth outcomes

We categorized children as low birth weight when they had a birth weight below the 10th percentile for gestational age on the basis of gender- and parity-specific standards from the PRN. We defined preterm birth as gestational age <37 weeks. We created a binary variable for artificial delivery (secondary section; vacuum delivery; or forceps delivery (yes/no)).

2.3.3. Infancy

The following child characteristics were included: sex of the child; accelerated growth between age 2 and 12 months (measured as change in SDS score of weight for length); and excessive crying at infant age three months (modified Wessel's criteria: more than 3 h a day, more than three days a week) [38,39]. Feeding practices were investigated with: breastfeeding (none, 1–6 months, >6 months); method of feeding (scheduled vs. on demand, other); number of feedings per day (≤8 feedings a day vs. > 8 feedings a day); number of feedings per night (≤1 feeding a night vs. >1 feeding a night);

and start of additional feeding (solid foods) (<4 months, 4–6 months, >6 months, unknown).

Parental nighttime behaviors at infant age three months were: sleeping place (in parents bed vs. elsewhere); swaddling at night (no, yes); pacifier when falling asleep at night (no, yes); and bottle feeding when falling asleep at night (no, yes). Infant sleep disturbances are assessed as potential long-term causes of sleep problems (ie, waking up by shortness of breath; cough; or itching rash during the last three months).

Maternal wellbeing was assessed with the CES-D, the STAI and the MFI again. Maternal sleep/resting duration in hours/day three months after birth was part of the MFI. Experience of parenthood was assessed with the Dutch questionnaire about the upbringing (Nederlandse vragenlijst voor de opvoedingsituatie) and the care list (Verzorgingslijst). The higher the score of the upbringing list, the more burden parents experienced in the upbringing [40]. The higher the score of the care list the more pleasure parents experienced in taking care of their baby [24].

Age at start daycare (0–6 months, 6–12 months, 12–48 months, >48 months) was self-reported by the parents in the seven-year questionnaire.

2.3.4. Context: demographic factors

Information on maternal and childhood demographics included: maternal age (years); single parent household; ethnicity (Dutch, African descent, Turkish, Moroccan, other based on country of birth of mother and grandmother) [41]; maternal education (0–6 years, 6–10 years, >10 years after primary education) [42]; and ≥1 older sibling in the household (no, yes). Maternal education was used to give an indication about the social economic position of the household [43].

2.3.5. Controlling factors for the outcome measurement

We added two controlling variables to all models as these might influence the outcome measurement of sleep problems: age of the child and depressive symptoms of the mother. The age of the child at the measurement of sleep problems was obtained from the seven-year questionnaire. Mothers with depressive symptoms might have filled out the questionnaires differently [44–46]. Therefore we additionally controlled for depressive symptoms assessed at the closest time point before the CSHQ questionnaire: at offspring age five years. We assessed depressive symptoms of the mother at this age with the Depression Anxiety Stress Scale (DASS21) [47], with a higher score indicating more problems. Anxiety symptoms of the mother during pregnancy and infancy are both in the model as a possible determinant.

2.4. Statistical analysis

Continuous variables were examined for a normal distribution and outliers. Outliers of maternal sleep or resting hours during pregnancy and infancy were removed and replaced with missing values if mothers reported >20 h or ≤2 h of sleep and if mothers reported long (>12) hours of sleep-rest and desire to sleep more (0.8%) or <8 h of sleep-rest and desire to sleep less (0.4%) or <6 h of sleep-rest and no desire to sleep less-more (0.4%). We tested correlation between variables within each category of potential determinants (ie, pregnancy, birth outcomes, infancy and demographics) to prevent collinearity in the multivariable model. In case of high correlation (r >0.6) we added the potential determinant with the strongest association with the outcome to the model and dropped other potential determinants. We performed multiple imputation on missing data of potential determinants using chained equations with the mi impute command making 20 imputed datasets. We inspected the distribution of the imputed variables and compared them with the original dataset.

Demographic characteristics of the baseline sample (approached for CSHQ questionnaire at age seven years); multiple imputation study sample; and complete cases are described using arithmetic means. Hereby we investigated selection bias due to loss to follow up and compared the multiple imputation means to the complete case means (Table 1). Means and standard deviations are reported for each sleep problem subscale and total sleep duration to compare children with low to moderate and high sleep problem scores (Table 2). Means of the potential determinants in the multiple imputations are reported for children with low to moderate versus high sleep problem score (Table 3). Linear regression models were used to explore the associations between the potential determinants and continuous sleep problem score. The regression model with minimal adjustment included two variables that could influence the outcome (age of the child and maternal depression) and was performed separately for each potential determinant. The main analyses (referred to as complete model) also included all potential determinants of all four categories at once. We performed four sensitivity analysis. At first we repeated the multivariable model for three subscales of the sleep problem score: bedtime resistance, daytime sleepiness and parasomnias. As a second sensitivity analysis we performed a separate multivariable model per category; and as a third sensitivity analysis we selected determinants by backward selection. In the fourth sensitivity analysis we did not control for maternal depression at the age of five years. We evaluated linearity for the significant associations by assessing the change in coefficients across categories.

All analyses were conducted using STATA version 15 (College Station TX, USA). We show results as unstandardized betas with their 95% confidence interval (CI) and used a threshold of $p < 0.05$ for significance. We did not adjust the threshold for multiple comparisons, as this is an explorative study.

3. Results

There are 7701 live-born singleton infants in the ABCD-study since phase 1. At phase 3b we approached 5768 parent–child pairs of which 2746 parents filled out the complete CSHQ questionnaire (36% of the 7701 eligible infants, Fig. 1).

Table 1 shows the comparison between mother–child pairs that were invited for the questionnaire at age 7–8 years base sample (n = 5768) with mother–child pairs that completed the HCSQ questionnaire (n = 2746) and complete cases with no missing potential determinants (n = 1626). Mother-child pairs with imputed or complete data had slightly lower anxiety scores during pregnancy, were less often from a single parent household, were more often of Dutch origin, had higher maternal education, and more often a higher BMI-SDS delta growth between age 2 and 12 months.

The mean (SD) sleep problem score in the total sample of 2746 children was 41.3 (4.5). We determined the p90 of sleep problem score within the cohort at a score of 49. Children with a high total CSHQ score scored on average higher on all subscales, most prominently on higher bedtime resistance and daytime sleepiness. Average sleep duration was also shorter in this group (10.3 h compared to 10.7 h per day) (Table 2).

Table 3 presents information on potential determinants among children with a low to moderate sleep problem score versus a high sleep problem score. All variables were normally distributed. In the pregnancy category STAI and CES-D were highly correlated (r = 0.86) and CES-D was correlated with MFI (r = 0.61). STAI had the strongest correlation with total CSHQ score, so CES-D and MFI sum scores during pregnancy and infancy period were omitted from the analysis.

Table 1
Demographic characteristics of baseline sample, multiple imputation sample and complete cases, showing selection bias and mean estimations of 20 multiple imputations.

	sample that was approached for questionnaire at age 7 years (n = 5768)	multiple imputation (n = 20) sample that completed CSHQ at age 7–8 years (n = 2746)	complete cases (no missing values outcome and covariates) (n = 1626)
Pre-pregnancy BMI (kg/m2)	23.0	22.8	22.7
Physical activity during pregnancy (%)			
None	15.9%	10.7%	8.5%
Low	40.5%	36.0%	31.8%
Moderate	35.1%	42.6%	47.1%
High	8.5%	10.7%	12.7%
Maternal psychological wellbeing during pregnancy (scoring range)			
Anxiety symptoms score (STAI 20–80)	37.9	36.1	35.4
Sex (male)	49.9%	51.5%	51.7%
BMI-SDS delta growth between age 2 and 12 months (SDS)	0.01	0.06	0.07
Single parent household (% yes)	12.0%	8.7%	7.4%
Ethnicity (%)			
Dutch	60.5%	72.2%	78.0%
African descent	9.9%	5.6%	3.4%
Turkish	4.2%	1.6%	1.1%
Maroccan	7.7%	3.8%	1.8%
Others	17.8%	16.9%	15.7%
Maternal education (%)			
low	19.2%	11.2%	7.8%
middle	37.6%	33.7%	32.3%
high	43.2%	55.1%	59.9%

Table 2
Child Sleep Habits Questionnaire (CSHQ) subscale scores in children with low to moderate versus high sleep problem score at age 7 years (n = 2746).

	low-moderate sleep problem score n = 2460	high sleep problem score (CSHQ ≥ 49) n = 286
Bedtime resistance (6 items, mean (SD))	6.7 (1.2)	9.4 (2.6)*
Sleep onset delay (1 item, mean (SD))	1.4 (0.7)	1.9 (0.9)*
Sleep duration (3 items, mean (SD))	3.5 (0.8)	4.7 (1.4)*
Sleep anxiety (4 items, mean (SD))	4.6 (1.1)	6.6 (1.9)*
Night wakening (3 items, mean (SD))	3.4 (0.8)	4.5 (1.4)*
Parasomnias (7 items, mean (SD))	8.3 (1.3)	9.9 (2.0)*
Sleep disordered breathing (3 items, mean (SD))	3.2 (0.6)	3.7 (1.1)*
Daytime sleepiness (8 items, mean (SD))	10.9 (2.4)	15.7 (3.2)*
Total sleep problem score (CSHQ) (mean (SD))	39.9 (3.9)	53.2 (4.5)*
Sleep duration in hours (mean (SD))	10.7 (0.7) (n = 2380)	10.3 (0.8)* (n = 259)

*: CSHQ score is significantly different between two groups, Mann–Whitney test $p < 0.0001$. The CSHQ items were rated on a 3-point scale; usually (5–7 times a week), sometimes (2–4 times a week), and rarely (0–1 time a week). A higher CSHQ score indicates more sleep problems on a continuous scale.

Results of the regression with minimal adjustment and multivariable regression analyses on the association between potential determinants and both total and high sleep problem score are shown in Table 4. We only describe the results on total sleep problem score in this results section (first and second column Table 4), giving a change in total sleep problem score for each potential determinant.

3.1. Pregnancy

There were two health indicators of the mother during pregnancy associated with a higher sleep problem score during childhood: pre-pregnancy BMI (β 0.12 (95% CI 0.05, 0.18)); and symptoms of anxiety (β 0.06 (95% CI 0.03, 0.09)). Sleep of the mother during early pregnancy was not associated with sleep problems during childhood, neither was gestational diabetes.

Both alcohol and tobacco use during early pregnancy (gestational week 14) were associated with higher sleep problem scores in the multivariable model. Children of mothers that reported drinking ≥1 glass of alcohol a day around 14 weeks of gestation had more than two points higher sleep problems scores (β 2.55 (95% CI 0.21, 4.89)) and children of mothers that reported smoking ≥1 cigarette per day in that period had approximately one point higher sleep problem scores (β 1.07 (95% CI 0.10, 2.03)). In the regression model with minimal adjustment, medication use during pregnancy was associated with more sleep problems. Associations for painkillers; sedatives or sleep medication; and antidepressants were in the same direction, but all associations were attenuated and non-significant in the multivariable analysis. Caffeine; cannabis; cocaine and XTC or speed intake during pregnancy were not associated with sleep problems.

3.2. Birth outcomes

Having a low birth weight was associated with a higher sleep problem score (β 0.90 (95% CI 0.12, 1.67)) in regression model with minimal adjustment only. Premature birth and artificial delivery were not associated with sleep problems.

Table 3
Mean and proportion calculated after multiple imputation of potential determinants in children with a low to moderate versus high CSHQ score at age 7 years (n = 2746).

	Low- moderate sleep problem score (n = 2460)	High sleep problem score (CSHQ ≥ 49, n = 286)
Pregnancy		
Pre-pregnancy BMI (kg/m2)	22.7	23.6
Gestational sleep/resting during pregnancy (hours)	8.8	8.9
Gestational diabetes (% yes)	1.4	2.1
Hypertensive condition during pregnancy (% yes)	14.7	14.2
Physical activity during pregnancy (%)		
None	10.3	14.0
Low	35.5	40.2
Moderate	43.4	36.4
High	10.8	9.4
Maternal psychological wellbeing during pregnancy (scoring range)		
Anxiety symptoms score (STAI 20–80)	35.7	40.2
Amount of caffeine intake a day (mg)	177.5	161.2
≥1 glass of alcohol a day during pregnancy (% yes)	0.7	1.4
≥1 cigarette a day during pregnancy (% yes)	5.2	8.4
Medication use during pregnancy (% yes)		
painkillers	22.5	28.3
sedatives or sleep medication	0.5	2.2
antidepressants	0.7	1.8
Drug use during pregnancy (% yes)		
Cannabis	1.4	0.7
Cocaine	0.2	0.7
XTC or speed	0.4	0
Birth outcomes		
Low birth weight <p10 (% yes)	7.8	10.5
Premature birth <36wk (% yes)	4.6	3.8
Artificial delivery (% yes)	9.5	12.5
Infancy		
Male sex (%)	51.9	48.6
Change in BMI SD score between age 2 and 12 months	0.085	−0.158
Excessive crying at age 3 months (% yes)	1.4	2.9
Breastfeeding (%)		
None	15.0	16.9
1–6 months	50.8	52.1
>6 months (reference)	34.1	31.0
Method of feeding at age 3 months (%)		
Scheduled	23.8	26.4
On demand (reference)	71.7	69.7
Other	4.4	3.9
>8 feedings a day at age 3 months (% yes)	3.1	6.9
>1 feeding during the night at age 3 months (% yes)	16.5	24.0
Start of additional (solids) feeding (%)		
<4 months	5.5	6.0
4–6 months	93.5	92.1
>6 months	1.0	1.9
Parental nighttime behaviors at age 3 months (% yes)		
Sleeping in parent's bed	7.9	14.1
Swaddling at night	20.1	24.8
Pacifier when falling asleep at night	54.9	58.9
Bottle feeding when falling asleep	3.9	8.3
Waking up during the first 3 months by (% yes)		
Shortness of breath	3.6	4.9
Dry cough	2.0	3.6
Itching rash	7.0	9.8
Maternal psychological wellbeing 3 months after birth (scoring range)		
Anxiety symptoms score (STAI 20–80)	33.6	37.2
Perceived burden of upbringing (NVOS 5–20)	5.9	6.1
Perceived pleasure of baby care (VL 5–20)	16.7	16.2
Maternal sleep/resting duration at 3 months (hours)	7.5	7.6
Start daycare before age 12 months (%)	37.5	46.7
Context		
Maternal age (years)	32.1	31.6
Single parent household (% yes)	8.0	14.7
Ethnicity (%)		
Dutch	73.5	60.8
African descent	5.0	10.5
Turkish	1.5	2.4
Moroccan	3.4	7.3
Others	16.6	18.9

(*continued on next page*)

Table 3 (*continued*)

	Low- moderate sleep problem score (n = 2460)	High sleep problem score (CSHQ ≥ 49, n = 286)
Maternal education (%)		
low	10.4	18.4
middle	33.3	37.1
high (reference)	56.3	44.6
≥1 older sibling(s) in household (% yes)	40.6	41.6
Controlling variables		
Maternal depression, anxiety stress score (DASS) at 5 years of age (SD)	7.8	11.0

CES-D: Center for Epidemiologic Studies Depression; STAI: State-Trait Anxiety Inventory; NVOS; Dutch questionnaire about the upbringing; VL, Dutch care list; CSHQ (Child Sleep Habit Questionnaire); DASS (Depression, Anxiety and Stress scales).

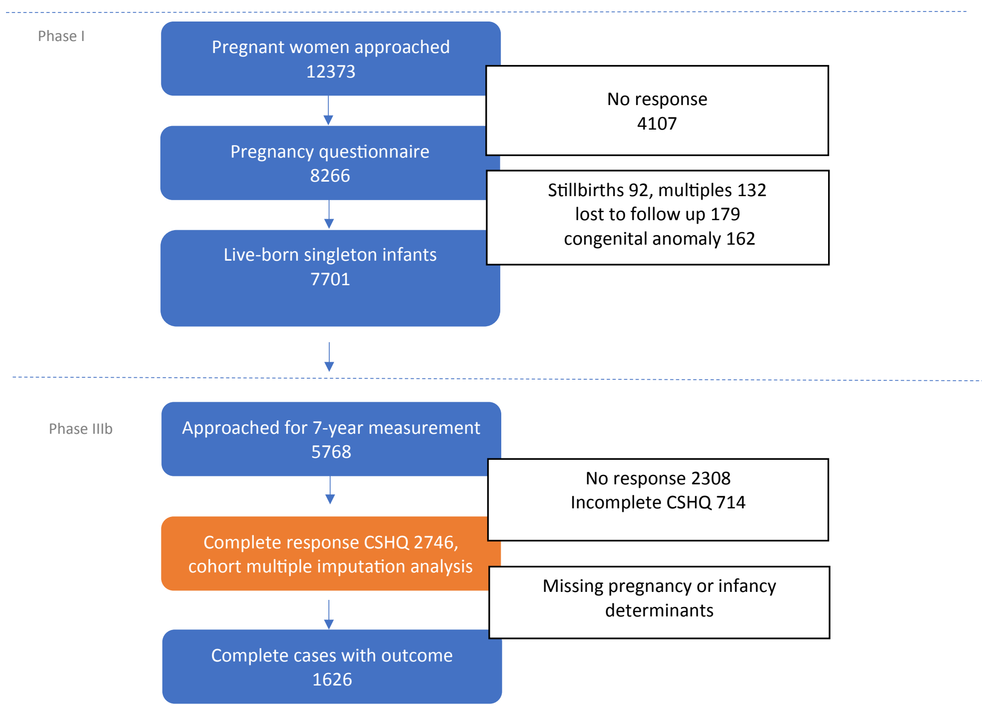

Fig. 1. ABCD-study cohort profile and selection process for this study.

3.3. Infancy

Being a mother with more symptoms of anxiety three months after delivery, independent of anxiety symptoms during pregnancy and all other potential determinants, was again associated with a higher sleep problem score for the child at age seven years, only for the continuous outcome (β 0.04 (95% CI 0.00, 0.07)). A higher perceived burden of the upbringing by the mother and lower pleasure in taking care of the baby three months after delivery were both associated with the more sleep problems in the regression model with minimal adjustment, but effects disappeared after adjustment for the other potential determinants. Children who had a relative larger increase in BMI SD score compared to their peers had a lower sleep problem score at age seven years (β −0.32 (95% CI -0.58, −0.05)).

Some infancy factors (eg, feeding and sleeping practices; and start of daycare) were associated with more sleep problems in the regression model with minimal adjustment, but after adjustment for all other potential determinants associations disappeared or were much smaller and non-significant. Gender, breastfeeding; on demand feeding; start of additional (solid) feeding; maternal sleep duration during infancy, excessive crying; and waking up by shortness of breath; dry cough; or itching rash were not associated with childhood sleep problems.

3.4. Context

Ethnicity, maternal education and single parenting were only associated with childhood sleep in the regression model with minimal adjustment, and associations were much smaller after adjustment for other variables in the complete model. The sensitivity analysis showed that single parent household; ethnicity; and maternal education level were significantly associated in the model with contextual factors only. Maternal age and older siblings in the household were not associated with childhood sleep problems.

3.5. Sensitivity analyses

Regression analysis for subscales of the CSHQ sleep problem score showed that the associations were in essence in the same direction compared to the total sleep problem score and often also significant on CSHQ subscales (Table S1). Bedtime resistance was more often significant than the other subscales and often without significance on the total sum score. Multivariable models ran separately for each category showed similar results than the complete model (Table S2). The beta's in these models are larger and more often significant. After backward selection of the potential determinants we identified the same factors, as well as single parent household and ethnicity to be significantly associated

Table 4
Associations between potential determinants and the total sleep problem score (n = 2746).

	Minimally adjusted	Multivariable (complete)
	β (95% CI)	β (95% CI)
Pregnancy		
Pre-pregnancy BMI (kg/m2)	**0.16 (0.10, 0.22)**	**0.10 (0.04, 0.17)**
Gestational sleep/resting (hours)	0.10 (−0.04, 0.23)	−0.04 (−0.18, 0.11)
Gestational diabetes (yes)	0.65 (−1.10, 2.39)	−0.64 (−2.39, 1.11)
Maternal psychological wellbeing during pregnancy (scoring range)		
Anxiety symptoms score (STAI 20–80)	**0.11 (0.08, 0.13)**	**0.06 (0.03, 0.09)**
Caffeine intake a day (mg)	−0.00 (−0.00, 0.00)	−0.00 (−0.00, 0.00)
≥1 glass of alcohol per day during pregnancy (yes)	**2.38 (0.01, 4.75)**	**2.55 (0.21, 4.89)**
≥1 cigarette per day during pregnancy (yes)	**1.46 (0.54, 2.39)**	**1.08 (0.11, 2.04)**
Medication use during pregnancy (yes)		
painkillers	**0.55 (0.04, 1.05)**	0.46 (−0.04, 0.96)
sedatives or sleep medication	2.48 (−0.10, 5.05)	1.49 (−1.11, 4.09)
antidepressants	1.83 (−0.52, 4.17)	1.17 (−1.17, 3.51)
Drug use during pregnancy (yes)		
Cannabis	−1.10 (−2.95, 0.76)	−1.72 (−3.59, 0.16)
Cocaine*	0.69 (−3.25, 4.62)	0.42 (−3.57, 4.41)
XTC or speed	−0.20 (−3.71, 3.30)	0.14 (−3.44, 3.72)
Birth outcomes		
Low birth weight < p10 (yes)	**0.90 (0.12, 1.67)**	0.24 (−0.54, 1.02)
Premature birth <36wk (yes)	0.03 (−0.98, 1.05)	−0.18 (−1.19, 0.84)
Artificial delivery (yes)	0.51 (−0.28, 1.31)	0.26 (−0.53, 1.04)
Infancy		
Male sex (yes)	−0.31 (−0.73, 0.11)	−0.35 (−0.77, 0.07)
Change in BMI SD score between age 2 and 12 months	**−0.32 (−0.58, −0.05)**	**−0.32 (−0.60, −0.04)**
Breastfeeding		
None	0.26 (−0.39, 0.92)	0.08 (−0.61, 0.77)
1–6 months	−0.06 (−0.53, 0.42)	−0.06 (−0.56, 0.45)
>6 months (reference)	reference	reference
Excessive crying at age 3 months (yes)	0.47 (−1.81, 2.75)	−0.39 (−2.71, 1.93)
Method of feeding at age 3 months		
Scheduled	−0.05 (−0.60, 0.50)	−0.13 (−0.70, 0.45)
On demand (reference)	reference	reference
Other	−0.28 (−1.52, 0.96)	−0.41 (−1.65, 0.82)
>8 feedings a day at age 3 months (yes)	**1.92 (0.52, 3.32)**	0.92 (−0.45, 2.29)
>1 feeding during the night at age 3 months (yes)	**1.36 (0.75, 1.98)**	0.44 (−0.24, 1.13)
Start of additional (solids) feeding		
<4 months	0.66 (−0.31, 1.63)	0.01 (−0.96, 0.98)
4–6 months (reference)	reference	reference
>6 months	0.47 (−2.19, 3.12)	−0.08 (−2.80, 2.64)
Parental nighttime behaviors at age 3 months (yes)		
Sleeping in parent's bed	**1.62 (0.71, 2.53)**	0.82 (−0.15, 1.80)
Swaddling at night	**0.62 (0.06, 1.19)**	0.28 (−0.30, 0.85)
Pacifier when falling asleep at night	0.30 (−0.14, 0.74)	0.40 (−0.06, 0.85)
Bottle feeding when falling asleep	**1.43 (0.19, 2.68)**	0.62 (−0.69, 1.92)
Waking up during the first 3 months by (yes)		
Shortness of breath	0.60 (−0.74, 1.93)	−0.32 (−1.68, 1.04)
Dry cough	1.51 (−0.44, 3.45)	0.54 (−1.46, 2.53)
Itching rash	0.46 (−0.50, 1.43)	0.01 (−1.01, 1.03)
Maternal psychological wellbeing 3 months after birth (scoring range)		
Anxiety symptoms score (STAI 20–80)	**0.09 (0.06, 0.12)**	**0.04 (0.00, 0.07)**
Perceived burden of upbringing (NVOS 5–20)	**0.16 (0.00, 0.31)**	−0.11 (−0.30, 0.08)
Perceived pleasure of baby care (VL 5–20)	**−0.18 (−0.28, −0.09)**	−0.09 (−0.22, 0.03)
Maternal sleep/resting duration (hours)	0.07 (−0.10, 0.25)	0.12 (−0.07, 0.30)
Start daycare before age 12 months (yes)	**0.77 (0.33, 1.20)**	0.02 (−0.46, 0.50)
Context		
Maternal age (years)	−0.04 (−0.09, 0.01)	−0.00 (−0.06, 0.05)
Single parent household (yes)	**1.73 (0.98, 2.48)**	0.71 (−0.10, 1.52)
Ethnicity		
Dutch (reference)	reference	reference
African descent	**2.48 (1.55, 3.40)**	0.88 (−0.13, 1.90)
Turkish	1.35 (−0.36, 3.05)	−0.55 (−2.34, 1.25)
Moroccan	**2.00 (0.89, 3.11)**	0.52 (−0.73, 1.77)
Others	**0.72 (0.15, 1.29)**	0.33 (−0.25, 0.91)
Maternal education		
low	**2.12 (1.43, 2.81)**	0.54 (−0.29, 1.38)
middle	**0.81 (0.35, 1.27)**	0.34 (−0.14, 0.82)
high (reference)	reference	reference
≥1 older sibling(s) in household (yes)	0.37 (−0.06, 0.80)	0.13 (−0.34, 0.60)

Regression model with minimal adjustment: adjusting for the maternal depression, anxiety and stress score (DASS21) at the 5-year questionnaire and the age of the child at the time of the outcome measurements. Multivariable regression model: also adjusted for all other factors added at once. **Bold:** statistically significant ($p < 0.05$), STAI: State-Trait Anxiety Inventory; NVOS: Dutch questionnaire about the upbringing situation; VL: Dutch caregiving list. *: wider 95% CI due to a low incidence of cocaine use.

(Table S2). Analysis without controlling for maternal depression did not change the results (data not shown).

4. Discussion

This study explores potential determinants during the first 1000 days of sleep problems at school age in an urban sample born in 2003–2004. Pregnancy factors positively associated with a higher sleep problem score at age 7–8 years were pre-pregnancy BMI; drinking ≥1 glass of alcohol or smoking ≥1 cigarette per day; and having more symptoms of anxiety during pregnancy. Maternal symptoms of anxiety and relative infant weight loss during infancy were also positively associated with more sleep problems.

We are the second study to report an association between pre-pregnancy BMI and a higher sleep problem score during childhood. Mina et al., studied the same association, with sleep problems measured at offspring age 3–5 years. They report that the average CSHQ sleep problem score was 6 points higher in children of mothers with extreme obesity (BMI>40 kg/m^2) compared to lean mothers (BMI 18.5–25 kg/m^2) and that the found association was independent of demographic factors, prenatal factors and maternal concurrent symptoms of anxiety and depression [48]. We calculated simple adjusted beta coefficients for problems scores of children of mothers with pre-pregnancy overweight, obesity and extreme obesity to compare our results and found similar effect sizes. Compared to children of lean mothers, we found a 1.26 point higher sleep problem score (95% CI 0.63, 1.89) in children of mothers with overweight; 1.99 for obesity (95% CI 0.81, 3.17); and 5.02 for extreme obesity (1.69, 8.35). The found association between maternal BMI and sleep problems is although small, in line with epidemiologic studies with other neurodevelopmental adverse outcomes [48–52]. A study in mice revealed an epigenetic biological pathway that could explain this association: maternal obesity disrupted epigenetic regulation of brain development in the offspring [53].

We explored associations for several medications and substances used during early pregnancy. We found that smoking ≥1 cigarette per day during pregnancy was associated with a higher sleep problem score, hereby confirming the findings of an earlier study in children up to age 12 years [21]. Both animal and human studies have shown abnormal cardiorespiratory response during sleep, less sleep and more fragmented sleep in newborns after prenatal nicotine exposure [54–57]. Furthermore, nicotine in breastmilk has been shown to decrease sleep length in infants [58]. Unknown is if these associations are still present during later childhood. The underlying mechanism for the association might be the interaction between nicotine with its nicotinic acetylcholine receptors [59]. Activation of these receptors alters the development of the fetal nervous system during the early prenatal stage. This may lead to a delayed neurodevelopment in the first few years of life; decreased cognitive functioning; and negative behavioral outcomes during childhood, which could all lead to sleep problems [59]. Next to smoking, we also found an association with alcohol use. Drinking ≥1 glass of alcohol a day during pregnancy was associated with a higher sleep problem score in our sample. In prior studies, maternal alcohol use during pregnancy has been associated with night terrors but not with other sleep problems at age four to nine years [20] and to shorter sleep and lower sleep efficiency at age eight years [19]. A possible mechanism is that prenatal alcohol exposure alters the function of the hypothalamic-pituitary-adrenocortical axis, which causes higher blood cortisol levels and influences sleep infrastructure in the child [60,61]. We found no significant association with drug use or medication use, probably due to the low prevalence. We therefore recommend further investigation of these associations in larger cohorts with more variation in medication use.

Both maternal psychological wellbeing during pregnancy and infancy were associated with a higher sleep problem score at age 7–8 years. Although the coefficients seem small, they reflect the change in sleep problem score per 1 point difference on the STAI, which has a range of 20–80. For a child of a mother with >2 SD higher STAI score, this means a two-and-a-half point higher sleep problem score (β2.49 (95% CI 1.36, 3.62)). Two other studies found an association between postnatal maternal mental health and childhood sleep problems [20,22], but the association with prenatal maternal mental health has not been assessed to our knowledge. The potential mechanism explaining pre- and postnatal effects of maternal mental health problems on the child's sleep is through dysregulation of the hypothalamic-pituitary-adrenal axis and higher levels of cortisol in mother and child [61–63]. A higher cortisol exposure effects the fetal programming of the nervous system and leads to an increased risk for behavioral problems [64]. Sleep problems might be associated through similar pathways as behavioral problems.

We found an association between relative infant weight loss (negative BMI SD change between infant age of two and 12 months) and sleep problems score during childhood. In clinical practice, attention is raised when the weight of a child changes with more than 0.67 SD between two measurements. For this reason we repeated the analysis with a categorical variable (delta BMI < −0.67; −0.67 to 0.67; and >0.67 SD) and noticed that the association with delta-BMI was mostly driven by a higher sleep problem score (>p90) in children with a large decrease in BMI (delta-BMI SD < −0.67), although associations were not significant (data not shown). Possible pathways for an association or common mechanism of relative weight loss and sleep problems would be self-regulation disturbance or neurodevelopmental problems causing both growth and sleep disorders. We are unaware of earlier studies that investigated relative weight loss during infancy and sleep problems during childhood.

Previous research is inconclusive on the effects of ethnicity on childhood sleep [25,65–67]. We did see a significant association between ethnicity and sleep problems in the regression model with minimal adjustment and in the contextual model, but not in the multivariable model. With backward selection however, ethnicity and also single parent household were significantly associated. A possible explanation is that differences between ethnicities and single versus double parenthood are due to cultural and environmental differences in upbringing and sleeping habits which were also included in the complete model [3]. In future studies it would be noteworthy to explore which factors contribute to the ethnic and socioeconomic differences in sleep problems observed in the regression models with minimal adjustment and previous studies.

4.1. Strengths and limitations

A strength of this study is the large sample size, followed from early pregnancy onwards. We explored potential early life determinants during pregnancy and infancy and measurements of parental wellbeing. Use of tobacco; alcohol; drugs; and medication was assessed during early pregnancy, which is the most important period of fetal neurodevelopment. Many potential determinants have not been studied before and there are many other contextual factors that have not been measured in the ABCD-study. Therefore we cannot rule out residual confounding. Another limitation is that we could have introduced colliders by adding all potential determinants at once. As previously suggested, we have added backward selection as a sensitivity analysis which provided similar results overall. Additionally, we provided possible explanations for the associations we found. This is an explorative study, we therefore recommend confirmation of our findings in future studies including mediation analysis and selection of relevant confounders based on causal models (also known as directed acyclic graphs [DAGs]). Due to multiple testing there is a higher chance of finding a positive association. This is however an explorative study, for which reason we do not want to tighten the threshold to a lower p-value. The findings need to be replicated in other populations, preferably combined with assessment of the mechanical pathways. A limitation was information bias as information on sleep problems and most potential determinants were based on self-report, which could suffer from socially desirable answers and recall bias. In the comparison with other studies, we noticed that there is a large variation in the assessment method of sleep problems, which limited the comparison with other studies. The mean CSHQ score in our sample was comparable to other studies, but close to the cut-off score used in a prior study [5]. For this reason, we used the 90th percentile as a cut-off for sleep problems in descriptive statistics. We used the total sum score and subscale scores and found comparable results. Bedtime resistance problems were more prevalent than other sleep problems and could influence sleep duration and sleep efficacy. As shown in Table 1 selection bias plays a role in our study as the mothers in the analyzed sample were more often of Dutch origin and had higher maternal education and less often living as a single parent. We minimized selection bias by performing multiple imputation for missing covariates. As this is an observational study, the results only show an association between potential determinants and sleep outcomes and do not assess causation.

4.2. Future recommendations

We recommend further research to reproduce our findings of potential determinants in the first 1000 days of life. Future studies may explore possible mechanisms of causality by conducting mediation analysis and selection of confounders could be done with the help of causal models (DAGs). Environmental factors during infancy that we could not include, but are recommended for future studies, are: screen time in the first two years of life; ambient noise (background noise from music or television; street sounds); and parenting practices (including bedtime routine and sleep initiation method) [25,68]. Uniform measurement of sleep problems can enhance comparability between studies.

5. Conclusions

We found the following factors as potential determinants of sleep problems among children aged 7–8 years as: pre-pregnancy BMI; alcohol and tobacco use during pregnancy; relative infant weight loss; and maternal mental health during pregnancy and infancy. If confirmed by other studies, these potential determinants may be used for early identification of children with increased risk of sleep problems. Early identification is the first step to early intervention and promotion of healthy sleep during the child's lifetime.

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Authors contribution

Study concept and design: All authors.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Harskamp, Kool.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Harskamp, Kool.
Obtained funding: Vrijkotte, Huss.
Study supervision: Vrijkotte, Chinapaw.

Data Access, Responsibility, and Analysis: Harskamp, Vrijkotte and Kool had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2019.12.020.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2019.12.020.

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