Sleep Trajectories Among Pregnant Women and the Impact on Outcomes: A Population-Based Cohort Study

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Running head: Sleep trajectories during pregnancy and outcomes

ABSTRACT

Objectives. Sleep problems and deprivation are common during pregnancy, particularly in the third trimester. Previous studies are mostly descriptive or focused on specific clinical groups and late pregnancy. We aimed to identify sleep duration trajectories during the pregnancy period, their associated factors, and impact on pregnancy and birth outcomes.

Methods. We studied 200 women from a mother-child cohort recruited in 2009-2011 from the French general population. We used semi-parametric models to analyze data collected through questionnaires.

Results. We detected three sleep duration trajectories during pregnancy: short-decreasing (<6.5h/night, 10.8% of the sample), medium-decreasing (6.5-8h/night, 57.6%), and long-increasing (>8h/night, 31.6%) trajectories. Factors associated with the short-decreasing trajectory relative to the medium-decreasing trajectory were older age (odds-ratio/year=1.13 [95%Confidence-Interval 1.00-1.29]) and working >28 weeks of gestational age (odds-ratio=0.30 [0.10-0.90]). Sleep duration during pregnancy in this trajectory group was modified by insomniac symptoms (regression coefficient/trimester=-0.74 [Standard-Error 0.12]) and naps (regression coefficient/trimester=0.58 [0.25]). Restless legs syndrome was the only factor associated with the long-increasing trajectory and decreased sleep duration (regression coefficient/trimester=-0.88 [0.25]). Assisted delivery (i.e. cesarean section and/or instrumental delivery) and post-partum depression were more frequent among women with the short-decreasing and long-increasing trajectories whereas cesarean section alone was more prevalent among those with the short-decreasing trajectory. Proportion of premature births was higher in the short-decreasing trajectory group. Birth-weight-z-score was lower in the long-increasing trajectory group.

Conclusion. We identified sleep trajectories among pregnant women with specific risk factors that could affect both pregnancy and birth outcomes. Taking these into consideration could improve both maternal and child health.

Significance: Pregnant women are at risk of sleep deprivation. Short sleep, particularly in late pregnancy, has been associated with adverse pregnancy outcomes. However, there are few studies that have assessed women's sleep during the entire pregnancy.

We identified three sleep duration trajectories during the pregnancy period in 200 women from the French general population: short-decreasing (<6.5h/night, 10.8% of the sample), medium-decreasing (6.5-8h/night, 57.6%) and long-increasing (>8h/night, 31.6%) trajectories. Both

short- and long-sleep duration trajectories were associated with adverse pregnancy outcomes, i.e. cesarean section and/or instrumental delivery and prematurity for short-sleep duration trajectory and instrumental delivery and low birth-weight-z-score for long-sleep duration trajectory.

Key words: Epidemiology; Public Health; Pregnancy outcomes; Longitudinal study; Sleep

INTRODUCTION

During pregnancy, women are at risk of sleep deprivation because of physical and hormonal changes and they report a higher incidence of disturbed sleep than non-pregnant women. Descriptive, cross-sectional studies, using questionnaires, actigraphy, or polysomnography, have reported a mean sleep duration of 6.8 to 7.8h/night before pregnancy, increasing during the 1st trimester, then decreasing during the 2nd and 3rd trimester, before returning to the reported pre-pregnancy levels in the postpartum period (Chang, Pien, Duntley, & Macones, 2010). This overall pattern was recently confirmed by a descriptive longitudinal study (Mindell, Cook, & Nikolovski, 2015). Up to 97% of pregnant women report disturbed sleep (Facco, Kramer, Ho, Zee, & Grobman, 2010), particularly during the third trimester of pregnancy. Increased restless legs syndrome (RLS), insomnia, snoring, and poor sleep quality are associated with decreased or short sleep duration (Facco et al., 2010; Micheli et al., 2011). This is particularly prevalent among older pregnant women who are less likely to be primiparae (Facco et al., 2010; Hedman, Pohjasvaara, Tolonen, Suhonen-Malm, & Myllylä, 2002). There are few studies that have assessed women's sleep during the entire pregnancy.

Research on sleep disorders during pregnancy and associated maternal complications and foeto-infant morbidity is growing. Evidence suggests that decreased sleep duration and/or sleep disturbances during pregnancy are associated with adverse maternal and neonatal outcomes (Chang et al., 2010; Pamidi et al., 2014). Indeed, short sleep duration and sleep disturbances during late pregnancy are associated with a higher occurrence of high blood pressure, preeclampsia, gestational diabetes (Chang et al., 2010; Pamidi et al., 2014), and post-partum depression (Chang et al., 2010; Nodine & Matthews, 2013). They are also associated with preterm labor and birth, longer labor, increased perception of labor pain and discomfort, and higher cesarean rates (Chang et al., 2010; Nodine & Matthews, 2013).

Most studies have been cross-sectional or case/control or have only focused on sleep duration during the third trimester of pregnancy. To our knowledge, there has been no publications on sleep trajectories, i.e. sleep evolution during the entire pregnancy, in the general population. Based on a mother-child birth cohort, we aimed to i) identify sleep duration patterns/trajectories during pregnancy; ii) simultaneously identify time-stable factors, explaining differences between patterns, and time-dependent factors associated with variations within patterns; and iii) study relationships between sleep patterns and both pregnancy and birth outcomes.

METHODS

1) Study design

This secondary analysis was carried out on a French cohort, AuBE, recruited in Saint-Etienne University Hospital between 2009 and 2011, for which the first aim was to evaluate the autonomic maturation profiles during the first two years of life and their impact on psychometric development at three years of age among term and preterm newborns (Patural et al., 2014). All consecutive mothers affiliated with a health plan were invited to participate. Exclusion criteria included a corrected postnatal age of less than 37 weeks, a documented familial history of cardiac disease, abnormality, or treatment. A total of 297 mothers and 302 children were enrolled. Written informed consent was obtained at enrolment. The local research ethics committee approved the study.

2) Data collection

All mothers completed a self-administered questionnaire within the first weeks post-delivery. Data concerning the newborns were: birthdate, term, sex, length, and weight. Data collected on the mother were: age, height, weight before and after pregnancy, parity, twin pregnancy, type of delivery (normal vaginal delivery versus instrumental and/or cesarean), premature membrane rupture, presence of chronic diseases (e.g. hypertension, diabetes), occupation, last date worked, and hospital anxiety and depression scale (HAD – a subscale score ≥ 8 defined a positive diagnosis of anxiety and/or depression)(Zigmond & Snaith, 1983), data on medication use, caffeine intake, tobacco use, alcohol intake,(> 1 glass a day more than 3 times a week) and illicit drug consumption. Data on the mothers' sleep before and during each trimester of the pregnancy were also collected, including questions on the estimation of sleep duration, nightmares, pain (all kinds), RLS (defined as an urge to move the legs accompanied or caused by unpleasant sensations, starting or worsening during periods of rest or inactivity, partially or totally relieved by movement, occurring or worsening in the evening or night), and the need for sleep treatment. An insomniac score (IS) was calculated before pregnancy and during each trimester based on 3 questions: "Do you have difficulties to fall asleep (> 30 min) at least 3 nights a week?" "Do you have night-awakenings (> 2-3/night, at least 3 nights a week)?" and "Do you experience early wake up (between 4 and 6 AM without being able to sleep again) at least 3 nights a week?". Each question had a yes/no answer. The score consisted of the sum of the answers ranging from 0 (all no) to 3 (all yes). A sleep-disordered breathing (SDB) variable was constructed for each time-point. A woman was considered to have SDB when she experienced sleep apnea (breathing-stops noted by the partner) or snored loudly (annoying the partner nearly every night) accompanied by daytime tiredness and drowsiness. A combined variable designated “work” was also created taking into account work and its duration during pregnancy using 28 weeks of gestational age (GA) (median of last date worked among pregnant women) as a threshold. A birth weight z-score was calculated for each child using Gardosi’s formula (Gardosi, Chang, Kalyan, Sahota, & Symonds, 1992) taking into account sex and gestational age and based on National Perinatal Surveys.

3) Statistical methods

We used group-based trajectory modeling (GBTM) to identify meaningful and distinct groups based on sleep duration throughout pregnancy as developed by Nagin (Nagin, 2005; Nagin & Odgers, 2010). We determined potential relationships between these groups and various time-stable or time-dependent factors. Time-stable factors included those such as age, whereas time-independent factors included those that varied during pregnancy, such as sleep disturbances.

The underlying hypothesis of GBTM is that there are inherent groups within a population, which evolve according to different patterns. The groups are not directly identifiable or pre-established by sets of characteristics, but are statistically determined through each series of responses, using maximum likelihood. The relationship between time (i.e. trimester of pregnancy) and the outcome (i.e. sleep duration) was modeled using polynomial equations to best define the trajectories. The most adequate model, in terms of number and shape of trajectories, was then determined using Bayesian Information Criteria and favored parsimony. The quality of the model was verified based on the recommended criteria: the average posterior probability (≥ 0.7), the odds of correct classification (≥ 5), and the similarity between the actual prevalence and that predicted by the model. Analyses were performed using the PROC TRAJ program SAS 9.4 (Nagin, 2005).

Unadjusted models were first estimated for all explanatory variables. Those with a p-value < 0.10 were included in the multivariable model. All analyses took into account the uncertainty of group assignment. Parameters were simultaneously estimated in multivariable models for time-dependent and time-stable variables.

GBTM makes it possible to link trajectory groups for a specified outcome (sleep duration) with another outcome variable measured only once that falls either on or beyond the end of the trajectory. This approach was used to study pregnancy and birth outcomes. Each model included all factors (time-stable and time-dependent) identified in the previous step.

Subjects with partial data for outcomes and time-dependent variables can be included assuming that the missing data are missing randomly. We included women with no more than one missing value for each time-dependent variable (N = 200) to obtain the most reliable trajectories. There were no missing values on time-stable variables for these subjects. Three women were pregnant with twins. Their exclusion did not change the results. Only the first child included in the database was considered for the analysis of birth outcomes. To verify the robustness of the model, sensitivity analysis was performed and the full procedure was carried out among women who had complete data for the outcome and each time-dependent variables (N=187). Results were very similar and we thus decided to present results for the largest sample size.

RESULTS

Approximately 67% of the women (200/297) reported three of four response points for sleep characteristics and were included in the analysis. The mothers who were included were more likely to work up to 28 GA (OR = 2.44 [1.15, 5.21]), to have a nap during the first trimester of pregnancy (47% versus 29%, p = 0.008), to sleep more on average during the second trimester (7.6 h versus 5.9 h/night, p = 0.01) than those not included. The mothers included in the analysis were also less likely to have a pre-term birth (7.0 % versus 14.6%, p = 0.04). The other factors studied were not significantly different.

The mean age of the included women was 30 years (range 18-43); the mean BMI before pregnancy was 23 (range 17-45); 43.5% were expecting their first child and 23.0% already had at least two children; 48.5% did not work or worked ≤ 28 GA; 22.0% smoked tobacco during pregnancy; 13.5% received treatment for sleep problems (alternative medicine for 74% of them); 4% and 7.5% developed gestational hypertension or diabetes, respectively; 9.5% had cesarean section; 44,5% delivered a female infant; the mean gestational age at delivery was 39.4 GA (26.5 – 41.9) and 7% had a delivery term < 37 GA; the mean birth weight-z-score was -0.42 (range -4.58, 2.00); 7.5% of the mothers had a HAD score ≥ 8 in the first week post-partum. Sleep characteristics are presented in Table 1.

We identified three sleep trajectories (Figure 1) labeled according to their shapes. We labeled the first trajectory showing short sleep before pregnancy (<6h30/night) that decreases throughout pregnancy and consisting of 10.5% of the population “short-decreasing”; the second trajectory showing medium sleep duration before pregnancy (around 7h30/night) that decreases throughout pregnancy and consisting of the majority of the women (57.6%) was labeled “medium-decreasing” and the last trajectory consisting of 31.9% of the women showing long sleep duration before pregnancy (around 8h30/night) that increases throughout pregnancy "long-increasing".

The relationships between the characteristics of the women and sleep trajectories are shown in Table 2. Among time-stable factors, older mothers were more likely to fall into the short-decreasing trajectory than the medium-decreasing trajectory whereas those that worked beyond 28 GA were less likely to fall into either the short-decreasing or long-increasing trajectories than the medium-decreasing trajectory. Among time-dependent factors, the insomniac score (IS) was strongly associated with decreased sleep duration among women of the short-decreasing and medium-decreasing trajectory groups (-45 and -36 minutes/symptom/trimester, respectively). RLS was associated with decreased sleep duration among women of the both medium-decreasing and long-increasing trajectory groups (-44 and -49 minutes/trimester, respectively). SDB was associated with decreasing sleep duration only among women of the medium-decreasing trajectory group (-44 minutes/trimester). Naps were strongly associated with increased sleep duration among women of both short-decreasing and medium-decreasing trajectory groups (+36 and +14 minutes/trimester, respectively).

The pregnancy and birth outcomes are shown in Figure 2. There were a higher proportion of assisted deliveries among both the short-decreasing and long-increasing trajectory groups whereas there were a higher proportion of cesarean section and preterm births only among the short-decreasing trajectory group. The mean birth weight-z-score was lower in the long-increasing trajectory group. Finally, there was a higher proportion of women with a positive HAD score in both short-decreasing and long-increasing trajectory groups.

DISCUSSION

We have used an original longitudinal developmental approach to identify three sleep duration trajectories covering the entire pregnancy: short-decreasing, medium-decreasing, and long-increasing. We reported a similar proportion of individuals in the short sleep trajectory group as that published for the general Canadian adult population using the same trajectory method (Gilmour et al., 2013). However, we reported a higher proportion of pregnant women in the long-increasing group, consistent with the prevalence observed by others (Signal et al., 2014). Increasing sleep during pregnancy may be a physiological mechanism to conserve energy or compensate for expected sleep troubles due to hormonal and physical changes (O'Keeffe & St-Onge, 2012). Descriptive studies showed that, during pregnancy, women experienced a global decrease in sleep duration and increased frequent snoring, insomnia, sleepiness, night awakenings, poor sleep quality, and RLS (Facco et al., 2010; Mindell et al., 2015). We confirmed the increase of these sleep troubles, particularly for the short- and medium-decreasing groups, but also showed the unexpected existence of a long-increasing sleep group for whom these troubles have a very low impact.

Short sleep has been associated with adverse health effects among the general population and has been studied among pregnant women with a specific focus on the third trimester of pregnancy. Risk factors for short sleep have been mostly described through cross-sectional studies (Facco et al., 2010; Matsuzaki, Haruna, Ota, Murayama, & Murashima, 2011). We confirmed the involvement of age independently of parity. We also showed that insomnia symptoms were responsible for decreased sleep duration among short-decreasing and medium-decreasing sleepers and quantified it (-44 min of sleep/symptom/trimester and -36 min of sleep/symptom/trimester, respectively). Unsurprisingly, naps independently increased sleep duration within both trajectory groups (+35 min and +14 min of sleep/trimester, respectively). We cannot draw conclusions on the relationship between naps and insomnia symptoms. However, these results suggest that sleep hygiene and behavioral approaches may be beneficial to these women (Gottlieb et al., 2006).

The only factor strongly influencing sleep duration within the long-increasing sleep trajectory group (≈ -1h/trimester) was RLS. Thought to involve dopaminergic dysfunction (Tamanna & Geraci, 2013), RLS is frequent among pregnant women in the third trimester (up to 30%) (Facco et al., 2010; Mindell et al., 2015; Oyiengo, Louis, Hott, & Bourjeily, 2014). Aside from iron deficiency, the main risk factor for RLS among pregnant women is an elevated estradiol concentration (Srivanitchapoom, Pandey, & Hallett, 2014) that may lower the RLS threshold through the dopamine neurotransmitter system. Indeed, pregnant women with RLS had higher blood concentrations of estrogen than those of pregnant, healthy controls during the third trimester (Dzaja, Wehrle, Lancel, & Pollmächer, 2009). Moreover, long sleep duration (> 10h/night) was recently associated with an increased risk for developing estrogen-related cancer among women from the general population (Hurley, Goldberg, Bernstein, & Reynolds, 2015) suggesting either a higher estrogen concentration or higher sensitivity to estrogen among them.

The GBTM method allowed the study of the relation between sleep duration trajectories and outcomes. It showed that both the short-decreasing and long-increasing trajectory groups were at higher risk of adverse and assisted delivery. We also showed that the short-decreasing sleep duration trajectory group was more at risk for preterm birth, possibly due to other associated pathology necessitating cesarean section and not studied here, such as preeclampsia. Short sleep duration, sleep deprivation, and insomnia are associated with preterm birth (Chang et al., 2010; Micheli et al., 2011). Insomnia in late pregnancy is also associated with adverse labor (pain, duration, operative birth) (Lee & Gay, 2004). Recently, short and long sleep duration associated with exhaustion were linked to preterm birth (Kajeepeta et al., 2014). To our knowledge, this is the first report of a positive association between long sleep duration during pregnancy and the occurrence of assisted delivery i.e. requiring at least instrumental use.

The analysis of the relation between sleep duration trajectories and birth outcomes showed the unexpected result of a lower mean birth weight-z-score for the long-increasing sleep duration group. Recently, it was shown in a case-control study that pregnant women who sleep more than 8 h/night during the last month of pregnancy were more prone to late stillbirth (OR = 1.83[1.14, 2.94]) than pregnant women sleeping 6-8 h/night (Stacey et al., 2011).This suggests that sleep duration increased throughout pregnancy because of lower sleep disturbances due to fetal movements and implies that longer sleep would not be the cause but the consequence of decreased fetal movements as already suggested for night fragmentation and fetal death (Chappell & Smith, 2011). Moreover, major decreases in fetal movement were associated with smaller babies (Scala et al., 2015; Sheikh, Hantoushzadeh, & Shariat, 2014) and stillbirths were shown to be more frequent among women followed for growth restriction (Gordon et al., 2015).

Finally, we showed a higher occurrence of mood disturbances among the short-decreasing sleep duration trajectory group, and to a lesser extent among the long-increasing sleep duration trajectory group, that paralleled assisted delivery. Short sleep duration is associated with mood disturbances and depression after delivery and preterm birth (Chang et al., 2010; Oyiengo et al., 2014). However, whether there is an association between the mode of birth and symptoms of postnatal depression is unclear. A very recent study failed to observe an association between operative birth and post-partum depression (Hanlon & Beckmann, 2015). We suggest that sleep trajectories during pregnancy may offer an explanation for these discrepancies.

This study presents three main strengths: i) the population sample derived from the general population delivering at the University hospital; ii) the longitudinal data up to delivery providing information on sleep duration and sleep troubles that may occur during pregnancy; iii) the method used that allowed the simultaneous estimation of time-stable, time-varying variables, and outcomes associated with each trajectory group. This study also has some limitations. The model was estimated on only 67% of the original cohort because of missing data. However, a comparison of the data for included and excluded women showed only small differences in sleep characteristics that would probably have a low impact on the modeled trajectories and associated factors. The total sample size was less than that recommended i.e. 300 cases (Nagin, 2005) and the number of explanatory variables was high leading to a small sample size for some categories and large confidence intervals. Nonetheless, goodness of fit criteria were met and sensitivity analyses using several coding schemes for explanatory variables gave very stable results. Finally, this study was a secondary analysis of retrospective data collected through self-questionnaires at the maternity. Women may have forgotten how long they slept and/or associated co-morbidities from a few months prior. We thus provided estimates of sleep disturbances and sleep durations before and during pregnancy. A prospective study, collecting the same data, and ideally, with objective measures of sleep through actigraphy, will be needed to confirm our results.

CONCLUSIONS FOR PRACTICE

Sleep and sleep troubles among pregnant women follow various trajectories. Some associated risk factors may be amenable to treatment or counseling. Clinicians should be encouraged to discuss sleep concerns with their pregnant patients, especially among short and long sleepers, as they may affect not only quality of life but may also lead to an increased risk of assisted delivery (including cesarean section), preterm birth, low birth weight, and post-partum depressive symptoms. Further studies are needed to confirm these results and to determine whether assessment and treatment of sleep disorders during pregnancy can improve quality of life and pregnancy outcomes.

Table 1. Sleep characteristics of the women before and at each trimester of pregnancy. Values presented are N (percentages) for all variables except sleep duration (mean (SE)).

Sleep characteristics	Before	1st trimester	2nd trimester	3rd trimester
Mean sleep duration (h)	7.7 (1.2)	8.0 (1.5)	7.6 (1.5)	7.2 (2.2)
Restless Legs Syndrome	18 (9.0)	24 (12.0)	40 (20.0)	65 (32.5)
Pain	5 (2.5)	16 (8.0)	26 (13.0)	81 (40.5)
Sleep disordered breathing	4 (2.0)	10 (5.0)	10 (5.0)	45 (22.5)
Bad dreams	19 (9.5)	19 (9.5)	25 (12.5)	44 (22.0)
Nap	25 (12.5)	94 (47.0)	68 (34.0)	130 (65.0)
Insomniac score ≥1	27 (26.5)	64 (32.0)	104 (52.0)	170 (85.0)

Table 2. Results of unadjusted and adjusted group-based trajectory models estimating i) the relationship between time-stable explanatory variables and probability of group membership, and ii) the change in average group sleep duration as a function of time-dependent explanatory variables.

	Unadjusted		**Simultaneously adjusted**	
Time-stable explanatory variables				
	OR (95%CI)[a]	**p-value**	**OR (95%CI)[a]**	**p-value**
1. Short-decreasing				
Age	1.11 (0.99 - 1.24)	0.06	1.13 (1.00 - 1.29)	0.06
Parity	2.92 (1.27 - 6.71)	0.03	1.83 (0.86 - 3.90)	0.12
Work ≤28GA[b]	-	-	-	-
>28GA[b]	0.26 (0.07 - 0.88)	0.03	0.30 (0.10 - 0.90)	0.03
Smoke	2.74 (0.93 - 8.06)	0.07	2.37 (0.75 - 7.50)	0.14
2. Medium-decreasing – Ref				
3. Long-increasing				
Age	0.91 (0.83 - 0.99)	0.03	0.92 (0.83 - 1.02)	0.12
Parity	0.58 (0.36 - 0.94)	0.03	0.74 (0.41 - 1.33)	0.31
Work ≤28GA[b]	-	-	-	-
>28GAb	0.76 (0.38 - 1.55)	0.47	0.46 (0.20 - 1.07)	0.07
Smoke	0.83 (0.34 - 2.06)	0.69	0.98 (0.36 - 2.64)	0.97
Time-dependent explanatory variables				
	β (SE)[c]	**p-value**	**β (SE)[c]**	**p-value**
1. Short-decreasing				
IS[d]	-0.87 (0.10)	$<10^{-4}$	-0.74 (0.12)	$<10^{-4}$
SDB[e]	-0.22 (0.04)	0.59	-0.29 (0.37)	0.43
RLS[f]	-1.05 (0.39)	0.007	-0.29 (0.29)	0.32
Pain	0.11 (0.37)	0.77	0.11 (0.29)	0.71
Nap[g]	0.94 (0.28)	0.001	0.58 (0.25)	0.02
2. Medium-decreasing				
IS[d]	-0.60 (0.08)	$<10^{-4}$	-0.60 (0.07)	$<10^{-4}$
SDB[e]	-0.88 (0.26)	0.001	-0.73 (0.21)	$<10^{-3}$
RLS[f]	-0.91 (0.18)	$<10^{-4}$	-0.42 (0.15)	0.007

Pain	-0.52 (0.20)	0.008	-0.23 (0.17)	0.18
Nap[g]	0.06 (0.13)	0.67	0.24 (0.12)	0.05
3. Long-increasing				
IS[d]	-0.11 (0.14)	0.44	-0.06 (0.13)	0.62
SDB[e]	0.10 (0.28)	0.71	0.02 (0.29)	0.95
RLS[f]	-0.69 (0.21)	0.001	-0.88 (0.25)	$<10^{-3}$
Pain	0.09 (0.25)	0.72	0.08 (0.25)	0.75
Nap[g]	0.04 (0.17)	0.81	-0.05 (0.19)	0.77

[a] Odds ratio and 95% confidence interval

[b] Weeks of gestational age

[c] Regression coefficient and standard error

[d] Insomniac score

[e] Sleep disordered breathing

[f] Restless legs syndrome

[g] Nap duration in hour/day

Figure 1. Estimated sleep duration trajectories and 95% confidence intervals in pregnant women (N=200).

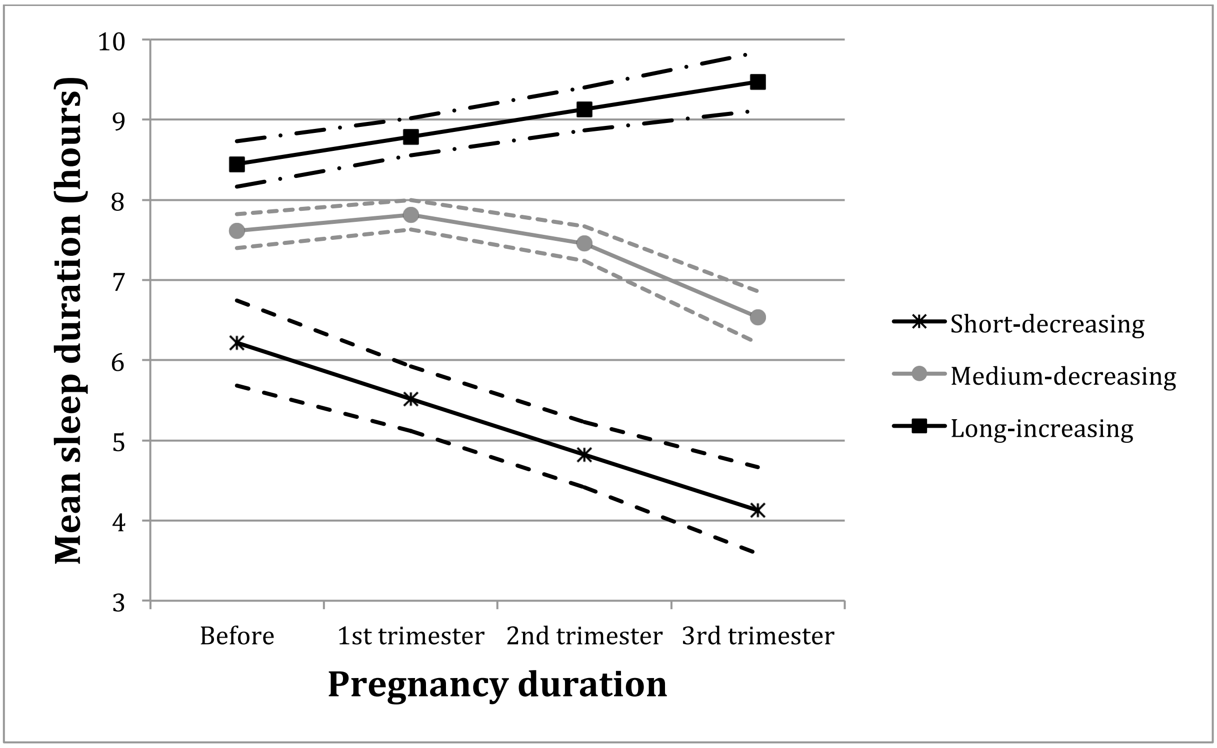
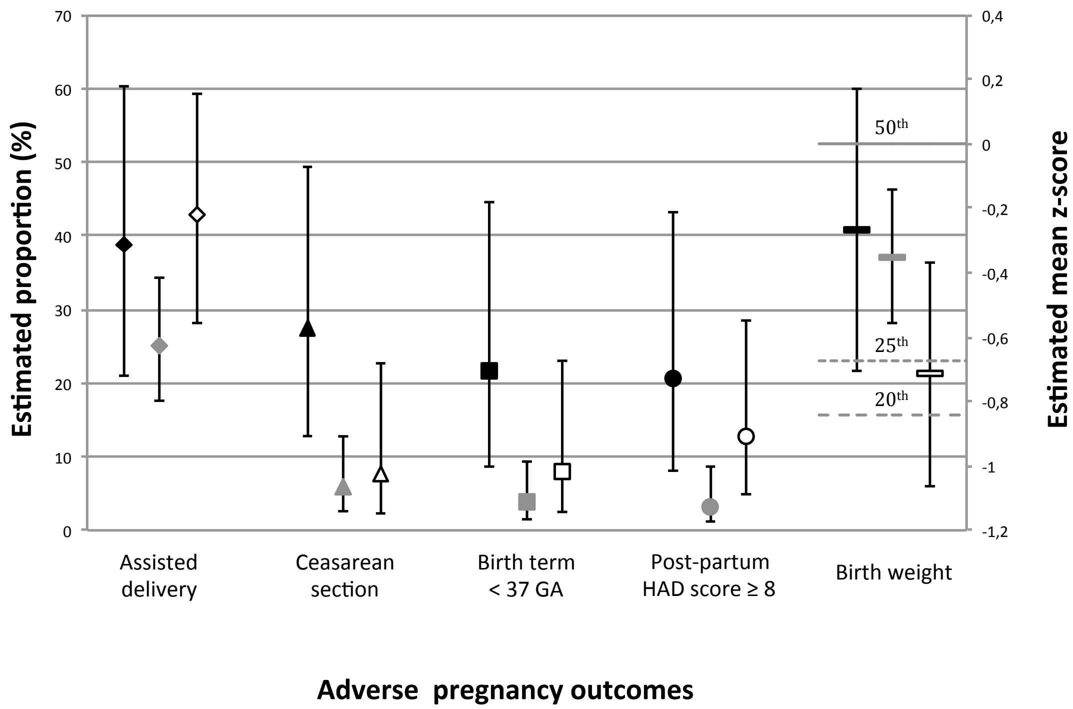


Figure 2. Estimated proportion and mean birth weight-z-score for adverse pregnancy outcomes. Trajectory groups are in black, grey and white for the short-decreasing, medium-decreasing and long-increasing groups, respectively. The birth weight-z-score was calculated for each child using Gardosi's formula (Gardosi et al., 1992), taking into account sex and gestational age and based on National Perinatal Surveys. The grey solid, short dash and long dash lines represent the 50th, 25th and 20th percentiles of expected birth weight, respectively.



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