TITLE PAGE

Night work and miscarriage: A Danish nationwide register-based cohort study

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ABSTRACT (215)

OBJECTIVE

Observational studies indicate an association between working night and miscarriage, but inaccurate exposure assessment precludes causal inference. Using payroll data with exact and prospective measurement of night work, the objective was to investigate whether working night shifts during pregnancy increases the risk of miscarriage.

METHODS

A cohort of 22 744 pregnant women was identified by linking the Danish Working Hour Database (DWHD), which holds payroll data on all Danish public hospital employees, with Danish national registers on births and admissions to hospitals (miscarriage). The risk of miscarriage during pregnancy week 4-22 according to measures of night work was analysed using Cox regression with time-varying exposure adjusted for a fixed set of potential confounders.

RESULTS

In total 377 896 pregnancy weeks (average 19.7) were available for follow-up. Women who had two or more night shifts the previous week had an increased risk of miscarriage after pregnancy week eight (HR 1.32 (95% confidence interval 1.07 to 1.62) compared to women, who did not work night shifts. The cumulated number of night shifts during pregnancy week 3-21 increased the risk of miscarriages in a dose-dependent pattern.

CONCLUSIONS

The study corroborates earlier findings that night work during pregnancy may confer an increased risk of miscarriage and indicates a lowest observed threshold level of two night shifts per week.

Keywords; Miscarriage, Night work, payroll data, pregnancy, cohort study

What is already known on this topic

Experimental studies indicate that endogenous melatonin contributes to the maintenance of a successful pregnancy. Night work causes exposure to light at night and circadian disruption, which decreases the release of melatonin.

Observational studies have indicated an association between working night and miscarriage, but inaccurate exposure assessment precludes affirmative risk assessment.

What this study adds

This is the first study to investigate the association between night work and miscarriage using detailed and prospective measurement of exposure to night work.

Our results indicate that women who work two or more night shifts per week may be at increased risk of miscarriage the following week. Furthermore, both the cumulated number of night shifts and consecutive number night shifts increased the risk of miscarriage in a dose-dependent pattern.

How might this impact on policy or clinical practice in the foreseeable future?

The findings increase the knowledge about exposure to night work and have relevance for working pregnant women as well as their employers, physicians and midwifes. Moreover, the results could have implications for national occupational health regulations.

INTRODUCTION (3.291)

In Europe around 14% of all women report working at night at least once a month.[1] Studies in humans have found lower levels of melatonin mediated by exposure to light-at-night and with no full catch-up during the day among night workers.[2, 3] Furthermore, several consecutive night shifts may cause circadian disruption by phase shifting the suprachiasmatic nucleus (master clock) desynchronising with the sleep cycle and the peripheral oscillators throughout the body.[4] Melatonin is primarily synthesised in the pineal gland, but also in peripheral organs such as the placenta and ovaries. It is thought to be an important free radical scavenger and play a role in preserving the optimal function of the placenta.[5] Furthermore, experimental studies have demonstrated the importance of tightly regulated circadian rhythms, in which melatonin also has a pivotal role in the maintenance of successful pregnancies.[6] Supporting this is the finding of a lower pregnancy success rate among mice exposed to shifting in light/dark cycle compared to controls.[7] However, many biological processes of the circadian regulation of reproduction in humans are still unknown.[8]

Around one-third of all human embryos are lost, the majority within six weeks from the last menstrual period, most often unnoticed by the pregnant women and only some 10-14% are recognised as clinical miscarriages.[9] More than half of miscarriages are due to chromosomal abnormalities, which could arise within the sperm, within the egg before a female is born, or during the completion of meiosis shortly before conception. Since only the latter mechanism could possibly be caused by the mother's occupational exposures, miscarriages related to maternal exposures is possibly more easily detected among non-chromosomal late miscarriages.[10]

Meta-analyses addressing the association between night work and miscarriage have reported a moderately increased risk of miscarriage in relation to fixed night work, whereas no or weak associations are reported for rotating shiftwork including night work.[11, 12] However, studies are few and exposure assessment primarily based on self-reports and limited by the inability to adjust for important factors such as sick-leave and number of working hours. Thus, there is a need for prospective studies with refined exposure assessments making it possible to explore the effect of the intensity of night work and the types of shift schedules used.

The aim of this study was to investigate whether women who worked night shifts during pregnancy had an increased risk of miscarriage. We investigated the risk of miscarriage after night work the previous week and among women who worked cumulated night shifts, consecutive nights shifts, and had quick returns back to work after a night shift (defined as shift return in <11 hours).

METHODS

Design and Study population

Our register-based cohort study includes all female employees working in the five Danish administrative regions, who became pregnant during the period from January 1, 2007 through to December 31, 2013. As the Danish Administrative regions run all public hospitals in Denmark, our cohort consist primarily of hospital-based employees, such as nurses and physicians.[13] Using their civil registration number we identified women who had given birth from the Danish Medical Birth Register (DMBR),[14] and women who had been treated at a Danish hospital for miscarriage, molar or ectopic pregnancy or induced abortion from the Danish National Patient Register (DNPR).[15] DNPR holds information on all hospital contacts including inpatient, outpatient and emergency contacts, but not on contacts to specialists outside hospitals.[15] Both DNPR and DMBR provide almost complete information on gestational age (GA) and day at delivery or submission to hospital. In Denmark all women are offered an ultrasound scan around pregnancy week 11-14 to screen for Downs syndrome. 95% of the Danish women have the scan. Thus, GA of births are, in most cases, based upon ultrasonography. Whereas GA of miscarriages before pregnancy week 11-14 are, most often, based on the last menstrual period. We estimated the date of conception of each pregnancy by subtracting the GA from the date of delivery or hospital submission for miscarriage. For three miscarriages and 271 births (1.35%) missing data on GA were replaced by the median values (8.5 weeks for miscarriages and 40 weeks for births). A number of 21 (1%) miscarriages occurred at four weeks. Miscarriages with registered GA less than four weeks (n=6), or more than 22 weeks (n=6) were excluded. Only the first registered pregnancy from January 1, 2007 through to December 31, 2013 with at least 28 days of employment after date of fertilisation was included (the index conception) (Figure 1).

Exposure assessment

Data on working hours were obtained from The Danish working hour database (DWHD), which is a national database of administrative payroll data.[13] For every working day DWHD provides information on the start and end time (date:hours:minutes) of a shift.[13] A night shift was defined according to the 2009 IARC working group on shiftwork, as working at least three hours between midnight and 5:00.[4] The sum of night shifts was computed for each consecutive pregnancy week from week three through to week 21. For descriptive purposes exposed employees were defined as study participants with one or more night shifts during pregnancy week 3-21.

The risk of miscarriage among women who were exposed to night work was examined as a ‘short term effect’ by the number of night shifts completed the previous week. Moreover a ‘cumulated effect’ was examined in three ways by adding the number of night shifts, by adding number of consecutive night shifts with spells of at least 2, 3, 4, 5, 6 or 7 night shifts, and by adding number of quick returns after a night shift *(initiating a new shift <11 hours after a night shift)*. All cumulated effects were calculated from pregnancy week 3 until the week before outcome, censoring or pregnancy week 22, whichever came first.

Outcome assessment

Data on hospital admissions due to miscarriages, molar or ectopic pregnancies, and induced abortions were retrieved from DNPR using the ICD-10 codes DO00-DO07. Using the median of registered GA, the miscarriages were categorised in two groups, namely miscarriages in pregnancy week 4-8 and miscarriages in week 9-22. Because late clinical miscarriages are defined as pregnancies terminating after pregnancy week 12, the association between night work and miscarriages in week 13-22 was also explored. The pregnancies were followed from week four until miscarriage (the outcome), molar or ectopic pregnancy (censoring), induced abortion (censoring), discontinuance of employment, or pregnancy week 22, whichever came first.

Covariates

Maternal date of birth was obtained from the DWHD, which enabled calculation of maternal age at the time of the index conception. The DMBR provided information on parity (completeness 97.7%), while this information was not available from DNPR. However, by linking women admitted for miscarriage to DMBR it was possible to retrieve data on parity for most of the women who had given birth before or after the time of the miscarriage (93.6%). For nulliparous women with miscarriage this information was missing (6.4%). Baseline smoking and BMI were retrieved from DMBR and based on the first midwife contact. For the women with miscarriage as index, pregnancy smoking status and BMI reported in relation to the birth closest in time to the hospital admission for the miscarriage was selected (median difference 42.9 months). Information on job title was retrieved from Statistics Denmark (DST) using DISCO-88 and DISCO-08, the Danish version of the International Standard Classification of Occupations in the calendar years 2007-2009 (DISCO-88) [16] and 2010-2013 (DISCO-08),[17] respectively. Classification of socioeconomic status (SES) into high, medium and low was derived from DISCO codes based on Statistics

Denmark's categorisation. Covariates were grouped according to the categories presented in Table 1.

Statistical methods

To determine the 'short-term effect' of night work, exposure data were used as both a continuous variable and as categorised into three groups: none, one, or two or more night shifts the previous week. Data on cumulated night shifts were also used both as a continuous variable and as categorised by 0, 1-10, 11-20, 21-25, and > 25 night shifts.

We estimated the risk of miscarriage by the different night work dimensions by discrete Cox regression with time varying exposure from pregnancy week four through to week 22, corresponding to the time after the implantation of the fertilised egg and until the week after which expulsion of the fetus is defined as a preterm birth or stillbirth. Each week was assigned week-specific exposure levels, and analyses were performed with and without adjustment for maternal age, BMI, smoking, parity, SES, and former miscarriages, which were chosen a priori.[18, 19] To ensure only night work prior to a miscarriage was taken into account, a lag of one week was used.

Competing risk by induced abortions[20] was examined in sensitivity analyses using the proportional hazard model proposed by Fine and Gray.[21] To account for possible differences between employees working and not working nights we performed sensitivity analyses within employees who had at least one night shift in pregnancy week 3-21. We observed a substantial decline in the number of registered miscarriages after 2010 (from 9.7% to 6%) and conducted a sensitivity analysis only including pregnancies registered between 2007 and 2010. Furthermore, we performed sensitivity analyses including only nulliparae and nurses as these represented the largest occupational group in the Danish regions. Effect modification by maternal age, BMI, smoking and SES were explored by adding interaction terms to the regression analyses.

Analyses were undertaken on pseudo-anonymised data at a remote platform at Statistics Denmark by SAS 9.4 software. Cox regressions were executed applying the PHREG procedure. A significance level of 0.05 was used.

RESULTS

A total of 22 744 pregnant employees and 377 896 pregnancy weeks at risk were included in the final analyses. Baseline characteristics of the study population by exposure to night work are presented in Table 1. Nearly half (44%) of the participants were exposed to night work with a median of nine night shifts during pregnancy weeks 3-21. Only 124 employees worked fixed nights with no registered day or evening shifts. A total of 1 889 women (8.5%) had a miscarriage. The exposed group had fewer miscarriages with a higher median for GA and fewer previous miscarriages compared to the reference group. A higher proportion of women in the exposed group were nulliparae, nurses and physicians, and had higher SES compared to the reference group.

Table 1 Characteristics of the study population according to exposure of night work (N=22 744)		
Characteristics	**Exposed** ≥ 1 registered night shift during pregnancy week 3-21 **(n=10 047)**	**Reference group** No registered night shifts during pregnancy week 3-21 **(n=12 697)**
Outcome of pregnancy, n (%)		
Births	9 089 (90)	11 007 (87)
Miscarriages	740 (8)	1 149 (9)
Molar and ectopic pregnancies	44	96 (1)
Induced abortions	174 (2)	445 (3)
Time for miscarriage (pregnancy week)		
Gestational age, median (min, max)	9.0 (4.0, 21.0)	8.0 (4.0, 21.0)
Follow-up weeks at risk, median (Pct 25, 75)	22 (22,22)	22 (22,22)
Work during pregnancy week 3-21, median (Pct 25,75)		
Number of day shifts	40 (25, 52)	50 (11, 80)
Number of evening shifts	6 (0, 16)	0 (0, 2)
Number of night shifts	9 (4,16)	
Maternal age at conception		
Mean years (SD)	30.5 (3.9)	30.9 (4.4)
≤ 25 years, n (%)	512 (5)	1 028 (8)
26-30 years, n (%)	4 531 (45)	4 701 (37)
>30 years, n (%)	5 004 (50)	6 968 (55)
Parity, n (%)		
0	5 948 (59)	6 967 (55)
1	2 442 (24)	3 434 (27)
2+	1 411 (14)	1 963 (15)
Missing	246 (2)	333 (3)
Former miscarriage, yes n (%)	736 (7)	1 104 (9)
BMI before pregnancy		
Mean (SD)	23.7 (4.3)	23.9 (4.6)
Underweight (<18.5 kg/m^2), n (%)	743 (7)	977(8)
Normal weight (18.5-24.9 kg/m^2), n (%)	6 646 (66)	8 167 (64)
Overweight (25.0-29.9 kg/m^2), n (%)	1 818 (18)	2 382 (19)
Obese (30+ kg/m^2), n (%)	840 (8)	1 171 (9)
Smoking during pregnancy, n (%)		
Non-smoker	9 252 (92)	11 579 (91)
Smoker	492 (5)	726 (6)
Missing	303 (3)	392 (3)
Socio-economic status (SES), n (%)		
Low	869 (9)	3 563 (28)
Medium	6 939 (69)	6 811 (53)
High	2 224 (22)	2 230 (18)
Missing	15	93 (1)
Most frequent occupation, n (%)[a]		
Nurse	6 242 (62)	3 405 (27)
Physicians	1 732 (17)	955 (8)
Medical secretary	53	1 373 (11)
Physiotherapist/Occupational therapist	29	1 175 (10)
Nurse assistant	510 (5)	727 (6)
Laboratory technician	233 (2)	642 (5)
Cleaning/kitchen worker	17	557 (4)
Pedagogue/care helper	230 (2)	383 (3)
Psychologist	<10	418 (3)
Midwife	305 (3)	41
Office worker	10	304 (2)
Teacher/scientist	81 (1)	300 (2)

217 [a]Among occupations with at least 100 employees

We found an increased short-term risk of miscarriage after pregnancy week eight with an adjusted HR of 1.32 (95% confidence interval 1.07 to 1.62) if the women had ≥ 2 night shifts the previous week (Table 2). The adjusted HR of late clinical miscarriage (pregnancy week 13-22) was 1.28 (95% confidence interval 0.70 to 2.34). Only 133 of the miscarriages (7%) were late clinical miscarriages.

Table 2 Risk of miscarriage by having night work the previous week

	All miscarriages (pregnancy week 4-22)			Miscarriages pregnancy week 4-8			Miscarriages pregnancy week 9-22		
	Cases[a]/ Risk time[c]	**Crude HR (95% CI)**	**Adjusted[b] HR (95% CI)**	**Cases[a]/ Risk time[c]**	**Crude HR (95% CI)**	**Adjusted[b] HR (95% CI)**	**Cases[a]/ Risk time[c]**	**Crude HR (95% CI)**	**Adjusted[b] HR (95% CI)**
Continuous exposure[d]	1 889/ 377 896	1.06 (1.00 to 1.11)	1.06 (1.01 to 1.12)	930/ 110 671	1.03 (0.96 to 1.11)	1.02 (0.95 to 1.10)	959/ 267 225	1.09 (1.01 to 1.17)	1.10 (1.03 to 1.19)
Categorical exposure									
No night shift	1 521/ 314 511	1	1	741/ 89 229	1	1	780/ 225 282	1	1
1 night shift	167/ 30 822	1.02 (0.87 to 1.20)	1.00 (0.85 to 1.18)	90/ 9 978	1.06 (0.85 to 1.32)	1.05 (0.84 to 1.32)	77/ 20 844	0.99 (0.78 to 1.25)	0.91 (0.71 to 1.17)
2+ night shifts	201/ 32 563	1.15 (0.99 to 1.33)	1.18 (1.01 to 1.37)	99/ 11 464	1.06 (0.86 to 1.31)	1.06 (0.85 to 1.31)	102/ 21 099	1.24 (1.01 to 1.53)	1.32 (1.07 to 1.62)

a Miscarriage

b Adjusted for maternal age, BMI and smoking in the beginning of pregnancy, parity, SES, former miscarriages

c Pregnancy weeks

d Mean effect of adding an additional night shift the previous week

Age modified the risk of miscarriage according to night work the previous week ($p<0.05$ for multiplicative interaction). Women in the age group 26-30 years had the highest risk of miscarriage after pregnancy week eight per additional night shift the previous week (HR 1.23 (95% confidence interval 1.11 to 1.37)). Neither SES, maternal BMI nor tobacco smoking modified the association between recent night work and risk of miscarriage (Appendix table 1).

All the sensitivity analyses were consistent with results from the main analyses (Appendix table 2). Taking competing risk of induced abortions into account did not affect the results.

A cumulated effect of number of night shifts during pregnancy week 3-21 was found with adjusted HR for miscarriage of 1.15 (95% confidence interval 1.02 to 1.29) per ten night shifts corresponding to one night shift every second week. In the categorised data, a dose-dependent risk of miscarriage was observed with an adjusted HR of 2.62 (95% confidence interval 1.30 to 5.29) among those with 26 or more night shifts during pregnancy week 3-21 (average of 35 night shifts, ranging from 26 to 79). However, this group had a risk time of only 4 246 pregnancy weeks and eight cases (Table 3).

Table 3 Risk of miscarriage pregnancy week 4-22 by cumulated night shifts during pregnancy

	Cases[b]	Risk time[c]	Crude HR (95% CI)	Adjusted[d] HR (95% CI)
Continuous exposure[a]				
Ten night shifts			1.13 (1.01 to 1.27)	1.15 (1.02 to 1.29)
Categorical exposure				
No night shifts	1 149	226 184	1	1
1-10 night shifts	646	113 058	1.03 (0.93 to 1.13)	1.05 (0.94 to 1.16)
11-20 night shifts	78	30 060	1.21 (0.96 to 1.53)	1.20 (0.94 to 1.53)
21-25 night shifts	8	4 348	1.59 (0.79 to 3.19)	1.70 (0.84 to 3.42)
26+ night shifts	8	4 246	2.48 (1.23 to 5.00)	2.62 (1.30 to 5.29)

a Effect per additional night shift during pregnancy week 3-21
b Miscarriages
c Pregnancy weeks
d Adjusted for maternal age, BMI and smoking during pregnancy, parity, SES, former miscarriages

A total of 6 435 pregnant employees (28%) had consecutive night shifts, the most frequent being two consecutive night shifts. The risk of miscarriage increased for each additional number of consecutive night shifts per spell; however, very few women (n=1.163) had ≥ four consecutive night shifts. (Figure 2). Quick return after night shift was registered for 810 pregnant employees during week 3-21 with a median of one quick return. No association was found between quick returns and the risk of miscarriage (HR 1.02 (95% confidence interval 0.85 to 1).

DISCUSSION

In our nationwide cohort of pregnant women, primarily employed at hospitals, we found an increased risk of miscarriage among women who had night work the previous week, and among women with cumulated numbers of night shifts. Two or more night shifts the previous week increased the risk of miscarriage after pregnancy week eight with 32% compared with women who had not worked night shifts the previous week. The number of night shifts and number of consecutive night shifts during pregnancy week 3-21 showed a dose-dependent increased risk. We found no association between quick returns after a night shift and risk of miscarriage, but due to the power constraints these results should be interpreted with caution.

Strengths and limitations of the study

To the best of our knowledge, our study represents the first to use prospective administrative data, which eliminates the risk of recall bias which is a common limitation in previous studies.[12] Furthermore, detailed payroll data accounted for sick-leave, which is common among pregnant women,[22, 23] and night work intensity.

However, some limitations need to be addressed. While all births in Denmark are registered in the DMBR, only miscarriages treated at hospitals are registered in DNPR. We lacked information on very early miscarriages, which may be unnoticed by the women or handled in primary care. However, this is a premise in register-based studies and might attenuate the risk estimates if exposures are assumed to be especially harmful in the first weeks of gestation. A Danish pregnancy-planner study using hCG analysis found that 12.4% of conceived pregnancies ended as clinically recognized miscarriages.[24] Reasons for the lower proportion of miscarriages found in our study could be, that our population was healthier and had less focus on pregnancy compared to the women in the pregnancy-planner study. However, it is more likely a reflection of organizational changes. In Denmark fewer miscarriages are being evacuated[25] and thus, a higher proportion of women may be treated by a primary care specialist. This may also partly explain the substantial decline in the proportion of registered miscarriages after 2010 relative to births, which is unlikely explained by biological causes. Nonetheless, place of treatment is likely independent of exposure and any potential misclassification would be non-differential with less risk of bias. This is supported by our sensitivity analysis, which was restricted to pregnancies registered between 2007 and 2010, which showed consistent results.

The difference in distribution of SES, occupations, parity and number of previous miscarriages between employees working night shifts and employees never working nights could potentially confound the results in the analyses. We adjusted for SES and parity and our sensitivity analyses including only nurses or nulliparae, respectively, were consistent with the results in the primary analyses. It is disputed whether to adjust for previous miscarriages or not. If previous miscarriages are caused by the exposure of interest, risk estimates might erroneously be attenuated. If previous miscarriages are due to other risk factors with an unbalanced distribution across exposure categories adjustment is needed.[9] However, the risk estimates did not change substantially whether adjustment was performed or not. We also observed a difference between employees having night shifts and employees never working nights regarding number and time of miscarriage. This could be explained by delayed entry in the exposed group (only women with no abortions before the first registered night shift were included) causing survivor bias. In the Cox analyses this was accounted for.

Also, we were unable to account for other work-related exposures such as lifting and non-sitting work posture, which may increase risk of miscarriage according to some studies.[12, 26, 27] Our sensitivity analysis only including nurses supported the primary results, but it has been shown in the American Nurses' Health Study cohort that nurses working day shifts have less strenuous work (lifting and standing) compared to nurses working fixed nights or shiftwork including night shifts.[28, 29]

In Denmark during the study's time-period about 8% of all pregnancies were conceived after fertility treatment. Being in fertility treatment could be a potential confounder due to increased risk of miscarriage and possible changed attitude towards working nights. The same could be the case for women with previous miscarriages. Unfortunately, we had no data on fertility treatment or cancelled night shifts. Because of this potential healthy worker selection our results could underestimate the effect of night work on miscarriage.

We found a stronger association between night work and risk of miscarriages after pregnancy week eight. This may be explained by the decline in proportion of chromosomally abnormal fetuses with gestational age, which makes an association with environmental exposure more easily detectable among later miscarriages.[30] The association between night shifts and late clinical miscarriage (after pregnancy week 12) was less strong, but with a wide confidence interval because of few cases.

Findings in relation to other studies

Our findings confirm results in previous studies on fixed night work and risk of miscarriage.[31, 29, 32-37] However, studies on shiftwork including night shifts and risk of miscarriage have been inconsistent and lacked information on number of consecutive shifts.[31, 36, 32, 29, 34, 38] To date, only three previous studies have been based on prospectively collected data.[37, 32, 38] An American study, with information on exposure retrieved from interviews before pregnancy week 13, found no effect of working evening/night, but non-significant increased odds of miscarriage if working rotating shifts (OR = 1.34 (95% confidence interval 0.77 to 2.34)). The extent to which shiftwork included night shifts was not indicated.[38] In two studies based on the Danish National Birth Cohort (DNBC) night work was measured by asking the women whether they primarily worked “fixed nights” or “shiftwork including night shifts”. Both studies reported an increased risk of miscarriage among women who worked fixed nights with corresponding risk estimates of HR 1.27 (95% confidence interval 0.89 to1.82)[37] and HR 1.81 (95% confidence interval 0.88 to 3.72)[32] respectively. For shiftwork including night shifts the HR was 1.21 (95% confidence interval 1.06 to 1.39)[37] and 1.10 (95% confidence interval 0.78 to 1.57),[32] respectively. The crude assessment of exposure in the earlier studies could result in misclassification and bias towards the null, especially in the group who had shiftwork. However, it is noteworthy that the pregnant women were included in DNBC in pregnancy week 11-25 (median 16)[37] and thus primarily addressed late miscarriages.[32] In our study we only observed a few late miscarriages. The stronger association between fixed night work and miscarriages could be explained by the intensity of night shifts, including a higher number of cumulated and consecutive night shifts, with a higher risk of circadian disruption and decrease in melatonin levels. This is consistent with our results which showed a dose-related effect of the cumulated number of night shifts.

Although our population was based on a nationwide cohort, it primarily consisted of women working in public hospitals, who may have more health-promoting behaviour compared with the general Danish population. This was indicated in our data showing a lower prevalence of smoking in early pregnancy [39] and a lower proportion of obese women.[40] However, we found no modifying effect of BMI and smoking.

CONCLUSION

The study corroborates earlier findings that night work during pregnancy may confer an increased risk of miscarriage and it indicates a lowest observed threshold level of two night shifts per week.

The new knowledge has relevance for working pregnant women as well as their employers, physicians and midwifes. Moreover, the results could have implications for national occupational health regulations.

(178)

Contributors

LMB, JPB, PECH, EMF and IOS conceived and designed the study. AHG, JH, ÅMH, HAK established and provided data from the DWHD. JPB analysed the data and EMF gave statistical support. LMB drafted the manuscript and all authors interpreted the data and revised the manuscript.

Competing interest

All authors have completed the ICMJE uniform disclosure from www.icmje.org/coi_disclosure.pdf and declare: support for the submitted work as described above; no financial relationship with any organisations that might have interest in the submitted work; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval

The study was approved by the Danish Data Protection Agency (though the notification system in the Capital region of Denmark, j.nr.: 2012-58-0004). By Danish law, no informed consent is required for a register-based study.

Acknowledgement

The results have been presented at the Reproyoung conference, Ystad 25th – 26th October. The authors thank Clara Helene Glazer for proof-reading the final manuscript.

Funding

This work was supported by the Danish Working Environment Research Fund grant 31-2015-03 2015001705.

Data Sharing

No additional data available.

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