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Shift work and subfecundity: a causal link or an artefact?

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Aims: The Danish National Birth Cohort (DNBC) was used to examine whether shift work is associated with reduced fecundity as estimated by time to pregnancy (TTP).
Methods: From 1 March 1998 to 1 May 2000, 39 913 pregnant women were enrolled in the DNBC. Data on job characteristics and TTP (0–2, 3–5, 6–12, and >12 months) were used for 17 531 daytime workers and 3907 shift workers who had planned the pregnancy. Fecundity odds ratios (ORs) were calculated with 95% confidence intervals using the discrete time survival analysis techniques performed by logistic regression. An OR above 1 expresses a shorter TTP and then a higher fecundity. Potential confounders, such as age at conception, gravidity, prepregnant body mass index, smoking, and alcohol consumption, as well as occupational characteristics, were also included in the model.
Results: Fixed evening workers and fixed night workers had a longer TTP. Compared with daytime workers, the adjusted ORs were 0.80 (95% CI 0.70 to 0.92) for fixed evening workers, 0.80 (95% CI 0.63 to 1.00) for fixed night workers, 0.99 (95% CI 0.91 to 1.07) for rotating shift (without night) workers, and 1.05 (95% CI 0.97 to 1.14) for rotating shift (with night) workers. When analysis was restricted to nulliparous women, the estimates remained unchanged. The proportions of unplanned pregnancies and contraceptive failures were higher among fixed evening and fixed night workers.
Conclusions: There was no unequivocal evidence of a causal association between shift work and subfecundity. The slightly reduced fecundity among fixed evening workers and fixed night workers may be mediated by pregnancy planning bias or differential options for sexual contacts.

Shift work, referring to hours of work occurring outside the regular daytime schedule, has been related to early fetal loss, preterm birth, and low birth weight.[1–3] The suggested mechanisms operate via hormonal disturbances, either as a direct effect of changes in circadian rhythm or indirectly through psychosocial stress. Melatonin, primarily secreted from the pineal gland, acts as a hormonal transduction of photoperiod influencing the timing of seasonal and circadian physiological rhythms.[4] If high melatonin concentrations in blood cause hypothalamic-pituitary-gonadal hypofunction, as seen in women with hypothalamic amenorrhoea,[5] one study showed that there was a trend towards amplifying the peak and rhythm amplitude of melatonin concentration after one year of rotating work.[6] Furthermore, decreased serum concentration and amplitude of the wave of cortisol, prolactin, and testosterone has been reported for shift workers.[7 8] Shift work is also a common stressor in the workplace,[9] and psychological stress has been associated with subfertility.[10 11]

A study from Sweden found that midwives who worked two-shift, three-shift, or fixed night work had reduced fecundability compared with those working in the daytime shifts.[12] A European multicentre study showed that rotating shift work for women was associated with an increased risk of subfecundity,[13] and a Japanese study on working conditions indicated that pregnancy rates were lower for women doing shift work compared with daytime workers.[14] However, three studies (from Denmark,[15] Italy,[16] and Thailand[17]) did not find an association between shift work and low fertility. These inconsistent results may reflect differences in shift work exposure or differences in work conditions, as well as methodological shortcomings.[18 19]

The Danish National Birth Cohort (DNBC), a nationwide study of pregnant women and their offspring, provides an opportunity to explore associations between potential hazardous occupational exposures and adverse reproductive outcomes.[20] This study aimed at examining whether exposure to various types of shift work was associated with low fecundity as measured by a prolonged waiting time to pregnancy (TTP). We especially expected rotating shift (with night) to be associated with a longer TTP, because it may be more difficult for the endogenous circadian system of the body to adjust to the changing rhythm of rotating shifts (with night). Rotating shifts may be a stressor in itself as well as interfering with coping with stress by interfering with maintaining a social network.

Main message

- There is no unequivocal evidence of a causal association between shift work and subfecundity.

Policy implication

- Further investigations are warranted to elucidate the risk of other adverse pregnancy outcomes due to shift work.

MATERIALS AND METHODS

Study population

The study was carried out within the DNBC, which has been described in detail elsewhere.[20–22] Candidates for the cohort were all pregnant women in Denmark who, at their first visit to their general practitioner, wanted to carry their pregnancy to term and who spoke Danish well enough to take part in the telephone interviews. Participants were given the possibility to indicate a preferred day and time for the interviews covering normal working hours, evenings, or weekends. Approximately 60% of all pregnant women accepted the invitation to join the cohort from almost 60% of the general practitioners who took part in the recruitment. From 1 March 1998 to 1 May 2000, 39 913 pregnant women (40 635 pregnancies) were enrolled in

Abbreviations: BMI, body mass index; CI, confidence interval; DNBC, the Danish National Birth Cohort; OR, odds ratio; TTP, time to pregnancy

Table 1 Exclusion criteria by work schedules

Pregnancies	Daytime work n (%)	Fixed evening work n (%)	Fixed night work n (%)	Rotating shift work (without night) n (%)	Rotating shift work (with night) n (%)
Total	24605	809	290	2334	2429
The second pregnancies†	184 (0.7)	7 (0.9)	1 (0.3)	21 (0.9)	17 (0.7)
Endometriosis	68 (0.3)	2 (0.2)	1 (0.3)	6 (0.3)	9 (0.4)
Ovarian or cervical cancer	18 (0.1)	0 (0.0)	0 (0.0)	3 (0.1)	0 (0.0)
Partly planned	2136 (8.7)	85 (10.5)	27 (9.3)	223 (9.6)	237 (9.8)
Unplanned	3078 (12.5)	167 (20.6)**	56 (19.3)**	365 (15.6)**	344 (14.2)*
Treatment for infertility	1590 (6.5)	55 (6.8)	28 (9.7)*	144 (6.2)	157 (6.5)
Final study pregnancies	17531 (71.2)	493 (60.9)	177 (61.0)	1572 (67.4)	1665 (68.5)

The numbers in parentheses represent percentages.
†One woman contributed two pregnancies during the study period.
*p<0.05 and **p<0.01, χ^2 test, compared with daytime workers.

the DNBC, giving their first telephone interview (12–16 completed gestational week), and still being pregnant at that time. They were asked to state their occupation and work schedule. We identified 30 467 pregnancies in women who had a job and had stated their occupation and work schedule. We excluded pregnancies in women with endometriosis, ovarian cancer, or cervical cancer. We excluded unplanned pregnancies, partly planned pregnancies, and pregnancies that occurred after infertility treatment from the main analysis. The proportions of unplanned pregnancies were higher among shift workers. Some women participated in the cohort with two pregnancies during the study period; we excluded the second reported pregnancies to achieve statistical independence. We ended up with 17 531 daytime workers, 493 fixed evening workers, 177 fixed night workers, 1572 rotating shift (without night) workers, and 1665 rotating shift (with night) workers, who were eligible for the main analyses (table 1).

Exposure assessment

In the first interview, the women were asked in detail about their occupation, including the number of jobs, their job title, type of work, working hours, work schedule, and number of night shifts. Their partners' occupations were also recorded. We grouped the women by occupation according to the Danish version of the International Standard Classification of Occupation (DISCO-88)[23] into: managers and professionals (0110–2470), technicians (3111–3480), service and sales workers (4111–6210), and industrial workers (7111–9333). We classified weekly working hours into two categories: <35 hours and 35+ hours. The work schedule question was asked as follows: "Do you primarily work during the day, during the evening or during the night, or do you have changing working hours?" The mutually exclusive answering categories were: 1, daytime; 2, fixed evening; 3, fixed night; 4, rotating shift (without night); 5, rotating shift (with night). We grouped the frequency of night shifts into 1–8 and 9+ times per month. We furthermore identified two specific job types with the largest numbers for an internal contrast in work schedules: nurses (n = 1624) and nursing assistants (n = 899). Their partners' jobs were classified in the same categories, except when they reported having no job.

Measurement of outcome and potential confounders

TTP was recorded according to the following questions: "How long did you try to become pregnant, before you succeeded? 0–2 months, 3–5 months, 6–12 months, or >12 months?" Additionally, the woman was asked if the pregnancy was planned, partly planned, or not planned. Only planned pregnancies were included in the analyses presented in the tables.

Potential confounders were categorised as shown in table 2. They included age at conception, gravidity, prepregnancy body mass index (BMI), smoking, and alcohol consumption. Maternal age at conception was computed by subtracting the woman's birth date from the last menstrual period and adding 14 days. Prepregnancy BMI was calculated on the basis of the women's report on height and weight before pregnancy. We used the question whether they had smoked at any time in the first trimester to categorise them as either smokers or non-smokers. Alcohol consumption was classified in categories as described elsewhere.[22] In brief, we added beer, wine, and spirits to one variable of total alcohol consumption per week, according to the woman's report on her drinking habits before pregnancy. One bottle of beer contains 11.6 g of alcohol, and 12 g of alcohol is an approximate average for one unit of wine or spirits in Denmark. If less than one unit per week was reported by the woman, 0.5 units were coded. We then grouped them by these levels: 0, 0.5–7, 7.5+ units (12 g alcohol per unit) per week. It has previously been shown[21] that neither interviewer's habits nor her attitudes towards smoking and alcohol consumption during pregnancy had consequences for responses obtained. Likewise, the education, age, or parity of the interviewer did not correlate with the answers obtained. We had limited data on the partner and no information on sexual activity or sperm quality.

Statistical analysis

In general, fecundability is defined as the probability to conceive in a menstrual cycle. In our study, we estimated the probability of obtaining a clinically recognised pregnancy in a waiting time interval among women not pregnant in the previous interval, conditionally that they did get pregnant. Fecundity odds ratio (OR) measures the odds of a conception within each waiting time interval among the exposed divided by the odds among those not exposed. This measure will correlate with fecundability under most conditions, but it is not a measure of fecundability. ORs were calculated with 95% confidence intervals (95% CI) using the discrete time survival analysis techniques performed by logistic regression, which is a non-proportional hazard model,[24] to estimate the effects on shift workers compared with daytime workers. TTPs in our study were measured in discrete times (four intervals). We first broke down each individual's TTP into a set of intervals that were treated as distinct observations. After pooling these observations, the next step was to estimate a binary regression model (logistic model) predicting whether a conception occurred in each interval and a variable to indicate that the interval was fitted into the model while covariates were allowed. We repeated all analyses for only those women who tried to become pregnant for the first time, since a previous TTP may modify risk behaviour in subsequent attempts in such a way that may be impossible to adjust for. All analyses were restricted to women who had a job at the first interview. We estimated the effect of night shifts on TTP by including only fixed night workers and rotating shift (with night) workers in the analysis. Potential confounders were included in the model, as well as a variable to indicate waiting time interval and the couple's occupational characteristics. Analyses were performed using SPSS 10.0.

Table 2 Characteristics of participants according to work schedules

	Daytime work		Fixed evening work		Fixed night work		Rotating shift work (without night)		Rotating shift work (with night)	
	n	%	n	%	n	%	n	%	n	%
Maternal age at conception										
<25	1639	9.3	85	17.2	31	17.5	173	11.0	103	6.2
25–29	7433	42.4	218	44.2	68	38.4	712	45.3	843	50.6
30–34	6730	38.4	144	29.2	65	36.7	520	33.1	558	33.5
35+	1729	9.9	46	9.3	13	7.3	167	10.6	161	9.7
Gravidity										
0	5529	31.5	137	27.8	45	25.4	549	34.9	564	33.9
1	6690	38.2	168	34.1	64	36.2	547	34.8	564	33.9
2+	5306	30.3	188	38.1	68	38.4	476	30.3	535	32.1
Missing	6	0.0	0	0.0	0	0.0	0	0.0	2	0.1
BMI										
<18.5	708	4.0	16	3.2	8	4.5	62	3.9	61	3.7
18.5–30	15350	87.6	421	85.4	145	81.9	1364	86.8	1480	88.9
>30	1214	6.9	48	9.7	20	11.3	120	7.6	112	6.7
Missing	259	1.5	8	1.6	4	2.3	26	1.7	12	0.7
Smoking										
No	13693	78.1	346	70.2	105	59.3	1161	73.9	1293	77.7
Yes	3835	21.9	147	29.8	72	40.7	410	26.1	371	22.3
Missing	3	0.0	0	0.0	0	0.0	1	0.1	1	0.1
Alcohol consumption										
None	1864	10.6	71	14.4	30	16.9	162	10.3	143	8.6
0.5–7	14170	80.8	391	79.3	133	75.1	1268	80.7	1395	83.8
7.5+	1419	8.1	29	5.9	14	7.9	137	8.7	122	7.3
Missing	78	0.4	2	0.4	0	0.0	5	0.3	5	0.3
Occupation, mother										
Managers and professionals	3785	21.6	15	3.0	7	4.0	299	19.0	259	15.6
Technicians	5117	29.2	176	35.7	49	27.7	631	40.1	1077	64.7
(Nurses)*	321		146		36		259		862	
Service and sales workers	7465	42.6	234	47.5	81	45.8	530	33.7	278	16.7
(Nursing assistants)*	521		137		43		106		92	
Industrial workers	1164	6.6	68	13.8	40	22.6	112	7.1	51	3.1
Occupation, father										
Managers and professionals	5204	29.7	94	19.1	26	14.7	458	29.1	541	32.5
Technicians	3313	18.9	72	14.6	24	13.6	278	17.7	334	20.1
Service and sales workers	2244	12.8	76	15.4	30	16.9	195	12.4	205	12.3
Industrial workers	5529	31.5	209	42.4	80	45.2	458	29.1	435	26.1
No job	754	4.3	26	5.3	10	5.6	126	8.0	105	6.3
Missing	487	2.8	16	3.2	7	4.0	57	3.6	45	2.7
Working hours per week										
<35	4110	23.4	389	78.9	109	61.6	455	28.9	467	28.0
35+	13397	76.4	101	20.5	68	38.4	1105	70.3	1187	71.3
Missing	24	0.1	3	0.6	0	0.0	12	0.8	11	0.7
Number of night shifts per month										
1–8					11	6.2			1555	93.4
9+					162	91.5			99	5.9
Missing					4	2.3			11	0.7

Percentages may not add to 100.0 because of rounding.
*Specific types of work, not included in column totals.

RESULTS

The proportion of shift work was 19.1% among women who had a job. Table 2 shows the primary characteristics of the study population. Characteristics of rotating shift workers (with or without night) were similar to that of daytime workers, except that most rotating shift workers were technicians and most daytime workers were service and sales workers. Fixed evening workers and fixed night workers were heterogeneous populations compared with others. They were younger, more often parous, obese, and smokers, and they more often worked as industrial workers, as did their partners. Their median weekly work hours were 28 hours and 30 hours, respectively, while daytime and rotating shift (with or without night) workers worked 37 hours per week. By agreement, full time employment in Denmark equals 37 hours a week. The median number of night shifts was 14 a month for fixed night workers and four for rotating shift workers (with night).

Compared with daytime workers, fixed evening workers and fixed night workers had a longer TTP, while rotating shift (with or without night) workers had similar TTP. The crude ORs were 0.83 for fixed evening workers, 0.75 for fixed night workers, 1.00 for rotating shift (without night) workers, and 1.11 for rotating shift (with night) workers. The adjusted risk estimates never changed more than the 10% limit (table 3). The adjusted OR for working at night more than nine times per month was 0.97 (95% CI 0.70 to 1.34) compared with 1–8 times per month.

The estimates did not change when we included only the first pregnancies (data not shown). When we restricted the analysis to nurses, none of the shift workers had a statistically significant low fecundity; the adjusted ORs were 0.99 (95% CI 0.71 to 1.38) for fixed evening work, 0.67 (95% CI 0.39 to 1.15) for fixed night work, 0.96 (95% CI 0.73 to 1.24) for rotating shift work (without night), and 0.99 (95% CI 0.81 to 1.22) for rotating shift work (with night), compared with daytime work (data not shown). When we did an analysis for nursing assistants, only fixed evening work (OR 0.73; 95% CI 0.54 to 0.99) showed a statistically significantly decreased fecundity (data not shown).

We performed separate analyses for smokers and non-smokers, since smoking was more prevalent among fixed evening work and fixed night work and correlated with TTP (OR 0.82; 95% CI 0.78 to 0.87). Shift work did not show any statistically significant association with fecundity among

Table 3 Time to pregnancy and adjusted fecundity odds ratios (ORs) for occupational exposures

	0–2 months		3–5 months		6–12 months		>12 months			
	n	%	n	%	n	%	n	%	OR	95% CI
Work schedule										
Daytime work	8700	49.6	4076	23.3	2958	16.9	1797	10.3	1	
Fixed evening work	219	44.4	113	22.9	96	19.5	65	13.2	0.80	0.70 to 0.92
Fixed night work	75	42.4	42	23.7	31	17.5	29	16.4	0.80	0.63 to 1.00
Rotating shift work (without night)	786	50.0	358	22.8	268	17.0	160	10.2	0.99	0.91 to 1.07
Rotating shift work (with night)	855	51.4	393	23.6	285	17.1	132	7.9	1.05	0.97 to 1.14
Occupation, mother										
Managers and professionals	2344	53.7	1007	23.1	624	14.3	390	8.9	1.09	1.02 to 1.16
Technicians	3581	50.8	1656	23.5	1178	16.7	635	9.0	1	
Service and sales workers	4071	47.4	2009	23.4	1550	18.0	958	11.2	0.87	0.82 to 0.91
Industrial workers	639	44.5	310	21.6	286	19.9	200	13.9	0.79	0.72 to 0.86
Occupation, father										
Managers and professionals	3316	52.4	1452	23.0	989	15.6	566	9.0	1.05	0.99 to 1.12
Technicians	2019	50.2	946	23.5	663	16.5	393	9.8	1	
Service and sales workers	1348	49.0	635	23.1	491	17.9	276	10.0	0.98	0.91 to 1.06
Industrial workers	3135	46.7	1560	23.2	1224	18.2	792	11.8	0.90	0.85 to 0.96
No job	528	51.7	242	23.7	171	16.7	80	7.8	1.10	0.99 to 1.23
Working hour										
35+	7769	49.0	3718	23.4	2713	17.1	1658	10.5	1	
<35	2841	51.4	1254	22.7	918	16.6	517	9.3	1.08	1.02 to 1.13
Number of night shifts per month*										
1–8	805	51.4	370	23.6	271	17.3	120	7.7	1	
9+	114	43.7	64	24.5	44	16.9	39	14.9	0.97	0.70 to 1.34

Discrete time survival analysis technique performed by logistic regression; adjusted for age at conception, gravidity, prepregnancy BMI, smoking, and alcohol consumption, as well as a variable to indicate time interval and a couple's occupational characteristics in the table except for number of night shifts per month; percentages may not add to 100.0 because of rounding.
*Only fixed night workers and rotating shift (with night) workers were included in the model, adjusted for age at conception, gravidity, prepregnancy BMI, smoking, and alcohol consumption, as well as a variable to indicate time interval and a couple's occupational characteristics in the table.

non-smokers. In smokers, fixed evening workers and fixed night workers had a decreased fecundity: OR 0.70 (95% CI 0.54 to 0.90) and 0.63 (95% CI 0.44 to 0.89), respectively (data not shown).

DISCUSSION

We did not find an association between rotating shift work (with or without night) and reduced fecundity. This finding was consistent for all, for nulliparous women, for nurses and nursing assistants, for non-smokers, and for smokers. The median number of working nights per month was only four for rotating shift workers (with night). If night shifts have only transient effects (say, few days), we may have limited possibility to detect it. We found no difference in TTP among women working at night more than 9 times per month and women working at night 1–8 times per month after adjusted for potential confounders.

Fixed evening workers and fixed night workers had different results. These workers were, however, very different from daytime workers and rotating shift workers. The proportions of unplanned pregnancies were much higher among these workers (table 1). Among unplanned pregnancies, the proportions of contraceptive failures were higher for fixed evening workers (21.8%) and fixed night workers (27.8%) than for daytime workers (17.0%). TTP is undefined for unplanned pregnancies, and because these unplanned pregnancies are excluded from the analysis of TTP, pregnancy planning bias could arise.[19 25 26] The highly fertile couples are more likely to have their children unintentionally (for example, as contraceptive failures) and thus never be eligible for the study of TTP. Meanwhile, the less fertile will be more likely to plan their pregnancies carefully, making themselves eligible for study. This self selection can produce an artefact by which shift work appears to impair fecundity, as seen in our study for fixed evening workers and fixed night workers. No effect for fixed evening work or fixed night work was seen when we restricted the analyses to nurses whose pregnancy planning status had no statistically significant difference among different work schedules. Infertile workers may also be overrepresented in the groups of fixed evening and night workers, as this type of work may be less adaptable to family life. Some families, however, argue that a fixed schedule is more conducive to family life, as it means better planning opportunities (you always know when to work) compared with the often irregular working schedules of the rotating staff. We also found that fixed evening and night workers were more often parous and had more children in the family.

Subfecundity is a couple's characteristic, but we have limited data on the male partner. We adjusted for their partners' occupations. Couples who have unprotected sexual intercourse around the time of ovulation are more likely to get pregnant in that cycle. Fixed evening and fixed night workers may have less opportunity for having sexual activity. However, both the Swedish study[12] and the European multicentre study[13] showed that the frequency of sexual intercourse was evenly distributed among daytime workers, rotating shift workers, and fixed night workers. Working time may affect the timing of intercourse, which is more important than frequency for conception.

We do expect that the effect of previous use of contraceptive pills[27 28] would bias our results since we had limited data on it. We asked the women about the use of oral contraceptives during the past four months before pregnancy and found that among those having TTP 0–2 months, the proportions of the previous use of pills were lower for fixed evening workers (27.9%) and rotating shift (with night) workers (32.2%), but not for fixed night workers (41.3%), and for rotating shift (without night) workers (38.5%), compared with daytime workers (38.8%). However, when we only looked at getting pregnant during 0–2 months of waiting time and performed an analysis after adjusting for the previous use of oral contraceptives and other potential confounders, we obtained similar results. Menstrual cycle characteristics are also known determinants of female fecundity, but we had only limited data to analyse the importance of this factor.

Three previous studies[12–14] found an association between shift work and women's fecundity, while three others[15–17] did not. The differences in working condition for shift workers in different populations and the pregnancy planning bias could

be major reasons for inconsistent results. Although the European multicentre study[13] concluded that data from the study were in favour of an association between shift work and prolonged TTP, they found no association between shift work and subfecundity in the population sample with first pregnancies (OR 1.0; 95% CI 0.7 to 1.5) and no effect of shift work on menstrual cycle length and irregular bleedings. They stated "it is likely that shift work is only a risk indicator".

The DNBC recruited about 60% of invited pregnant women (30–40% of all pregnant women). The response rate could cause selection bias if the decision to participate was associated with both exposure to shift work and TTP. We believe this to be unlikely, since studying determinants of subfecundity was not specified as the aim of the birth cohort.

This study included only women who had a clinically recognised pregnancy and all effect measures were restricted to pregnancies that survived the first 12–16 weeks of gestation. If the exposures under study lead to an all or none effect or early fetal loss, we had no possibility of detecting such an effect. Most experiences so far show that only few exposures have such an effect.[25]

We used telephone interviews to obtain information on TTP. Validation studies of TTP have shown that recall of TTP is accurate, even over longer time periods.[26 29] In our study they only had to remember a few months back in time.

We asked for work schedules in the first interview. We have no data on work status at the start of pregnancy planning. If women who experience unsuccessful pregnancy attempt to change their work schedules, the results may be misleading. We believe this to be a minor problem. The proportion of shift work in our study population was comparable with the previous reports in Denmark.[30] Secondly, it is unlikely that a woman would change daytime work to shift work after getting pregnant. In order to minimise the potential bias of behaviour modification and the female reproductively unhealthy worker effect, we restricted the analysis to the women who conceived their first pregnancy and obtained the same results.

To study determinants of subfecundity also assumes comparable persistence in pursuing a pregnancy attempt among the compared groups.[31] We expect this problem to be of minor importance after correction for age and gravidity.[32] Other potential confounders, such as prepregnant BMI, smoking, and alcohol consumption,[33–35] were also controlled in the analyses. Since BMI is associated to shift work and may be related to a biological effect due to hormone disturbances,[36] we performed the same analyses without this variable in the models and found that the estimates remained unchanged.

In conclusion, we found no evidence of a causal association between shift work performed in our study and subfecundity. The slightly reduced fecundity among fixed evening workers and fixed night workers may be mediated by pregnancy planning bias.

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