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Sickness absence among pregnant women is frequent. Sickness absence has in particular been related to occupational exposures. Little is known of other potentially influencing factors. This large population-based study investigates associations between a number of relevant predictors and risk of sickness absence in pregnancy. We found associations between these predictors and risk of sick leave in pregnancy.

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Predictors of sickness absence in pregnancy: a Danish cohort study

by Mette Lausten Hansen, MD,¹ Ane Marie Thulstrup, PhD,¹ Mette Juhl, PhD,² Jette Kolding Kristensen, PhD,³ Cecilia Høst Ramlau-Hansen, PhD⁴

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Objective The aim of this cohort study was to investigate associations between parity, pre-pregnancy body mass index (BMI), assisted reproductive therapy (ART), time to pregnancy (TTP), and engagement in physical exercise and the risk of sickness absence in pregnancy from 10–29 completed pregnancy weeks.

Methods Data from 51 874 pregnancies in the Danish National Birth Cohort collected from 1996 until 2002 were linked to the Danish Register for Evaluation of Marginalization. Exposure information was based on questionnaires. Hazard ratios (HR) with 95% confidence intervals (95% CI) were calculated by Cox regression, using time of first episode of sickness absence as the primary outcome.

Results Multiparity 1.26 (95% CI 1.10–1.45), overweight 1.13 (95% CI 1.08–1.18), obesity 1.23 (95% CI 1.15–1.31), ART 1.10 (95% CI 1.01–1.20), and TTP >12 months 1.06 (95% CI 0.99–1.13) were associated with higher HR of sickness absence. Physical exercise of >120 minutes per week was associated with lower HR 0.84 (95% CI 0.75–0.95).

Conclusion Risk for sickness absence was higher among women who were multiparous, overweight, obese, received ART, and had prolonged TTP, and lower among women engaged in leisure-time physical exercise. Few studies have investigated these associations, and the results should be confirmed in other studies of pregnant women.

Key terms assisted reproductive therapy; body mass index; Danish National Birth Cohort; Denmark; parity; physical exercise; time to pregnancy.

Sickness absence among pregnant women is frequent (1–5). A number of studies indicate that the amount of sickness absence in pregnancy has increased over the past decades, yet without clear medical explanations (5–8). Factors such as course of pregnancy (9), occupational exposures (10), levels of social benefits (8, 11), and attitudes towards sickness absence, experiences and worries (2) have been associated with levels of sickness absence. However, a number of other factors could potentially also influence sickness absence levels.

The combination of work outside the home, domestic duties, and natural physical fatigue increases the total strain among pregnant women, and this may particularly affect sickness absence among multiparous women (9, 12). Body mass index (BMI) could be hypothesized as a risk factor for sickness absence in pregnancy, as BMI is positively associated with pregnancy-related pelvic

pain (13), and high BMI has been suggested to reduce the capability to perform manual work during pregnancy (14). BMI among European women has increased in the past decades, which also affects an increasing number of pregnant women (15).

The number of assisted reproductive therapy (ART) treatments has increased steadily during the past 15 years, and today 8% of childbirths arise from ART (16). ART is often linked to prolonged waiting time to pregnancy (TTP), and women who become pregnant after ART experience more pregnancy-focused anxiety compared to women conceiving spontaneously (17, 18). We hypothesize that this could lower thresholds for sickness notification among ART-pregnant women and women with prolonged TTP.

Physical exertion at work and risk of adverse pregnancy outcome has been investigated in numerous stud-

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ies with conflicting results (19–24). In consequence, precautionary principles are followed, and pregnant women are advised to reduce occupational exposures like heavy lifting as well as prolonged walking and standing, especially late in pregnancy (22, 25, 26). On the other hand, pregnant women are not discouraged from leisure time physical activity – hereafter referred to as physical exercise – and the Danish Health and Medicines Authority currently recommends physical exercise at a moderate intensity level for a minimum of 30 minutes per day for women with uncomplicated pregnancies (25).

On the basis of limited knowledge about how these factors are associated with sickness absence, we aimed to investigate associations between parity, pre-pregnancy BMI, ART, TTP and engagement in physical exercise and the risk of sickness absence in pregnancy from 10–29 completed pregnancy weeks.

Methods

Study population

We used data from the Danish National Birth Cohort (DNBC), a population-based pregnancy cohort, including 100 418 pregnancies enrolled between 1996–2002. Women were invited to participate at the first antenatal visit with their general practitioner. Inclusion criteria were: (i) Danish residency, (ii) an intention to complete pregnancy, and (iii) sufficient fluency in Danish to participate in four telephone-based interviews. The basic data collection in DNBC included four computer-assisted telephone-based interviews, three blood samples, and a food frequency questionnaire. Two interviews were conducted during pregnancy (around pregnancy week 17 and 30) and two postpartum (6 and 18 months). The cohort is described in detail elsewhere (27). In this study, we included pregnancies where information was collected in the first pregnancy interview (N=92 891). For definition of the studied pregnancies, see (figure 1). The final number of pregnancies studied was 51 874 among 49 708 women, as some women contributed with more than one pregnancy. The Scientific Ethical Committee approved the cohort, and the Danish Data Protection Agency and the DNBC Steering Committee approved storage, handling, and linkage of data for the current study (approval number 2012-41-0086 and 2012-06).

Predictors

All independent variables came from the first pregnancy interview (in completed pregnancy weeks: 18 (mean); 17 (median); 25th percentile: 14, and 75th percentile: 20). The following questions and corresponding answer

categories all available at www.dnbc.dk were used (translated from Danish). Parity [yes/no (reference)]: “Have you given birth before?” BMI: “What was your weight before the pregnancy?” and “How tall are you?” BMI was calculated as weight (kg)/[height (m)]² and grouped according to WHO classification: underweight (<18.5 kg/m²), normal weight (18.5–<25 kg/m² [reference]), overweight (25–<30 kg/m²) and obese (≥30 kg/m²) (28). TTP: “For how long time did you try to get pregnant before you succeeded?” (Did not try to get pregnant, got pregnant immediately (reference), 1–2 months, 3–5 months, 6–12 months, for more than 12 months). TTP for women reporting not trying to get pregnant were coded as missing. ART [yes/no (reference)]: “Did you get any infertility treatment prior to this pregnancy?” Engagement in physical exercise (yes/no): “Do you get any kind of exercise during pregnancy?” If yes, “What kind of exercise?”, “How many times a week do you exercise?” and “How many minutes at a time do you exercise?” Minutes of weekly physical exercise were calculated and categorized in five groups: 0, 1–30 (reference), 31–60, 61–120, and >120 minutes. All independent variables that were answered “do not know” or “do not want to answer” were coded as missing.

Sickness absence

We used the Danish Register for Evaluation of Marginalisation (DREAM) to measure sickness absence (29). DREAM contains weekly information on more than 100 types of public benefit payments, varying from state educational funds to retirement pension. Each type of benefit is characterized by a unique code, sickness benefits are coded according to the type of employment preceding sick leave. In Denmark, sickness during pregnancy is classified as sickness absence or pregnancy-related sickness absence, the latter due to either abnormal course of pregnancy or due to conditions in the work environment potentially harmful in pregnancy. At the time of data collection, reimbursement of sickness absence benefit, a prerequisite for DREAM registration, was conditional on a minimum of two weeks of consecutive sickness absence paid by the employer. Thus, sick leave <15 consecutive days was not registered in DREAM. As for pregnancy-related sickness absence, employers received reimbursement from the first days of sickness absence. Finally, a weekly registration in DREAM requires merely one day of sickness benefit payment during the week in question.

For each completed pregnancy week from 10–29, we estimated sickness absence for gainfully employed women, using the following DREAM codes: 774 (sickness absence from flexi-jobs – jobs for people with reduced ability to work because of chronic illness), 881 (maternity leave and pregnancy-related sickness

Figure 1. Number of pregnancies included in the study.

absence), 890, 892, 893, 894, 895, 896, 897, 898, and 899 (all sickness absence codes for either ordinary employment, various job training programs, apprenticeships or part-time sick leave) (29).

Time of first episode of sickness absence from 10 to 29 completed pregnancy weeks was the primary outcome in this study.

Potential confounders

We adjusted for the following *a priori* selected potential confounders based on the literature: age, daily smoking, weekly intake of alcoholic drinks, physical and psychological demanding work environment, socioeconomic status, weeks of sickness absence two years prior to the DNBC pregnancy, and chronic diseases. Parity analyses were furthermore adjusted for family structure. The variable age was the women's age at the time of first pregnancy interview. Mean of self-reported alcohol intake (drinks/week) and daily tobacco smoking (yes/no) were generated from questions in the first pregnancy interview. Physical and psychological job demands (often, from time to time, seldom) were generated based on

first pregnancy interview data. Socioeconomic status in five categories (unemployed, unskilled workers, skilled workers, lower grade professionals, higher grade professionals) was based on educational level and the Danish version of International Standard Classification of Occupations (DISCO-88). If educational level or DISCO-88 codes were missing for the pregnant women, information for the spouse or cohabiting partner was used. The women provided this information at the first pregnancy interview. Sickness absence prior to the DNBC pregnancy was assessed using DREAM data. We included information 104 weeks back in time from the onset of the DNBC pregnancy and counted the number of weeks each woman received sickness benefit payment (excluding pregnancy benefits). Sickness absence prior to the DNBC pregnancy was categorized in five groups (≥ 26 , 9–25, 5–8, 1–4, and 0 weeks). The variable “chronic diseases” (yes/no) was generated from information on self-reported diseases and included cardiovascular, metabolic, musculoskeletal, epilepsy, and psychiatric disorders as well as other diseases classified as severe. Finally, a variable family structure was created, which included information on civil status and having children in the household.

Statistical analysis

Data were analyzed by multivariate Cox regression models using pregnancy week as the underlying time variable. The calculation of pregnancy week was based on self-reported due date from the first pregnancy interview and the date was based on last menstrual period. If these data were missing, data from the late pregnancy interview were used.

Time at risk started at first pregnancy interview, and ended at first episode of sickness absence, pregnancy termination (abortion, preterm delivery or still birth), or end of the study period at 29 completed pregnancy weeks, whichever came first. Pregnancies of women with sickness absence at the time of first pregnancy interview or prior to the first interview were excluded from the analyses.

Risk estimates are presented as crude and adjusted hazard ratios (HR) for the whole study period and for four pre-defined completed pregnancy week periods; (week 10–14, 15–19, 20–24, and 25–29). Time at risk in each of the four pregnancy week period started at the beginning of the time intervals and ended at first episode of sickness absence, pregnancy termination (abortion, preterm delivery, or still birth), or end of the time period, whichever came first. No pregnancies were included in the pregnancy week period analyses before time of first pregnancy interview. Women on sick leave were excluded from the analyses in the following pregnancy week periods. Trend test estimates for dose–response relations rep-

represent the following unit changes: BMI (one-unit change in BMI), TTP (one-unit change in TTP category), and physical exercise (one-unit change in exercise category). We calculated time-varying coefficients for all the predictors to estimate time-dependent effects of the predictors with time since 10 completed pregnancy weeks. Trend tests were calculated for the time-varying coefficients, and represent trends on weekly HR from 10–29 completed pregnancy weeks for the predictors. Finally, we conducted three sub-analyses in which we (i) excluded ART pregnancies to take the close relation between ART and TTP into account, (ii) further adjusted for selected pregnancy-related disorders (vaginal bleeding, painful Braxton hick's contractions, risk of giving preterm birth, nausea and vomiting during pregnancy), and (iii) restricted the analysis to the first DNBC participation for women participating more than once in DNBC in order to estimate possible clustering of events. Pregnancy-related disorders were included, because they are risk factors for sickness absence. Data on the pregnancy-related disorders were obtained from the second pregnancy interview at (mean) 32.2 completed pregnancy weeks.

Data were analyzed using STATA, version 13.0 (STATA Corp LP, College Station, Texas, USA).

Results

In 12 585 pregnancies (19.5%), the first episode of sickness absence occurred before the first pregnancy interview. Cumulative incidence proportion of sickness absence was 36.0% from onset of pregnancy until 29 completed pregnancy weeks and 20.6% from first interview until 29 completed weeks. Table 1 gives a description of sickness absence prevalence for each pregnancy week from 10–29 completed pregnancy weeks. In the study period, the prevalence of sickness absence increased from 2% to 17%.

Table 2 provides a description of the pregnancies according to the first episode of sickness absence between 10–29 completed pregnancy weeks or no sickness absence. There were small and probably not clinically important differences in mean age and mean pregnancy week at first interview between pregnancies in women with and without sickness absence. Pregnancies with sickness absence were more frequent among women who were smokers and alcohol abstainers compared to pregnancies in women without sickness absence. Larger proportions of pregnancies resulted in sickness absence among women, who suffered from chronic diseases, and who reported physically and psychologically demanding working conditions. Sickness absent women were more often skilled and unskilled workers and sickness absent the two years prior to study entry and had more often

children in the household compared to non-sickness absent women.

Table 3 shows crude and adjusted HR with 95% confidence intervals (95% CI) for first episode of sickness absence from 10–29 completed pregnancy weeks. In the adjusted analyses, multiparity, overweight, obesity, ART, and no engagement in physical exercise were associated with higher HR of sickness absence compared to the reference groups. HR increased in a dose-dependent way with increasing BMI and TTP in crude as well as adjusted analyses. Engagement in physical exercise of >120 minutes per week was associated with lower risk of sickness absence compared with the reference group, and physical exercise was associated with lower risk of sickness absence in a dose-dependent way.

The study period was split into four time periods to evaluate time-dependent effects of the predictors measured by time-varying coefficients (table 4). We found increased HR for sickness absence during all four time periods for multiparity, overweight, obesity and ART. HR for TTP of 6–12 months and TTP >12 months were in most intervals increased compared to the reference groups. The effects of multiparity and TTP >12 months were time dependent, as HR decreased with number of completed pregnancy weeks in a statistically significant way. Time dependent effects indicated increasing hazards of sickness absence with time at levels of physical exercise between 31–60 minutes per week. There was no substantial difference in HR according to time period for BMI, ART, and remaining TTP and physical exercise intervals.

To address the possible close relation between ART and TTP, we made a sub-analysis in which pregnancies resulting from ART (N=2859) were excluded (supplementary table A, www.sjweh.fi/data_repository.php). Overall, the results were in the same direction as in the main analyses. We did not adjust for pregnancy-related disorders in the main analyses, as we did not have such information by the time-of-first-pregnancy interview. In a sub-analysis, we used data from the late pregnancy interview to adjust for self-reported pregnancy complications. However, these adjustments did not change the results appreciably (supplementary table B, www.sjweh.fi/data_repository.php). The sub-analysis for possible clustering of events did not change the results either (data not shown).

Discussion

We found multiparity, overweight, obesity, ART and TTP >12 months to be associated with a higher risk of sickness absence. Physical exercise was associated with a lower risk.

Table 1. Prevalence of sickness absence according to pregnancy week from 10–29 completed pregnancy weeks (N=51 874).

Completed pregnancy week	Pregnancies with sickness absence		Prevalence of sickness absence %	Total pregnancies
	Yes	No ^a		
10	4	200	2.0	204
11	35	1416	2.4	1451
12	86	4189	2.0	4275
13	189	8581	2.2	8770
14	341	13 461	2.5	13 802
15	524	18 566	2.7	19 090
16	787	23 364	3.3	24 151
17	1041	27 802	3.6	28 843
18	1343	31 712	4.1	33 055
19	1719	35 162	4.7	36 881
20	2200	38 021	5.5	40 221
21	2686	40 373	6.2	43 059
22	3213	42 015	7.1	45 228
23	3781	43 210	8.1	46 991
24	4493	43 848	9.3	48 341
25	5300	44 062	10.7	49 362
26	6136	43 919	12.3	50 055
27	6962	43 631	13.8	50 593
28	7871	43 060	15.5	50 931
29	8793	42 377	17.2	51 170

^a Pregnancies ending as an abortion or preterm birth were excluded from the denominator week by week in total (N=704) exclusions.

In Scandinavian studies, the reported cumulative incidence of sickness absence during pregnancy varies from 29% to 72% (9, 10, 30–32). These variations can largely be explained by differences in definitions of sickness absence. We found a cumulative incidence proportion of 36.0% from onset of pregnancy until 29 completed pregnancy weeks and of 20.6% from 10–29 completed weeks. These results are in accordance with results from the Norwegian Mother and Child Cohort Study that is similar to DNBC in structure, where the authors reported 36.2% of the participants having >14 days of sickness absence by pregnancy week 28 (32). Absence risk between pregnancy week 17–30 in the Norwegian Mother and Child Cohort Study was associated with young age (55%), low education (45%), high parity (40%), multiple pregnancies (87%), and smoking (35%) (32). Risk associated with parity ranged from 26% (nulliparous) to 40% (para ≥ 4). Although we classified multiparity differently from the Norwegian Mother and Child Cohort Study, our results are in accordance with the Norwegian results. Other studies have also investigated associations between parity and sickness absence with conflicting results (3, 31, 33). A Danish study found no significant association between multiparity and sick leave among hospital employees [odds ratio (OR) 1.3, 95% CI 0.9–1.9] (3), whereas two Norwegian studies found significant associations between multiparity and measures of sick leave in pregnancy (OR 1.40; 1.55) (31, 33). A Swedish study investigated sex differ-

ences in sickness absence patterns in relation to parental status and found a relation between having custody of children and sickness absence among women (34). These results suggest that women in general might be more sensitive to imbalances between work and personal life compared with men, and this could at least partially explain the observed association between parity and sick leave in pregnancy.

To our knowledge, only one previous study has examined the associations between obesity and sickness absence and social benefit payments among pregnant working women (14). In Sweden, there are two types of benefits additional to sick leave, parental benefit, and pregnancy benefit. Parental benefit ensures women the right to take time off after delivery, yet up to 60 days of the parental benefit can be used before delivery. These days will subsequently be subtracted from the after-delivery parental benefit period. Pregnancy benefit can be granted to women having demanding and monotonous jobs from between 60 to 10 days before delivery and granting is not based on the women's actual health. In the Swedish study, authors found that obese women made more use of both parental benefits and pregnancy benefits compared to normal weight women, suggesting that there may be a possible incompatibility between pregnancy, obesity, and engagement in employment (14). Surprisingly, the authors did not find obesity to be predictive of increased number of sick leave days (14). Sickness absence without relation to pregnancy has been found to be associated with obesity in several studies (35–37). Associations are first of all believed to originate from obesity-related co-morbidities, possible susceptibility to non-chronic health problems, longer recovery time or even discrimination, but obesity could also reduce the ability to meet physical work load requirements in some jobs (36). We do not know whether the association we found between BMI and sickness absence was due to obesity, per se, or a combination of obesity and pregnancy.

Only one study previously investigated associations between ART and sick leave during pregnancy (33); the authors found an association between ART and sick leave in all three trimesters (OR 1.77; 95% CI 1.27–2.46), which is in agreement with our results. However, the authors included multiple pregnancies and did not adjust for co-morbidities and measures of work load in their study, which makes both interpretation and comparison with our results difficult. The findings, though, are not surprising, as we expect ART-pregnant women to be more anxious about the course of pregnancy and more alert and worried about natural pregnancy-related discomfort compared to women conceiving naturally. We found no studies in our literature search investigating associations between sickness absence and TTP.

Several studies using prospectively collected data have found that physical exercise is associated with

Table 2. Characteristics of the pregnancies (N=51 874) according to first episode of sickness absence from 10–29 completed pregnancy weeks. [SD=standard deviation]

Parameter	Sickness absence ^a [N=10 667 (20.6%)]				No sickness absence ^a [N=41 207 (79.4%)]			
	N	%	Mean	SD	N	%	Mean	SD
Pregnancy week in interview 1			16.4	3.8			17.6	4.2
Age (years)			30.1	4.2			30.7	4.0
Age group (years)								
<20	21	0.2			85	0.2		
20–< 30	4967	46.6			16 473	40.0		
30–< 40	5488	51.4			23 891	58.0		
≥40	191	1.8			758	1.8		
Smoking	1904	17.9			4722	11.5		
Lifestyle alcohol, weekly intake (drinks ^b)								
0	6213	58.3			20 555	49.9		
≤2	3910	36.7			17 938	43.5		
2–7	514	4.8			2606	6.3		
>7	18	0.2			61	0.2		
Self-reported physical demanding work								
Often	3722	34.9			5281	12.8		
Sometimes	2831	26.5			8559	20.8		
Rarely	3960	37.1			26 780	65.0		
Self-reported psychological demanding work								
Often	2384	22.4			5950	14.4		
Sometimes	3972	37.2			15 839	38.4		
Rarely	4156	39.0			18 833	45.7		
Socioeconomic status								
Higher grade professionals	1279	12.0			10 176	24.7		
Lower grade professionals	3619	33.9			13 755	33.4		
Skilled workers	4844	45.4			15 501	37.6		
Unskilled workers	889	8.3			1651	4.0		
Sickness absence two years before study entry (weeks)								
0	6836	64.1			32 389	78.6		
1–4	2146	20.1			4501	10.9		
5–8	528	5.0			895	2.2		
9–26	599	5.6			1492	3.6		
>26	558	5.2			1930	4.7		
Chronic diseases ^c (yes)	1263	11.8			3463	8.4		
Family structure								
Not single, no children in the household	4160	39.0			19 244	46.7		
Not single, children in the household	6338	59.4			21 404	51.9		
Single, no children in the household	82	0.8			362	0.9		
Single, children in the household	77	0.7			166	0.4		

^a Non-adjusted differences between groups tested by: t-test (mean age, mean body mass index), Wilcoxon Mann Whitney test (pregnancy week at interview 1), Chi2 test (parity, assisted reproductive therapy, smoking, and chronic diseases), Spearman's rank correlation test (age group, alcohol intake, physical- and psychological demanding work, socioeconomic status, sickness absence two years preceding study entry and family structure). Percentages do not add up to 100 due to the following missing values: smoking (N=16), alcohol intake (N=59), physical demanding work (N=741), psychological demanding work (N=740), socioeconomic status (N=160), chronic diseases (N=86), family structure (N=41).

^b One drink=12 grams of alcohol: corresponds to either one beer (33 cl), one glass of wine (12.5 cl) or one glass of spirits (4 cl).

^c Self-reported in early pregnancy interview. Combined into a measure of diseases that have been present and caused symptoms during pregnancy; the variable included (metabolic diseases, hypertension, urinary tract diseases (not cystitis), musculoskeletal diseases, psychiatric disorders and other severe somatic diseases).

reduced sickness absence (38–40). A Norwegian study found an association between no weekly exercise and increased odds for sick leave in pregnancy (OR 1.79; 95% CI 1.69–2.31) (33). Our results corroborate these findings. However, pregnant women who exercise may be of better health than non-exercising pregnant women, and, thus, our results could overestimate the presumed beneficial effect of exercise. Furthermore, if some of the pregnant women stopped exercising due to pregnancy disorders associated with future sickness absence, we might overestimate the beneficial effect of exercise due to reverse causation.

Strengths of our study include the large sample size and the ability to adjust for a wide range of prospectively collected potential confounders. The overall participation rate in DNBC was approximately 31% and varied according to education, occupation, income, and civil status (41). Non-participation in DNBC was either caused by the general practitioners (approximately 50% participated) or the women themselves (approximately 60% participated). This selection, partially associated with socioeconomic factors, could cause confounding. However, we believe that the adjustment for socioeconomic status in the statistical analyses minimizes important confounding due

Table 3. Crude (HR_{crude}) and adjusted (HR_{adj}) hazard ratios of first episode of sickness absence from 10–29 completed pregnancy weeks according to predictors N=51 874. [95% CI=95% confidence interval; BMI=body mass index; ART=assisted reproductive therapy; TTP=time to pregnancy.]

	Completed pregnancy week 10–29							
	Events (N)	Subjects in analyses ^a	HR _{crude}	95% CI	Events (N)	Subjects in analyses	HR _{adj} ^b	95% CI
Parity								
Nulliparous	4352	24 418	Ref		4314	24 216	Ref	
Multiparous	6314	27 454	1.35	1.30–1.40	6151	26 651	1.26	1.10–1.45
BMI (kg/m ²)								
<18.5	423	2082	1.08	0.98–1.20	415	2031	1.01	0.92–1.12
18.5–25	6802	35 755	Ref		6680	35 115	Ref	
>25–30	2272	9643	1.26	1.21–1.33	2238	9467	1.13	1.08–1.18
>30	997	3590	1.64	1.44–1.64	974	3515	1.23	1.15–1.31
BMI continuous trend ^c			1.03	1.03–1.04			1.02	1.01–1.02
ART								
No	10 081	48 991	Ref		9896	48 055	Ref	
Yes	583	2859	1.01	0.93–1.10	576	2829	1.10	1.01–1.20
TTP (months)								
0–2	4207	21 037	Ref		4125	20 614	Ref	
3–5	1903	9764	0.97	0.92–1.02	1875	9624	0.98	0.93–1.03
6–12	1643	7704	1.06	1.00–1.12	1625	7616	1.03	0.97–1.09
>12	1437	6794	1.08	1.02–1.15	1421	6713	1.06	0.99–1.13
TTP continuous trend ^c			1.03	1.01–1.05			1.02	1.00–1.04
Physical exercise (min/week)								
0	7382	32 992	1.26	1.14–1.40	7229	32 288	1.16	1.04–1.28
0–30	391	2165	Ref		388	2127	Ref	
30–60	986	5440	0.99	0.88–1.11	975	5376	0.98	0.87–1.10
60–120	926	5319	0.95	0.84–1.06	912	5240	0.96	0.85–1.08
>120	958	5825	0.87	0.77–0.98	947	5750	0.84	0.75–0.95
Physical exercise continuous trend ^c			0.91	0.89–0.92			0.93	0.92–0.94

^a Number of missing predictors: parity (N=2), BMI (N=780), ART (N=24), TTP (N=6341) and physical exercise (N=127)^b Adjusted for age, smoking status, alcohol intake, self-reported strenuous physical and psychosocial work environment, socioeconomic group, level of sickness absence two years preceding the Danish National Birth Cohort pregnancy, and chronic diseases. The parity analysis was in addition adjusted for family structure.^c Trend test variables entered as: BMI (continuous), TTP and physical exercise (continuous categorical).

to this selection. Even so, the selection into DNBC can affect the external validity of our study, and our results may not apply to other populations of pregnant women.

Information on predictors and covariates was based on self-reports and could be subject to misclassification. Yet, if present, misclassification is not believed to be related to sickness absence, and our results would therefore most likely be biased towards the null. The outcome of interest (ie, sickness absence) was based on register information from DREAM. This register has recently been validated in a study comparing employer registration of sickness absence with DREAM registration (42). Sensitivity and specificity were very high for ordinary sickness absence but very low for pregnancy-related sickness absence (42). We believe this could be due to exclusion of pregnancy-related sickness absence or maternity leave (DREAM code “881”) from the analyses. A validation of DREAM data in relation to sickness absence in pregnancy is thus still required. We have included women, who refrain from working due to exposures in their work environment. These women are not specifically identifiable in DREAM because they have no specific DREAM code. However, we do not believe misclassification of their

outcome is concurrently associated with the predictors. The misclassification may therefore most probably lead to bias towards the null.

We adjusted for a number of possible confounders, yet residual confounding and confounding by variables not included in the models cannot be ruled out. Adjustment for pregnancy-related disorders diagnosed by the women’s general practitioner or obstetrician would have been relevant, but unfortunately we did not have these data.

In summary, we found higher risk of sickness absence in pregnancy with multiparity, overweight, obesity, ART, and prolonged TTP, and lower risk with leisure-time physical exercise. Only few studies have investigated these associations, and our results should be confirmed in other studies of pregnant women.

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Table 4a. Crude (HR_{crude}) and adjusted (HR_{adj}) hazard ratios of first episode of sickness absence from 10 until 29 completed pregnancy weeks according to predictors in four pregnancy week period intervals. Follow-up started at time of first pregnancy interview, pregnancies of sickness absent women at that time of or before time of follow-up started were excluded from the analyses N=51874^a [95% CI=95% confidence interval; BMI=body mass index; ART=assisted reproductive therapy; TTP=time to pregnancy; TVC=time varying coefficient.]

	Pregnancy weeks 10–14 (N=13 980)				Pregnancy weeks 15–19 (N=36 663)				TVC ^b	95% CI
	HR _{crude}	95% CI	HR _{adj} ^c	95% CI	HR _{crude}	95% CI	HR _{adj} ^c	95% CI		
Parity										
Nulliparous	Ref		Ref		Ref		Ref			
Multiparous	1.39	1.15–1.69	1.99	1.02–3.87	1.37	1.25–1.50	1.24	0.89–1.71	0.99	0.98–0.99 ^e
BMI (kg/m ²)										
<18.5	0.95	0.56–1.63	0.86	0.50–1.48	1.15	0.91–1.45	1.04	0.82–1.32	1.00	0.98–1.03
18.5–<25	Ref		Ref		Ref		Ref			
25–<30	1.55	1.24–1.93	1.35	1.08–1.69	1.30	1.16–1.45	1.13	1.01–1.27	0.99	0.98–1.00
≥30	1.58	1.15–2.19	1.17	0.84–1.62	1.69	1.46–1.96	1.32	1.13–1.53	0.99	0.97–1.00
BMI continuous trend ^d	1.05	1.03–1.07	1.03	1.01–1.05	1.04	1.03–1.05	1.02	1.01–1.03		
ART										
No	Ref				Ref					
Yes	1.21	0.82–1.80	1.19	0.80–1.80	1.16	0.96–1.40	1.27	1.05–1.54	0.99	0.97–1.01
TTP (months)										
0–2	Ref		Ref		Ref		Ref			
3–5	0.95	0.73–1.25	0.95	0.72–1.26	0.97	0.86–1.11	0.99	0.87–1.13	1.00	0.99–1.02
6–12	1.17	0.89–1.54	1.07	0.80–1.41	1.09	0.95–1.24	1.06	0.93–1.21	1.00	0.99–1.01
>12	1.22	0.91–1.63	1.10	0.81–1.49	1.20	1.04–1.38	1.18	1.02–1.35	0.99	0.97–0.99 ^e
TTP continuous trend ^d	1.07	0.98–1.17	1.03	0.94–1.13	1.06	1.01–1.10	1.05	1.00–1.10		
Physical exercise (min/week)										
0	1.18	0.70–1.99	1.11	0.66–1.86	1.30	1.02–1.67	1.15	0.90–1.48	1.01	0.98–1.03
1–30	Ref		Ref		Ref		Ref			
31–60	0.73	0.40–1.34	0.74	0.40–1.36	0.77	0.57–1.03	0.74	0.55–1.00	1.03	1.01–1.05 ^e
61–120	0.90	0.50–1.63	0.97	0.54–1.76	0.99	0.74–1.31	0.99	0.74–1.31	1.00	0.98–1.01
>120	0.67	0.36–1.22	0.72	0.39–1.32	0.83	0.63–1.11	0.81	0.61–1.08	1.01	0.99–1.03
Physical exercise continuous trend ^d	0.87	0.81–0.93	0.91	0.85–0.97	0.88	0.86–0.91	0.91	0.88–0.94		

Table 4b.

	Pregnancy week 20–24 (N=46 154)				Pregnancy week 25–29 (N=45 597)				TVC ^b	95% CI
	HR _{crude}	95% CI	HR _{adj} ^c	95% CI	HR _{crude}	95% CI	HR _{adj} ^c	95% CI		
Parity										
Nulliparous	Ref		Ref		Ref		Ref			
Multiparous	1.47	1.37–1.57	1.46	1.14–1.88	1.26	1.19–1.34	1.09	0.89–1.34	0.99	0.98–0.99 ^e
BMI (kg/m ²)										
<18.5	1.06	0.89–1.27	1.01	0.85–1.20	1.08	0.94–1.25	1.02	0.88–1.18	1.00	0.98–1.03
18.5–<25	Ref		Ref		Ref		Ref			
25–<30	1.24	1.14–1.35	1.10	1.01–1.20	1.24	1.16–1.33	1.13	1.05–1.21	0.99	0.98–1.00
≥30	1.59	1.42–1.78	1.25	1.11–1.41	1.43	1.29–1.58	1.17	1.06–1.30	0.99	0.97–1.00
BMI continuous trend ^d	1.04	1.03–1.04	1.02	1.01–1.03	1.03	1.02–1.04	1.01	1.01–1.02		
ART										
No	Ref		Ref		Ref		Ref			
Yes	0.94	0.81–1.09	1.07	0.92–1.24	0.98	0.87–1.11	1.06	0.93–1.20	0.99	0.97–1.01
TTP (months)										
0–2	Ref		Ref		Ref		Ref			
3–5	0.93	0.85–1.03	0.94	0.85–1.04	0.99	0.92–1.08	1.00	0.93–1.09	1.00	0.99–1.02
6–12	1.00	0.91–1.11	0.98	0.89–1.09	1.08	1.00–1.18	1.05	0.96–1.14	1.00	0.99–1.01
>12	1.09	0.98–1.21	1.09	0.98–1.21	1.02	0.93–1.12	1.00	0.91–1.10	0.99	0.97–0.99 ^e
TTP continuous trend ^d	1.02	0.99–1.06	1.02	0.99–1.05	1.02	0.99–1.04	1.01	0.98–1.04		
Physical exercise (min/week)										
0	1.28	1.08–1.51	1.16	0.97–1.40	1.23	1.06–1.43	1.15	0.99–1.34	1.01	0.98–1.03
1–30	Ref		Ref		Ref		Ref			
31–60	1.05	0.86–1.29	1.03	0.84–1.26	1.04	0.88–1.24	1.06	0.89–1.26	1.03	1.01–1.05 ^e
61–120	0.94	0.76–1.16	0.95	0.77–1.17	0.94	0.79–1.12	0.96	0.80–1.14	1.00	0.98–1.01
>120	0.86	0.69–1.05	0.81	0.66–1.00	0.91	0.77–1.09	0.89	0.75–1.05	1.01	0.99–1.03
Physical exercise continuous trend ^d	0.90	0.88–0.92	0.92	0.90–0.95	0.92	0.90–0.94	0.94	0.92–0.96		

^a Number of eligible participants for the analyses. Numbers of participants in each pregnancy week period differ from the number of eligible participants, owing to differences in time of first interview, time of the events and missing values on predictors and covariates.

^b HR for each pregnancy week can be calculated using the formula: HR pregnancy week(x) = HRpregnancyweek 10 × TVC raised to the power of pregnancy week(x), if TVC>1 HR increases with time and if TVC<1 HR decreases with time.

^c Adjusted for age, smoking, alcohol intake, self-reported physical and psychological demands in the work environment, socioeconomic group, sickness absence prior to the DNBC pregnancy and chronic diseases. The parity analyses were in addition adjusted for family structure.

^d Variables entered as: BMI (continuous), TTP and physical exercise (continuous categorical).

^e P for trend <0.05. Trend test for weekly HR from 10 to 29 completed pregnancy weeks.

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