

Sick leave in pregnancy – risk factors and prognosis Studies among Danish employed women

PhD dissertation

Mette Lausten Hansen

Health Aarhus University 2016



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PREFACE

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> Mette Lausten Hansen Aarhus, March 2016

PAPERS IN THE DISSERTATION

I.	Predictors of sickness absence in pregnancy: a Danish cohort study.
	Scand J Work Environ Health. 2015 Mar;41(2):184-93.
II.	Occupational exposures and sick leave in pregnancy: Results from a
	Danish cohort study.
	Scand J Work Environ Health. 2015 Jul 1;41(4):397-406.
III.	Does sick leave in pregnancy predict labour market attachment post
	partum? – An 8-year follow-up study among Danish women
IV.	Are lifestyle and occupational exposures still risk factors for sick leave
	in pregnancy?

LIST OF ABBREVIATIONS

ART: assisted reproductive therapy BMI: body mass index CDR: Central Denmark Region CI: confidence interval COPSOQ II: Copenhagen Psychosocial Questionnaire II DISCO-88: Danish version of International Standard Classification of Occupations DKK: Danish Kroner DNBC: The Danish National Birth Cohort DREAM: Danish Register for Evaluation of Marginalisation HR: hazard ratio IRR: incidence rate ratio IVF: in vitro fertilization JEM: Job Exposure Matrix OR: odds ratio SGA: small for gestational age TTP: time to pregnancy

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1. INTRODUCTION

Most women work during their reproductive years. Pregnancy is in general widely considered as a natural and healthy condition - not as a disease. In spite of this, high levels of sick leave among pregnant women have been found in several studies¹⁻⁵, and some studies indicate that the levels have increased over the past decades without medical explanation⁶⁻⁹. Pregnancy-related sick leave is estimated to constitute around 4,000 full-time employed, corresponding to a yearly cost of 1.4 billion DKK¹⁰. Besides being costly to society, sick leave also includes adverse economic effects for employers, more work for colleagues and potentially economic burdens for the pregnant women. Research within the area of pregnancy and sick leave is sparse. Knowledge on potential risk factors for sick leave in pregnancy is limited, and so is knowledge about the future labour market prognosis of women with high levels of sick leave in pregnancy.

European legislation protects pregnant women from potentially harmful occupational exposures. Furthermore, pregnant women should have the possibility to obtain adjustments in their occupational exposures, if necessary. With this legal protection it seems to be a paradox that sick leave among pregnant women has increased during recent decades, suggesting that the intention of the legislation is difficult to adhere to in practice.

Physical, psychological and organisational occupational exposures are risk factors for sick leave in pregnancy^{1,2,4}. Other important factors are course of pregnancy¹¹, levels of social benefit when sick^{12,13}, and attitudes towards reporting sick^{7,12}. If occupational exposures cause illness among pregnant woman, or lower the threshold for reporting sick, at least some pregnancy-related sick leave can possibly be prevented. However, more information about occupational exposures and their associations with sick leave is necessary in order to undertake preventive initiatives. It is also of importance to investigate whether sick leave in pregnancy has potential side effects beyond pregnancy like future vulnerable attachment to the labour market or even drop out. Such information can be obtained from longitudinal studies with comprehensive information on exposures and covariates.

1

2. AIMS

The primary aim of the dissertation was to investigate associations between (i) Lifestyle, (ii) Obstetric and fertility factors, (iii) Physical and (iiii) Psychosocial occupational factors and the risk for sick leave during pregnancy by using two pregnancy cohorts separated in time by more than a decade. A further aim was to investigate if pregnancy-related sick leave during pregnancy predicts exit from the labour market or a vulnerable position in the labour market. Four studies were conducted with the following aims:

- Study I: To investigate associations between parity, pre-pregnancy body mass index, assisted reproductive therapy, time to pregnancy and engagement in physical exercise and the risk of sick leave in pregnancy from 10–29 completed pregnancy weeks.
- Study II: To investigate associations between work posture, lifting at work, shift work, work hours and job strain and the risk of sick leave from 10–29 completed pregnancy weeks.
- Study III: To investigate if pregnancy-related sick leave during pregnancy together with a number of occupational and lifestyle factors predict poor labour market attachment, or even exit from the labour market in an 8-year follow-up period starting one year after child birth.
- Study IV: To investigate if lifestyle, obstetric history and occupational exposures in the years of 2013–2014 were associated with increased risk for sick leave during pregnancy.

3. BACKGROUND

The main focus of this thesis is sick leave during pregnancy used as either an outcome or an exposure. Sick leave during pregnancy in three of the studies is used as the primary outcome of interest and in one study pregnancy-related sick leave is used as the exposure of interest. Below follows a description of the literature on sick leave, sick leave measures and risk factors for sick leave in working populations. Next follows a description of the literature on sick leave in pregnancy. Finally, a description of antenatal care, legislation and sick leave notification is given.

3.1 Sick leave

Sick leave has received increasing attention during the past decades in Denmark as well as in other European countries. It is a common belief that sick leave rates have increased over time, even though no national statistics clarify this completely. A recent study within groups of health workers in Norway and Denmark supports the conception of an increase in sick leave¹⁴. There are different ways of assessing sick leave: (i) *absence incidence* (number of absence spells per year per employee), (ii) *duration* (length of absence spells), (iii) *prevalence* (absentees at a given time point) or (iiii) *sick leave rate* (number of sick leave days per year divided by the possible number of work days)¹⁵.

In the latest Danish sick leave report published by The Ministry of Employment, a total of 150,000 persons were daily on sick leave, which is equivalent to about 5% of the Danish work force¹⁶. The expense of sick leave was estimated to amount to 37 billion DKK annually¹⁶. From 2003 to 2006, the mean number of sick leave recipients increased by 18% for employed people, and the increase was partly attributable to women, people aged 30–59 years and immigrants from non-western countries¹⁶. Not only had the number of people on sick leave increased, the duration of sick leave spells had also increased¹⁶. The annual number of mean sick leave days differs between sectors: state (8.3 days), municipal (12.5 days), and private sector (8.1 days). The duration of sick leave spells are often divided into short-term and long-term sick leave spells in epidemiological studies. These definitions are, however, inconsistent and vary across studies¹⁷⁻¹⁹. Some Danish studies used 8 weeks as the cut-point between short-term and long-term sick leave, and 8 weeks is also the time limit for municipal case management in prolonged sick leave cases. Short- and long-term sick

leaves are believed to differ in aetiology, short-term leave reflecting lack of motivation, skiving or homely burdens, whereas long-term sick leave reflects illness or disease. Sick leave is often used as a health indicator and is associated with mortality rates^{19,20}. In the prospective Whitehall II study, hazard ratios for all cause mortality increased linearly with number of medically certified absence spells the previous 10 years²⁰. Long-term sick leave reduces probability of returning to work, and is a risk factor for receiving disability pension²¹⁻²⁴. In consequence, sick leave and its derived adverse effects are of public health concern, and initiatives have been made to reduce sick leave²⁵.

3.2 Risk factors for sick leave

Well-known risk factors for sick leave include age, gender, education, job group sector, lifestyle, physical and psychological work environment and disease^{17,26-32}. The mechanisms by which these risk factors affect sick leave are complex and poorly investigated. Having a disease influences sick leave rates, but sometimes in a non-predictable way, as some employees having a disease go to work, and employees without disease choose not to go to work. Factors also associated with sick leave are illness/disease perceptions¹⁵, levels of sick leave benefits³⁰, previous sick leave patterns³³ and size of the work place³⁴. Local cultures at work places may also be potential determinants of sick leave. One study suggests that sick leave theory should include environmental factors as well as personal factors and that interaction between the two within a social framework predicts sick leave patterns¹⁵.

3.3 Pregnancy and work

The majority of Danish women (81%) work during their reproductive years³⁵. Potential adverse effects of occupational exposures on outcomes like preterm birth, miscarriage, low birth weight and malformations have been investigated in a large number of epidemiological studies with conflicting results³⁶⁻⁴³. Two recent meta-analyses investigated miscarriage, pre-maturity, low birth weight and pre-eclampsia according to a number of occupational exposures as shift work, lifting, standing and working hours, and the authors concluded that the results were largely reassuring as none of the investigated occupational exposures entails large risks for women with uncomplicated pregnancies^{44,45}. However, the results did not suggest beneficial effects of the exposures. In spite of there being no considerable risk for adverse pregnancy

outcomes in relation to these investigated occupational exposures, some occupational exposures involve aggravation of discomfort during pregnancy, discomfort which is considered non-pathological, but an inherent part of pregnancy. The Danish Working Environment Authority (WEA) issues guidelines for management of work environments for pregnant women⁴⁶. These guidelines are not binding; but they are based on binding legislation. Work places must assess the work environment for pregnant women according to the guidelines by WEA, and react, if the requirements in the guidelines are not met.

All things considered, pregnant women constitute a vulnerable group of employees, and a number of health promoting and legal initiatives are launched to protect them and their fetuses. These initiatives include statutory protection against harmful occupational exposures⁴⁷ and an antenatal care programme comprising general practitioners and maternity wards⁴⁸.

3.4 Sick leave in pregnancy

A Danish report on sick leave among pregnant women was published in 2010^{10} . In 2005–2007, around 66% of pregnant women were on sick leave before beginning maternity leave, with an average number of 48 sick leave days. This is more than 6 times higher than the background level of sick leave days. From 2002–2004 to 2005–2007, pregnancy-related sick leaves increased by 2.1%, which was less than the concurrent 5% increase in general sick leave^{10,16}. Results from Norway showed a 50% increase in the sick leave rate in pregnancy relative to pre-pregnancy sick leave from 1995–2007, indicating a considerable increase in sick leave among pregnant women over time⁴⁹.

Reference	Design	Study population	Outcome	Exposure	Covariates	Results	Summary of results
Kaerlev, 2004 ¹	Cross- sectional	Danish hospital employees 1995-1999 (N≡773)	>10% absence of scheduled work time	Lifting Walking/standing Variation/sedentary Comfort Chemicals Infections Shifts Work speed Stressful events	Age Occupation Full time/ part time Previous sick leave	Sick leave rate 18.6% 7.3 times higher sick leave rate compared to non- pregnant Rates increase with pregnancy week Sick leave associated with a large number of the exposures	High level of sick leave among hospital employees Work conditions are strongly related to sick leave
Strand, 1997^2	Cross- sectional	National survey in Norway octnov. 1989. (N=2,713)	LSC>3 weeks LSC>8 weeks	Physical effort Heavy lifting Heetic work tempo Weekly working hours Work schedules Job control	Domestic conditions Socio demographics Previous sick leave	63.4% had sick leave (yes/no) 26% eight weeks before 51% three weeks before LSC>8 weeks and LSC> 3 weeks associated with many of the exposures	The study population had the same level of sick leave the year before pregnancy as non- pregnant women. Dose response relation for some exposures - indicating causality.
Alexanderson, 1995 ¹¹	Cross- sectional	Sweden 1985-1987 (N=6,933)	Sick leave rate: Pregnant women on sick leave divided by number of women giving birth	Occupational group (9 & 30 levels) Male-female domination at work	Age	Large variation between occupations Occupation related to sick leave rates Male/female domination associated with sick leave	Not a clear relation between occupation and sick leave. Age of little importance
Saurel-Cubizolles, 1987 ⁴		France, 1981 (N=2,387)	Birth outcomes and Sick leave (yes/no) No of sick leave days Stopped work before 3rd trimester	Standing Lifting Assembly line work Physical effort Night work Work hours	Parity, smoking	More sick leave in exposed groups	Sick leave associated with strenuous work

Table 1 Associations between occupational exposures and sick leave in pregnancy

The results from the Danish report¹⁰ are largely consistent with results from epidemiological studies conducted in Norway and Denmark^{1,2,50}. Self-reported data on sick leave prevalence during pregnancy ranged in Norwegian studies from 71.5%² to 75.3%⁵⁰. Among Danish hospital employees, the average number of sick leave days was 56 days¹. Results on sick leave levels vary according to definitions of sick leave and available data sources. In a Swedish study using register data including sick leave spells exceeding 7 days, 37% of women aged 16–44 years were on sick leave during pregnancy¹¹. In spite of high levels of sick leave, a very small number of studies have been conducted with the purpose of investigating potential external risk factors for sick leave in pregnancy.

3.5 Occupational risk factors for sick leave in pregnancy

Associations between different occupational exposures and sick leave in pregnancy have been investigated in a limited number of studies^{1,2,4,11}, see Table 1. Among 2,713 pregnant women in Norway, increased odds ratios for sick leave either 3 or 8 weeks before delivery were found for non-daytime work, standing with the back bent forward, working with hands above shoulder levels, twisting/bending and lifting between 10–20 kilos². A Danish hospital employee study found heavy lifting, walking or standing, uncomfortable working positions and high work speed to be associated with sick leave rates of more than $10\%^{1}$. Self-reported psychosocial work conditions like low job control, lack of support from colleagues or supervisors and need for change in work tasks were also associated with higher odds for sick leave¹. Carrying heavy loads, having assembly line work or having considerable physical effort were associated with frequent sick leave in a French study⁴. A Swedish study used occupational groups as proxies for exposures and found a large variation of pregnancy-related sick leave rates between occupations; the largest rates were found in occupations with work assumed to be physically demanding¹¹. Furthermore, pregnancy-related sick leave rates were related to gender domination at work, with sick leave rates being lower in gender-integrated jobs¹¹. Major limitations of these studies are small size, retrospectively collected exposure information, use of crude exposure estimates and limited confounder adjustment.

Three studies have investigated if adjustments in exposures can reduce sick leave in pregnancy^{4,51,52}. The results suggest that there are potential preventive initiatives and that the legal rights for job adjustment are not fully implemented at the work sites. A

total of 62% of the women working in pregnancy needed job adjustment, and only 55% of these obtained adjustments⁵¹. In the group of women needing job adjustment and not obtaining it, almost 80% were sick leave notified before delivery and furthermore, this group of women was accountable for 44.5% of all sick leave weeks during pregnancy in the study population⁵¹. If a causal association between not obtaining job adjustment and sick leave exists, the results suggest an immense potential for sick leave reduction in pregnancy. A larger Norwegian study gave similar results⁵². Surprisingly, women in jobs with need of adjustment seemed less likely to obtain job adjustments. Furthermore, organisational factors such as decision latitude, pace and monotony were more important factors than physical job load when population attributable fractions were calculated⁵².

3.6 Other possible risk factors for sick leave in pregnancy

Non-occupational factors associated with sick leave in pregnancy have also been investigated and include course of pregnancy³, social benefits and economic compensation during sick leave^{12,13} and attitudes to sick leave^{7,53}. Sick leave in pregnancy may, however, also relate to a number of other factors including lifestyle, already having children and effort to become pregnancy.

Overweight and obesity is of growing public health concern and is now considered as a global epidemic⁵⁴. In Denmark, 32% of women aged 25–34 years and 41% of women aged 35–44 years are overweight $(BMI \ge 25)^{55}$, this means that overweight and obesity is a problem affecting a large number of pregnant women. A number of studies have found associations between non-pregnancy-related sickness absence (short-term and long-term) and high BMI^{32,56-58}. A high BMI is a risk factor for pregnancy-related pelvic pain, and pelvic pain is the most frequent diagnosis for sick leave in pregnancy⁵⁹. This suggests that there may be a pathway from a high BMI to sick leave in pregnancy.

Physical activity is beneficial for pregnant woman and exerts no potential adverse effects on the fetus^{60,61,62,63}. Accordingly, physical activity at moderate intensity levels is recommended for at least 30 minutes daily for women with uncomplicated pregnancies⁴⁸. Physical leisure time activity is beneficial in relation to reducing sick leave in populations of non-pregnant women^{57,64}. A recent study found an odds ratio

of 1.79 for sick leave in pregnancy for women not exercising compared to exercisers⁵⁰. Reluctance to exercise in pregnancy is therefore a possible risk factor for sick leave, and inactivity is, moreover, frequent among pregnant women^{65,66}.

The balance between work life and private life is challenging to women, which is reflected in gender differences in sick leave⁶⁷. In the literature this difference is often referred to as "the double burden of women". The challenge between work life and private life may be even harder during pregnancy because pregnancy induces fatigue and is an inherent strain on these women⁶⁸. An association between parity and sick leave in several studies has suggested this^{3,51,69}, and multiparous women may consequently need more rest during pregnancy⁷⁰.

The number of couples seeking help to conceive has increased markedly during the past decades. Today, 8% of all births arise from assisted reproductive therapy (ART)⁴⁸, these pregnancies have an inherent prolonged time to pregnancy (TTP) compared to couples conceiving naturally. Infertility treatment in a Norwegian study was associated with an odds ratio of 1.77 for sick leave compared to the reference group of natural conceivers⁵⁰. This is, however, not surprising as women conceiving though ART have more pregnancy-focused anxiety and a more intense emotional attachment to the fetus, which may lower the threshold for reporting sick^{71,72}. In addition, ART more frequently gives rise to multiple pregnancies, these pregnancies inherently comprise sick leave. Altogether, this knowledge suggests that ART could be a considerable risk factor to investigate further.

3.7 Antenatal care

All Danish citizens are covered by tax-financed health insurance, which includes antenatal care. The antenatal care programme encompasses three visits to the general practitioner, two ultrasound scans and 6–7 maternity ward contacts⁴⁸. If risk assessment of occupational exposures is found to be indicated at the general practitioners or maternity wards, referral to departments of occupational medicine for risk assessment is instituted. Less than 1% of pregnancies are referred to a specialist in occupational medicine⁷³.

3.8 Legislation covering pregnant working women

If occupational exposures are harmful or suspected to be harmful to the fetus or to the course of pregnancy, actions should be taken in the following sequence: (i) provision of personal protection or aid facilities, (ii) referral to other work tasks, or if not possible (iii) leave from work until beginning of maternity leave. Employers are responsible for making the assessments of the work environment and dealing with possible harmful exposures. There are three types of leave from work during pregnancy: (i) sick leave with no relation to pregnancy (termed ordinary sick leave in Table 2B, (ii) pregnancy-related sick leave, e.g. nausea, pelvic pain, or (iii) leave due to harmful occupational exposures: in Danish "fraværsmelding". Economic compensation varies according to the type of leave. Working women on sick leave or pregnancy-related sick leave receive either wages paid by the employer or sick leave benefits. The type of payment depends on the collective agreements covering the women. Leave due to harmful occupational exposures prompts full wage payment⁷⁴. Employers receive reimbursement equivalent to sick leave benefits after the "employer period" has passed. The duration of the employer period has changed over time: 2 weeks in the years 1989–2007, 21 days in the years 2008–2012, 30 days from 2012. Reimbursement is paid from the first day of sick leave in the event of pregnancy or harmful occupational exposures⁷⁵. Reimbursement is also paid to employers from the first day of sick leave if (i) the employee holds a flexi-job, (ii) the employee is chronically ill and has a municipality grant of a §56 agreement or (iii) the employer holds an insurance for short term sick leave, which is possible for either self-employed or small companies. Sick leave compensation is set at a fixed level, and the compensation rate varies thus according to wage level.

3.9 Sick leave notification

The prevalence of sick leave in pregnancy increased almost linearly with gestational week from 17.0% (week 13–16) to 44.6% (week 25–28) in a Norwegian study⁵². The tendencies were similar in a Danish study, with the following prevalences: 23.8% (1st trimester), 34.6% (2nd trimester) and 41.6% (3rd trimester) ⁷⁶. Predominant diagnoses prerequisite for pregnancy-related sick leave are pelvic pain (28.1%), risk of preterm birth and/or bleeding in the third trimester (19.4%) and risk of miscarriage (11.5%)⁶⁹. There is no registration which makes it possible to separate pregnancy-related sick

leave from leave due to a harmful occupational environment. Less than 5% of sick leaves in pregnancy in a Danish study were explained by hazards in the work environment⁶⁹. However, work environment contributes in some degree to 50.2% of leaves⁷⁷. Certification of sick leave is most often given by general practitioners (86.7%) and less often by hospital doctors (12.1%)⁷⁷. The certifying doctors are often put in a dilemma between being the pregnant women's confidant/e and preventing unnecessary sick leave⁷⁸. Moreover, the distinction between pregnancy-related sick leave and sick leave due to occupational exposures is not always straight forward for sick leave certifying medical doctors. Often even distinction between sick leave in pregnancy and pregnancy-related sick leave is ambiguous.

Summing up, pregnant women are frequently on sick leave and sick leave incidence has increased. The influence of occupational exposures as well as other potential risk factors needs to be investigated further because current knowledge is limited. Prospective studies carried out among working pregnant women will add to the existing knowledge in this field.

	STUDY IV	Follow-up study	ties from the DNBC 1,028 pregnancies from CDR	n pregnancy Physical occupational exposures Psychosocial occupational exposures	Questionnaire data	First episode of sick leave	on from survey-29 completed	leave weeks pregnancy weeks	DREAM*	lcohol, Chronic diseases, educational class, previous	up, sick leave	al and	vrk, chronic	s sick leave,		ere	ill models	ion Cox regression
	STUDY III	Follow-up study	54,997 pregnanc	Sick leave rate it	DREAM*	Flexi-job	Disability pensic	Number of sick l	DREAM*	Age, smoking, ai	occupational gro	strenuous physic	psychosocial wo.	disease, previous	health worries	All covariates we	not included in a	Logistic regressi
iccording to study	STUDY II	Follow-up study	51,874 pregnancies from the DNBC	Physical occupational exposures Psychosocial occupational exposures	Questionnaire data	First episode of sick leave	from 10-29 completed	pregnancy weeks	DREAM*	Age, smoking, alcohol intake,	occupational group,	previous sick leave,	chronic disease, BMI,	ART, collegial support				Cox regression
w of materials and methods a	STUDY 1	Follow-up study	51,874 pregnancies from the DNBC	Obstetric history Lifestyle	Questionnaire data	First episode of sick leave	from 10-29 completed	pregnancy weeks	DREAM*	Age, smoking, alcohol intake,	strenuous physical and	psychosocial work, socioeconomics,	previous sick leave, chronic disease	*Parity analysis for family structure				Cox regression
Table 2A Overviev		Design	Population	Exposure	Exposure assessment	[Outcome	1	Outcome assessment	7		H	1	COVAILAICS				Statistical analyses (

* For more details see table 2B

Sick leave in pregnancy	Insurance scheme ≥1 calendar day §56 agreement ≥1 calendar day	774, 881, 890, 892, 893, 894, 895, 896, 897, 898, 899
STUDY III Pregnancy-related sick leave Sick leave certified as related to pregnancy or Leave due to potential harmful occupational exposures Registered from first day Registered from first day Number of sick leave weeks in follow-up Flexi-job in follow-up Disability pension in follow-up Disability code (yes/no) Disability code (yes/no) Disability code (yes/no) Disability code (yes/no) Disability code (yes/no) Disability code (yes/no) Cumulated number of sick leave codes: (>14 calendar davs, insurance scheme holder ≥1	calendar day, §56 agreement ≥1 calendar day	771, 772, 773, 774, 781, 782, 783, 890, 892, 893, 894, 895, 896, 897, 898, 899
STUDY II Sick leave in pregnancy - - - - - - - - - - - - - - - - - - -	Insurance scheme holder ≥1 calendar day §56 agreement ≥1 calendar day	774, 881, 890, 892, 893, 894, 895, 896, 897, 898, 899
STUDY I Sickness absence in pregnancy - - First episode of sick leave from 10-29 completed pregnancy weeks from flexi job ≥1 calendar days Sick leave from flexi job ≥1 calendar day Pregnancy-related sickness absence ≥1 calendar day	Insurance scheme holder ≥1 calendar day §56 agreement ≥1 calendar day	774, 881, 890, 892, 893, 894, 895, 896, 897, 898, 899
Sick leave term DREAM DREAM DREAM DREAM DREAM DREAM DREAM DREAM DREAM		DREAM codes 79

Table 2B Overview of sick leave definitions based on DREAM data according to study

4. MATERIALS AND METHODS

In the next sections follows a description of the cohorts and registers used in the studies underlying this dissertation. After that, a brief description of the methods used in each of the studies I–IV is given. An overview of the studies is given in Table 2A. In table 2B is given an overview of sick leave measures used in studies I-IV according to DREAM data. Definitions of study populations are described in Figures 1 and 2. More detailed method descriptions are available in the appended papers I–IV.

4.1 The Danish National Birth Cohort: the DNBC

The Danish National Birth Cohort (DNBC) is a population-based pregnancy cohort, including 100,418 pregnancies enrolled between 1996 and 2002. The primary objective of the DNBC was to investigate how environmental, social and lifestyle exposures in the pregnancy period affect maternal and offspring health⁸⁰. This knowledge is important to make preventive measures for pregnant women and their children. The women were invited to participate at the first antenatal visit at their general practitioner, normally around gestational weeks 6–12. More than 95% of the women in the cohort were recruited at their general practitioner, the rest by a back-up recruitment at the maternity wards⁸⁰. 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 women were followed during pregnancy until birth or alternative outcomes of the pregnancy. The basic data collection included four computer-assisted telephone interviews, three blood samples and a food frequency questionnaire. Two interviews were conducted during pregnancy (around pregnancy weeks 17 and 30) and two postpartum (6 months and 18 months). Detailed information on the interviews is available at www.dnbc.dk. Data collection at the first interview included information on obstetric history, lifestyle, health, medication, education, occupational exposures and socio-demographics. The questionnaires were developed in cooperation with specialists within the subject areas. The large number of questions in the first interview enabled us to measure a number of occupational and non-occupational exposures and covariates. By using Danish civil registration numbers it is possible to link the DNBC with national registers.

4.2 Central Denmark Region: CDR

Central Denmark Region (CDR) is the second largest of five administrative health service units in Denmark. CDR covers a population of nearly 1,275,000 people, which is approximately 23% of the Danish population. The yearly birth rate in CDR is around 15,000 births. We conducted an internet-based study ("Gravid i job") in cooperation with the six maternity wards in CDR from April 2013 until August 2014. Pregnant women were invited to participate at their first midwife consultation, normally around gestational weeks 16–18. The only eligibility criterion was fluency in Danish language to complete the internet-based questionnaire. The women were informed about the study by the midwives and were given a four-page information leaflet. Further information about the study and login to the questionnaire was available at <u>www.gravid-i-job.dk</u>. A total of 1,748 women participated in the study, which was estimated to 21% of eligible women. The study included baseline questions on education, employment, occupational exposures, somatic and psychological disorders, as well as questions about the pregnancy. Some women (n=1,501, (86%)) gave us permission to contact them again by e-mail after having given birth. These women were sent a follow-up questionnaire, which included questions on time of birth, maternity leave and sick leave. The participation rate in the follow-up was 84%. The reason for establishing the CDR cohort was to investigate the associations found in study I and study II in another cohort of pregnant women at a minimum of 11 years later.

4.3 Danish Register for Evaluation of Marginalisation: DREAM

Danish Register for Evaluation of Marginalisation (DREAM) is a translation from the Danish acronym "Dansk Register for Evaluering **a**f Marginalisering". DREAM is a database falling under The Danish Agency for Labour Market and Recruitment. DREAM contains weekly information on more than 100 different types of public benefit payments, ranging from state education fund grants to unemployment benefits, sick leave benefits and old age pension⁷⁹. Each benefit is characterised by a unique code. Registration in DREAM is conditional on just one day of benefit payment. Only one code is registered weekly, and as codes are arranged hierarchically, change of codes during a week entails overwriting according to the hierarchy of codes. In the study populations of this thesis, codes for sick leave, flexi-job and disability pension

are high-ranking just below the code for death. Depending on studies I–IV, one or more of the following codes from DREAM were used: 771, 772, 773 (flexi-jobs, i.e. jobs for people with reduced work ability because of chronic illness), 774 (sickness absence from flexi-jobs) 783 (disability pension), 881 (maternity leave and pregnancy-related sickness absence), 890, 892, 893, 894, 895, 896, 897, 898, and 899 (all sickness absence codes for either ordinary employment, various job training programmes, apprenticeships or part-time sick leave)⁷⁹. Reimbursement is prerequisite to a registration in DREAM in working populations. The time from beginning of sick leave to reimbursement differs according to type of benefit, as earlier described. Owing to differences in time of reimbursement, the sick leave measures used in this thesis include a mix of short-term sick leave (\geq 1 day study I-IV) and long-term (>14 days in study I – III and > 30 days in study IV). For further details see Table 2B.

Below follows a description of the study populations, exposures, outcomes, covariates and statistical methods used in the studies underlying the dissertation. The study populations for studies I–III are derived from the DNBC, and for study IV CDR. DREAM data is included in all four studies, either as an outcome (studies I, II and IV) or as exposure and outcome study III.

4.4 Studies I and II

4.4.1 Population

The study population is described in Figure 1. A total of 92,891 women participated in the first pregnancy interview in the DNBC. We excluded 41,017 pregnancies according to the exclusion criteria listed in Figure 1. The final study population comprised (N=51,874) pregnancies of employed women (employed, self-employed, holding a flexi-job). Students, unemployed, rehabilitees and pensioners were not included in the study population.

4.4.2 Exposure

In study I, we used information from the first pregnancy interview on parity, prepregnancy weight and height, from which pre-pregnancy body mass index (BMI) was calculated⁸¹, use of any ART, TTP and engagement in physical exercise. Weekly engagement in physical exercise (minutes) was calculated based on duration and frequency of exercise sessions.

In study II, information from the DNBC was used for the occupational exposures: work posture, daily lifts medium weight (11–20 kilos), daily lifts heavy (>20 kilos), work shift, average monthly night shifts, weekly work hours, job demands and control. Daily cumulative lifting was calculated from frequency and weights of the daily lifts: medium weight lifts were assigned the value of 15.5 kilos and heavy lifts 22.5 kilos. Job strain was measured using the job strain model developed by Karasek⁸². Demands and control dimensions were derived from the questions: "Do you feel overworked in your job?" (Demand dimension) "Do you have any influence on your working conditions?" (Control dimension). Answer categories were given on a 3-point nominal scale for both dimensions: (often, from time to time, seldom). High demands were defined by the "often" answer category and low control by the "seldom" answer category.

4.4.3 Outcome

Time of first episode of sick leave from 10 to 29 completed pregnancy weeks was the primary outcome, regardless of the duration of the episode. Based on due date information from the first pregnancy interview, we calculated time of first day of last menstrual bleeding, which was set as the time of conception (due date minus 280 days). If the due date was missing at first interview, data from the late pregnancy interview were used. The conception date was linked to DREAM data, and for each pregnancy, we made a time line. If time of conception was on a Monday, Tuesday, Wednesday or Thursday, time of conception was set to Monday in the conception week. Fridays, Saturdays and Sundays were set at Monday the following week. For each completed pregnancy week from 10 to 29, we estimated the time of first episode of sick leave. Sick leave was defined as the first occurrence of one of the DREAM codes listed in Table 2B. The lower limit of 10 completed pregnancy weeks was

Figure 1 Flow chart of pregnancies – investigating lifestyle, obstetric and occupational exposures as risk factors for sick leave in pregnancy (studies I and II) and labour market attachment after sick leave in pregnancy (study III).



arbitrarily set, because the DNBC contains no information on the exact time of recruitment, but most women have seen their general practitioner at 10 completed pregnancy weeks, which was set as the time of cohort entry. The upper limit was set at 29 completed pregnancy weeks, since it is not possible to distinguish maternity leave from pregnancy-related sick leave in DREAM. The upper limit did not collide with maternity leave, as Danish women at earliest begin maternity leave at 31 completed pregnancy weeks.

4.4.4 Covariates

Covariates in both studies were age (continuous), smoking, alcohol intake, chronic diseases, (somatic and psychological) and previous sick leave. The variable previous sick leave was generated based on DREAM data and covered sick leave two years before the DNBC pregnancy. From time of conception, we looked two years back in time and counted the number of weeks each woman received sick leave benefits. Pregnancy-related sick leave was not included in the previous sick leave variable. In study I, analyses were further adjusted for job demands (physical and psychological) and socioeconomic status based on educational level and the Danish version of International Standard Classification of Diseases (DISCO-88). Parity analyses were additionally adjusted for family structure, a variable including information on marital status and having children in the household. In study II, we further adjusted for occupational class based on DISCO-88, parity, pre-pregnancy BMI, ART and collegial support.

4.4.5 Statistical analyses

Data were analysed by multivariate Cox regression models using pregnancy week as the underlying time variable. Time at risk started at first pregnancy interview and ended at first episode of sick leave, 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 sick leave at the time of inclusion or prior to the first interview were excluded from the analyses. Hazard ratios (HR) were calculated for the whole study period and in four pre-defined completed pregnancy week periods; (weeks 10–14, weeks 15–19, weeks 20–24 and weeks 25–29). Time at risk in each of the four pregnancy week periods 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 at the beginning of the pregnancy week periods were excluded from the analyses in the following pregnancy week periods. Time-varying coefficients were calculated for all the exposures to estimate time-dependent effects with time since 10 completed pregnancy weeks. Finally, a number of sub-analyses from study I and study II are described in the appended papers (I–II).

4.5 Study III

4.5.1 Population

The study population is described in Figure 1. A total of 92,891 women participated in the first pregnancy interview in the DNBC. We excluded 37,894 pregnancies according to the exclusion criteria listed in Figure 1. The final study population comprised (N=54,997) pregnancies of employed women (employed, self-employed, holding a flexi-job). Students, unemployed, rehabilitees and pensioners were not included in the study population.

4.5.2 Exposure

A number of occupational exposures and lifestyle factors were investigated as predictors of poor labour market attachment, but the main predictor of interest was percentage of pregnancy-related sick leave weeks from conception until maximum 29 completed pregnancy weeks. This percentage was calculated as the number of weeks with a pregnancy-related sick leave code in DREAM divided by the number of weeks each woman was observed pregnant until a maximum of 29 completed pregnancy weeks. This exposure measure was chosen in an attempt to eliminate sick leave not related to pregnancy, as this type of sick leave could be related to the outcomes.

4.5.3 Outcomes

Outcomes were cumulated number of sick leave weeks in DREAM regardless of duration (continuous), flexi-job (yes/no), and disability pension (yes/no) in an 8-year follow-up period starting one year after child birth. These data were obtained from DREAM.

4.5.4 Covariates

Covariates for the continuous outcome cumulated number of sick leave weeks were age, smoking, alcohol intake, BMI, occupational group, strenuous physical and psychosocial work demands, chronic disease, previous sick leave and health worries. Covariates for the dichotomous outcomes flexi-job and disability pension were selected based on univariable analyses and likelihood ratio tests in the model building process. Covariates included, but not in all models, were age, smoking, BMI, occupational group, strenuous physical and psychosocial work demands, chronic disease, previous sick leave and health worries.

4.5.5 Statistical analyses

We built a model including predictors available from antenatal care. The continuous outcome cumulated number of sick leave weeks during follow-up was analysed by a multivariable zero-inflated Poisson regression model (zip). A zip model is useful when the outcome has a high number of zeros, and there is a right skewed distribution among the non-zeros. Results are given as odds ratios (OR) and incidence rate ratios (IRR) in the zip model.

The dichotomous outcomes flexi-job and disability pension were analysed by multivariable logistic regression models, with results presented as odds ratios (OR). Predictors with $p \le 0.20$ from the univariable analysis were included in the multivariable model. Second, predictors were selected by a backward selection procedure ($p \le 0.05$) from the full model using likelihood ratio tests. Predictors eliminated by this procedure were re-entered in the final model and included at the level of $p \le 0.05$ significance. The final models did not include the same combination of covariates. A number of sub-analyses were conducted, see appended paper (III).

4.6 Study IV

4.6.1 Population

The definition of the study population is described in Figure 2. A total of 1,748 women completed the baseline questionnaire. A number of women (n=720) were excluded based on the exclusion criteria listed in Figure 2, giving a study population of 1,028 employed women. A sub-population of (n=636) women with follow-up data

collected after childbirth comprised the sub-population for an analysis including birth data.

4.6.2 Exposure

From the CDR survey, we used information on parity, pre-pregnancy weight and height to calculate BMI, TTP and weekly engagement in physical exercise. Occupational exposures were work shifts, weekly work hours, work posture, daily lifts medium weight (11–20 kilos), daily lifts heavy (> 20 kilos), cumulative number of daily lifts (kilos), cumulative number of kilos pushed daily, number of daily person lifts and job strain. Medium and heavy lifts were assigned weights in kilos as in study II. Job strain was measured using selected questions from the Copenhagen Psychosocial Questionnaire II (COPSOQ II)⁸³.

4.6.3 Outcome

Outcome data were obtained from DREAM and the outcome was first episode of sick leave from baseline until 29 completed pregnancy weeks, regardless of the duration of the episode. As for studies I and II, due date information was based on the baseline questionnaire. We calculated time of first day of last menstrual bleeding, which was set as the time of conception (due date minus 280 days). Women with missing due date information were excluded. The conception date was linked to DREAM data and time lines were made as for studies I and II. For each completed pregnancy week from baseline to 29 pregnancy weeks, we estimated sick leave. The upper limit was set at 29 completed pregnancy weeks, since it is not possible to distinguish maternity leave from pregnancy-related sick leave in DREAM. **Figure 2** Flowchart of pregnancies included in the CDR study investigating lifestyle, obstetric and occupational exposures as risk factors for sick leave in pregnancy (study IV).


4.6.4 Covariates

Covariates were occupational group, self-reported number of sick leave days one year before pregnancy and chronic diseases.

4.6.5 Statistical analyses

Data were analysed by a multivariate Cox regression model using pregnancy week as the underlying time variable. Time at risk started at baseline, and ended at first episode of sick leave or 29 completed pregnancy weeks, whichever came first. Women with sick leave at baseline or pregnancy sick leave before baseline were excluded from the analyses. For the 636 women, we used birth date given in the follow-up questionnaire.

5. RESULTS

The following section summarises main findings from the individual studies. More results are available in the appended papers I–IV.

5.1 Studies I and II

The cumulative incidence proportion of sick leave was 36% from time of conception until 29 completed pregnancy weeks. Prevalence of sick leave increased from 2% to 17% from 10 to 29 completed pregnancy weeks. Table 3 shows weekly prevalence of sick leave.

Table 3 Prevalence of sickness absence according to pregnancy week from 10 to 29completed pregnancy weeks. N=51,874

Completed pregnancy week	Pregnancie sickness at	es with osence	Prevalence of sickness absence %	Total number of pregnancies
	Yes	No ^a		
10	4	200	2.0	204
11	35	1,416	2.4	1,451
12	86	4,189	2.0	4,275
13	189	8,581	2.2	8,770
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	1,041	27,802	3.6	28,843
18	1,343	31,712	4.1	33,055
19	1,719	35,162	4.7	36,881
20	2,200	38,021	5.5	40,221
21	2,686	40,373	6.2	43,059
22	3,213	42,015	7.1	45,228
23	3,781	43,210	8.1	46,991
24	4,493	43,848	9.3	48,341
25	5,300	44,062	10.7	49,362
26	6,136	43,919	12.3	50,055
27	6,962	43,631	13.8	50,593
28	7,871	43,060	15.5	50,931
29	8,793	42,377	17.2	51,170

^aPregnancies ending as abortions, miscarriages or preterm births were excluded week by week (N=704).

Sick leave in pregnancy was more frequent among working women who were smokers, alcohol abstainers, suffered from chronic diseases and were skilled and unskilled workers. There were differences among sick leave groups in the perception of physical and psychosocial demands at work. Furthermore, women with sick leave were more frequent on sick leave during the two years before pregnancy.

All predictors in study I were associated with the overall risk (HR) for sick leave from 10 to 29 completed pregnancy weeks. Multiparity was associated with a HR of 1.26 (95% CI: 1.10–1.45) compared with nulliparous pregnancies, and ART with a HR of 1.10 (95% CI: 1.01–1.20) compared to natural conceivers. There were dose-dependent effects for BMI (HR_{trend} 1.02 (95% CI: 1.01–1.02)), TTP (HR_{trend} 1.02 (95% CI: 1.00–1.04)) and physical exercise (HR_{trend}0.93 (95% CI: 0.92–0.94)). These results were largely confirmed by dividing the pregnancy period into four periods. Decreasing time-dependent effects were found for multiparity and TTP > 12 months and increasing effects for exercising 31–60 minutes per week. Selected results for study I are shown in Table 4.

In study II, a range of work postures were associated with elevated risks (HR) for sick leave compared to the reference (sitting); standing 2.75 (95% CI: 2.51–3.02), walking 2.96 (95% CI: 2.74–3.20) and standing and walking 2.98 (95% CI: 2.79–3.18). Daily lifting, cumulative as well as individual medium or heavy lifts were associated with higher risk for sick leave compared to the reference groups. There was a dose-response relation for cumulative lifting HR_{trend}1.33 (95% CI: 1.31–1.35). Work shift different from day was associated with elevated risk for sick leave, so was average number of night shifts HR_{trend} 1.05 (95% CI: 1.04–1.06). Weekly work hours showed a decreasing dose-response relation HR_{trend} 0.90 (95% CI: 0.88–0.92). Finally, high job strain increased the risk for sick leave compared to the reference group 1.60 (95% CI: 1.49–1.71). There were decreasing time-dependent effects of the exposures for work postures classified as other, medium and heavy lifts and a passive job strain. In addition, there were increasing time dependent effects for a shifting work shift. Selected results for study II are shown in Table 5.

Study	γ I		Study IV		
Predictor	$\mathrm{HR}^{\mathrm{adj}}$	95% CI	Predictor	$\mathrm{HR}_{\mathrm{adj}}{}^{\mathrm{b}}$	95% CI
Multiparity (yes) BMI (kg/m ²)	1.26	1.10-1.45	Multiparity (yes) BMI (kg/m²)	1.71	1.26 –2.31
<18.5 18.5 - <25	1.01 1.00	0.92 –1.12	<25	1.00	I
25- <30 >30	1.13 1.23	1.08 –1.18 1.15 –1.31	≥25	1.50	1.11 -2.03
ART (yes)	1.10	1.01 - 1.20			
TTP (months)			TTP (months)		
0 – 2	1.00		0 - <3	1.00	I
3 -5	0.98	0.93 - 1.03	3 –6	1.25	0.82 - 1.90
6-12	1.03	0.97 - 1.09	>6	1.11	0.79 - 1.58
>12	1.06	0.99 - 1.13			
Physical exercise (min/week)			Physical exercise (hours/week)		
0	1.16	1.04 - 1.28			
1 - 30	1.00		0 – 1	0.86	0.59 - 1.24
31 -60	0.98	0.87 - 1.10			
61 – 120	0.96	0.85 - 1.08	1-2	1.00	I
>120	0.84	0.75 - 0.95	>2	0.56	0.39 - 0.80

^aAdjusted for age, smoking, alcohol intake, strenuous physical and psychosocial work environment, socioeconomic group, prior sick leave level and chronic diseases. Parity analysis furthermore adjusted for family structure ^bAdjusted for chronic diseases, educational class and prior sick leave days

according to study Table 4 Selected results for lifestule obstatric and fertility factors

Table 5 Selected results for occupationa	al exposures	according to study			
Study II			Study IV		
Predictor	${ m HR}_{ m adj}{}^{ m a}$	95% CI	Predictor	$\mathrm{HR}_{\mathrm{adj}}^{\mathrm{b}}$	95% CI
Work posture			Work posture		
Primarily standing	2.75	2.51 -3.02			
Primarily walking	2.96	2.74 - 3.20			
Primarily standing and walking	2.98	2.79 - 3.18	Primarily standing and/or walking	1.51	1.02 - 2.19
Primarily sitting	1.00	I	Primarily sitting	1.00	I
Changeable	1.56	1.47 - 1.65	Changeable	1.13	0.76 - 1.67
Other	2.36	1.87 –2.98			
Daily lifts 11 –20 kilos (yes)	1.92	1.84 -2.00	Daily lifts 11 –20 kilos (yes)	1.58	1.15 -2.18
Daily lifts >20 kilos (yes)	1.96	1.87 –2.06	Daily lifts >20 kilos (yes)	1.60	1.03 –2.49
Cumulative daily lifting (kilos)			Cumulative daily lifting (kilos)		
0 -14	1.00	I	0	1.00	I
15 -100	1.70	1.61 - 1.79	1 -100	1.35	0.89 -2.03
101 -200	2.19	2.03 -2.36	>100	1.70	1.01 -2.87
201 –500	2.39	2.21 -2.58			
501 -1000	2.51	2.21 -2.84			
>1000	3.55	3.00 -4.21			

^aAdjusted for age, smoking, alcohol intake, prior sick leave level and chronic diseases, parity, BMI, ART and support from colleagues. ^bAdjusted for chronic diseases and prior sick leave days.

Table 2 Colle Survey Logard Totale 101 Occu	<u>אסטוומו הא</u>	onsure according to a	iuuy		
Study II			Study IV		
Predictor	HRadj ^a	95% CI	Predictor	HRadj ^b	95% CI
Work shift			Work shift		
Fixed day	1.00	I	Fixed day	1.00	I
Fixed evening	2.08	1.89 - 2.29		000	
Fixed night	1.54	1.16 - 2.03	Fixed evening or night	0.88	0.21 - 2.93
Shifting, without night shifts	1.44	1.35 - 1.54	Shifting, without night shifts	1.84	1.25 -2.69
Shifting, with night shifts	1.58	1.39 - 1.80	Shifting, with night shifts	1.28	0.82 -2.01
Weekly work hours			Weekly work hours		
< 30 hours	1.12	1.07 - 1.19		1 1 4	031 000
$30 - \langle 37 \rangle$ hours	1.26	1.19 - 1.34	STUOLI / C >	1.14	00.1-20.0
37 hours	1.00	I	37 hours	1.00	I
>37 hours	0.81	0.76 -0.87	>37 hours	09.0	0.35 -1.06
Job strain			Job strain		
High strain	1.60	1.49 - 1.71	High strain	0.75	0.34 -1.68
Passive	1.02	0.95 - 1.10	Passive	0.56	Ι
Active	1.00	I	Active	1.00	0.36 -0.85
Low strain	0.70	0.67 -0.74	Low strain	0.79	0.54 - 1.14

Table 5 cont. Selected results for occupational exposures according to study

^aAdjusted for age, smoking, alcohol intake, prior sick leave level and chronic diseases, parity, BMI, ART and support from colleagues. ^bAdjusted for chronic diseases and prior sick leave days.

5.2 Study III

The cumulative incidence proportion of pregnancy-related sick leave was 28% from conception until 29 completed pregnancy weeks. Sick leave rates were less than 20% in 8,548 (15%) of pregnancies, and above 20% in 6,970 (13%) of pregnancies. The mean number of sick leave weeks was 2.3 weeks, and in pregnancies with sick leave 8.3 weeks. During follow-up 738 (1.3%) of women received flexi-job benefits, and 443 (0.8%) received disability pension. The mean number of sick leave weeks during follow-up was 11.5 weeks.

Table 6 shows selected results from study III. Pregnancy-related sick leave was associated with a 62% (95% CI: 52–72%) higher risk for at least one sick leave week in follow-up. Number of sick leave weeks in follow-up was 17% (95% CI: 16–18%) higher for women with pregnancy-related sick leave compared to women without sick leave. A 10% increase in pregnancy-related sick leave proportion was associated with OR 1.09 (95% CI: 1.07–1.11%) for at least one sick leave week in follow-up. Correspondingly, a 10% increase in pregnancy-related sick leave week in follow-up. Correspondingly, a 10% increase in pregnancy-related sick leave weeks in the follow-up period. Smoking, overweight and obesity, low occupational group, strenuous physical and psychological job demands, chronic disease and prior sick leave were also predictors of increased odds for sick leave during follow-up. Pregnancy-related sick leave was associated with both flexi-job and disability pension. Having pregnancy-related sick leave in more than 20% of the pregnancy was associated with an OR of 2.56 (95% CI: 2.11–3.11) for flexi-job and an OR of 3.21 (95% CI: 2.53–4.07) for disability pension.

5.3 Study IV

The cumulative incidence proportion of sick leave from conception until 29 completed pregnancy weeks was 38%, and from time of study inclusion until 29 completed weeks 19%. Working women having sick leave in pregnancy suffered more frequently from chronic diseases and were of lower occupational groups. Selected results for study IV are shown in Tables 4 and 5. BMI > 25 was associated with a HR of 1.50 (95% CI: 1.11–2.03) for sick leave compared to women with BMI < 25.

Predictor	At least of in follow	one week sick y-up	Number of given sick in fol	of weeks llow-up
	OR ^a	95% CI	IRR ^a	95% CI
Pregnancy-related sick leave (per 10%) Pregnancy-related sick leave (yes)	1.09 1.62	1.07 –1.11 1.52 –1.72	1.06 1.17	1.05 –1.06 1.16 –1.18
-	Flexi-job)	Disability	pension
	OR^b	95% CI	OR ^c	95% CI
Pregnancy-related sick leave (%) 0 ≤ 20 > 20	1.00 1.51 2.56	- 1.23 -1.86 2.11 -3.11	1.00 1.33 3.21	0.99 -1.79 2.53 -4.07

Table 6 Selected results for cumulated sick leave weeks, flexi-job, disability pension according to pregnancy-related sick leave (Study III)

^aAdjusted for age, smoking, alcohol intake, BMI, occupational group, strenuous physical and psychosocial job demands, chronic diseases, prior sick leave, health worries

^bAdjusted for age smoking, occupational group, strenuous physical and psychosocial job demands, chronic diseases, prior sick leave, health worries

^CAdjusted for age smoking, occupational group, strenuous physical and psychosocial job demands, chronic diseases, prior sick leave, health worries

For multiparous women, we found a HR for sick leave of 1.71 (95% CI: 1.26–2.31) compared to nulliparous women, and for physical exercise > 2 hours weekly a HR of 0.56 (95% CI: 0.39–0.80). TTP was not associated with risk for sick leave in pregnancy. Occupational exposures such as walking and/or standing posture were associated with sick leave with HR of 1.51 (95% CI: 1.02–2.19). Lifting 11–20 kilos items was associated with a HR of 1.58 (95% CI: 1.15–2.18) for sick leave and lifting items > 20 kilos was associated with a HR of 1.60 (95% CI: 1.03–2.49). For lifting > 100 kilos daily the HR for sick leave was 1.70 (95% CI: 1.01–2.87) compared to no lifting. Daily pushing of >200 kilos was associated with a HR of 2.21 (95% CI: 1.44–3.39) and daily person lifts between 1-5 times was associated with a HR of 1.58 (95% CI: 1.06–2.36) compared to the zero categories. A passive job strain was associated with a HR of 0.56 (95% CI: 0.36–0.85) for sick leave reduced risk for sick leave, whereas weekly work hours were not associated with risk for sick leave. Finally, work shift was not associated with sick leave in a clear-cut way.

6. DISCUSSION

One of the aims in this dissertation was to study predictors of sick leave among working pregnant women in studies with a prospective collection of exposure data. We found that a number of lifestyle and obstetric factors were associated with higher risk for sick leave in pregnancy. A large number of occupational exposures were also found to be associated with an increased risk of sick leave in pregnancy. The associations found in the DNBC were largely supported by the study conducted in the CDR. Another aim was to investigate labour market prognosis for women with pregnancy-related sick leave. Pregnancy-related sick leave was associated with increased risks for future sick leave, flexi-job and disability pension during 8- years of follow-up after child birth. The absolute risk for receiving flexi-job or disability pension during follow-up were, however low, as was the positive predictive value of pregnancy-related sick leave.

The studies included in this thesis are all follow-up studies. No studies are designed perfectly – there are strengths and limitations in all epidemiological studies. Below follows a discussion of bias in studies I–IV. Bias determines the internal validity of the studies.

6.1 Methodological considerations

6.1.1 Selection bias

Selection bias occurs when the relation between exposure and the outcome is different for those who participate compared to all of those who in theory were eligible for the study, including those who do not to participate⁸⁴. The overall participation rate in the DNBC was low, around 30%⁸⁵. There were two levels of selection into the DNBC (i) selection at the general practitioner level, accounting for 50% of non-participation, and (ii) selection at the individual level of pregnant women, accounting for another 50% of non-participation. Nohr et al. found that the participation rate in the DNBC was higher for women of normal weight, non-smokers or previous smokers and women receiving in vitro fertilization (IVF) treatment⁸⁵. These differences were investigated for the following exposure-outcome relations: IVF-preterm birth, smoking-small for gestational age (SGA) and BMI-stillbirth. The participation rate,

however, did not bias the estimates for the exposure-outcome relations investigated when compared to estimates in the source population for the DNBC in two geographical areas⁸⁵. This is reassuring, even though selection bias in relation to other outcomes is possible. Participation in the DNBC was also associated with socioeconomics, a higher participation was found among women with academic educations, incomes above the 75th percentile and being employed⁸⁶. This socioeconomic-driven selection into the DNBC may have introduced confounding, and to minimise this, we adjusted for socioeconomic status or occupational class in our analyses. Selection into the DNBC may have influenced the external validity of the results, and the results may not be generalisable to other populations of pregnant women.

In the CDR cohort, participation was even lower than in the DNBC. By keeping track of the number of leaflets handed out and the number of replies, we calculated a participation rate of 21% (range between maternity wards 15–25%). Selection mechanisms were possible at the level of the midwives and at the level of individual participants. Selection at the midwife level would be essential if midwives systematically discarded or invited pregnant women based on their exposures and/or outcomes. As all midwives were given the same information about inclusion procedures, we consider this selection to be of little importance. At the level of the pregnant women selection bias was possible. The women knew about the overall purpose of the study, and we cannot rule out possible selection bias if women having a strenuous work environment and at the same time feeling need for a sick leave notification decided to participate more than women without these characteristics.

6.1.2 Information bias

Information bias is caused by measurement errors in the exposure, outcome or covariates⁸⁴. The direction and magnitude of information bias depends on whether the measurement error in one variable depends on the value of that particular variable, values of other variables or errors in measuring other variables. Measurement errors are called misclassification, which can be either non-differential or differential. Non-differential misclassification of a variable occurs when the misclassification is unrelated to other variables. Non-differential misclassification will bias estimates towards the null hypothesis of no association between exposure and outcome (type II error). Differential misclassification can bias estimates in any direction.

The predictors/exposures studied were, except for study III, based on self-reports, and self-reports are by nature imprecise, questions may be misunderstood, questions may be difficult to answer or study subjects may have recall problems. This leads to exposure/predictor misclassification and could potentially bias results. For example, the precision of self-reports in weight studies has been validated, and weights are, especially for women, most often underestimated⁸⁷.

Self-reported exposure data does, however, bias results towards the null if the inherent misclassification is unrelated to the outcomes of interest. For the majority of exposures in studies I, II and IV, misclassification is most likely non-differential, because subjects who at the time of interview were on sick leave were not included in the analyses. Hence, misclassification and imprecision of exposures would bias results towards the null hypothesis. We did not account for work adjustments in the exposure assessment. It is possible that women in the high exposure groups with progression of pregnancy obtained adjustments in their exposures; such misclassification of the high exposed groups could underestimate the true effect of the exposures. In study III, we cannot rule out the possibility of differential misclassification of the exposure, because sick leave in pregnancy as a behaviour or trait may correlate with future sick leave; this could overestimate the predictive effect of the exposure sick leave in pregnancy on sick leave during the 8-year follow-up period after childbirth. Information bias should also be considered for the outcomes. Outcome data were register-based, which generally limits information bias if the register information is valid. A further advantage in using register-based outcome data is the completeness of follow-up. DREAM has been used in a number of studies investigating outcomes like return to work^{88,89}, sick leave⁹⁰⁻⁹² and disability pension^{23,24}. The register has been validated in two studies, one against self-reported sickness benefit payment⁹³ and another against work-place registration of sick leave⁹⁴. Stapelfeldt et al. concluded that there was an excellent agreement between work-place-registered sick leave and DREAM-registered sick leave⁹⁴. The authors found, however, a poor agreement between work-place registration and DREAM registration for pregnancy-related sick leave. This finding may be because the authors excluded DREAM code number 881 (maternity leave), a code also used for pregnancy-related sick leave. A validation of DREAM data in relation to sick leave in pregnancy is thus still required. We used a combined measure of sick leave in studies I, II and IV consisting of pregnancy-related sick leave and general sick leave for employed women. We did this because we

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wanted to investigate overall sick leave in pregnancy and because there may be inconsistencies in the registration of sick leave. This non-homogeneous measure of sick leave includes a mixture of short-term and long-term sick leave which entails misclassification of the outcome. Owing to the weekly registration, DREAM generally overestimates duration of sick leave. Short periods of general sick leave not exceeding the employer period are not registered in DREAM, which means that DREAM underestimates the prevalence of sick leave. In study III, we used only the code for pregnancy-related sick leave, because we sought to investigate the specific impact of pregnancy-related sick leave on future labour market attachment, as inclusion of normal sick leave was thought to be possibly related to the outcomes. This measure of exposure is not unambiguous as classification of sick leave as pregnancy-related or not depends on medical judgements, consequently some women in the exposed category are misclassified, but the misclassification will most likely be unrelated to the future outcomes. However, there may be an association between future general sick leave and pregnancy-related sick leave in cases where sick leave is a pattern of behaviour more than a consequence of disease.

These evident inaccuracies in DREAM in relation to both the exposure pregnancyrelated sick leave and sick leave as an outcome are, however, believed to be unrelated to the exposures, and misclassification of outcomes is therefore non-differential and would potentially bias the results towards the null. It is also possible that some participants in studies I, II and IV may have had short periods of sick leave before the interview, which was not registered in DREAM. This misclassification would most likely not be related to specific exposures either. In study III, any misclassification of the three outcomes sick leave, flexi-job or disability pension is believed to be nondifferential.

6.1.3 Confounding

Confounding is an important issue in observational studies and is best described as a confusion of effects⁸⁴. A confounder must fulfil three criteria: (i) it must be associated with the exposure either causally or non-causally, (ii) it must be an independent risk factor for the outcome and (iii) it must not be on the causal pathway from exposure to outcome. Confounding either overestimates or underestimates the effect of an exposure and can be accounted for in the statistical analyses.

We decided *a priori* to adjust for a number of potential confounders in studies I, II and IV based on the literature. In study I, where we investigated associations between lifestyle and obstetric factors, we adjusted for age^{3,30,95}, alcohol intake, smoking⁹⁶, physical and psychosocial demanding work⁹⁶, socioeconomic status⁹⁷, previous sick leave³³ and chronic diseases³¹. In study II, investigating the association between a number of occupational exposures and sick leave, we furthermore adjusted for parity, BMI, ART based on the findings in study I. In addition, we adjusted for collegial support, as this factor in qualitative research has been found important in relation to sick leave notification⁹⁸. The work exposures were omitted in study II, because they were the independent variables. Owing to the close correlation between socioeconomic group and occupational exposures, we only adjusted for occupational class in a sub-analysis in study II. Sick leave in pregnancy according to selected confounders for studies I, I and IV is displayed in Table 7.

The size of the study population in study IV together with the available data limited the number of confounders we could adjust for, and we therefore only adjusted for chronic diseases, educational class and number of previous sick leave days.

Confounder adjustment in study III was determined on the basis of the univariable analyses for the outcomes flexi-job and disability pension. For cumulated number of sick leave weeks, we adjusted for the same confounders as in study I, and in addition, the variable health worries, which was considered as a proxy for sick leave behaviour.

It would seem relevant to adjust for diagnoses related to sick leave in pregnancy, i.e. nausea, vomiting, pelvic pain, painful Braxton hick's contractions and vaginal bleeding, as at least some of these diagnoses most likely are associated with both the exposures and risk factors for the outcome sick leave. To investigate this, we used information from the late pregnancy interview in the DNBC (pregnancy week 32), which, however, did not cause any appreciable changes in the risk estimates.

We believe that adjustment for the chosen confounders has minimised the possibility of confounded risk estimates; however, there is still the possibility of residual confounding and unknown confounding. In study IV, unmeasured confounding is a possibility, because we did not have information on the lifestyle exposures smoking and alcohol intake.

6.2 Main findings in the light of other studies

A very limited number of studies have investigated the association between occupational and lifestyle exposures and sick leave in populations of employed pregnant women. This also applies to studies concerning labour market position after sick leave in pregnancy. Incidence proportions of sick leave in pregnancy vary across studies according to how sick leave is defined^{2,3,11,50,52}. The cumulative incidence proportion we found from beginning of pregnancy until 29 completed pregnancy weeks (36% in the DNBC) and (38% in the CDR) is in accordance with results from the Norwegian MoBA cohort, which is similar to DNBC in structure⁵². The associations between parity and risk for sick leave are consistent with finding from two other studies^{2,50}, whereas a Danish study among hospital employees found no association¹. Our findings of associations in studies I and IV between obesity and sick leave in pregnancy are in agreement with results from studies conducted in general working populations^{56,99}. To our knowledge only one previous study has investigated the influence of obesity on sick leave¹⁰⁰. The authors found a higher frequency of obese women in occupations with manual work, and within manual work occupations obese women made more use of parental leave compared to normal weight women¹⁰⁰. Parental leave is a benefit which can be used before delivery instead of sick leave. These findings suggest an incompatibility between concurrent employment, pregnancy and obesity. To fully investigate the significance of pregnancy and obesity on sick leave, comparisons should be made with groups of non-pregnant overweight employees.

ART as a risk factor for sick leave has only been investigated in one previous study⁵⁰; no earlier studies have investigated associations between TTP and sick leave. Study I supports the findings from Dorheim et al.'s study⁵⁰. One possible causal pathway from ART to sick leave goes through pregnancy-related anxiety. Studies have shown that women who become pregnant after ART have more pregnancy-focused anxiety compared to women conceiving naturally^{71,72,101}; these findings are not consistent though, and Poikkeus et al. found no difference between these groups¹⁰².

			St	udy I & I	II (N=51,87	4) ^a					-1	Study IV	(N=1,02	(8)		
Parameter	Sick lear N=10,66	ve 7 (21%)			No sick N=41,2	: leave 07 (79%)			Sicl N=]	k leave 192 (819	(%)		No s. N=8	ick leave 36 (19%)		
	z	%	Mean	SD	Z	%	Mean	SD	z	%	Mean	SD	z	%	Mean	SD
Age (years) Mean (SD)			30.1	(4.2)			30.7	(4.0)			31.2	4.0			31.2	4.0
Socioeconomic status^b, no. (%) Higher grade professionals Lower grade professionals Skilled workers Unskilled workers	1.279 3.619 4.844 889	12.0 33.9 45.4 8.3			10.176 13.755 15.501 1.651	24.7 33.4 37.6 4.0			28 98 5	14.7 51.3 31.4 2.6			264 339 201 28	31.7 40.8 24.2 3.4		
Sickness absence before study entry (weeks/days ^c), no. (%) 0 1 -4 5 -8 9 -26 >26	6.836 2.146 528 599 558	64.1 20.1 5.0 5.2			32.389 4.501 895 1.492 1.930	78.6 10.9 2.2 3.6 4.7			21 77 55 31	10.9 40.1 28.7 16.2 2.6			179 411 164 58 7	21.4 49.2 19.6 6.9 0.8		
Chronic diseases Yes, no. (%)	1.263	11.8			3.463	8.4			33	17.2			100	12.0		
Lifestyle smoking Smoking no. (%)	1.904	17.9			4.722	11.5										
Lifestyle alcohol, weekly intake (drinks), no. (%) 0 2 - 7 >7	6.213 3.910 514 18	58.3 36.7 4.8 0.2			20.555 17.938 2.606 61	49.9 43.5 6.3 0.2										

*Not directly comparable between study I, II and IV. In study I and II number of weeks according to DREAM two years prior to pregnancy, in study IV number of days (self-reported) one year prior to pregnancy.

Dorheim et al. found a positive association between no weekly exercise and increased OR for sick leave in the three pregnancy trimesters⁵⁰; our results in studies I and IV corroborate these findings. In addition, our data suggested a negative dose-response relation. We found no other studies on exercise in pregnancy and sick leave, whereas a preventive effect of physical exercise has been found in working populations^{64,103}. The beneficial effect of physical activity could be overestimated in our studies, because "a healthy exerciser effect" may play a role. Furthermore, if pregnant women stop exercising because of pregnancy-related disorders associated with future sick leave, an overestimation of a beneficial exercise effect is possible due to reverse causation.

The results for occupational exposures are in agreement with the existing literature among pregnant women^{1,2,4}. Different outcome definitions across these studies make comparison of risk estimates difficult. The Norwegian study by Strand et al. found sick leave at either 3 or 8 weeks before delivery to be associated with non-daytime work, standing bent forward, work with hands above shoulder level, twisting and bending and lifting 10–20 kilos; all results were, however, not statistically significant². Long-term sick leave defined as sick leave for more than 10% of scheduled time was in a Danish study by Kaerlev et al. statistically significantly associated with heavy lifting, walking or standing, uncomfortable working positions, night or shift work, long work days, low job control, low collegial support¹. Saurel-Cubizolles et al. found a higher frequency of sick leave among women carrying heavy loads, having considerable physical effort in their work or having a combination of position, heavy loads or assembly line work⁴. All of these three studies used exposure information collected retrospectively that encompassed the risk of differential misclassification of the exposure, and this may have led to an overestimation of the risk estimates. Our findings are, furthermore, corroborated by results from general working populations of both genders, because both physical and psychosocial work factors have been found to be associated with sick leave ^{32,104-107}. These parallel findings in working populations imply caution in the interpretation of results, as the risk estimates could reflect the effect of the exposures per se and not the effect of exposure and pregnancy. The associations we found could be influenced by risk perceptions among pregnant working women and/or their surroundings, instead of reflecting causal associations from the exposures to risk of sick leave in pregnancy. Women believing that the exposures constitute a risk to their pregnancy may be more

reluctant to seek for a sick leave notification, such risk perceptions may even be intensified if colleagues, work place culture and work place exposures support it. The association between sick leave in pregnancy and labour market position has not previously been investigated. In working population studies, sick leave is associated with disability pension^{21-24,108-110}. A few studies have investigated sick leave in sub-groups of pregnant women and did not find an association with future disability pensioning¹¹⁰⁻¹¹². The association we found between sick leave in pregnancy and future sick leave is corroborated by general population studies concluding that previous sick leave is associated with future sick leave is discussed with future sick leave to future sick leave, or even on a pathway from occupational and/or lifestyle exposures to sick leave or labour market marginalisation.

7. CONCLUSION

In two cohorts with prospectively collected data, lifestyle, obstetric and fertility factors and a number of physical and psychosocial occupational exposures were associated with increased risk for sick leave in pregnancy.

A dose-response relation between BMI, TTP and physical exercise and risk of sick leave was found. Also, cumulative daily lifting, monthly night shifts and weekly work hours were associated with the risk of sick leave in a dose-dependent way. Physical exercise and more than 37 hours weekly work were associated with a lower risk for sick leave in pregnancy. There were time-dependent effects of parity, and TTP above 12 months resulting in decreasing risk for sick leave with elapsed pregnancy weeks in study I. Some of the not time-stable exposures in studies I and II also suggested timedependent effects, but the importance of these findings may be questionable, as the exposures likely change with progression of pregnancy.

Increasing levels of pregnancy-related sick leave among employed women was associated with higher levels of future sick leave as well as a risk for flexi-job and disability pensioning. But pregnancy-related sick leave was not a strong predictor of the outcomes.

The findings were based on cohorts with exposure and covariate data obtained through questionnaires, which inherently encompasses the risk of potential selection bias. This may compromise the generalisability of the results to other populations of working pregnant women.

To conclude, these findings first of all stress that working pregnant women constitute a vulnerable group in the labour market, and that workplaces do not accommodate the needs of pregnant women. The associations we found between a large range of occupational exposures and risk of sick leave indicate that the intentions of the compulsory protection of pregnant women and their fetuses are difficult to adhere to at workplaces. Cooperativeness and adaptability amongst employers and employees are requisite to fulfil the intentions of the legislation. Adjustments in occupational exposures may be an area of focus to reduce sick leave rates in pregnancy if our results reflect causal associations. Our findings are of importance for general practice, maternity wards and work places, as information on lifestyle and occupational risk factors is important regarding prevention of sick leave.

8. PERSPECTIVES

This dissertation contributes by use of prospectively collected data to a limited amount of studies regarding predictors of sick leave in pregnancy.

An urgent future perspective of our findings would be to validate the DREAM register for pregnant women either by use of self-reported or by employer-registered sick leave data.

We investigated the effects of individual exposures. It would be of interest in future studies to investigate the combined effect of concurrent occupational and lifestyle exposures.

In future studies, selection bias in cohort studies could be circumvented by using Danish health registers in combination with exposure information from validated job exposure matrices (JEM). Linkage of the birth register, IVF register, occupational register, the Danish national patient register and DREAM with a JEM containing information on, e.g. occupational lifting or other occupational exposures, would provide risk estimates for the entire population of employed pregnant Danish women.

In future studies use of the new Danish Register of Sickness Absence Compensation Benefits and Social Transfer Payments (RSS) instead of DREAM would enable us to assess duration and prevalence of sick leave periods, because RSS holds information on sick leave data on a day-to-day basis.

Other perspectives of the findings include their use in the development of interventions that could be of use in general practice, departments of occupational medicine and work places to investigate what adjustments in occupational exposures would be effective in reducing sick leave rates among pregnant women. A randomised controlled trial with work exposure adjustments as intervention in large workplaces with high sick leave rates could be the focus of such an investigation.

9. ENGLISH SUMMARY

Background

Most women work during their reproductive years. High levels of sick leave among pregnant women have been found in several studies, and studies indicate that the levels have increased over the past decades. Research within the area of pregnancy and sick leave is limited; however, information on risk factors for sick leave is necessary in order to make preventive initiatives. Knowledge about potential adverse effects of sick leave in pregnancy is also needed.

Aims

To investigate (1) associations between (i) Lifestyle, (ii) Obstetric and fertility factors, (iii) Physical and (iiii) Psychosocial occupational factors and the risk for sick leave during pregnancy using two different cohorts separated in time and (2) to investigate whether sick leave during pregnancy predicts exit from the labour market or a vulnerable position in the labour market.

Materials and methods

We used data from two pregnancy cohorts. The Danish National Birth Cohort (DNBC) with pregnancies enrolled between the years 1996–2002 (N=100,418) was used in studies I-III. A cohort established for this project in the Central Denmark Region (CDR) with enrolment from 2013–2014 (N=1,748) was used in study IV. Self-reported cohort data obtained through questionnaires were linked to Danish Register for Evaluation of Marginalisation (DREAM), a national register containing information on public benefit payments. Measures of exposures were parity, body mass index (BMI), assisted reproductive therapy (ART), time to pregnancy (TTP) and physical leisure time activity in studies I and IV. In studies II and IV, the exposures were physical and psychosocial occupational factors (i.e. work posture, occupational lifting, work shift, job strain). The outcome in studies I, II and IV was the first episode of sick leave. The measure of exposure in study III was proportion of sick leave in pregnancy. Outcomes in an 8-year follow-up period one year after child birth were (i) cumulated number of sick leave weeks, (ii) receiving flexi job benefits and (iii) receiving disability pension. Data were analysed using multivariable Cox regression analysis, logistic regression and zero-inflated Poisson regression.

Results

In studies I, II and IV, a number of lifestyle and obstetric factors were associated with higher risk for sick leave in pregnancy. Furthermore, a large number of occupational exposures were found to be associated with an increased risk of sick leave. The associations found in the DNBC were largely corroborated by results from the CDR. Pregnancy-related sick leave was associated with of future sick leave, flexi-job and disability pension in study III.

Conclusion

The findings first of all stress that pregnant women constitute a vulnerable group in the labour market. The findings furthermore indicate that the compulsory protection of pregnant women and their fetuses is difficult to adhere to at workplaces. Adjustments in occupational exposures may be an area of future focus to reduce sick leave rates in pregnancy if our results reflect causal associations. The findings are of importance for general practice, maternity wards and work places, as information on lifestyle and occupational risk factors is important regarding prevention of sick leave.

10. DANISH SUMMARY

Baggrund

De fleste danske kvinder arbejder i deres reproduktive alder. Gravide har et højt niveau af sygefravær, og niveauet er steget de seneste årtier. Forskning indenfor området graviditet og sygefravær er begrænset. For at kunne forebygge sygefravær under graviditet, er det nødvendigt at have kendskab til, hvilke risikofaktorer der er af betydning for fravær under graviditet. Ligeledes er det vigtigt at belyse, om meget sygefravær under graviditeten kan forudsige arbejdsmarkedstilknytningen fremadrettet.

Formål

Ved brug af data fra to graviditetskohorter: (1) at undersøge associationen mellem (i) Livsstil, (ii) Fertilitetsfaktorer, (iii) Fysiske og (iiii) Psykosociale arbejdsmiljøeksponeringer og risikoen for sygefravær under graviditeten, samt (2) at undersøge, om sygefravær under graviditet prædikterer en sårbar arbejdsmarkedstilknytning.

Materialer og metoder

Den Nationale Fødselskohorte – Bedre Sundhed for Mor og Barn (BSMB) indeholdende 100.418 graviditeter tilmeldt mellem 1996-2002 blev brugt i studie I-III. En kohorte etableret i Region Midtjylland (RM) fra 2013-2014 til brug for dette projekt med 1.748 graviditeter, blev brugt i studie IV. Spørgeskemadata fra kohorterne blev koblet med Dansk Register for Evaluering af Marginalisering (DREAM), som indeholder oplysninger om offentlige overførselsindkomster. Eksponeringsmålene i studie I og IV var paritet, body mass index (BMI), assisteret reproduktiv terapi (ART), ventetid til graviditet (TTP) og fysisk fritidsaktivitet. I studie II og IV anvendtes fysiske og psykosociale arbejdsmiljøeksponeringer (bl.a. arbejdsstilling, løft, skiftende arbejdstid, job strain). Udfald i studie I, II og IV var første episode af sygefravær. I studie III var eksponeringen den procentuelle andel af sygefravær i graviditeten og udfaldene henholdsvis (i) kumuleret antal sygefraværsuger, (ii) fleksjob og (iii) førtidspensionering. Udfaldene blev bestemt i en 8 års opfølgningsperiode begyndende 1 år efter BSMB fødsel. Data blev analyseret ved multivariable regressionsanalyser: Cox regression (studie I, II, IV), logistisk regression og zero-inflated Poisson regression (studie III).

Resultater

I studie I, II og IV var en række livsstils- og fertilitetsfaktorer associeret med højere risiko for sygefravær i graviditeten. Et stort antal af arbejdsmiljøeksponeringerne var ligeledes associeret med en øget risiko for sygefravær. Retningen af resultaterne fra BSMB, blev overvejende genfundet i studiet fra RM om end med noget mindre præcision. Mere end 20% sygefravær i graviditet var associeret med fremtidigt sygefravær, fleksjob og førtidspension i studie III.

Konklusion

Resultaterne understreger først og fremmest, at gravide kvinder er en sårbar gruppe på arbejdsmarkedet. Resultaterne indikerer endvidere, at den af lovgivningen bestemte beskyttelse af gravide kvinder og deres fostre er svært at efterkomme og effektuere på arbejdspladserne, idet mange af eksponeringerne er forbundet med en øget risiko for sygemelding. Justeringer i arbejdsmiljøeksponeringer bør være et område af fremtidigt fokus for at nedbringe sygefraværet blandt gravide, såfremt resultaterne afspejler kausale sammenhænge. Resultaterne er af betydning for almen praksis, jordemoder konsultationer og arbejdspladser, idet oplysninger om livsstil og arbejdsmiljøeksponeringerne kan være vigtige i forhold til forebyggelse af sygefravær.

11. REFERENCES

1. Kaerlev L, Jacobsen LB, Olsen J, Bonde JP. Long-term sick leave and its risk factors during pregnancy among danish hospital employees. *Scand J Public Health*. 2004;32(2):111-117.

2. Strand K, Wergeland E, Bjerkedal T. Work load, job control and risk of leaving work by sickness certification before delivery, norway 1989. *Scand J Soc Med.* 1997;25(3):193-201.

3. Alexanderson K, Hensing G, Leijon M, et al. Pregnancy related sickness absence in a swedish county, 1985-87. *J Epidemiol Community Health*. 1994;48(5):464-470.

4. Saurel-Cubizolles MJ, Kaminski M. Pregnant women's working conditions and their changes during pregnancy: A national study in france. *Br J Ind Med.* 1987;44(0007-1072; 0007-1072; 4):236-243.

5. Saurel-Cubizolles MJ, Subtil D, Kaminski M. Is preterm delivery still related to physical working conditions in pregnancy? *J Epidemiol Community Health*. 1991;45(0143-005; 0143-005; 1):29-34.

6. Sydsjo A, Sydsjo G, Alexanderson K. Influence of pregnancy-related diagnoses on sick-leave data in women aged 16-44. *J Womens Health Gend Based Med*. 2001;10(7):707-714.

7. Sydsjo G, Sydsjo A. Newly delivered women's evaluation of personal health status and attitudes towards sickness absence and social benefits. *Acta Obstet Gynecol Scand*. 2002;81(2):104-111.

8. Petersen KR, Hording U, Roepstorff C, Kamper-Jorgensen F, Larsen JF. Self-reported pattern of illness and hospitalization during pregnancy. results from a nation-wide questionnaire study. *Ugeskr Laeger*. 1989;151(10):621-625.

9. Markussen S, Rogeberg O. Sickness absence associated with major life events - original language sykefravær rundt større livshendelser. *Tidsskr Nor Laegeforen*. 2012;132(10):1231-1234.

10. Beskæftigelsesministeriet, Danish Ministry of Employment. Analyse af graviditetsbetinget fravær - analysis of pregnancy related sick leave. 2010.

11. Alexanderson K, Hensing G, Carstensen J, Bjurulf P. Pregnancy-related sickness absence among employed women in a swedish county. *Scand J Work Environ Health*. 1995;21(3):191-198.

12. Sydsjo A, Sydsjo G, Kjessler B. Sick leave and social benefits during pregnancy--a swedishnorwegian comparison. *Acta Obstet Gynecol Scand*. 1997;76(8):748-754.

13. Sydsjo G, Sydsjo A, Wijma B. Variations in sickness absence and use of social benefits among pregnant women in a swedish community 1978-1997. *Acta Obstet Gynecol Scand*. 1999;78(5):383-387.

14. Krane L, Johnsen R, Fleten N, et al. Sickness absence patterns and trends in the health care sector: 5-year monitoring of female municipal employees in the health and care sectors in norway and denmark. *Hum Resour Health*. 2014;12:37-4491-12-37.

15. Kristensen TS. Sickness absence and work strain among danish slaughterhouse workers: An analysis of absence from work regarded as coping behaviour. *Soc Sci Med.* 1991;32(1):15-27.

16. Beskæftigelsesministeriet - The Danish Employment Ministry. Analyse af sygefraværet - analyses of sick leave. . 2008.

17. Eshoj P, Jepsen JR, Nielsen CV. Long-term sickness absence - risk indicators among occupationally active residents of a danish county. *Occup Med (Lond)*. 2001;51(0962-7480; 0962-7480; 5):347-353.

18. Labriola M, Holte KA, Christensen KB, Feveile H, Alexanderson K, Lund T. The attribution of work environment in explaining gender differences in long-term sickness absence: Results from the prospective DREAM study. *Occup Environ Med.* 2011;68(1470-7926; 1351-0711; 9):703-705.

19. Vahtera J, Pentti J, Kivimaki M. Sickness absence as a predictor of mortality among male and female employees. *J Epidemiol Community Health*. 2004;58(0143-005; 0143-005; 4):321-326.

20. Kivimaki M, Head J, Ferrie JE, Shipley MJ, Vahtera J, Marmot MG. Sickness absence as a global measure of health: Evidence from mortality in the whitehall II prospective cohort study. *BMJ*. 2003;327(7411):364.

21. Kivimaki M, Forma P, Wikstrom J, et al. Sickness absence as a risk marker of future disability pension: The 10-town study. *J Epidemiol Community Health*. 2004;58(8):710-711.

22. Borg K, Hensing G, Alexanderson K. Predictive factors for disability pension--an 11-year follow up of young persons on sick leave due to neck, shoulder, or back diagnoses. *Scand J Public Health*. 2001;29(2):104-112.

23. Lund T, Kivimaki M, Labriola M, Villadsen E, Christensen KB. Using administrative sickness absence data as a marker of future disability pension: The prospective DREAM study of danish private sector employees. *Occup Environ Med.* 2008;65(1):28-31.

24. Labriola M, Lund T. Self-reported sickness absence as a risk marker of future disability pension. prospective findings from the DWECS/DREAM study 1990-2004. *Int J Med Sci.* 2007;4(1449-1907; 1449-1907; 3):153-158.

25. Danish Government. Sick leave - a joint challenge. The government's action plan to reduce sick leave. Sygefravær - en fælles udfordring. regeringens handslingsplan for at nedbringe sygefraværet. . *Ministry of Employment*. 2008.

26. Lund T, Labriola M, Villadsen E. Who is at risk for long-term sickness absence? A prospective cohort study of danish employees. *Work*. 2007;28(1051-9815; 1051-9815; 3):225-230.

27. Lu X, Laaksonen M, Aittomaki A, et al. Sickness absence, employment history, and high-risk employees: A 10-year longitudinal study. *J Occup Environ Med.* 2010;52(1536-5948; 1076-2752; 9):913-919.

28. Bang CK, Lund T, Labriola M, Villadsen E, Bultmann U. The fraction of long-term sickness absence attributable to work environmental factors: Prospective results from the danish work environment cohort study. *Occup Environ Med.* 2007;64(1470-7926; 1351-0711; 7):487-489.

29. Christensen KB, Lund T, Labriola M, Bultmann U, Villadsen E. The impact of health behaviour on long term sickness absence: Results from DWECS/DREAM. *Ind Health*. 2007;45(2):348-351.

30. Allebeck P, Mastekaasa A. Swedish council on technology assessment in health care (SBU). chapter 5. risk factors for sick leave - general studies. *Scand J Public Health Suppl.* 2004;63:49-108.

31. Eriksen W, Bruusgaard D, Knardahl S. Work factors as predictors of sickness absence: A three month prospective study of nurses' aides. *Occup Environ Med.* 2003;60(4):271-278.

32. Alavinia SM, van den Berg TI, van Duivenbooden C, Elders LA, Burdorf A. Impact of workrelated factors, lifestyle, and work ability on sickness absence among dutch construction workers. *Scand J Work Environ Health.* 2009;35(5):325-333.

33. Roelen CA, Koopmans PC, Schreuder JA, Anema JR, van der Beek AJ. The history of registered sickness absence predicts future sickness absence. *Occup Med (Lond)*. 2011;61(2):96-101.

34. Virtanen P, Siukola A, Luukkaala T, et al. Sick leaves in four factories--do characteristics of employees and work conditions explain differences in sickness absence between workplaces? *Scand J Work Environ Health.* 2008;34(4):260-266.

35. Statistics Denmark. AKU120: Arbejdsmarkedstilknytning (procent) efter beskæftigelsesstatus, alder og køn - labour market participation (percent) according to employment status, age and gender. http://www.statistikbanken.dk/10309. Accessed 06/13, 2015.

36. Fortier I, Marcoux S, Brisson J. Maternal work during pregnancy and the risks of delivering a small-for-gestational-age or preterm infant. *Scand J Work Environ Health*. 1995;21(6):412-418.

37. Snijder CA, Brand T, Jaddoe V, et al. Physically demanding work, fetal growth and the risk of adverse birth outcomes. the generation R study. *Occup Environ Med.* 2012;69(8):543-550.

38. Henriksen TB, Hedegaard M, Secher NJ, Wilcox AJ. Standing at work and preterm delivery. *Br J Obstet Gynaecol*. 1995;102(0306-5456; 0306-5456; 3):198-206.

39. Pompeii LA, Savitz DA, Evenson KR, Rogers B, McMahon M. Physical exertion at work and the risk of preterm delivery and small-for-gestational-age birth. *Obstet Gynecol*. 2005;106(6):1279-1288.

40. Juhl M, Strandberg-Larsen K, Larsen PS, et al. Occupational lifting during pregnancy and risk of fetal death in a large national cohort study. *Scand J Work Environ Health*. 2013;39(4):335-342.

41. Juhl M, Larsen PS, Andersen PK, et al. Occupational lifting during pregnancy and child's birth size in a large cohort study. *Scand J Work Environ Health*. 2014;40(4):411-419.

42. Ahlborg G,Jr, Bodin L, Hogstedt C. Heavy lifting during pregnancy--a hazard to the fetus? A prospective study. *Int J Epidemiol*. 1990;19(1):90-97.

43. Zhu JL, Knudsen LE, Andersen AM, Hjollund NH, Olsen J. Laboratory work and pregnancy outcomes: A study within the national birth cohort in denmark. *Occup Environ Med*. 2006;63(1):53-58.

44. Bonde JP, Jorgensen KT, Bonzini M, Palmer KT. Miscarriage and occupational activity: A systematic review and meta-analysis regarding shift work, working hours, lifting, standing, and physical workload. *Scand J Work Environ Health*. 2013;39(4):325-334.

45. Palmer KT, Bonzini M, Harris EC, Linaker C, Bonde JP. Work activities and risk of prematurity, low birth weight and pre-eclampsia: An updated review with meta-analysis. *Occup Environ Med.* 2013;70(4):213-222.

46. Danish Work Environment Authority. Guidance of pregnant and/or breast feeding employees. <u>http://arbejdstilsynet.dk/~/media/at/04-regler/05-at-vejledninger/a-vejledninger/a-1-8-gravide-og-ammende/gravide-og-ammende/20pdf.ashx</u>. Updated 2009. Accessed 02/11, 2014.

47. European Economic Community. Directive 95/85/EEC - pregnant workers. . 1992:<u>http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31992L0085&from=EN</u>.

48. Danish Health and Medicines Authority - Sundhedsstyrelsen. Anbefalinger for svangreomsorgen - recommendations for antenatal care. . 2013(2nd).

49. Rieck KME, Telle K. Sick leave before, during and after pregnancy. *Acta Sociologica*. 2013;56(2):117-137.

50. Dorheim SK, Bjorvatn B, Eberhard-Gran M. Sick leave during pregnancy: A longitudinal study of rates and risk factors in a norwegian population. *BJOG*. 2013;120(5):521-530.

51. Strand K, Wergeland E, Bjerkedal T. Job adjustment as a means to reduce sickness absence during pregnancy. *Scand J Work Environ Health*. 1997;23(5):378-384.

52. Kristensen P, Nordhagen R, Wergeland E, Bjerkedal T. Job adjustment and absence from work in mid-pregnancy in the norwegian mother and child cohort study (MoBa). *Occup Environ Med*. 2008;65(8):560-566.

53. Melsom AM. Long-term sickness absence during pregnancy and the gender balance of workplaces. *Scand J Public Health*. 2014;42(7):627-634.

54. World Health Organisation. Obesity: Preventing and managing the global epidemic. 2000.

55. Danish Health and Medicines Authority - Sundhedsstyrelsen. Danskernes sundhed - den nationale sundhedsprofil 2013 the danes' health - national health profile 2013. . 2014(1 st).

56. Harvey SB, Glozier N, Carlton O, et al. Obesity and sickness absence: Results from the CHAP

study. Occup Med (Lond). 2010;60(5):362-368.

57. Quist HG, Thomsen BL, Christensen U, et al. Influence of lifestyle factors on long-term sickness absence among female healthcare workers: A prospective cohort study. *BMC Public Health*. 2014;14:1084-2458-14-1084.

58. Labriola M, Lund T, Burr H. Prospective study of physical and psychosocial risk factors for sickness absence. *Occup Med (Lond)*. 2006;56(7):469-474.

59. Biering K, Nohr EA, Olsen J, Andersen AM, Hjollund NH, Juhl M. Pregnancy-related pelvic pain is more frequent in women with increased body mass index. *Acta Obstet Gynecol Scand*. 2011;90(10):1132-1139.

60. Marcoux S, Brisson J, Fabia J. The effect of leisure time physical activity on the risk of preeclampsia and gestational hypertension. *J Epidemiol Community Health*. 1989;43(2):147-152.

61. Sorensen TK, Williams MA, Lee IM, Dashow EE, Thompson ML, Luthy DA. Recreational physical activity during pregnancy and risk of preeclampsia. *Hypertension*. 2003;41(6):1273-1280.

62. Juhl M, Andersen PK, Olsen J, et al. Physical exercise during pregnancy and the risk of preterm birth: A study within the danish national birth cohort. *Am J Epidemiol*. 2008;167(1476-6256; 0002-9262; 7):859-866.

63. Juhl M, Olsen J, Andersen PK, Nohr EA, Andersen AM. Physical exercise during pregnancy and fetal growth measures: A study within the danish national birth cohort. *Am J Obstet Gynecol*. 2010;202(1097-6868; 0002-9378; 1):63-68.

64. Eriksen W, Bruusgaard D. Physical leisure-time activities and long-term sick leave: A 15-month prospective study of nurses' aides. *J Occup Environ Med*. 2002;44(6):530-538.

65. Zhang J, Savitz DA. Exercise during pregnancy among US women. *Ann Epidemiol*. 1996;6(1):53-59.

66. Haakstad LA, Voldner N, Henriksen T, Bo K. Physical activity level and weight gain in a cohort of pregnant norwegian women. *Acta Obstet Gynecol Scand.* 2007;86(5):559-564.

67. Akerlind I, Alexanderson K, Hensing G, Leijon M, Bjurulf P. Sex differences in sickness absence in relation to parental status. *Scand J Soc Med.* 1996;24(1):27-35.

68. Bialobok KM, Monga M. Fatigue and work in pregnancy. *Curr Opin Obstet Gynecol*. 2000;12(6):497-500.

69. Rasmussen OB, Sorensen AU, Nielsen CV. [Sick leave for pregnant women in the municipality of fjend 1987-1990]. *Ugeskr Laeger*. 1996;158(0041-5782; 0041-5782; 49):7069-7073.

70. U H, Petersen K.R, C R, Kamper-Joergensen F, Larsen J.F. Pregnancy related disease, hospital admission and sick leave: A danish national representative sample. *Journal of Obstetrics and Gynaecology*. 1989.

71. McMahon CA, Boivin J, Gibson FL, et al. Age at first birth, mode of conception and psychological wellbeing in pregnancy: Findings from the parental age and transition to parenthood australia (PATPA) study. *Hum Reprod.* 2011;26(6):1389-1398.

72. Hammarberg K, Fisher JR, Wynter KH. Psychological and social aspects of pregnancy, childbirth and early parenting after assisted conception: A systematic review. *Hum Reprod Update*. 2008;14(5):395-414.

73. Pedersen J, Viskum S. [Pregnancy and occupational environment. counseling of pregnant women in the department of occupational medicine during the period 4 january--31 december 1992]. *Ugeskr Laeger*. 1996;158(0041-5782; 0041-5782; 49):7064-7068.

74. Beskæftigelsesministeriet - The Danish Employment Ministry. Bekendtg¢relse af lov om ret til orlov og dagpenge ved barsel - act on the right to leave and social benefits in the event af maternity . . 2011.

75. Beskæftigelsesministeriet - The Danish Employment Ministry. Bekendtgørelse af lov om dagpenge ved sygdom eller fødsel - act on the right to social benefits in event of sickness or delivery. 2011.

76. Tophoj A, Sabroe S. [Duration of maternity leave and sick leave during pregnancy]. *Ugeskr Laeger*. 1999;161(0041-5782; 0041-5782; 36):5014-5019.

77. Tophoj A, Mortensen JT. Pregnancy-related and work-related sick leave of pregnant women. *Ugeskr Laeger*. 1999;161(36):5009-5013.

78. Larsson C, Sydsjo A, Alexanderson K, Sydsjo G. Obstetricians' attitudes and opinions on sickness absence and benefits during pregnancy. *Acta Obstet Gynecol Scand*. 2006;85(0001-6349; 0001-6349; 2):165-170.

79. Rasmussen J. DREAM, danish ministry of employment, copenhagen. <u>http://www.dst.dk/da/TilSalg/Forskningsservice/Data/Andre_Styrelser.aspx</u>. Updated 2012. Accessed 01/30, 2014.

80. Olsen J, Melbye M, Olsen SF, et al. The danish national birth cohort--its background, structure and aim. *Scand J Public Health*. 2001;29(4):300-307.

81. World Health Organisation. BMI database - classification of BMI. <u>http://apps.who.int/bmi/index.jsp?introPage=intro_3.html</u>. Updated 2014. Accessed 02/13, 2014.

82. Karasek RA. Job demands, job decision latitude, and mental strain: Implications for job redesign. *Administrative Science Quarterly*. Jun., 1979;Vol. 24(No.2):285-308.

83. Pejtersen JH, Kristensen TS, Borg V, Bjorner JB. The second version of the copenhagen psychosocial questionnaire. *Scand J Public Health*. 2010;38(3 Suppl):8-24.

84. Rothman K, Greenland S, Lash T. *Modern epidemiology*. 3rd ed. Philadelphia, USA: Lippincott Williams & Wilkins; 2008.

85. Nohr EA, Frydenberg M, Henriksen TB, Olsen J. Does low participation in cohort studies induce bias? *Epidemiology*. 2006;17(4):413-418.

86. Jacobsen TN, Nohr EA, Frydenberg M. Selection by socioeconomic factors into the danish national birth cohort. *Eur J Epidemiol*. 2010;25(5):349-355.

87. Connor Gorber S, Tremblay M, Moher D, Gorber B. A comparison of direct vs. self-report measures for assessing height, weight and body mass index: A systematic review. *Obes Rev.* 2007;8(4):307-326.

88. Labriola M, Christensen KB, Lund T, Nielsen ML, Diderichsen F. Multilevel analysis of workplace and individual risk factors for long-term sickness absence. *J Occup Environ Med.* 2006;48(1076-2752; 1076-2752; 9):923-929.

89. Lund T, Labriola M, Christensen KB, Bultmann U, Villadsen E. Return to work among sicknessabsent danish employees: Prospective results from the danish work environment cohort Study/National register on social transfer payments. *Int J Rehabil Res.* 2006;29(0342-5282; 0342-5282; 3):229-235.

90. Bang Christensen K, Lund T, Labriola M, Villadsen E, Bultmann U. The fraction of long-term sickness absence attributable to work environmental factors: Prospective results from the danish work environment cohort study. *Occup Environ Med.* 2007;64(7):487-489.

91. Andersen LL, Clausen T, Mortensen OS, Burr H, Holtermann A. A prospective cohort study on musculoskeletal risk factors for long-term sickness absence among healthcare workers in eldercare. *Int Arch Occup Environ Health*. 2011(1432-1246; 0340-0131).

92. Burr H, Pedersen J, Hansen JV. Work environment as predictor of long-term sickness absence: Linkage of self-reported DWECS data with the DREAM register. *Scand J Public Health*. 2011;39(1651-1905; 1403-4948; 7):147-152.

93. Hjollund NH, Larsen FB, Andersen JH. Register-based follow-up of social benefits and other transfer payments: Accuracy and degree of completeness in a danish interdepartmental administrative database compared with a population-based survey. *Scand J Public Health*. 2007;35(1403-4948; 1403-4948; 5):497-502.

94. Stapelfeldt CM, Jensen C, Andersen NT, Fleten N, Nielsen CV. Validation of sick leave measures: Self-reported sick leave and sickness benefit data from a danish national register compared to multiple workplace-registered sick leave spells in a danish municipality. *BMC Public Health*. 2012;12:661-2458-12-661.

95. Ariansen AM, Mykletun A. Does postponement of first pregnancy increase gender differences in sickness absence? A register based analysis of norwegian employees in 1993-2007. *PLoS One*. 2014;9(3):e93006.

96. Lund T, Christensen KB, Vaez M, et al. Differences in sickness absence in sweden and denmark: The cross national HAKNAK study. *Eur J Public Health*. 2009;19(1464-360; 1101-1262; 3):343-349.

97. Feeney A, North F, Head J, Canner R, Marmot M. Socioeconomic and sex differentials in reason for sickness absence from the whitehall II study. *Occup Environ Med.* 1998;55(2):91-98.

98. Alstveit M, Severinsson E, Karlsen B. Living on the edge of being overstretched--a norwegian qualitative study of employed pregnant women. *Health Care Women Int.* 2010;31(6):533-551.

99. Ferrie JE, Head J, Shipley MJ, Vahtera J, Marmot MG, Kivimaki M. BMI, obesity, and sickness absence in the whitehall II study. *Obesity (Silver Spring)*. 2007;15(6):1554-1564.

100. Sydsjo A, Claesson IM, Ekholm Selling K, Josefsson A, Brynhildsen J, Sydsjo G. Influence of obesity on the use of sickness absence and social benefits among pregnant working women. *Public Health.* 2007;121(9):656-662.

101. McMahon CA, Ungerer JA, Beaurepaire J, Tennant C, Saunders D. Anxiety during pregnancy and fetal attachment after in-vitro fertilization conception. *Hum Reprod.* 1997;12(1):176-182.

102. Poikkeus P, Saisto T, Unkila-Kallio L, et al. Fear of childbirth and pregnancy-related anxiety in women conceiving with assisted reproduction. *Obstet Gynecol*. 2006;108(1):70-76.

103. van Amelsvoort LG, Spigt MG, Swaen GM, Kant I. Leisure time physical activity and sickness absenteeism; a prospective study. *Occup Med (Lond)*. 2006;56(3):210-212.

104. Foss L, Gravseth HM, Kristensen P, et al. The impact of workplace risk factors on long-term musculoskeletal sickness absence: A registry-based 5-year follow-up from the oslo health study. *J Occup Environ Med*. 2011;53(12):1478-1482.

105. d'Errico A, Costa G. Socio-demographic and work-related risk factors for medium- and long-term sickness absence among italian workers. *Eur J Public Health*. 2012;22(5):683-688.

106. Voss M, Floderus B, Diderichsen F. Physical, psychosocial, and organisational factors relative to sickness absence: A study based on sweden post. *Occup Environ Med.* 2001;58(3):178-184.

107. Clausen T, Burr H, Borg V. Do psychosocial job demands and job resources predict long-term sickness absence? an analysis of register-based outcomes using pooled data on 39,408 individuals in four occupational groups. *Int Arch Occup Environ Health*. 2014;87(8):909-917.

108. Stapelfeldt CM, Nielsen CV, Andersen NT, et al. Sick leave patterns as predictors of disability pension or long-term sick leave: A 6.75-year follow-up study in municipal eldercare workers. *BMJ Open*. 2014;4(2):e003941-2013-003941.

109. Hultin H, Lindholm C, Moller J. Is there an association between long-term sick leave and disability pension and unemployment beyond the effect of health status?--a cohort study. *PLoS One*. 2012;7(4):e35614.

110. Gjesdal S, Ringdal PR, Haug K, Maeland JG. Predictors of disability pension in long-term sickness absence: Results from a population-based and prospective study in norway 1994-1999. *Eur J Public Health*. 2004;14(1101-1262; 1101-1262; 4):398-405.

111. Gjesdal S, Bratberg E. Diagnosis and duration of sickness absence as predictors for disability pension: Results from a three-year, multi-register based* and prospective study. *Scand J Public Health*. 2003;31(1403-4948; 1403-4948; 4):246-254.

112. Pedersen J, Bjorner JB, Burr H, Christensen KB. Transitions between sickness absence, work, unemployment, and disability in denmark 2004-2008. *Scand J Work Environ Health*. 2012;38(6):516-526.

113. Davey MM, Cummings G, Newburn-Cook CV, Lo EA. Predictors of nurse absenteeism in hospitals: A systematic review. *J Nurs Manag*. 2009;17(3):312-330.
12. ORIGINAL ARTICLES

- **PAPER I:** Predictors of sickness absence in pregnancy: a Danish cohort study

 Link:
 <u>https://pubmed.ncbi.nlm.nih.gov/25469623/</u>
- PAPER II: Occupational exposures and sick leave during pregnancy: Results from a Danish cohort study

Link: https://pubmed.ncbi.nlm.nih.gov/26047490/

- PAPER III: Manuscript not published
- PAPER IV: Manuscript not published