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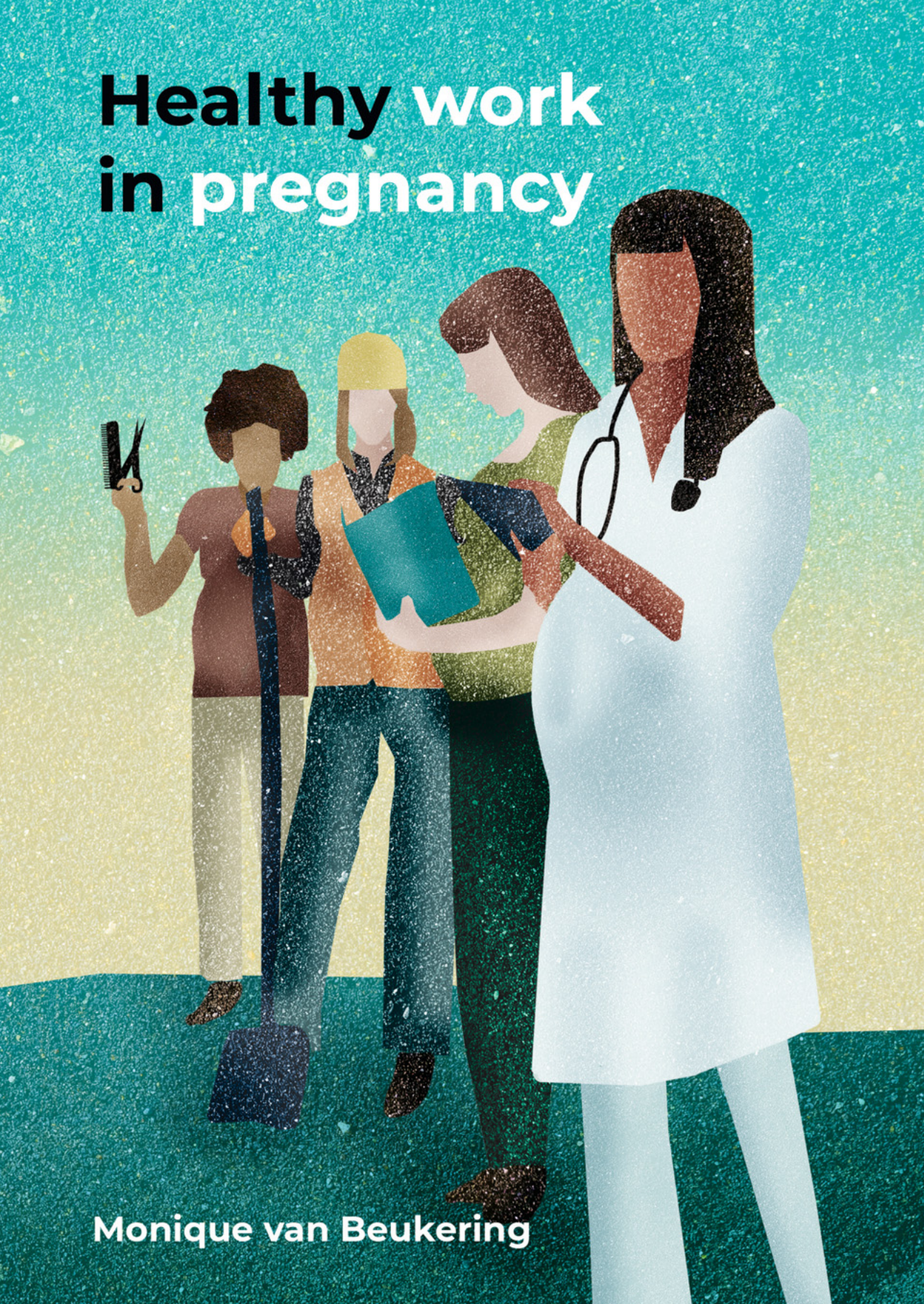

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Healthy work in pregnancy

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Introduction

Background

Working women

From the beginning of the twentieth century, there was an increase in working women in all early industrialised countries [1]. By the 1960s, the employment rate of women in countries from Organisation for Economic Co-operation and Development (OECD, a collaboration of, at that time 20, predominantly prosperous countries from Europe, Canada and the USA) had risen to 41%.

Worldwide, this growth continued into the early twenty-first century and then slowed down. In some high-population countries [2] such as China, Russia and India, numbers have decreased, causing the number of women in paid work worldwide to fall slightly: from 56% in 1990 to 53% in 2019 (Figure 1).

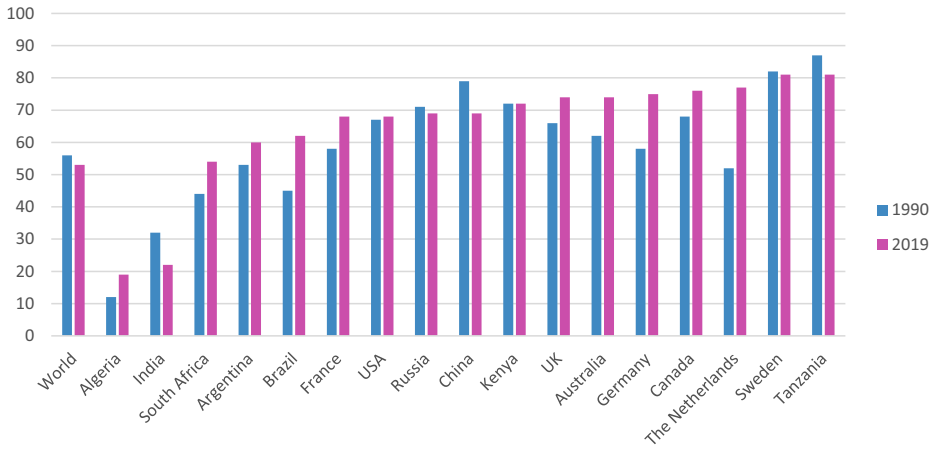

Figure 1. Labour force partition rate 1990-2019, female (% of female population ages 15-64), **by country** (World Bank, 2021)

More than half of women aged 15 to 65 years on almost all continents have paid work (Figure 2). High- and low-income women are more likely to work than middle-income women (Figure 3) [2].

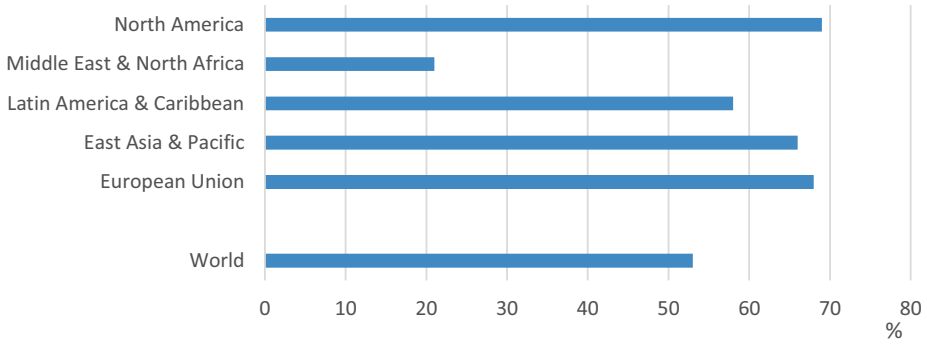

Figure 2. Labour force participation rate, 2019, female (ages 15-64), **by continent**, (World Bank, 2021)

Globally, women are less likely to work full-time, more often have lower-paid occupations and make less progress in their careers than men [3]. As a result, gender pay gaps persist, and women are more likely to end their lives in poverty. Even when women work full-time, they bear the burden of domestic and family responsibilities.

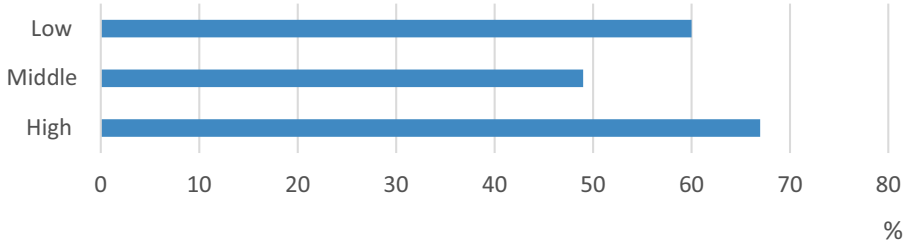

Figure 3. Global labour force participation rate, 2019, female (ages 15-64), by income (World Bank, 2021)

The Netherlands

In the Netherlands, the number of working women increased by almost 25% between 1990 and 2019 [2]. In 2019, 76% of women aged 15 to 65 (who were not in education) were in paid work, compared to 86% of men [4]. While in all other EU Member States the majority (70%) of working women have a full-time job, in the Netherlands almost three quarters work part-time.

The average working time of women in 2009 was almost 27 hours a week; in 2019 this had increased to 28.5 hours. Highly educated women work an average of 31 hours a week, almost one day more than less educated women. In each generation of births, women at 35 years of age work fewer hours than at 25 years of age, often due to the birth of children. But the youngest generation of women shortens their working week

less than the older generations, so women of the age when many of them have children work more hours on average than before [4]. Currently in 2021, 82% of women at work are of childbearing age between 25-45 [5].

In 2019, 70% of women (15 to 65 years old) with paid work had a permanent employment relationship (an employment contract for an indefinite period and a fixed number of hours per week). The proportion with a flexible employment relationship was 16%. The remaining 14% were self-employed (Figure 4).

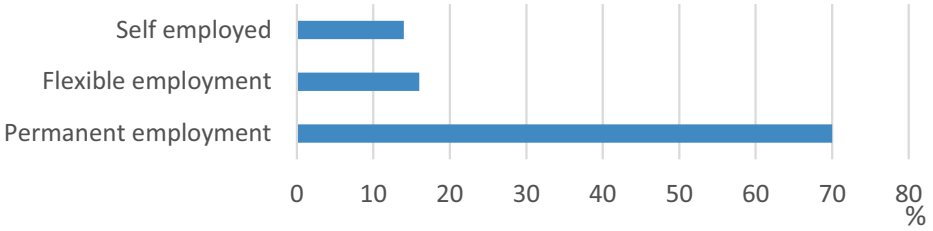

Figure 4. Women in paid or self-employment in the Netherlands, ages 15-64, 2019 (CBS/SCP)

At work while pregnant

As the number of women in the workforce of most western countries continues to grow, so has the number of women working during their pregnancy [6]. In the United States, 66% of mothers who gave birth to their first child between 2006 and 2008 worked while pregnant [7]. For comparison, in the early 1960s, only 44% worked during pregnancy. In the Netherlands, more than nine in ten pregnant women are in paid employment and continue to work in their first pregnancy, an average of 30 hours a week [8] (Figure 5). Most pregnant women have a position (health) care and social service, followed by pedagogical and service professions. An increasing number of women (60%) continue to work the same number of hours after becoming a mother for the first time. The other young mothers usually work fewer hours, and one in ten young mothers stops working temporarily or otherwise [9] (Figure 5).

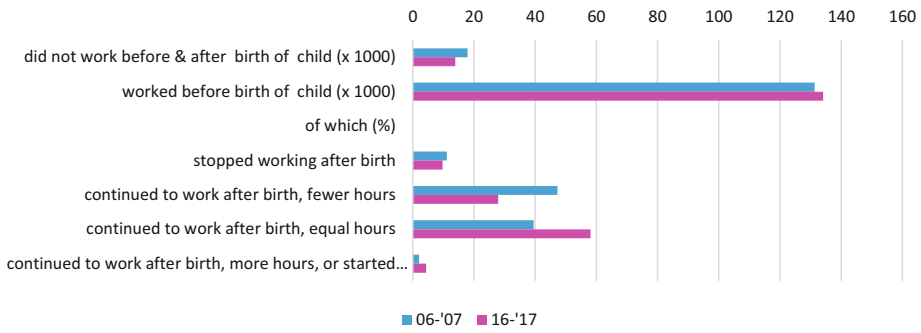

Figure 5. Women's work pattern, before and after birth of the first child, 2006-2017 (in absolute numbers x 1000) (Portegijs W, van den Brakel M, 2018)

Working pregnant women are a vulnerable group on the labour market. The Netherlands Institute for Human Rights concludes from a survey of 1,150 women that pregnancy discrimination occurred on a large scale in the Netherlands between 2016 and 2019: 43% of women on the labour market with a child experienced one or more situations that indicate discrimination due to pregnancy or recent motherhood [10]. In another study of the Netherlands Institute for Human Rights, 19 employers from the healthcare, education, business services and financial services sectors, both large and small companies (between 10 and 16,000 employees) were interviewed [11]. They mentioned not having major organisational problems related to pregnancies at work and did not recognise there was any pregnancy or motherhood discrimination. However, sometimes business interests can be affected. For example, if someone is needed in the short term, in such cases, some employers may prefer to choose someone else than the pregnant applicant. Some employers were confronted with extra costs, in case a woman with a difficult job or a managerial position goes on pregnancy leave. The interviews with employers suggest that their dealings with pregnant job applicants are more likely to be influenced by the particular managers' perspective on pregnancy than by the type of organisation involved. Although almost half of women have experienced a situation suggesting discrimination, only a few report their experience, which explains why employers indicate that they rarely receive complaints [11]. In general, employees in a managerial position, with a temporary contract, in the profit sector, women with illness or complications during pregnancy and childbirth and women with a child that suffers from health problems run the greatest risk of possible discrimination.

Core concept: pregnancy and work

During pregnancy, there are two types of risks to consider in the workplace: *work-related and personal risk factors* [12]. Adjustment of working conditions can prevent disorders in mother and child (Figure 6).

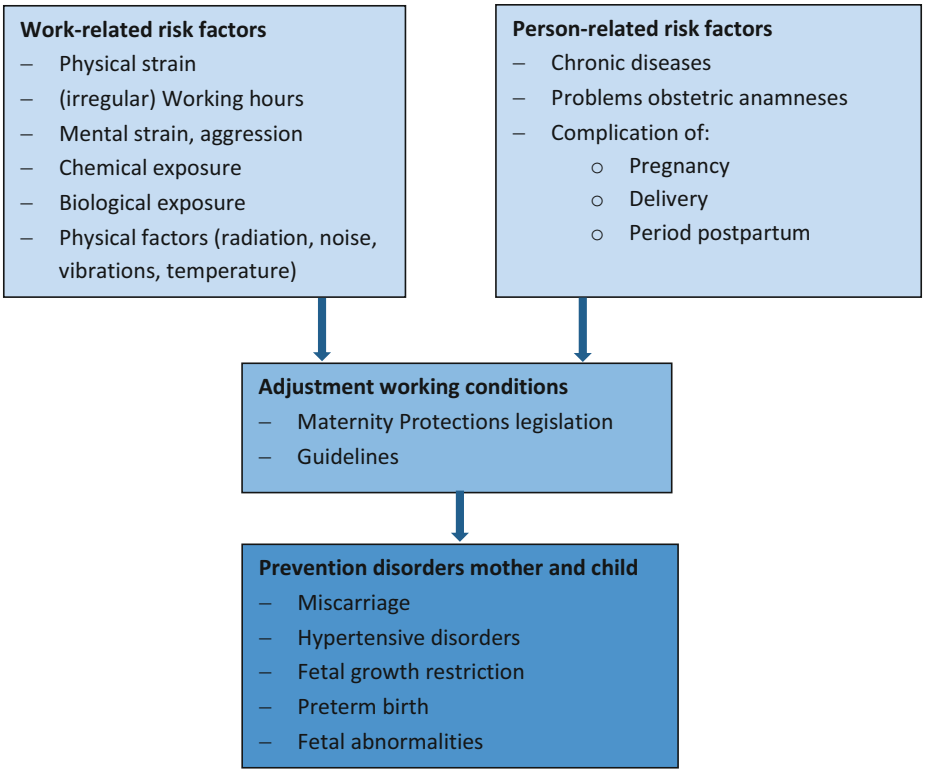

Figure 6. Pregnancy and work: the core concept 2018 (NVAB)

Several types of work-related factors can increase the risk of adverse pregnancy outcomes: physically demanding work, (irregular) working hours, mental strain, aggression, chemical exposure, biological exposure and physical factors (radiation, noise, vibrations, temperature) (Figure 6). In addition, personal risks such as chronic diseases, the medical (obstetric) history or complications during pregnancy can be a reason for pregnant women to adjust her work. These necessary work adjustments are laid down in *legislation and (medical) guidelines* [13-19]. Adjustment of working conditions can prevent disorders in mother and child such as miscarriage, hypertensive disorders, foetal growth restriction, preterm birth and foetal abnormalities [20-32].

Work-related risk factors

Hazardous working conditions, including physically demanding and irregular work, increase the risk of adverse pregnancy outcomes such as miscarriage and preterm birth (PTB) [20-32]. Two recent systematic reviews based on 80 observational studies of adverse pregnancy outcomes related to work showed that various types of physically demanding work, shift work and working >40 hours per week increased the risk of preterm birth by 10 to 31%. The risk of miscarriage increased by 23%, 38% and 35%,

respectively, when performing fixed night shifts, working >40 hours a week and lifting >10 kg [20,21].

Work adjustment can prevent these adverse pregnancy outcomes. In Canada, the implementation of legal measures which eliminate harmful workplace exposures before 24 weeks of gestation resulted in a 30 to 50% reduction in the risks of and foetal growth restriction [33] and preterm birth [34].

Person-related risk factors

As the pregnancy progresses, the body of a woman adjusts itself to the growing foetus(es) through several important physiological and anatomical changes [35]. These changes have an impact on her physical performance and therefore affect her capacity to work [12]. Furthermore, pregnancy can lead to a variety of medical problems that do not affect non-pregnant women. Therefore, while a woman is pregnant, her capacity to work is susceptible to change. After giving birth, it takes a while before her capacity for work returns to normal, of which the duration of breastfeeding is a significant factor.

During pregnancy and the postpartum period, complications can occur that affect a woman's ability to work [12]. This also applies to problems in the obstetric history or suffering from a chronic disease. In the development in 2007 and revision in 2018 of the Guideline 'Pregnancy, postpartum period and work', from the Netherlands Society of Occupational Medicine [12], the authors point out that there is hardly any research on the influence of working conditions for pregnant women with a personal risk factor. Based on 'expert opinion', the project group advised adjusting the work of women with certain personal risk factors during pregnancy and post-partum, for example, a recurrent miscarriage, preterm birth or growth restriction in order to avoid the risk of recurrence due to the work. This also applies to complications during pregnancy such as gestational hypertension, gestational diabetes or multiple pregnancy.

Legislation and guidelines

Recommendations for work adjustments during pregnancy are set down in maternity protection legislation (MPL) and guidelines are available in many countries [12-19]. They address restrictions on night work, overtime and hazardous work, and are aimed at preventing adverse pregnancy outcomes. The International Labour Organization (ILO) has established common principles regarding work and pregnancy, based on information from 111 countries. These principles include: (i) risk assessment and education for pregnant workers; (ii) work adjustments or other temporary work, without risk of pregnancy complications; (iii) temporary leave, with the retention of financial compensation for the employee [14,15].

In the Netherlands, there are two guidelines for employers and health care providers regarding working conditions of pregnant women. Based largely on the results of

scientific research, occupational physicians of the Dutch Association for Occupational Medicine (NVAB) have developed a guideline *'Pregnancy, Postpartum and Work'* in collaboration with other experts. With the recommendations of the guideline, regarding work-related and personal risk factors, occupational physicians can advise pregnant employees and their employers about work adjustment [12]. Based on the NVAB guideline and European legislation, the Dutch Social and Economic Council (SER) has developed a '*Guide to Occupational Health and Safety Measures Pregnancy & Work*' for employers and employees [36]. In both guidelines, where no results of scientific research or legislation were available, recommendations were formulated based on practice.

Although there is maternity protection legislation in many countries, implementation is lagging behind [13, 37]. This is due to unawareness among employers, employees and health care providers, lack of risk analysis in the companies, difficult co-operation with employers, lack of competences in the field of occupational health and safety and the design of MPL and incentives for implementation. The result is that pregnant women continue to work in hazardous workplaces. Others decide to stop working and call in sick.

Prevention

There are only a few examples of preventive interventions concerning the working conditions of pregnant workers. In Ghana, midwives were trained to implement an intervention that reduces lifting and carrying during pregnancy for a five-week trial period [38]. The intervention of this pilot study, in preparation for an RCT with a larger sample size of 1,000 participants, appears to have the potential to reduce physical exertion and adverse outcomes in pregnant women and their (unborn) children. Additional focus is needed on recruiting and retaining both participants and trained midwives. A recent Swiss study showed that training on the Ordinance on Maternity Protection at Work (OProMa), a legal framework that refers to the protection of pregnant workers, has a positive effect on the knowledge of the obstetrician and the implementation of MPL [37].

In 2007, the NVAB guideline introduced a new intervention: a 'preventive consultation' for all pregnant working women. At the start of their pregnancy, their occupational physician gives personal advice about work and personal risk factors, the necessary work adjustment and information about rest times and breastfeeding [12]. When this guideline was revised in 2018, it appeared that preventive consultation has added value, but only a few pregnant women had access to this preventive consultation [39]. The intervention resulted for almost all participants (95%) in advice on adjusting work or working time and encouraged pregnant women to discuss the recommendations for work adjustment with their employers (86%) [40]. In two discussion groups in the context of the revision of the NVAB guideline, occupational physicians unanimously agreed that preventive consultation in pregnant women should remain a recommendation in the guideline. They indicated that they offered a preventive consultation (and 'pregnancy

policy') to pregnant women with certain employers but not with all. They didn't have the impression that employers didn't want that, but that they didn't think it was important.

Opportunities for research and prevention

Many studies evaluated the impact of several *work-related risk factors* on different pregnancy outcomes. Focusing on the impact of two common risk factors, physically demanding work and (irregular) working hours, on preterm birth, provides the opportunity to explore this mechanism in more detail. Preterm birth occurs in 7% of pregnancies in the Netherlands and is the leading cause of morbidity and mortality worldwide [41].

All kinds of physiological processes change during pregnancy to ensure that the foetus develops properly and to prepare the pregnant woman for delivery [35]. Studies on the impact of working conditions on preterm birth usually do not distinguish the impact per trimester (1, 2 or 3). In addition, these studies often include non-working women in their control group.

Physical work can involve various activities: standing and walking, lifting and carrying, physical effort and demanding posture. At work, people often combine different physical activities. Only a few studies evaluated the impact of a combination of risk factors (Croteau 2006, 2007, Vrijkotte 2007, 2021). We expect that the effect of the combination of different tasks with physical load or another exposure is not exactly equal to the sum of the effects of the individual risk factors, possibly slightly lower. Employment in general is associated with better pregnancy outcomes [42], but not all studies exclude non-working women from the control group.

As with most *personal risk factors*, there are no published studies on the influence of working conditions in multiple pregnancies. Women with multiple pregnancies have an increased risk of preterm birth, babies of a multiple pregnancy have a ten times higher risk to be born preterm [43]. In the Netherlands, the NVAB guideline provides advice for the guidance of working women with a multiple pregnancy (NVAB 12). Due to the increased risk of preterm birth, the advice aims to limit working conditions with a risk of PTB and foetal growth restriction, supplemented with experts' advice (practice-oriented).

Identifying the working conditions that contribute to an increased risk of preterm birth in multiple pregnancies can improve the advice on preventive measures on the job for these women. In working women with a low-risk pregnancy, the risk of preterm birth increases due to physically demanding work and long and irregular working hours

[22,28,30,33]. We expect that these working conditions also increase the risk of preterm birth in working women with a multiple pregnancy.

Little is known about the *implementation of legislation and guidelines* in the Netherlands. One study in the Netherlands shows that information provision by the employer is relatively rare: 27% of the employees who were pregnant in the two years before the 2005 NEA survey indicated that they had been informed by the employer [44]. Even in a sector such as healthcare with a relatively large number of young working women, with a lot of physically demanding work, night shifts and with biological and chemical risks, the percentage that claims to have received information does not exceed 40%. Analyses of the NEA data showed that the provision of information is associated with a lower absenteeism due to illness. These analyses point out that international research shows that work adaptations also lead to better health for mother and child [44]. Another study shows that there is a large difference between working pregnant women in access to and guidance by occupational physicians [45]. Especially in small and medium-sized enterprises, access to occupational health and safety care is very limited, while self-employed persons usually do not have an occupational physician [45].

In summary, in the Netherlands, there are up-to-date guidelines on MPL and guidance of pregnant employees for all stakeholders: employees, employers, health care providers and policymakers (NVAB, SER). We know that in many countries the implementation of MPL is lagging behind [13], but figures from the Netherlands are missing or dated. In addition to general advice for low-risk pregnant women, the NVAB guideline also provides recommendations aimed at working women with a high-risk pregnancy, such as multiple pregnancies. Also unknown is whether the recommendations from the NVAB guideline for women with multiple pregnancies are applied. If reliable figures show that implementation is marginal, this can convince stakeholders to improve compliance and provide starting points for change.

Although hardly any *preventive interventions* are available for working pregnant women so far, mobile health applications (mHealth apps) have the potential to support them in (realising) work adjustment. Both working pregnant women and their health care professionals are often unaware of the importance of safe working conditions and of maternity protection legislation [13]. Providing information on work adjustments through obstetric care can offer a solution, because most women receive guidance from a midwife or obstetrician early in pregnancy [46]. MHealth applications will increasingly be used in counselling pregnant women [47,48]. Mobile health (mHealth) applications are suitable for educating women who are expecting a child, are frequent consumers of web-based health information [49-51] and they consider them useful [52,53]. However, the evidence for its effectiveness is limited [47]. The connection and adherence between client and therapist improve by combining face-to-face counselling with online support [54] and may also increase the efficiency of occupational health education [55]. For

example, in a blended application, occupational hygiene e-courses for students were positively evaluated on effectiveness [56]. This can also apply to working pregnant women and their obstetric care providers.

This thesis

Aims

The aims of this thesis are as follows:

1. to identify the effect of physical load and (irregular) working hours for working pregnant women on preterm birth
2. to identify working conditions with an increased risk of preterm birth in multiple pregnancies
3. to examine whether the Dutch MPL and guidelines have been implemented and, if not, which work-related risk factors are involved in adverse pregnancy outcomes
4. to provide pregnant women and their obstetrical caregivers with personalised advice on work adjustment with a blended care program called 'Pregnancy and Work' which consists of a training session for professionals and a mobile health (mHealth) application (the P&W app)

Research questions

To address these aims, we want to answer the following questions:

1. Do pregnant workers in paid or self-employment who are exposed to different kinds of physically demanding work during the pregnancy have a higher risk of preterm birth, defined as delivery before 37 weeks gestations, compared to their colleagues who are not or are to a lesser extent exposed to physically demanding work (Chapter 2)?
2. Do pregnant workers in paid or self-employment, with shift work or long working hours, have a higher risk of preterm birth compared to their colleagues who are not or are to a lesser extent exposed (Chapter 3)?
3. Are pregnant employees informed about the risks at work and necessary work adjustments according to the Dutch MPL and guidelines, and have any work adjustments been made, in a low-risk group (Chapter 4) and a group with a personal risk factor on the other, that being women with a multiple pregnancy (Chapter 5)?
4. Which working conditions contribute to an increased risk of preterm birth in multiple pregnancies up to 20 weeks of gestation (Chapter 6)?
5. What are the perceived facilitators and barriers according to pregnant women, medical professionals, and employers for the use of a mobile application in obstetric care to prevent occupational-related pregnancy complications (Chapter 6)?
6. What is the usability of the mHealth Pregnancy and work application (P&W app) and the perceived usefulness of the work advice of the P&W application by potential end users (Chapter 7)?

7. Does the blended care program Pregnancy and Work, which consists of a training session for professionals and a mobile health (mHealth) application (the P&W app), lead to more advice about work adjustment from obstetric caregivers to their clients, and do these pregnant women realise more work adjustments than those receiving care as usual (Chapter 8)?

Outline

In Part 1, the effect of physically demanding work **(Chapter 2)** and (irregular) working hours **(Chapter 3)** for working pregnant women on preterm birth is evaluated in two meta-analyses. We present the results of both the impact of various individual forms of physically demanding work (standing and walking, lifting and carrying, physical effort and demanding posture), and the combination of two or more tasks involving physical exertion, or physically demanding work with other occupational exposures and shift work and/or long working hours in working pregnant women. We differentiated these risks per trimester.

Part 2 describes two prospective cohort studies in different groups of pregnant women in which the implementation of legislation and guidelines of the NVAB and SER was investigated: a low-risk group **(Chapter 4)** and a group with multiple pregnancies **(Chapter 5)**. We report the results of a survey on work status and (adjustment of) working conditions (physically demanding work, irregular and long working hours, job strain and exposure to chemical and biological exposure) at different times during the pregnancy. In addition, we evaluate whether working conditions increased the risk of preterm birth in multiple pregnancies **(Chapter 5)**.

In Part 3, we report on the development and evaluation of a blended care program called 'Pregnancy and Work' (a training for professionals and a mobile health application (the P&W app) for their clients, working pregnant women and their obstetric caregivers). The P&W application was first developed on the basis of a focus group **(Chapter 6)** and a think-aloud study **(Chapter 7)**. The blended care program was then tested in an intervention study using a questionnaire among working pregnant women **(Chapter 8)**. We evaluated whether the blended care program 'Pregnancy and Work' led to more 'work advice' and 'work adjustment' than pregnant women receiving usual care.

In the general discussion, we evaluate the results of this thesis and we discuss the implications for policy, clinical practice and future perspectives to improve 'healthy work in pregnancy' **(Chapter 9)**.

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Physically demanding work and preterm delivery: a systematic review and meta-analysis

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2

Abstract

Objective: Physically demanding work may increase the risk of preterm delivery (PTD), defined as delivery before 37 weeks. We assessed the available evidence.

Methods: A systematic search in Medline, Embase and Nioshtic for the period 1990 to June 2012 for observational and intervention studies on physically demanding work (prolonged standing, heavy lifting, physical exertion, occupational fatigue and demanding posture) and PTD,. Selected studies were assessed for their risk of bias, and pooled using a random effects model. Results of case-control and cohort studies were reported separately in sub-groups.

Results: We found 10 studies with low risk of bias and seven studies with moderate risk of bias. Standing and walking at work during pregnancy for more than three hours per day was associated with an increased risk for PTD (OR 1.3 (95% CI 1.1-1.6)), just as lifting and carrying > 5 kg (OR 1.3 (95% CI 1.05-1.6)) or lifting and carrying in the third trimester of the pregnancy (OR 1.3 (95% CI 1.01-1.8)). Jobs that required physical effort or physical exertion were associated with an increased risk of PTD (OR 1.4 (95% CI 1.19-1.66)). Working during pregnancy in jobs with a combination of two or more physical tasks, physical effort or occupational fatigue was also associated with an increased risk of PTD (OR 1.5 (95% CI 1.1- 2.0)).

Conclusions: Physically demanding work during pregnancy is associated with an increased risk of preterm delivery, especially in jobs with a combination of tasks with physical effort. In general, only small to moderate elevations of risks were found.

Keywords
Physically demanding work; preterm delivery; pregnancy outcome; occupational exposure.

Introduction

In most parts of the world, women work during pregnancy. Some working conditions are suspected to increase the risk of adverse outcomes of pregnancy, such as preterm delivery (PTD) or low birth weight. PTD, defined as the birth of a living fetus before 37 completed weeks of gestation, is the leading cause of perinatal morbidity and mortality in the developed world. The frequency of PTD varies between 5-9% in developed countries; however, the rate of preterm birth has increased in many locations, predominantly because of increasing indicated preterm births and PTD of artificially conceived multiple pregnancies [5, 20]

The main causes of preterm birth are spontaneous preterm labour, divided into spontaneous labour (preterm premature rupture of membranes (PPROM) (25%; 7.1-51.2%) and spontaneous (idiopathic) preterm birth with intact membranes (50%; 23.2-64.1%)) and medically indicated (iatrogenic) preterm birth (25%; 18.7-35.2%) [42]. From 2000-2007, the risk for preterm birth in the Netherlands in singleton pregnancies decreased significantly from 6.4% to 6.0%, mainly as a result of the decrease in PPROM (3.6-3.1%) [62]. Globally, there is a rise in the incidence of preterm birth [13].

PTD has a multifactorial origin, including feto-maternal conditions, infection and lifestyle. The pathway to PTD is not fully understood, and probably not all causes have been identified [20]. Better understanding of the mechanisms underlying spontaneous and iatrogenic PTD is important, as it can help to take preventive measures.

The last decade, two systematic reviews, including meta-analyses, have been published about the relation between adverse pregnancy outcomes and occupational exposures [6, 44]]. For PTD, Bonzini et al. (2007) found extensive and generally consistent associations with exposures such as prolonged working hours, shift work, lifting, standing and heavy physical workload. This tended to rule out more than moderate effects (relative risks (RR) > 1.4). Mozurkewich et al. (2000) estimated that physically demanding work, including lifting, was significantly associated with PTD (OR 1.2), small for gestational age (SGA) (OR 1.4) and hypertension or pre-eclampsia (OR 1.7), and that the risks of PTD were also higher in those with prolonged standing (OR 1.3) and shift or night work (OR 1.2). One study observed the influence of changing working conditions during pregnancy on PTD and found that this risk increased with the increase of a cumulative index composed of nine work conditions [15]. Changing of working conditions in the course of pregnancy, due to legally justified job withdrawal or reassignment was associated with a lower risk of PTD.

As the labour participation of women continues to grow, it is increasingly common for (occupational) physicians to be confronted with questions concerning work, pregnancy and the postpartum period.

More evidence based information about the work-related and personal risk factors that increase the risk of preterm delivery is necessary. The objective of this systematic review is to study the association between exposure to physically demanding work-related factors (prolonged standing, heavy lifting, physical exertion, occupational fatigue and demanding posture) of pregnant workers and the risk of PTD. By focusing on a more specific exposure category (physically demanding work) and a selected outcome parameter (preterm delivery), we expected to increase the homogeneity of studies for a meta-analysis. Because the last systematic review [6] included papers until 2005, we also wanted to provide an update of the published evidence until the first half of 2012.

Our research question was whether pregnant workers in paid employment who are exposed to physically demanding work during the pregnancy have a higher risk of preterm delivery compared to their colleagues who are not or to a lesser extent exposed to physically demanding work.

Methods

We performed a systematic review and meta-analysis on the association between physically demanding work and PTD. The review was performed according to the PRISMA statement [35]

Literature Search

A series of literature searches was conducted using the electronic databases MEDLINE (by PubMed), EMBASE and NIOSH-TIC 2. We limited our search to the articles written in English, German, French, and Spanish. We included studies published between 1990 and July 1st 2012 using MeSH or key terms related to the disease (pre-term delivery), the exposure (physically demanding work) and population (working pregnant women). Search terms included combinations of the following terms: "pregnancy, pregnant, work, employ*, occupation*, work*, lifting, carrying, manual lifting, carrying heavy load, heavy physical work, stand*, prolonged standing, postural balance, walking, kneeling, squatting, trunk bending, physical exercise, physical activity, physical fitness, workload, occupational activity, preterm, premature, delivery, birth, labour, adverse pregnancy outcome, pregnancy complications, labour complications, gestational age, trimester, fetal morbidity, maternal morbidity". We checked reference lists of relevant studies to identify additional relevant citations not captured by the electronic searches. Appendix 1 includes a summary of search strategies.

Study selection

Two authors independently screened titles and abstracts for relevance (MvB and MvM), and full reports of potentially relevant articles were reviewed by these two investigators.

Disagreements were resolved through consensus, and when needed using the opinion of a third author (CH)

Studies were included if they met the following criteria: (1) inclusion of pregnant women in paid employment in control and exposure group for at least eight hours per week for four weeks during pregnancy (2) report on PTD between 26+0 and 36+6 weeks (3), data collection from 1990 and (4) observational and intervention studies with original data.

Data collection process

We developed a data extraction sheet based in Access, pilot-tested it on five included studies, and refined it accordingly. One review author (MvB) extracted the data from the included studies and the second author (MvM) checked the extracted data. Disagreements were resolved by discussion between the two authors; if no agreement could be reached, a third author decided (CH).

Data items

Information was extracted from each included study on: characteristics of the study, characteristics of the study population, information about the exposure, outcome defined, and information on the results.

Risk of Bias Assessment

We have scored each article on risk of bias based on the methodology used in a UK guideline on physical and shift work in pregnancy (NHS Plus 2009). Two authors (MvB, MvM) performed this quality assessment. Disagreements were resolved with a third author (CH). We scored the studies on 13 items related to clarity of information on population, exposure, and outcome and to the quality of the study design and the analysis. The total score ranged from 0 to 18 points. Studies with a score below 10 were considered as high risk of bias and were excluded. We defined studies with a score from 10 to 13 points as moderate risk of bias and studies scoring more than 13 points as low risk of bias. We have judged studies on having low, moderate, or high risk of bias.

Data Analysis

We performed a meta-analysis with a random effects model using RevMan 5 software (RevMan 2012). We used the generic inverse variance method to pool the studies. The odds ratios and the 95% confidence intervals as reported by the original authors were recalculated into the natural log of the OR and its Standard Error, which were used as input for RevMan. Because the incidence of the events was under ten per cent in all cases, we equated odds ratios with relative risks and finally present the results as odds ratios or risk ratios. From the studies, we always took the risk estimate that was most adjusted for confounders. We reported the results of case control and cohort studies separately in sub-groups and depending on heterogeneity combined them in a single summary estimate.

In case the authors had not provided an effect estimate, we calculated a relative risk and its standard error [57].

We combined studies according to the following exposure categories:
- Standing and walking for more than 3 hours per day versus less,
- Lifting more than 5 kg versus less than 5 kg,
- Reporting the job requires physical effort or physical exertion versus no physical exertion
- Job with a combination ≥ 2 tasks with physical effort or Occupational Fatigue Score (OFS) ≥ 2 versus < 2 tasks or OFS.

If results were reported per trimester, we combined these first in a separate meta-analysis and used the pooled estimate of the three trimesters as input in the main analysis. We measured statistical heterogeneity with the I^2 statistic with the following interpretation of its value: less than 30%: not important; 30% to 60%: moderate heterogeneity; 50% to 90%: substantial heterogeneity, and more than 75% considerable heterogeneity.

We made separate analyses of studies that measured exposure during the first, second and third trimester when there were more than three studies available that reported these results.

We also performed a separate analysis to find out how sensitive the results were for the risk of bias in the included studies. For this analysis we included only studies with a score of at least 14 which is about 75% on our risk of bias checklist with a maximum score of 18.

Results

Study selection

The flow chart in Figure 1 summarises the selection of studies through the review. The search of the computerised databases identified a total of 616 citations. After checking for doubles, and excluding studies clearly not related to the objective of our review, 33 papers were retrieved for detailed evaluation. Screening of the references of all relevant papers resulted in 21 additional studies. Of these 54 studies, 36 were excluded because they did not meet the inclusion criteria. One of the remaining 18 papers that were scored for their quality in information was at high risk of bias [34]. Finally, 17 studies were included in the review.

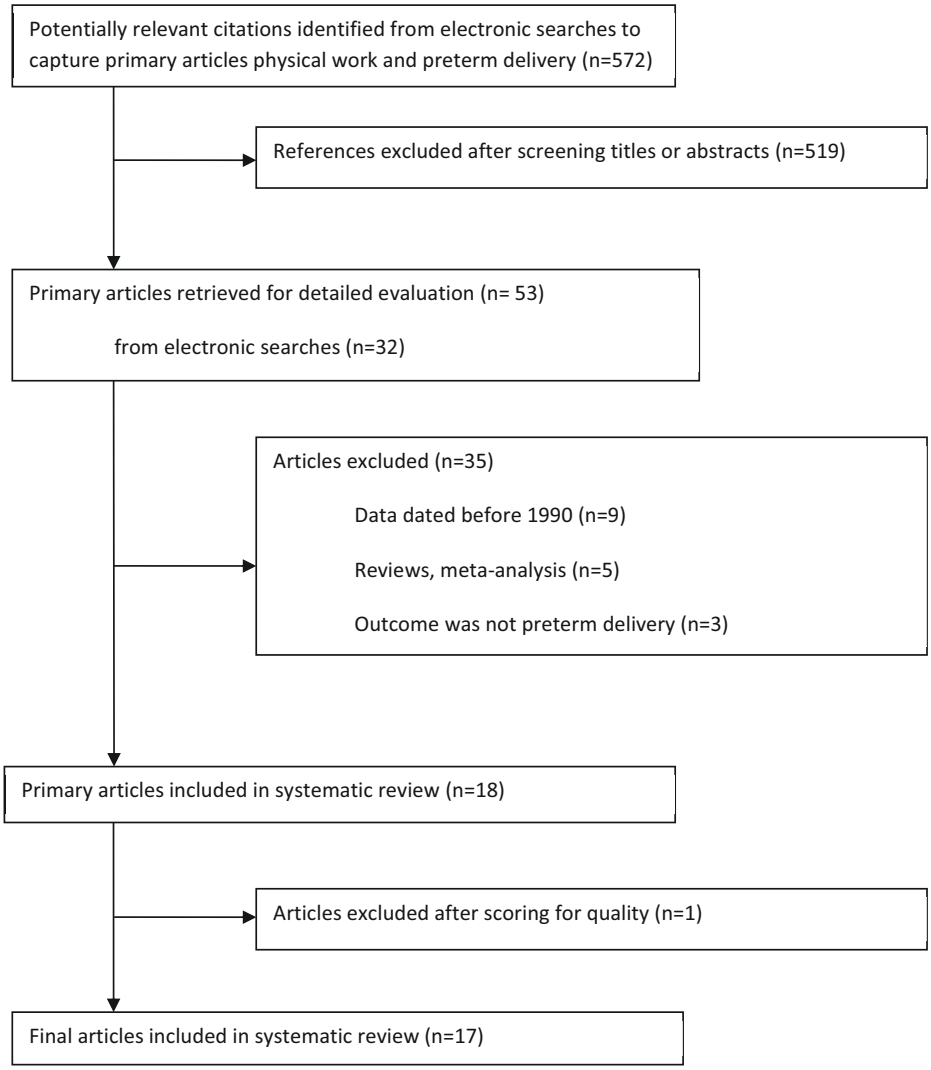

Figure 1. Flowchart literature selection physically demanding work and preterm delivery

Description of Included Studies

Table 1 presents a summary of the study characteristics of the 17 included articles. There were six European studies [7, 9, 17, 31, 45, 59], five studies from United States [33, 36, 37, 53, 66] two from Africa [1, 51], two from Thailand [55, 69], and one from Mexico [12] and Canada [15].

Table 1. Details of included studies

First author (year)	Country	Study period	Study design	Exposure	Method of exposure assessment	Outcome: Preterm Delivery
Agbla F (2006)	Benin	2000-2002	Case control	Carrying heavy loads Standing Tiredness at end working day	Interview in family home >1-<30 months after delivery	PTD < 37 weeks
Bonzini M (2009)	United Kingdom	1999-2003	Pro/ retrospective cohort	Lifting Standing Walking Kneeling Squatting Trunk bending	Interview 34 weeks gestations	PTD 34-37 weeks
Brink-Hendriksen T (1995)	Denmark	1989-1991	Prospective cohort	Standing Walking Standing and walking	Self-administered questionnaire during pregnancy at 16 and 30 weeks gestation	PTD <37 weeks
Céron-Mireles P (1996)	Mexico	1992	Retrospective cohort	Standing Physical effort	Personal interview, 24 h after delivery	PTD: <37 weeks
Croteau A (2007)	Canada	1997-1999	Case control	Demanding posture Cumulative index: no of occupational cond. present at beginning pregnancy: > 5 consecutive working days, irregular or shift work-schedule, demanding posture ≥ 3h/day, whole body vibrations, very hot or very cold temperature, mod. active or high strain job with low or mod. social. Support	Interviewed by telephone max 32 days after delivery	PTD: <37 weeks

Table 1. Continued.

First author (year)	Country	Study period	Study design	Exposure	Method of exposure assessment	Outcome: Preterm Delivery
Escribà-Agüir V (2001)	Spain	1995-1996	Case control	Lifting Standing Physical workload indicator: Sum of standing, lifting and strenuous position	Interview 2 days after delivery	PTD: 22-36 weeks
Koemeester A (1995)	Netherlands	1989-1990	Prospective cohort	Physical load: combination of walking, standing, lifting, stooping, squatting, without resting	Questionnaire 15 an 20 weeks Interview 20 weeks	Gestational age at delivery
Lawson C (2009)	USA	1993-2001	Retrospective cohort	Lifting Standing Walking	Questionnaires (up to 8 years) after delivery	PTD <37 weeks
Luke B (1995)	USA	1995	Case control	Standing Physical exertion Occupational fatigue score	Mailed Questionnaire after delivery	PTD <37 weeks
Magann EF (2005)	USA	4 years, not specified	Prospective cohort	Lifting Standing	Questionnaire initial 8 weeks gestation update throughout pregnancy	20-37 weeks and PTlabor
Niedhammer I (2009)	Ireland	2001	Prospective cohort	Physical work demands Cumulative index, at least two of the factors: sum of work contract, working hours, shift work, physical demands	Questionnaire (moment unknown)	PTD < 37 weeks
Omokhodion FO (2010)	Nigeria	2008	Retrospective cohort	Standing Physical exertion	Interview by trained nurses within 2 days after delivery	PTD < 37 weeks

Table 1. Continued.

First author (year)	Country	Study period	Study design	Exposure	Method of exposure assessment	Outcome: Preterm Delivery
Pompeii LA (2005)	USA	1995-2000	Prospective cohort	Lifting Standing	Telephone interview (at 24-31 weeks) Face-to-face interview after delivery, before discharge from the hospital	PTD < 37 weeks
Ritsmitchai S (1997)	Thailand	1993	Case control	Standing Physical exertion	Interview using structured questionnaire	PTD 28-37 weeks
Saurel-Cubisolles MJ (2004)	16 European countries	1994-1997	Case Control	Lifting Standing	Questionnaires Interviews after delivery	PTD < 37 weeks
Stinson J (2003)	USA	Not noted	Prospective cohort	Fatigue score	Self-administered questionnaire during pregnancy, monthly phone call	PTD < 37 weeks
Tuntiseranee (1998)	Thailand	1994-1995	Prospective cohort	Lifting Standing Physical job demand squatting	Expert Interview at 17 and 32 weeks, n=130 after delivery	PTD < 37 weeks

The study design of the 17 included studies was mostly a prospective cohort (8), retrospective cohorts (3) or case control (6). In 11 studies the method of exposure assessment was a personal interview (sometimes by phone), two times before and eight times after delivery, one study both before and after. In seven studies a self-administered questionnaire was used, before (4) or after (3) delivery. One study used a questionnaire and an interview before delivery. After quality assessment, seven studies were considered as of moderate risk of bias, whereas the quality of the other ten studies was considered as low risk of bias.

Twelve studies focussed on the effect of standing and walking on PTD; nine studies on lifting and carrying, nine on physical exertion/occupational fatigue, three on demanding posture and two on tiredness/fatigue. The outcome of 16 studies was PTD, defined as the birth of a living fetus before 37 completed weeks of gestation, while two studies reported on a substantial smaller period: delivery between 28-37 weeks [55] or 34-37 weeks [7]. One study described of each birth the gestational age [31].

Standing and walking

The relationship between occupational standing and walking and PTD was examined in 12 studies (table 2) [7, 9, 12, 17, 33, 36, 37, 51, 53, 55, 59, 69]. Of these studies five were prospective, four case control and three retrospective. Five of them were of moderate risk of bias, the other seven were of low risk of bias. Studies differed substantially in timing and duration of exposure. Timing of exposure was mostly first trimester, five studies described the exposure more or less specified per trimester. It is noteworthy that as pregnancy progressed, fewer women were reported to standing or walking for a longer time. The results were significant with OR from 1.1 to 4.1.

Table 2. summary of findings standing and walking

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Significance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm Delivery
Bonzini M (2009)	Pro/ Retrospective cohort	1327	Standing or walking>4 h/day in total	AD 11 exposed n=484 (37%)/ exposed cases 16	AD 11: OR 0.92 (0.49 to 1.70)	NS	11 weeks	No data available of changing	14	PTD 34-37 weeks
				AD 19: exposed n=432 (34%)/ exposed cases n= 12	AD 19: OR 0.76 (0.39 to 1.49)	NS	19 weeks	working conditions		
				AD 34: exposed n= 201 (24%)/ exposed cases n=6	AD 34 OR: 0.99 (0.39 to 2.51)	NS	34 weeks			
Brink-Hendriksen T (1995)	Prospective cohort	4259	Standing > 5 h/day ref: 0-2h/day	total n= 4259/ exposed n=197	RR: 1.2 (0.6 to 2.4)	NS	16 weeks	Working at wk 16, change in exposure noted	14	PTD <37 weeks
			Walking >5 h/day ref: 0-2 h/day	total n= 4259/ exposed n=243	RR: 1.4 (0.7 to 2.5)	NS	16 weeks 30 weeks	Working at wk 16, change in exposure noted	14	
			Standing and/or walking > 5h/day ref: 0-2h/d	total n= 4259/ exposed n=52	RR:3.3 (1.4 to 8.0)	S	16 weeks 30 weeks	Working at wk 16, change in exposure noted	14	
Céron-Mireles P (1996)	Retrospective cohort	2429	Standing >7h/d	not exposed n= 1937/ exposed n=463	OR 1.16 (0.89-1.51)	NS	not stated	At least 3 months (also change workstation/ sick leave noted)	11	PTD: <37 weeks
				PTD not exposed 223/ exposed n=62						
Escribà-Agüir V (2001)	Case control	676	Standing	228 cases/ 345 controls			First trimester	Worked at least the first 3 months	14	PTD: 22-36 weeks

Table 2. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Significance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm Delivery
			Standing ≤2h/d	35.7%	≤2h/d: reference			Missing data excluded?		
			Standing 2-6h/d	31.9%	2-6 h/d OR 1.28 (0.82-1.99)	NS				
			Standing ≥6h/d	32.5%	≥6h/d 1.51 (0.97-2.35)	NS				
Lawson C (2009)	Retrospective cohort	6977	Standing/walking ≥9 vs 5-8 h/shift	151 (25.8%/ controls 1323 (20.7%)	RR: 1.3 (1.0-1.7)	S	First trimester	≥ 1h/wk during 1st trimester Missing data excluded	11	PTD <37 weeks
Luke B (1995)	Case control	1470		cases 210/ controls 1260			Whole pregnancy	at least 20 weeks gestation		PTD <37 weeks
			Standing ≥4 vs <4 h/shift	Cases 92.3%/ controls 84.8%	OR 2.4 (1.4-4.3)	S		Missing data excluded	10	
Magann EF (2005)	Prospective cohort	814	Standing ≥ 4h/d vs < 4 h/d	n= 215 (26.4% total 814)	OR: 1.636 (0.884-3.063) preterm birth	NS	8 weeks gest. until delivery	First trimester, update throughout pregnancy	14	20-37 weeks
					OR 2.179 (1.105-4.444) preterm labor	S				and PTlabor
		623 standing	Standing without vs with altering standing at wk 21	n= 132 vs n= 481	OR: 1.69 (1.03-2.8) preterm birth	S				
					OR : 1.69 (1.05-3.16) preterm labor	S				

Table 2. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Significance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm Delivery
Omokhodion FO (2010)	Retrospective cohort	980	Standing>6h vs <6 h/d	<6 h/d 939; preterm 10	reference		not noted	not noted	11	PTD < 37 weeks
			univariate analyse	>6 h/d 45; preterm 11	1.1 (0.42-2.85)	NS		Stopped work in pregnancy no/yes 1.36 (0.74-2.49)		
				unknown 13; preterm 8						
Pompeii LA (2005)	Prospective cohort	977 standing	Standing: > 30 vs 6-15 h/wk	1st trim: 1796, 229 cases; 453 (25%) >30h/wk	Trimester 1 RR 1.2 (0.9 to 1.7)	NS	1-12 weeks	Working women for at least 28	12	PTD < 37 weeks
			reference:6-15 h/wk	2nd trim: 1711, 210 cases; 323 (18.8%)	Trimester 2 RR 0.9 (0.6 to 1.2)	NS	13-27 weeks	days during the 1st trimester		
			5-15 h/wk: n=524 (trimester not noted)	3rd trim: 444, 135 cases; 99 (22,3%)	Trimester 3 RR 1.3 (0.8 to 2.3)	NS	28-31 weeks	Missing data excluded		
			>30h/wk: n=453 (trimester not noted)							
Ritsmitchai S (1997)	Case control	446	Standing > vs< 3 h/d				Whole pregnancy	Trimester: 1, 1+2, 1+2+3, 2+3	15	PTD 28-37 weeks
			not	191cases/ 206 controls	OR 1					
			1st trimester	8 cases/4 controls	OR 0.93 (0.11-8.13)	NS				
			1st+2nd trimester	5 cases/ 7 controls	OR 0.58 (0.12-2.75)	NS				
			1st +2nd+trd trimester	19 cases/ 4 controls	OR 4.1 (1.29-13.10)	S				

Table 2. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Significance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm Delivery
Saurel-Cubisolles MJ (2004)	Case Control	6353	Standing 6 vs 2 h/day	2317 cases, 4036 control	OR 1.26 (1.1 to 1.5)	S	First trimester	Worked at least 3 months from the start of pregnancy	15	PTD < 37 weeks
			Countries A1 Standing <2 vs >6 h/day	n=936	OR 1.06 (0.8-1.3)	NS				
			Countries A2 Standing <2 vs >6 h/day	n=859	OR 1.38 (1.1-1.7)	S				
			Countries B Standing <2 vs >6 h/day	n=534	OR 1.55 (1.1-2.3)	S				
Tuntiseranee P (1998)	Prospective cohort	1121	Standing ≥5 vs ≤4h/d:	148 (13%) ; preterm 4,8% 973 (87%) preterm 5.2	OR 0.9 (0.3 -2.3)	NS	Second trimester Third trimester	Missing data excluded Not stated, working at 17 and or 32 weeks. At 32 weeks: 41% stopped working	16	PTD < 37 weeks

We pooled the data from all 12 studies that compared women standing and walking at work during their pregnancy for more than 3 h/d with standing less than 3 h/d. The summary estimate OR was 1.33 (95% CI 1.11-1.59) (p= 0.002, I2=62%) (Figure 2). For the subset of seven studies to have low risk of bias, the corresponding summary OR was 1.41 (95% CI 1.06-1.89) (p=0.02, I2=63%) (Figure 3). The pooled OR of two studies specified for the risk in the third trimester was 1.22 (95% CI 0.77-1.93) (p=0.40, I2=0%).

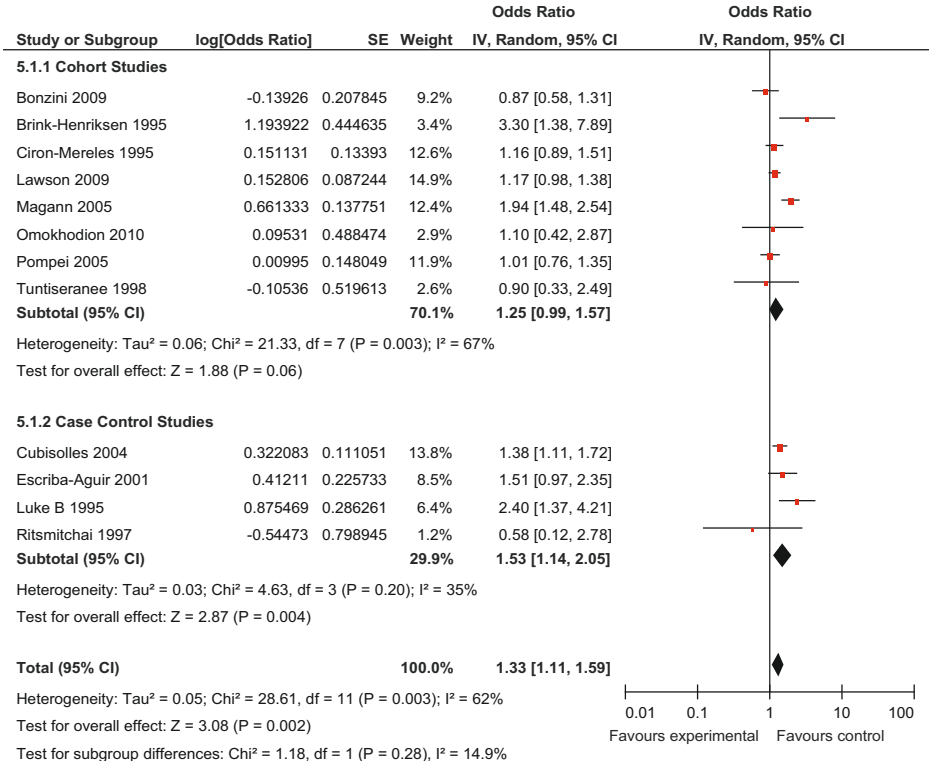

Figure 2. Forest plot of comparison: standing and walking > 3 hours/day versus no standing and walking, outcome: preterm delivery (PTD)

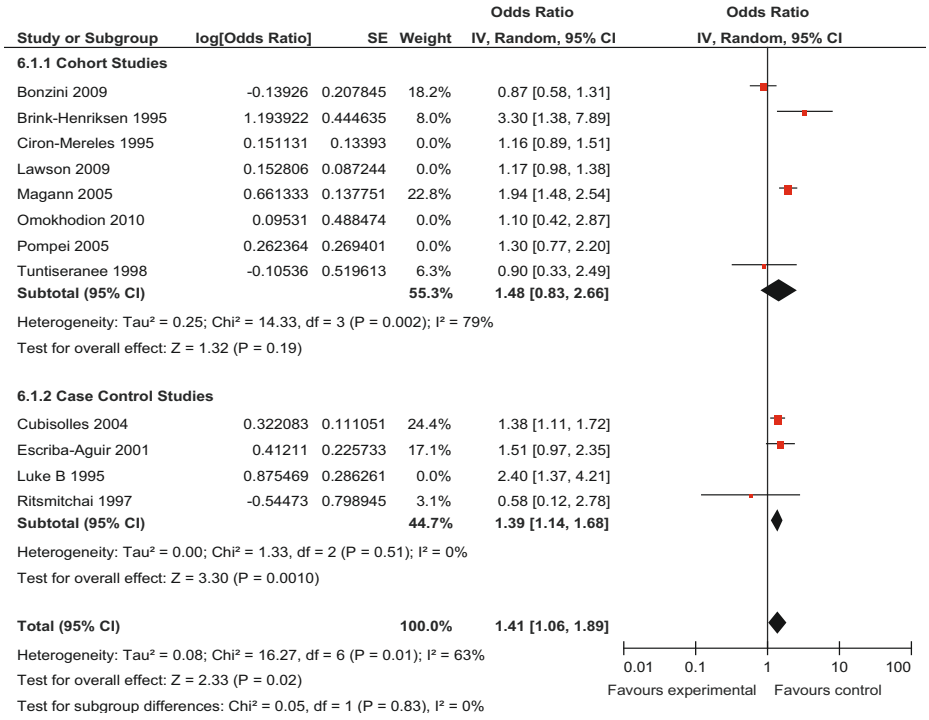

Figure 3. Forest plot of comparison: standing and walking > 3 hours/day versus no standing and walking, sensitivity analysis, outcome: preterm delivery (PTD)

Lifting and carrying

The relationship between occupational lifting and PTD was examined in nine studies [1, 7, 17, 33, 37, 53, 55, 59, 69]((Table 3). Of these studies, four were prospective cohort studies, one a retrospective cohort study. and four studies had a case control design. Six studies were of low risk of bias, three were moderate.

Substantial differences in definition of exposure occurred. Timing of exposure was mostly first trimester; three studies described the exposure specified per trimester. In these studies the number of pregnant employees with exposure to lifting or carrying decreased obviously in second and third trimester. Four studies showed significant results with OR's from 1.7-5.0.

Table 3. summary of findings lifting and carrying

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm delivery
Agbla F (2006)	Case control	203	Carrying loads (12 kg) > 5 days /week	Total n=203 Cases n=99 Controls=104	OR: 5.0 (1.38-18.8)	S	not noted	Not noted	11	PTD < 37 weeks
Bonzini M (2009)	Pro/ retrospective	1327	Lifting weights >25kg by hand vs no lifting	AD 11 exposed n=121 (9%)/ exposed cases n=3	AD 11: OR 0.69 (0.21 to 2.26)	NS	11 weeks	No data available of changing	14	PTD 34-37 weeks
	cohort			AD 19: exposed n=83 (6%)/ exposed cases n= 3	AD 19: OR 1.10 (0.33 to 3.05)	NS	19 weeks	working conditions		
				AD 34: exposed n= 24 (3%)/ exposed cases n=2			34 weeks			
Escribà-Agüir V (2001)	Case control	676	Carrying >5kg	228 cases/ 345 controls			First trimester	Worked at least the first 3 months	14	PTD: 22-36 weeks
				never 79.1%	never: reference			Missing data excluded?		
				occasionally/ often/very often 20.9%	OR 1.73 (1.17-2.57)	S				
Lawson C (2009)	Retrospective cohort	676	Lifting: ≥16 vs <1 times/day 11 kg	cases 36 (6.1%)/ controls 266 (4.2%)	RR: 1.2 (0.8-2.0)	NS	First trimester	≥1h/wk during 1st trimester Missing data excluded	11	PTD <37 weeks

Table 3. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm delivery
Magann EF (2005)	Prospective cohort	814	lifting yes vs no	n=48 (5.9%) total 814	OR1.13 (0.319- 3.179) preterm birth	NS	8 weeks pregnancy until delivery	First trimester, update throughout pregnancy	14	20-37 weeks
		318 lifting			OR 1.219 (0.273-3.921) preterm labor	NS				and PTlabor
			lifting > 4h/d and stopped lifting at 21-28 weeks vs no lifting	cases=2 (total 5) vs cases=78 (total 809)	p= 0.025 preterm birth	S				
			lifting > 11 kg and altered lifting at 21-28 weeks vs no lifting		p= 0.021 preterm labor	S				
Pompeii LA (2005)	Prospective cohort	977 standing	Lifting >11 kg >13 vs 0 times/ wk	1st trim: 1796, 229 cases; 453 (25%) >30h/wk	Trimester 1 RR 1.3 (0.9 to 1.8)	NS	1-12 weeks	Working women for at least 28 days during the 1st trimester	12	PTD < 37 weeks
		1176 lifting	reference: no lifting	2nd trim: 1711, 210 cases	Trimester 2 RR 1.3 (0.8 to 2.1)	NS	13-27 weeks			

Table 3. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm delivery
			0 times /wk: 1001 trimester not noted >13 times/wk: 175 trimester not noted	3rd trim: 444, 135 cases	Trimester 3 RR 1.3 (0.6 to 2.9)	NS	28-31 weeks	Missing data excluded		
Ritsmitchai S (1997)	Case control	446	Physical exertion: lifting or carrying anything ≥10 kg ≥3 /d				Whole pregnancy	Trimester: 1, 1+2, 1+2+3, 2+3	15	PTD 28-37 weeks
			not	160 cases/ 172 controls	OR 1					
			1st trimester	14 cases/ 21 controls	OR 0.50 (0.23-1.09)	NS				
			1st+2nd trimester	18 cases/ 18 controls	OR 0.86 (0.39-1.89)	NS				
			1st +2nd+trd trimester	28 cases/12 controls	OR: 2.91 (1.29-6.58)	S				
Saurel-Cubisolles MJ (2004)	Case Control	6353	Lifting 20 kg vs none	2314 cases, 4025 control	OR 1.02 (0.8 to 1.2)	NS	First trimester	Worked at least 3 months from the start of pregnancy	15	PTD < 37 weeks
Tuntiseranee P (1998)	Prospective cohort	1108	no lifting	933 (83%); preterm 4.9%	OR 1		Second trimester	Missing data excluded	16	PTD < 37 weeks

Table 3. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome Preterm delivery
			Lifting 12 kg ,10 times /d vs none	175 (16%); preterm 5.8%	OR 0.9 (0.4-2.1)	NS	Third trimester	Not stated, working at 17 and or 32 weeks.		
			Lifting 12 kg , >10 times /d vs none	13 (1%); preterm 7.7%	OR 1.6 (0.1-20.4)	NS		At 32 weeks: 41% stopped working		
				unknown 21; preterm 14						

The overall meta-analysis included all nine studies. We pooled data of pregnant women lifting more than five kg versus less lifting. The summary OR was 1.29 (95% CI 1.05-1.57) (p=0.01, I^2=34) (Figure 4).

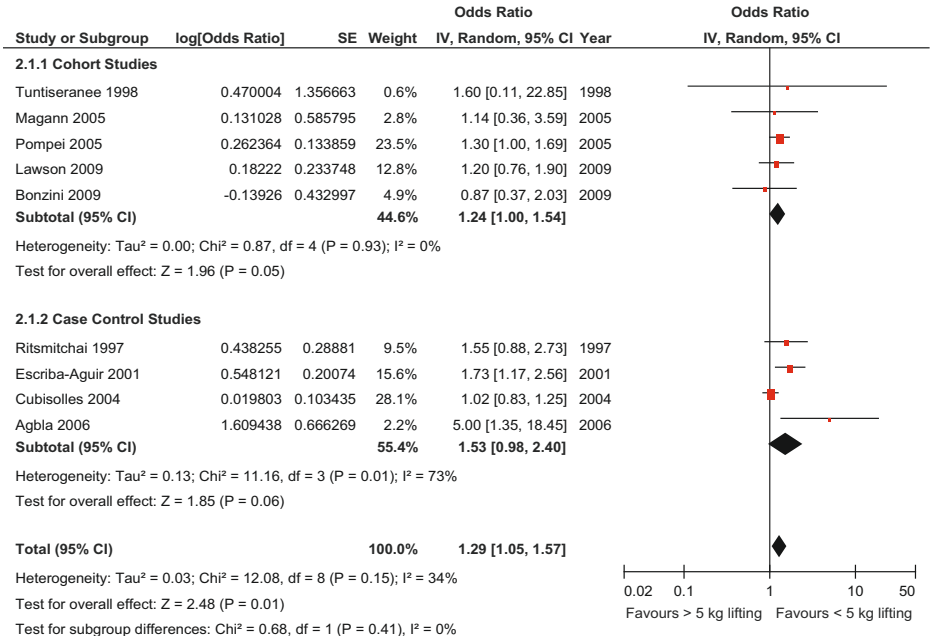

Figure 4. Forest plot of comparison: lifting > 5 kg vs less lifting, outcome: preterm delivery (PTD)

For the six studies that met our criteria for low risk of bias, OR was 1.24 (95% CI 0.96-1.61) (p=0.10, I^2=29) (Figure 5).

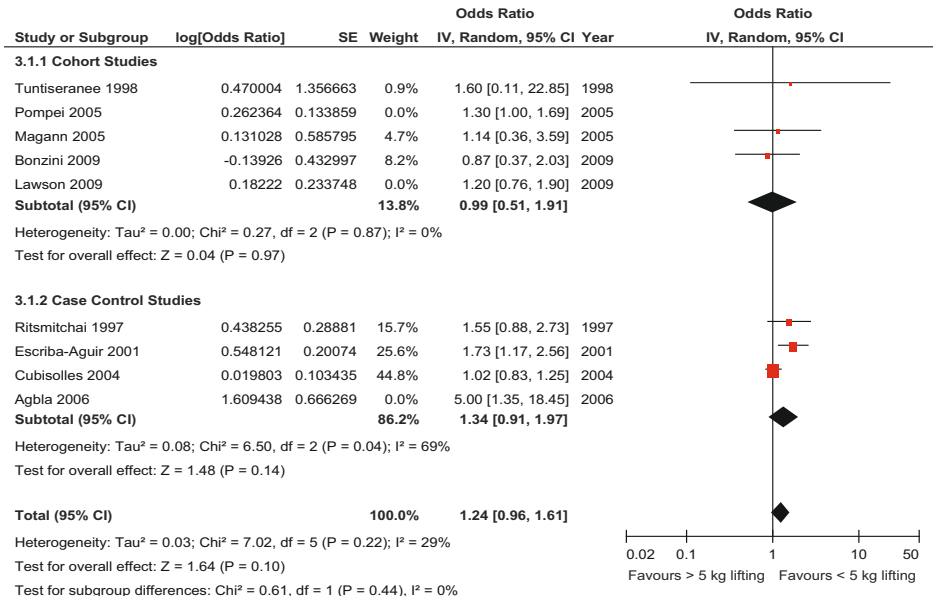

Figure 5. Forest plot of comparison: lifting > 5 kg, sensitivity analysis, outcome: PTD

The pooled OR of two studies specified for the risk in the third trimester was 1.30 (95% CI 1.01-1.76) (p=0.04, I^2=0%). The meta-analysis on lifting and carrying shows little heterogeneity (Figure 6).

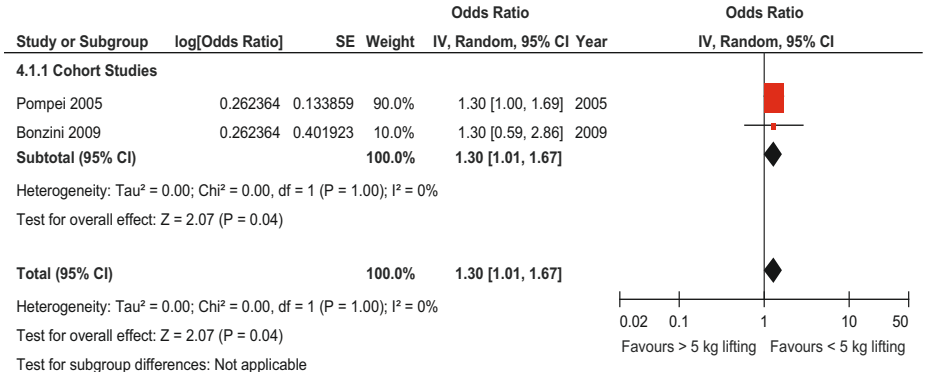

Figure 6. Forest plot of comparison: lifting > 5 kg, 3rd trimester only, outcome: PTD

Physical exertion/ Occupational Fatigue Score

The relationship between Physical exertion/ Occupational Fatigue and PTD was examined in nine studies [1, 12, 15, 17, 31, 36, 48, 51, 69] (Table 4): three prospective cohort studies,

two retrospective cohort studies, and four case control studies. Four studies were of low risk of bias, five were moderate.

Exposure was defined in two ways. In five studies, the exposure was defined as "job requires physical effort or physical exertion". We pooled the data from these five studies to evaluate the relationship between pregnant women with jobs that require physical effort or physical exertion vs no physical exertion. The summary OR for these studies was 1.4 (95% CI 1.19-1.66)(p=0.0001, I^2=0%). The meta-analysis shows no heterogeneity (Figure 7).

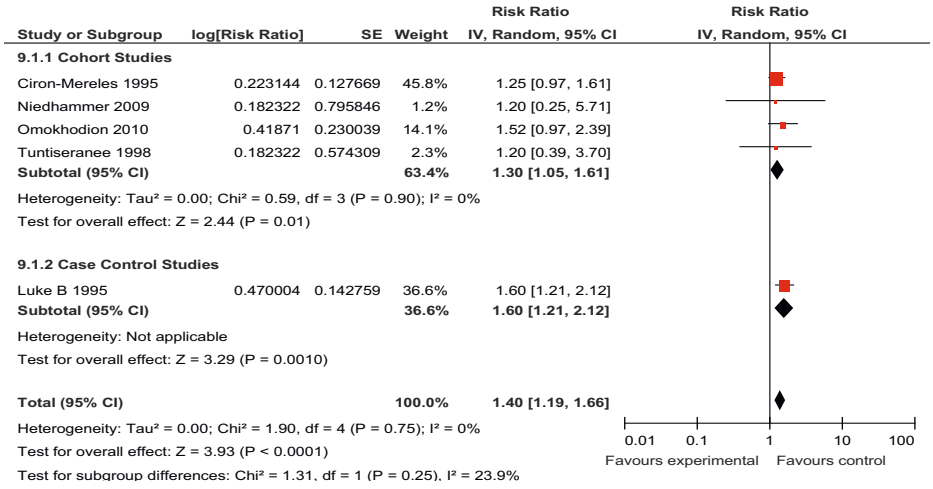

Figure 7. Forest plot of comparison: job requires physical effort or physical exertion vs no physical effort or exertion, outcome: PTD

In six studies, a combination of two or more tasks with physical effort (e.g. carrying, walking and/or a demanding posture or tasks combined in a cumulative work fatigue score) was examined. This cumulative index, the Occupational Fatigue Score, was developed by [39]. In line with Mozurkewich (2000) [44], exposures were all scored as 1 and totaled: standing position for more than three hours per day; working on a strenuous industrial machine or conveyor belt; important physical exertion or load carrying; routine work or task without mental stimulation; and one or more of the following factors: noise, cold temperature, wet atmosphere, or manipulation of chemical substances. In all these six studies, a cumulative index of at least two or more tasks or exposures showed a positive association with PTD. There were trends in increasing number of tasks with OR from 1.2 to 6. Timing of exposure was mostly in the first trimester.

Table 4.A Summary of findings physical exertion : combination of 2 or more tasks with physical effort or Occupational Fatigue score

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome: Preterm delivery
Agbla F (2006)	Case control	203	Carrying loads (12 kg) + Walking > 5 days/week vs < 5 d/week	Total n=203 Cases n=99 Controls=104	OR: 6.88 (1.45-32.2)	S	not noted	Not noted	11	PTD < 37 weeks
Croteau A (2007)	Case control	5755 4513 controls 1242 cases	Cumulative index: no of occupational cond. present at beginning pregnancy. > 5 consecutive working days irregular or shift work schedule demanding posture ≥ 3h/d whole body vibrations very hot or very cold temperature mod. active or high strain job with low or mod. social. Support				exposure at beginning exposure eliminated <24 weeks exposure not eliminated	At least 4 weeks from the first month At least 20h/wk Missing data excluded	15	PTD: <37 weeks
			0	controls 1549/ cases 357 PTD/ cases very PTD 59	reference OR 1					
			1	controls 1637/ cases 449 PTD/ cases very PTD 89	PTD: OR 1.2 (1.0-1.4)/ Very PTD: OR 1.4 (1.0-2.0)	S				
			2	controls 814/ cases 238 PTD/ cases very PTD 46	PTD: OR 1.2 (1.0-1.5)/ Very PTD: OR 1.5 (1.0-2.2)	S				

Table 4.A Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome: Preterm delivery
			3	controls 390/ cases 131 PTD/ cases very PTD 26	PTD: OR 1.4 (1.1-1.8)/ Very PTD: OR 1.7 (1.1-2.8)	S				
			4-6	controls 117/ cases 58 PTD/ cases very PTD 12	PTD: OR 2.0 (1.4-2.8)/ Very PTD: OR 2.7 (1.4-5.1)	S				
			When eliminated trends stronger when not eliminated early by preventive measures							
Escribà-Agüir V (2001)	Case control	676	Physical workload indicator:	228 cases/ 345 controls			First trimester	Worked at least the first 3 months	14	PTD: 22-36 weeks
			Sum of standing, lifting and strenuous position	low 61.7%	never: reference			Missing data excluded?		
				medium 25.2%	medium OR 1.59 (1.05-2.39)	S				
				high 13.0%	high OR 2.31 (1.43-3.73)	S				
Koemeester A (1995)	Prospective cohort	116	higher duration of tasks with physical work load: combination of walking, standing, lifting, stooping, squatting, , without resting	116	correlation with shorter gestational age p= 0.004	S	Not stated	≥12 weeks	14	Gestational age at delivery

Table 4.A Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome: Preterm delivery
Luke B (1995)	Case control	1470	Occupational Fatigue Score ≥3 vs<3	cases 210/ controls 1260 Cases ≥3 59% / controls ≥3 49%	OR 1.4 (1.1-1.9)	S	Whole pregnancy	at least 20 weeks gestation Missing data excluded	11	PTD <37 weeks
Niedhammer I (2009)	Prospective cohort	676	Cumulative index, at least two of the factors: sum of work contract, working hours, shift work, physical demands	≥2 98 (15.22%) 5 cases <2 478 (84.88%) 17 cases	OR: 5.18 (1-27.01)	S	Unclear 2e and 3e trimester	Unclear No data available of changing working conditions	13	PTD < 37 weeks

Table 4.B Summary of findings physical exertion : job requires physical effort or physical exertion

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome: Preterm delivery
Céron-Mireles P (1996)	Retrospective cohort	2429	Job requires physical effort yes/no	not exposed n= 1897/ exposed n=504 PTD not exposed 214/ exposed n=71	RR 1.25 (0.97 to 1.60)	NS	not stated	At least 3 months change workstation/ sick leave	11	PTD: <37 weeks
Luke B (1995)	Case control	1470	Physical exertion yes vs no	cases 210/ controls 1260 Cases 56.2%/ controls 44.6%	OR 1.6 (1.2-2.1)	S	Whole pregnancy	at least 20 weeks gestation Missing data excluded	10	PTD <37 weeks
Niedhammer I (2009)	Prospective cohort	676	Physical demands: Very vs not/ not very/fairly physically work	very: 122 (18.15%)/: 4 cases not/ not very/ fairly 550 (81.85%) 20 cases	OR: 1.2 (0.25-5.66)	NS	Unclear 2e and 3e trimester	Unclear No data available of changing working conditions	13	PTD < 37 weeks
Omokhodion FO (2010)	Retrospective cohort	980	Physical exertion no vs yes multivariate anal.	no 704; preterm 9 yes 272; preterm 14 unknown 21; preterm 14	reference 1.52 (0.97-2.39)	NS	not noted	not noted Stopped work in pregnancy no/yes 1.36 (0.74-2.49)	11	PTD < 37 weeks

Table 4.B Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome: Preterm delivery
Tuntiseranee P (1998)	Prospective cohort	1142	Physical job demand high vs moderate vs mild	high 122 (11%); preterm 7.4 %	OR 1.2 (0.4-3.8)	NS	Second trimester		16	PTD < 37 weeks
				moderate 769 (69%) mild 224 (20%)	OR 0.6 (0.3-1.3 OR 1	NS	Third trimester	Missing data excluded Not stated, working at 17 and or 32 weeks. At 32 weeks: 41% stopped working		

In one study it was found that the associations for the cumulative index of most of the work conditions with PTD were weaker when exposures were eliminated or changed due to a legally justified preventive measure (Croteau et al. 2007). In the meta-analysis five studies were included. This shows an increased risk of PTD for women working during their pregnancy in jobs with a combination two or more tasks with physical effort or an Occupational Fatigue Score of ≥ 2: summary OR = 1.49 (95% CI 1.12- 1.99)(p=0.0007, I^2=54) (Figure 8).

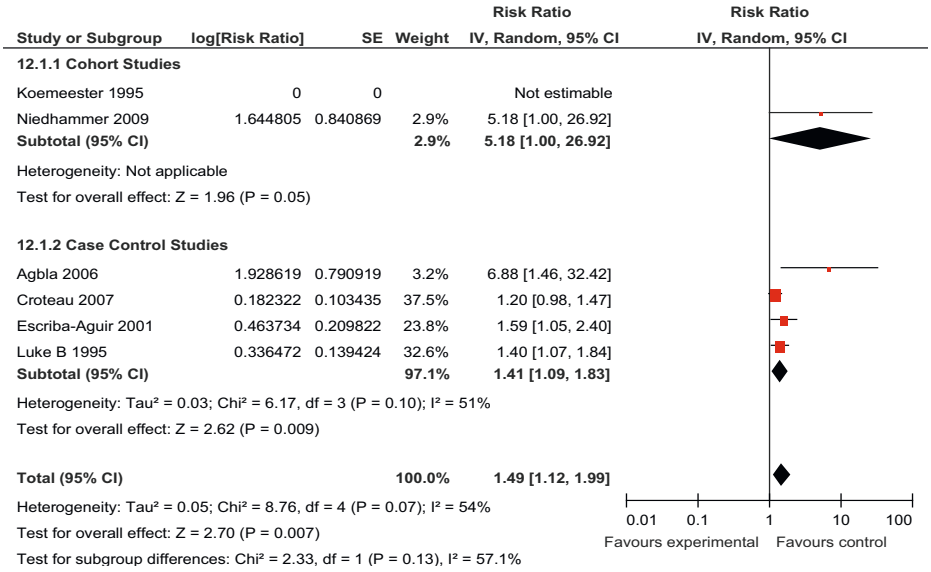

Figure 8. Forest plot of comparison: combination ≥ 2 tasks with physical effort or an Occupational Fatigue Score of ≥ 2. outcome: PTD.

Demanding Posture

The relationship between demanding posture in work and PTD was examined in three studies (Table 5) [7, 15, 69]. Of these studies, two were prospective cohort studies and one had a case control design. All three were assessed as low risk of bias studies. Exposure was defined as one or more kinds of demanding posture: kneeling, squatting, trunk bending, arms raised above shoulder level, during more than one, three or five hours a day. Risk of PTD was elevated threefold in women whose work at 34 weeks entailed trunk bending for more than one hour/day [7]. In the study of Croteau et al. (2007) the occupational conditions present at the beginning of pregnancy, demanding posture (bending, squatting, arms raised above shoulder level) for at least three hours per day, was significantly associated with PTD. The association was higher when not eliminated by preventive measures (OR 1.7) than when they were eliminated early during pregnancy (OR 1.4).

Table 5. Summary of findings demanding posture

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Method off Exposure assessment	Outcome Preterm Delivery
Bonzini M (2009)	Pro/ retrospective cohort	1327	Kneeling or Squatting>1 h/d in total vs no kneeling or Squatting or < 1h/d	AD 11 exposed n=219 (17%)/ exposed cases 6	AD 11: OR 0.77 (0.32 to 1.84)	NS	11 weeks	No data available of changing working conditions	14	Interview 34 weeks gestations	PTD 34-37 weeks
				AD 19: exposed n=209 (16%)/ exposed cases n= 6	AD 19: OR 0..86 (0.36 to 2.06)	NS	19 weeks				
				AD 34: exposed n= 82 (10%)/ exposed cases n=3	AD 34 OR: 0.1.25 (0.37 to 4.28)	NS	34 weeks				
			Trunk bending >1 h/d in total vs no trunk bending or < 1h/d	AD 11 exposed n=589 (23%)/ exposed cases n=23	AD 11: OR: 1.25 (0.69 to 2.26)	NS	11 weeks	No data available of changing working conditions	14		
				AD 19: exposed n= 569 (23%)/ exposed cases n= 23	AD 19: OR 1.47 (0.80 to 2.71)	NS	19 weeks				
				AD 34: exposed n= 315 (16%)/ exposed cases n=39	AD 34 OR: 2.92 (1.27 to 6.70)	S	34 weeks				

Table 5. Continued.

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Method off Exposure assessment	Outcome Preterm Delivery
Croteau A (2007)	Case control	5755	Demanding posture ≥3 h a day:	cases 498/ controls 2023	reference: 0 h/d			At least 4 weeks from the first month	15	Interviewed by telephone max 32 days after delivery	PTD: <37 weeks
		4513 controls 1242 cases	Bending, squatting, arms raised above shoulder level, or other demanding posture	cases 312/ controls 917	OR 1.4 (1.2-1.7)	S	exposure at beginning	At least 20h/wk			
				cases 125/ controls 404	OR 1.4 (1.2-1.7)	S	exposure eliminated <24 weeks	Missing data excluded			
				cases 138/ controls 356	OR 1.7 (1.3-2.1)	S	exposure not eliminated				
Tuntiseranee P (1998)	Prospective cohort	1121	squatting ≥5 vs ≤4h/d	≤ 4h/d 1114 (99%), preterm 5.0			Second trimester	Missing data excluded	16	Expert Interview at 17 and 32 weeks, n=130 after delivery	PTD < 37 weeks
				5+h/d 7 (1%) preterm 14.3	OR 2.2 (0.2-24.4)	NS	Third trimester	Not stated, working at 17 and or 32 weeks. At 32 weeks: 41% stopped working			

Table 6. Summary of findings tiredness/ fatigue score

First author (year)	Study design	Study population	Exposure Comparison	Number in analysis	Measure of association	Signi-ficance	Exposure Timing	Minimal duration exposure	Risk of bias score	Outcome:
Agbla F (2006)	Case control	203	Tiredness at end working day OR: ref=extremely tired.	Total n=203 Cases n=99 Controls=104			not noted	Not noted	11	PTD < 37 weeks
			extremely tired		ref: OR=1					
			vs very tired		vs very tired : 1.0 (0.20-4.96)	NS				
			vs tired		vs tired : 0.84 (0.20-3.59)	NS				
			vs not tired		vs not tired: 1.18 (0.24-5.86)	NS				
Stinson J (2003)	Prospective cohort	359	(perceived Fatigue) Fatigue Score >660 (severe) vs (0-660) low	cases: >660 cases 15 (28.8%) vs 35 (67.38%) (Preterm Labor)	P=3.782	NS	Second trim. (22-26weeks)	Not noted	14	PTD < 37 weeks
			Term labour n= 307 PTlabour n=52	controls: >660 138 (44.7%) vs 171 (55.7%) term labour	Less fatigue OR 1.79 (0.93-3.44) (ref=no PTD)	NS	Monthly	Not noted		
			Term birth n=325 PTB n=34	cases: >660 cases 14 (41.2%) vs 20 (58.8%) (Preterm Birth) controls: >660 134 (41.2%) vs 178 (54.7%) term labour	p=0.039	S				

Tiredness/ Fatigue

In two studies on physically demanding work, the relationship between tiredness or fatigue among employees and PTD was also discussed (Table 6). One study was a case control study with moderate risk of bias [1]. The other was a prospective cohort with low risk of bias [66] These last authors examined military women in their pregnancy and found a trend for preterm labour to be associated with lower perceived fatigue severity. Findings indicate that the perception of fatigue may be protective against PTD. Agbla et al. (2006) found no significant results.

Discussion

Principal findings

Ten low risk of bias studies and seven moderate studies were included in this systematic review. Several studies found significant positive associations between PTD and standing and walking, lifting and carrying and demanding posture. Six studies examined a combination of two or more tasks with physical effort, like carrying, walking and/ or a demanding posture, or used a cumulative occupational fatigue score. In all six studies a cumulative index of at least two or more tasks showed a positive association with PTD. Meta-analyses were performed with a random effects model. The results of case-control and cohort studies were reported separately in sub-groups. Depending on heterogeneity we combined the results in a single summary estimate. Physically demanding work during pregnancy, including standing and walking at work during pregnancy for more than three hours per day, lifting more than five kg, physical effort or physical exertion and jobs with a combination of two or more tasks with physical effort or an Occupational Fatigue Score of ≥ 2, is significantly associated with an increased risk of PTD. The exposure to physically demanding work mostly occurred during the first trimester. Six studies specified the exposure per trimester. In all of these studies the number of women exposed to physically demanding work diminished substantially as pregnancy progressed.

Strengths and weaknesses of the review

We feel that the strength of this review is that we focused on the effect of physical activities on the risk of PTD only among women working during pregnancy. Several recent publications have examined the effect of physical activity on pregnancy outcome [8, 16, 41, 61, 67, 68]. Takito et al. (2009) draws attention to the influence of different domains of daily physical activity which can have influence upon outcomes in pregnancy: occupational, household, leisure-time and commuting. In a recent review, Savitz and Murnane (2010) note that some studies of recreational physical activity have generated mixed results regarding PTD. In most European countries, socioeconomic inequalities in ill health are an important determining factor for entering and maintaining paid employment [63]. In some studies, working women are, on average, healthier and at

lower a priori risk of PTD and other adverse pregnancy outcomes than women who do not work [45, 56, 65]. Other studies could not confirm this association [27]. We assume that working women have a comparable lifestyle. To prevent bias, we only included studies with pregnant women in paid employment in exposure and control group.

This review deals with work-related physical load during pregnancy. Physical work can involve various activities. We distinguished lifting and carrying, prolonged standing and walking, demanding posture and physical effort. Employees often combine different physical activities. Therefore, we examined the effect of individual kinds of exposure, but also of a combination of two or more tasks with physical effort, or physically demanding work with other occupational exposure.

Strength of this review is that we included requirements for information about the exposure in the quality assessment (e.g. minimal duration, period or trimester of exposure, measured at different moments, timing and reason of reduced exposure). Three studies scored on three of the four items 9, [33, 53, 69]. Eight studies scored on two items [15, 17, 31, 37, 55, 59, 66]. The exposure mostly occurred during first trimester. It is obvious that the number of women exposed to all kinds of physically demanding work diminished substantially as pregnancy progressed.

A limitation of our review relates to the definition or determination of the level of exposure: in most studies it was based on self-assessment by the women. In 12 of the 17 studies, data on this were collected by interviewers (mostly trained nurses or experts) giving possibilities to go more into details about parts of the questions. In the meta-analyses we combined studies according to exposure categories with cut-off points mainly determined by the number of available data: standing and walking for more than three hours per day versus less than three hours, however in most studies this was actually more than five hours per day. For lifting, the cut-off point was more than 5 kg versus less than 5 kg but in some studies this was in reality more than 10 or sometimes 20 kg.

A possible source of error may be a wrong interpretation of health outcomes or response rates. All studies except one (Luke et al. 1995) obtained outcome data from hospital records, registers or birth certificates. Response rates were usually higher than 85%. In two studies the response rate was much lower [51, 53], leading to a moderate risk of bias score. Therefore, we think that this source of error may be limited.

In research on the effect of occupational exposure on PTD, bias and confounding may influence the results significantly. A substantial part of our data on physical work and pregnancy outcome is found in observational studies. Retrospective studies in particular can be susceptible to recall bias. Several maternal or fetal risk characteristics exist that have been associated with an increased risk of PTD. On one hand, we eliminated any

intrinsic differences between exposed and unexposed women, by including only studies in which controls also were engaged in the work force. On the other hand, our score on risk of bias assessed individual studies' attention to equal clinical and demographic factors.

A last limitation of our review may be that we did not consider work leave policies. Conflicting findings from studies on this topic could be related to the social and legislative environment. Saurel-Cubizolles et al. (2004) analysed the relation between PTD and working conditions in Europe to test whether employment-related risks varied by country of residence. Their findings suggest that employment related risks could be mediated by the social and legislative context in the country.

Strengths and weaknesses in relation to other studies

The results of the reviews and meta-analyses of Mozurkowich et al. (2000) and [6] that focus on physically demanding work and PTD are, for a major part, comparable to our results.

Bonzini et al. (2007) reviewed the relationship between PTD and five occupational exposures (long working hours, shift work, lifting, standing and heavy physical workload). They pooled 12 studies that compared standing for at least three hours with lower exposures. The summary estimate OR was 1.28 (95% CI 1.11 - 1.47), and that for the subset of six studies with low risk of bias was 1.26 (95% CI 0.96 - 1.66). An important difference between our review and Bonzini's is that we only included studies with pregnant women in paid employment in both exposure and control group. Bonzini included also studies with unemployed women. In particularly in the review by Bonzini et al. (2007) this resulted in a higher number of included studies. Mozurkowich et al. (2000) examined the association between prolonged standing, defined as more than three hours per day or the predominant occupational posture and PTD. This association, which was statistically significant (OR 1.26, 95% CI 1.13 - 1.40), was consistent across all study designs and meta-analytic methods. Physically demanding work, defined as heavy and/or repetitive lifting or load carrying, manual labor, or significant physical exertion was significantly associated with PTD (OR 1.22, 95% CI 1.16 - 1.29). On the basis of data from six studies with a total of 7719 women, Mozurkowich evaluated the association between a cumulative work fatigue score and PTD. This association was also significant (OR 1.63, 95% CI 1.33 - 1.98), and the results were consistent across analytic methods.

A difference between our review and the ones by Bonzini and Mozurkowich is the period of included studies. They also used data collected before 1990. Moreover, in our review we included detailed information about duration, period and timing of reduced exposure in the assessment of risk of bias. Work and exposure status tended to change during pregnancy towards lower levels of physically demanding work. Consequently, some women may have been considered as exposed to physically demanding work

although they rapidly benefit from a modification in their work. This would lead to an underestimation of the association between exposure and PTD. With our method of quality assessment we might have reduced the probability of this underestimation.

A last difference is that we included a study which also focussed on the results of eliminated or decreased exposure, due to legally justified preventive measures [15]. This study showed promising effects of preventive measures.

Meaning of the study: implications for clinicians or policymakers, unanswered questions and future research

Our findings should be interpreted with caution because of the limitations of observational studies and because of the fact that in general only small elevations of risks were found. However, the results are consistent with earlier meta-analyses and indicate a slight to moderate but consistent association of physically demanding work with an increased risk of PTD. PTD has proved resistant to many interventions (Goldenberg et al. 2008), but working conditions can be adjusted and remain a modifiable risk factor.

It is remarkable that, although the earlier reviews by Mozurkowich et al. (2000) and Bonzini et al. (2007) lead to similar results, the authors of these reviews drew different conclusions regarding the implications for work adjustment. While Mozurkowich et al. believe that their findings lend support to a call for a better national maternity leave policy for working women, Bonzini et al. are much more cautious. The evidence does not convince the authors enough to warrant restrictions on any of the activities considered in their review. However, they do recommend avoiding long work hours, prolonged standing, and physically demanding work, especially late in pregnancy, due to some uncertainties and the apparent lack of significant beneficial effects [6].

Some years ago, the reviews by Mozurkowich et al. (2000) and Bonzini et al. (2007) were used in the development of two evidence based guidelines on pregnancy and work, respectively in the Netherlands and in the UK (Netherlands Society of Occupational Medicine (NVAB) 2007; NHS Plus 2009). The difference in conclusions of these both reviews is reflected in the recommendations of these guidelines, regarding physically demanding work. The recommendation of the Dutch Guideline, partly based on the review by Mozurkowich et al. (2000) and studies by Koemeester et al. (1993; 1997), is to adjust working conditions after the 20th week of pregnancy. The limits recommended are the same as those referred to in legislation. They recommend to carry out these preventive measures at 16 weeks gestation. The Dutch government used the finding of the studies by Koemeester et al. (1993; 1997) for legislation on pregnancy.

The English guideline indicates that employers should reduce lifting, standing for >3 hours/day and very heavy physical activities for pregnant workers where possible, particularly in late pregnancy. However, if a pregnant worker who has been informed

of the possible risks wishes to continue, then there are insufficient grounds upon which to impose restrictions against her will.

Only one study included in our review was an intervention trial. More intervention studies are needed to confirm the effect of preventive measures on physically demanding work.

Based on our (and earlier) findings we recommend pregnant employees with increased risk on PTD, to adapt physically demanding work early in pregnancy, at 12 weeks. However, the effect of this recommendation also needs more research.

Conclusion

Physically demanding work, standing and walking, lifting and carrying, physical exertion and demanding posture during pregnancy may increase a woman's risk of PTD. A cumulative index of at least two tasks with physical effort or physically demanding work shows a positive association with PTD. In general, small to moderate elevations of risks were found. These results should be interpreted with caution because of the lack of accurate and objective exposure measurement.

Preventive measures on physically demanding work, taken before 20 weeks gestation, may reduce the risk of PTD in pregnant workers and health problems for the pregnant women herself. Future research with reliable determination of exposure is needed to confirm the effect of preventive measures. Furthermore, we recommend pregnant employees with increased risk on PTD, to adapt physically demanding work early in pregnancy, at 12 weeks. The effect of such recommendation needs to be evaluated.

Conflict of interest The authors declare that they have no conflict of interest.

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APPENDIX 1 SUMMARY OF SEARCH STRATEGIES

PubMed: combinations of amongst others:
"Pregnancy"[Mesh] OR "Pregnant Women"[Mesh]
"Work"[Mesh] OR work* OR occupation* OR employ*
"Premature Birth"[Mesh] OR "Infant, Premature"[Mesh]
"Lifting"[Mesh] OR manual* OR pull* OR load* OR handl* OR push* OR lift* OR stand* OR kneel* OR "squat" OR "Physical Exertion"[Mesh]

EMBASE and NIOSHTIC-2: Combinations of amongst others:
(pregnant or pregnancy) and (lifting or manual* or pull* or load* or handl* or push* or lift* or stand* or kneel* or squat* or prolonged standing or physical load) and (preterm or premature)

Shift work, long working hours and preterm birth: a systematic review and meta-analysis

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3

Introduction

In Europe, as in most parts of the world, women of reproductive age now comprise a substantial proportion of the total workforce [1]. In the Netherlands, the average proportion of women with paid employment is 65% [8]. At present, women continue with their work during pregnancy, in The Netherlands often even to a gestational age of 36 weeks. Current European Union legislation requires employers to assess health and safety risks to pregnant workers, and where possible to minimize them. Especially in the health care sector, where the majority of employees is female, several potential hazardous factors for pregnancy exist, such as physically demanding work, shift work, long working hours or heavy workload that could have an adverse effect on pregnancy outcome.

In the past decades ample research has been done to investigate the relationship between working conditions and adverse pregnancy outcomes. Among those adverse pregnancy outcomes, preterm birth (PTB), i.e. live birth before 37 weeks of gestation, is still considered to be the most important cause of perinatal mortality and morbidity. In 2000, Mozurkewich et al. published a meta-analysis in which they evaluated the association between shift work and long working hours and preterm birth. They found that, taking all study designs into account, for shift work and long working hours the pooled odds ratios were respectively 1.24 (95% CI 1.06-1.46) and 1.03 (95% CI 0.92-1.16). Their findings lend further support to calls for a better national maternity leave policy for working women{15}. In 2007, Bonzini et al. performed a comparable meta-analysis with similar results concerning shift work (pooled RR 1.20 (95% CI 1.01-1.42)). They concluded that the evidence was not sufficiently compelling to justify mandatory restrictions on physical activities and working conditions, but that it would be prudent to advice against long working hours, prolonged standing and heavy physical work [1]. They also stated that there seemed to be no reason to recommend discontinuation of shift work during pregnancy [1]. In 2011, Bonzini et al. repeated their meta-analysis concerning shift work and preterm delivery and included also more recent studies. Again they found small elevations of risk (pooled RR 1.16 95% CI 1.00-1.33) on PTB as well as small for gestational age (SGA) and low birth weight (LBW). Again they concluded that the available evidence does not make a compelling case for mandatory restrictions on shift work in pregnancy, but that it would be prudent to reduce the exposure to shift and night working [3].These findings suggest that it is still difficult to provide an explicit advice to pregnant women whether or not change there working conditions concerning shift work. The absence of consistent statistically significant results still produces indecisiveness upon health professionals.

Over the years, not only the female proportion of the workforce changed but also the working conditions for pregnant women. It is more common to have modifications of working conditions during pregnancy, a paid maternity leave or health benefits by law.

To provide a more contemporary answer whether or not nowadays specific physical activities or working conditions exert an influence on preterm birth we conducted a meta-analysis. Therefore we used only more recent studies for this systematic review instead of some of the more dated studies in earlier reviews [1, 3, 15]. Using more recent studies will give a better reflection of today's risk of PTB. In this way we are taking the changes in working population and also the changes in working conditions for pregnant women into account. In their reviews, Bonzini et al. (2007 and 2011) compared women who had a paid employment during their pregnancy with women who did not. We believe that those two groups are not comparable because of the difference in exposure to certain kinds of risk factors. For that reason we only included studies that compared women who had a paid employment during pregnancy and had differences in the degree of exposure to probable risk factors. We focused on the potential hazardous activities shift work and long working hours. Our aim was to review and summarize the pre-existing evidence concerning the effect of shift work or long working hours on the risk of preterm birth in order to try to provide a more concrete advice that can be given to pregnant employees whether or not they are at risk for PTB.

Methods

We performed a systematic review and meta-analysis on the association between shift work, long working hours and PTB. This review was performed according to the PRISMA-statement [13].

Search strategy

A series of literature searches was conducted using the electronic databases MEDLINE (by PubMed) and EMBASE. We limited our search to the articles published between 1990 and November 1st 2013 written in English, German, French, or Spanish. Our search aimed at the gestational age at delivery (outcome) for pregnant women (population) who were exposed to shift work or long working hours (exposure) during their pregnancy. Medical subject heading terms and keywords were chosen that represented our population and the specific exposure related to the outcome preterm birth. For this search we used all combinations of the following terms: "pregnancy, pregnant women, expect*, mother*, reproductive health, women, work, employ*, occupation*, work* hours, shift work, work shifts, night shift, night work, long working hours, irregular working hours, excessive hours, overtime, work schedule tolerance, regular working hours, preterm birth, premature, premature birth, delivery, birth, labour, adverse pregnancy outcome, pregnancy complications, labour complications, gestational age, trimester, fetal morbidity, maternal morbidity". Reference lists of relevant studies were checked to identify possible additional relevant citations not captured by the electronic searches.

Study selection

Titles and abstracts were examined independently by two reviewers (MM and MB) and duplicates or irrelevant references were eliminated. In case of disagreement or doubt, the abstracts or articles were assessed in a discussion panel (MM, MB, CH) and either included or excluded from the list of remaining articles. Studies were included if they met the following criteria: (1) the exposure was shift work or long working hours, (2) the outcome was preterm birth, i.e. birth between 26 and 37 weeks of gestation, (3) studies were observational or interventional with original data, (4) the data in the study had to be obtained after 1990. Full reports of all relevant articles were retrieved on paper and reviewed by two reviewers (MM and MB). After performing this selection, a list of primary articles remained that was eligible for detailed evaluation.

Data collection

Every selected article that seemed relevant was submitted to a detailed evaluation. For this evaluation a data extraction form was developed in Microsoft Office Access that was pilot-tested and refined on five included articles. In this form all data on study characteristics, methodology (i.e. specification of study population, definitions and assessment of exposure, data collection, duration of follow up), results and potential bias were extracted from the papers. All data of the included studies were extracted by one reviewer (MM) and checked by a second reviewer (MB). Possible disagreements were discussed mutually (MM, MB). When no consensus could be reached, a third reviewer (CH) was consulted.

Quality assessment

Every included article was scored for its quality according to a standardized form based on the methodology developed by the Scottish Intercollegiate Guidelines Network (SIGN –methodology). The same methodology was used by the UK Royal College of Physicians when they developed the national guideline 'Physical and shift work in pregnancy' [16]). Quality assessment was conducted by two reviewers (MM and MB) and disagreements were resolved with a third reviewer (CH). Studies were scored by giving a proportional amount of points for degree of presence of the following eight items: (1) the transparency of population sampling (maximum 2 points), (2) whether or not a power analysis was performed (maximum 1 point), (3) the response rate (maximum 3 points), (4) the intelligibility of exposure assessment (maximum 5 points), (5) outcome defined (maximum 1 point), (6) whether or not bias occurred (maximum 2 points), (7) consideration of potential confounders (maximum 2 points), (8) whether or not an effect size (OR or RR) was rated including a confidence interval (maximum 2 points). For these items there was a maximum score of 18 points. When a paper scored more than 13 points (approximately 75% of the maximum score)it was qualified by us as a high quality study. When the score was between 9 and 13 points the study was qualified as moderate and with less than 9 points (approximately 50% of the maximum score) it was qualified as poor. These last studies were excluded from further analysis.

Data analysis

A meta-analysis with a random effects model was performed using RevMan 5 software (RevMan 2012). The generic inverse variance method was used to pool the studies. The odds ratios and the 95% confidence intervals as reported by the authors were recalculated into the natural log of the OR and its standard error, which were used as input for RevMan. Because the incidence of the events was under 10% in all cases, we equated odds ratios with relative risks and finally present the results as relative risks. From the studies, we always took the risk estimate that was most adjusted for confounders. We reported the results of case-control and cohort studies separately in sub-groups and depending on heterogeneity combined them in a single summary estimate. In case the authors had not provided an effect estimate, we calculated a relative risk and its standard error [20]. Studies were combined according to the following exposure categories: 1) working more than 40 hours per week versus fewer hours per week, 2) working in shift work versus no shift work.

If results were reported per trimester, we combined these first in a separate meta-analysis and used the pooled estimate of the three trimesters as input in the main analysis. We measured statistical heterogeneity with the I^2 statistic with the following interpretation of its value [10]: less than 40% not important, 30% to 60% moderate heterogeneity, 50% to 90% substantial heterogeneity and more than 75% considerable heterogeneity.

We made separate analyses of studies that measured exposure during the first, second and third trimester when more than three studies were available that reported these results. We also performed a separate analysis to find out how sensitive the results were for the risk of bias in the included studies. For this analysis only studies with a score of at least 14 were included.

Results

Study selection

The electronic search resulted in a total of 530 citations. They were checked on titles and abstracts and from this 26 primary articles were selected. From the reference lists of these articles another 16 eligible articles were retrieved which lead to an initial 42 primary articles for further evaluation. After verification of the data, 25 articles were excluded because they did not meet our criteria (exposure, outcome, study type and timing or data obtainment). The remaining 17 articles were included in the primary review. After scoring their quality assessment only one paper [27] was of poor quality. This paper was excluded from this meta-analysis leaving 16 final articles for inclusion in this systematic review [2, 4, 5, 6, 9, 11, 12, 14, 17, 19, 21, 23, 24, 25, 26, 28]. A summary of this selection process is shown in Figure 1.

Study characteristics

The general characteristics of the included articles are shown in Table 1. There were six prospective cohort studies and five retrospective cohort studies; four studies had a case-control design and one study was cross-sectional. The method of exposure assessment most often used was the questionnaire, five times after delivery, four times antenatal and in one case there was an unknown timing of assessment. A personal interview (sometimes by phone) was used seven times of which three times antenatal, three times after delivery and in one case both before and after delivery. Of the included sixteen studies, eight studies were qualified to be of high quality [2, 6, 9, 21, 24-26, 28]. Not all of the included studies examined the association of both shift work and working hours on preterm birth. Therefore a distinction was made between the studies that examined the exposure shift work and the studies that examined the exposure working hours.

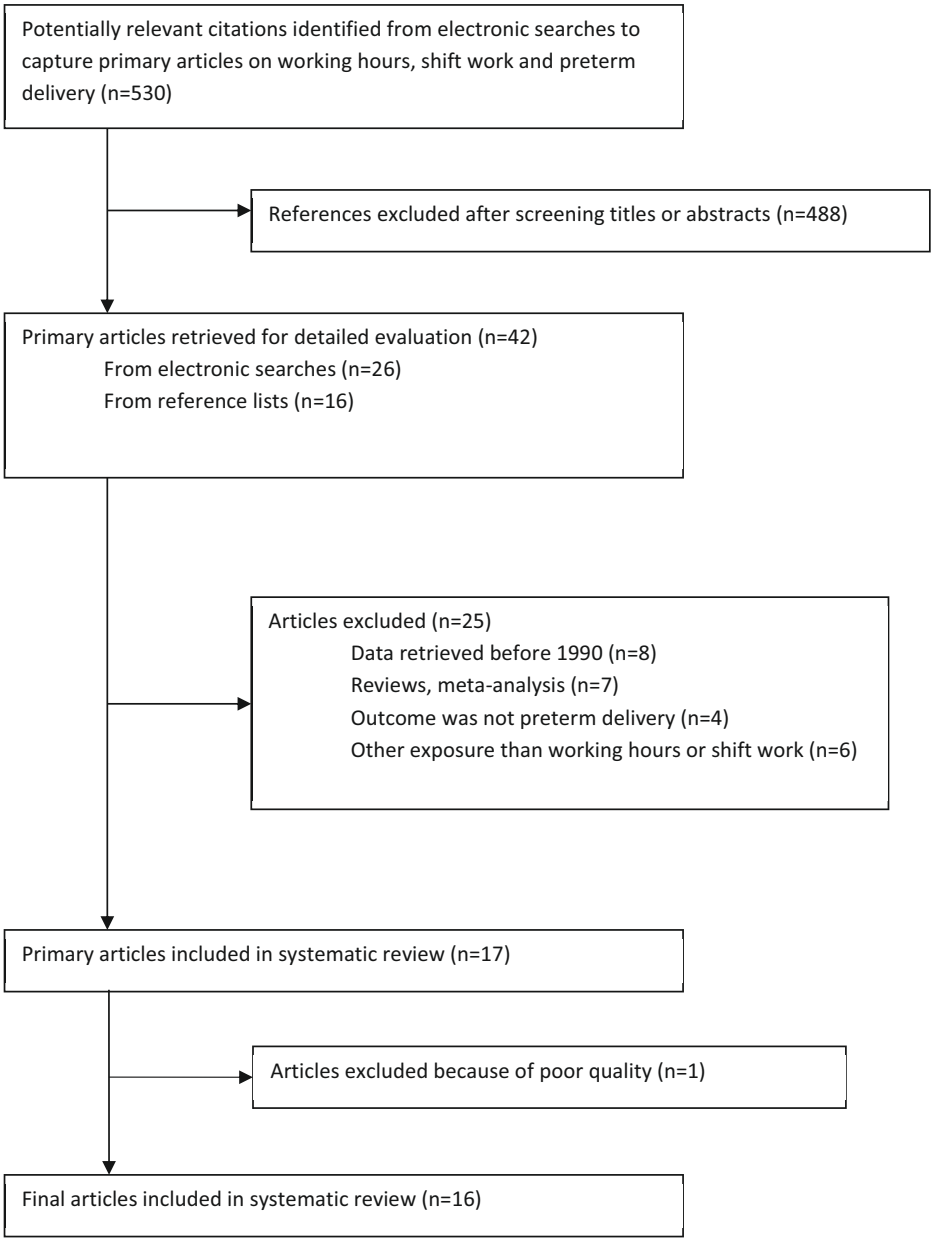

Figure 1. Flowchart selection process included articles

Table 1. General study characteristics of the included articles

First author (year)	Country	Study period	Study Design	Exposure(s)	Method of exposure assessment	Outcome
Bonzini (2009)	United Kingdom	1999 - 2003	Prospective cohort	Working hours Working night shifts	Interview at 34 weeks gestation	Preterm delivery (34-37 weeks)
Both (2010)	United Kingdom	1991 - 1992	Retrospective cohort	Shift work	Antenatal questionnaire	Preterm delivery (<37 weeks)
Cerón-Mireles (1996)	Mexico	1992	Cross-sectional	Working hours	Interview within 24 hours after delivery	Preterm delivery (<37 weeks)
Croteau (2007)	Canada	1997 - 1999	Case-control	Working hours Shift work Schedule regularity	Computer assisted telephone interview (within one month after delivery)	Preterm delivery (<37 weeks)
Escribà-Agüir (2001)	Spain	1995 - 1996	Case-control	Working hours	Questionnaire (2 days after delivery) by trained interviewer	Preterm delivery (22-36 weeks)
Jansen (2010)	The Netherlands	2002 - 2006	Retrospective cohort	Working hours	Questionnaire at >= 25 weeks	Preterm delivery (<37 weeks)
Lawson (2009)	USA	2001	Retrospective cohort	Work schedule Night work Working hours	Questionnaires (up to 8 years) after delivery	Preterm delivery (<37 weeks)
Luke (1995)	USA	1995	Case-control	Working hours Shift work	Questionnaire after delivery	Preterm delivery (<37 weeks)

Table 1. Continued.

First author (year)	Country	Study period	Study Design	Exposure(s)	Method of exposure assessment	Outcome
Niedhammer (2009)	Ireland	2001	Prospective cohort	Work schedule Working hours	Questionnaires (moment unknown)	Preterm delivery (<37 weeks)
Pompeii (2005)	USA	1995 - 2000	Prospective cohort	Night work Long working hours	Telephone interview (at 24-31 weeks) Face-to-face interview after delivery, before discharge from the hospital	Preterm delivery (<37 weeks)
Saurel-Cubizolles (2004)	16 European countries	1994 - 1997	Case control	Night work Shift work Working hours	Questionnaires after delivery Interview after delivery	Preterm delivery (<37 weeks)
Shirangi (2009)	Australia	2002	Retrospective cohort	Working hours	Questionnaire (self-administered) after delivery	Preterm delivery (<37 weeks)
Snijder (2012)	The Netherlands	2002-2006	Prospective cohort	Working hours Night work	Questionnaire during mid-pregnancy (at 30 weeks)	Preterm delivery (<37 weeks)
Stinson (2003)	USA	Unclear	Retrospective cohort	Shift work	Questionnaire (at 22-26 weeks) Phone call	Preterm delivery (<37 weeks)
Tuntiseranee (1998)	Thailand	1994 - 1995	Prospective cohort	Working hours	Expert Interview at 17 and 32 weeks	Preterm delivery (<37 weeks)
Zhu (2004)	Denmark	1998 - 2001	Prospective cohort	Shift work	Telephone interview (11-25 weeks and 27-37 weeks	Preterm delivery (34-37 weeks) Very preterm birth <34 weeks

Shift work

Of the sixteen studies that were analysed eleven [2, 4, 6, 12, 14, 17, 19, 21, 24, 25, 28] examined the relationship between shift work and preterm birth (Table 2). Most of the articles did not find a statistically significant relationship between shift work and preterm birth. Only Both et al. (2010) and Luke et al. (1995) described a significant relationship between shift work and preterm birth. However they described conflicting results. Both et al. (2010) reported that working night shifts in the third trimester of the pregnancy was a protective factor for the occurrence of preterm birth (OR 0.67 (95% CI 0.47-0.95). Luke et al. (1995) reported that both working evening shifts and night shifts during the whole pregnancy increased the risk of preterm birth (respectively OR 1.6 and OR 1.4). The other articles [2, 6, 12, 17, 19, 21, 24, 25, 28] presented results that show a trend of a negative influence of working other moments than daytime on preterm birth but these results do not reach statistical significance.

The data of all eight cohort studies and three case control studies that compared women working in rotating shifts or night shifts only during their pregnancy with women that worked regular day-time hours were pooled. The summary estimate OR was 1.04 (95% CI 0.90-1.20) (p=0.39, I^2=29%) showing no significant association between shift work and PTB (Figure 2). With the I^2 being 29%, it represents a relative homogeneous group of studies.

Table 2. Evidence table exposure to shift work and preterm birth (PTB)

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
Bonzini (2009)	*Night shifts*:		11 weeks	Not stated	14
	11 weeks: 131	11 weeks: OR 1.14 (95% CI 0.43-2.93)	19 weeks	No data available of changing working conditions	
	19 weeks: 116	19 weeks: OR 1.07 (95% CI 0.37-3.05)	34 weeks		
	34 weeks: 33	34 weeks: -			
Both (2010)	Preterm birth: 494	Night shifts (3rd trimester): OR 0.67 (95% CI 0.47-0.95)	Whole pregnancy	Not stated Unclear if missing data is excluded	13
Croteau (2007)	*Work schedule:*	*Schedule:*	Whole pregnancy	At least 4 weeks from the first month	15
	Days: 757cases/ 2772controls	Days: reference		At least 20h/wk	
	Evenings: 345cases/ 1218controls	Evenings: OR 1.0 (95% CI 0.8-1.2)		Missing data excluded	
	Nights: 126cases/ 483controls	Nights: OR 0.9 (95% CI 0.7-1.2)			
	Unknown: 7cases/ 24controls				
	Schedule regularity:	*Regularity*:			
	Regular 1045cases/ 3803controls	Regular: reference			
	Irregular/shift work: 190cases/ 694controls	Shift work: OR 1.0 (95% CI 0.9-1.3)			
Lawson (2009)	*Shifts*:	*Shifts*:	First trimester	Min 1h/wk during 1st trimester	11
	Days only: 409	Days: Reference		Missing data excluded	

Table 2. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	Nights only: 52	Rotating day/evening: RR 1.0 (95% CI 0.7-1.3)			
	Rotating shifts, including nights: 35	Nights only: RR 1.1 (95% CI 0.8-1.5)			
	Day/evening rotating: 91	Rotating shifts, including nights: RR 1.1 (95% CI 0.5-1.1)			
	Missing: 1				
Luke (1995)	*Shift work*:	*Shift work*:	Whole pregnancy	Not stated	10
	Days: 114cases/ 813 controls	Days: reference		Missing data excluded	
	Evenings: 60 cases/ 268 controls	Evening: OR 1.6			
	Nights: 36 cases/ 179 controls	Nights: OR 1.4 (p=0.01)			
Niedhammer (2009)	*Shift work*:	*Shift work*:	Unclear	Not stated	13
	No: 17	No: Reference		No data available of changing working conditions	
	Yes: 6	Yes: OR 1.68 (95% CI 0.44-6.34)			
Pompeii (2005)	*Regular night work:*	*Regular night work*:	1-12 weeks	Working women for at least 28 days during the 1st trimester	13
	1st trim: 229 cases	No: Reference	13-27 weeks	Missing data excluded	
	2nd trim: 210 cases	Yes: 1st trim: OR 1.5 (95% CI 1.0-2.1)	28-31 weeks		
	3rd trim: 135 cases	2nd trim: 1.6 (95% CI 1.0-2.3)			
		7th month: OR 1.8 (95% CI 0.8-3.9)			

Table 2. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
Saurel-Cubizolles (2004)	*Night work*: 2300	*Night work:* Yes: OR 0.92 (95% CI 0.7-1.1)	First trimester	Worked at least 3 months from the start of pregnancy	15
	Shift work: 2300	*Shift work:* Yes: OR 0.97 (95% CI 0.8-1.1)		Unclear if missing data is excluded	
Snijder (2012)	*Night shifts:*	*Night shifts:*	Whole pregnancy	Worked before pregnancy or started working during the first trimester	15
	No: 4069	No: Reference			
	Occasionally: 137	Occasionally: OR 0.87 (95% CI 0.38-2.01)			
	Often: 60	Often: OR 1.29 (95% CI 0.46-3.65)			
Stinson (2003)	Works at night: 22	*Night work*: OR 1.80 (95% CI 0.93-3.53)	Second trimester (22-26weeks)	Not stated	14
			Monthly	Unclear if missing data is excluded	
Zhu (2004)	*Preterm birth*:	*Preterm birth:*	Whole pregnancy	Not stated	15
	Daytime work: 1374	Daytime work: reference		Missing data taken into account	
	Evening work: 41	Evening work: OR 0.88 (95% CI 0.63-1.63)			
	Night work: 13	Night work: OR 0.70 (95% CI 0.33-1.75),			
	Rotating (no night): 145	Shift work (no night): OR 1.09 (95% CI 0.76-1.30)			
	Rotating: 126	Shift work (with night): OR 0.97 (95% CI 0.61-1.11)			

Table 2. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	Very preterm birth: Daytime: 348 Evening 12 Night 3 Rotating (no night) 36 Rotating 34	*Very preterm birth:* Daytime work: reference Evening work: OR 1.00 (95% CI 0.55-1.82)			

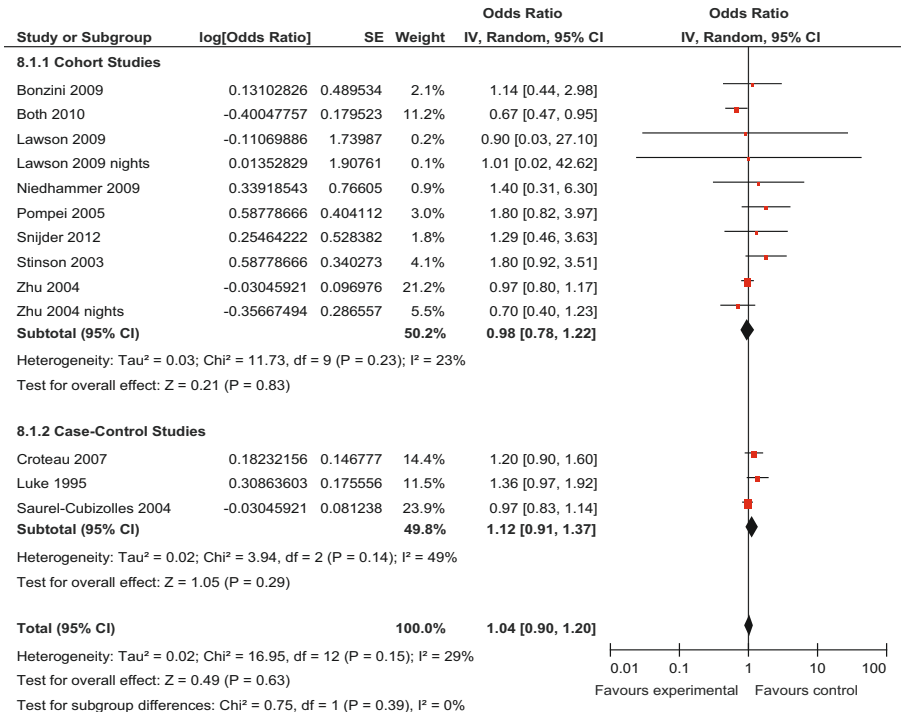

Figure 2. Forest plot of comparison shift work versus no shift work

Working hours

Thirteen of the sixteen studies [2, 5, 6, 9, 11, 12, 14, 17, 19, 21, 23, 24, 26] analysed the relationship between the amount of working hours per week and preterm birth (Table 3). Among these thirteen studies there were five prospective cohort studies, four case-control studies, three retrospective cohort studies and one cross-sectional study. In most of the studies a slightly positive association between working hours and PTB was seen. Only the study by Pompeii et al. (2005) and partly the study by Bonzini et al. (2009) -in the last trimester- found an inverse relationship between long working hours and preterm birth. In all other studies association between working more than 40 hours a week and preterm birth was found [6, 9, 11, 14, 21, 23, 24, 26] although in most of the studies this did not reach statistical significance.

Table 3. Evidence table exposure to long working hours and preterm birth (PTB)

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
Bonzini (2009)	*Working hours:*	*Working hours (>= 40h/wk):*	11 weeks	Not stated	14
	11 weeks: 244	11 weeks: OR 1.03 (95% CI 0.49-2.15)	19 weeks	No data available of changing working conditions	
	19 weeks: 236	19 weeks: OR 1.01 (95% CI 0.47-2.17)	34 weeks		
	34 weeks: 130	34 weeks: 0.59 (95% CI 0.17-2.03)			
Cerón-Mireles (1996)	*Working hours:*	*Working hours:*	Whole pregnancy	Worked at least 3 months during pregnancy	11
	3-25: 22	3-25: OR 0.78 (95% CI 0.51-1.19)		Missing data taken into account	
	26-40: 136	26-40: reference			
	41-50: 76	41-50h/week: OR 0.91 (95% CI 0.70-1.19)			
	> 50: 54	>50h/week: OR 1.21 (95% CI 0.90-1.62)			
Croteau (2007)	*Working hours/wk:*	*Working hours:*	Whole pregnancy	At least 4 weeks from the first month	15
	20-34: 325cases/ 1335controls	20-34 h/wk: reference		At least 20h/wk	
	35-40: 775cases/ 2729controls	35-40h/wk: OR 1.2 (95% CI 1.0-1.4)		Missing data excluded	
	>40: 135cases/ 433controls	>40h/wk: OR 1.2 (95% CI 1.0-1.6)			
Escribà-Agüir (2001)	*Weekly working hours:*	*Working hours:*	First trimester	Worked at least the first 3 months	14
	< 35h/wk: 54 cases/ 77 controls	<35h/wk: reference		Unclear is missing data is excluded	

Table 3. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	35-40h/wk: 121 cases/ 204 controls >40h/wk: 53 cases/ 67 controls	35-40h/wk: OR 0.98 (95% CI 0.63-1.52) >40h/wk): OR 1.06 (95% CI 0.62-1.80)			
Jansen (2010)	*Weekly working hours: 4408*	*Working hours:* 1-24h/wk: reference 25-39 h/wk: OR 1.37 (95% CI 0.91-2.06) >40h/wk: OR 1.30 (95% CI 0.81-2.10); p for trend 0.345	5-18 weeks 18-25 weeks 25-39 weeks	Min 1h/wk Non-response analyses	13
Lawson (2009)	*Hours worked:* 1-20 h/wk: 101 21-40 h/wk: 371 >= 41 h/wk: 116	*Working hours:* 1-20h/wk: RR 0.7 (95% CI 0.6-1.0) 21-40: reference >= 41h/wk: RR 1.0 (95% CI 0.8-1.4)	First trimester	Min 1h/wk during 1st trimester Missing data excluded	11
Luke (1995)	*Working hours:* >= 36/wk: 69 cases/ 559 controls >36h/wk: 141 cases/ 701 controls	*Working hours un-adjusted* =<36h/wk: reference >36h/wk: OR 1.6 (95% CI 1.1-2.2) *Working hours Adjusted (=<36h or >36h):* OR 1.6 (95% CI 1.1-2.2)	Whole pregnancy	Not stated Missing data excluded	10
Niedhammer (2009)	*Working hours:*	*Working hours:*	Unclear	Not stated	13

Table 3. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	<40h/wk: 14	<40h/wk: reference		No data available of changing working conditions	
	>= 40 h/wk: 9	>= 40h/week: OR 2.25 (95% CI 0.69-7.32)			
Pompeii (2005)	*Hours worked/wk:*	*Working hours: <34 h/wk:*	1-12 weeks	Working women for at least 28 days during the 1st trimester	13
	1st trim 299 cases	1st trim: OR 1.0 (95% CI 0.8-1.3)	13-27 weeks	Missing data excluded	
	2nd trim: 210 cases	2nd trim OR 1.0 (95% CI 0.8-1.4)	28-31 weeks		
	3rd trim: 135 cases	3rd trim OR 1.0 (95% CI 0.7-1.3) *Working hours 35-45 h/wk: reference* *Working hours >46h/week:* 1st trim: 0.6 (95% CI 0.4-0.9) 2nd trim OR 0.4 (95% CI 0.2-0.8) 3rd trim OR 0.3 (95% CI 0.1-0.7)			
Saurel-Cubizolles (2004)	*Working hours: 2221cases*	*Long working hours:*	First trimester	Worked at least 3 months from the start of pregnancy	15
		<30h/wk: OR 1.06 (95% CI 0.9-1.3)			
	Countries A1: 936	30-39 h/wk: reference			

Table 3. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	Countries A2: 859 Countries B: 534	40-42h/week: OR 1.09 (95% CI 0.9-1.3) >43h/week: OR 1.33 (95% CI 1.1-1.6) *Countries A1:* < 30h/wk: OR 1.0 (95% CI 0.8-1.3) 40-42h/wk: OR 0.85 (95% CI 0.7-1.1) >=43 h/wk: OR 1.12 (95% CI 0.8-1.5) *Countries A2:* <30h/wk: OR 1.04 (95% CI 0.8-1.4) 40-42h/wk: OR 1.20 (95% CI 0.9-1.5) >=43 h/wk: OR 1.4 (95% CI 1.0-1.9) *Countries B:* <30h/wk: OR 1.38 (95% CI 0.9-2.2) 40-42h.wk: OR 1.43 (95% CI 1.0-2.1) >=43 h/wk: OR 1.65 (95% CI 1.0-2.7)			
Shirangi (2009)	*Working hours:* <35h/wk: 323	Working hours: <35h/wk: reference	Whole pregnancy	Not stated Missing data excluded	10

Table 3. Continued.

First author (year)	Number in analysis (n)	Association size (CI 95%)	Exposure timing	Minimal duration exposure	Quality score
	35-45h/wk: 214	35-45h/week: Crude RR 1.61 (95% CI 0.84-3.07)			
	>45h/wk: 199	>45h/week: Crude RR 1.93 (95% CI 1.03-3.61)			
Snijder (2012)	*Work hours:*	Work hours:	Whole pregnancy	Worked before pregnancy or started working during the first trimester	15
	1-24h/wk: 1191	1-24 h/wk: Reference			
	25-39 h/wk: 2214	25-39 h/wk: OR 1.29 (95% CI 0.89-1.87)			
	>40 h/wk: 1084	>40 h/wk: OR 1.32 (95% CI 0.85-2.03)			
Tuntiseranee (1998)	*Working hours:*	*Long working hours:*	Second trimester	Not stated	16
	<=50h/wk: 49	<=50h/wk: reference	Third trimester	Missing data excluded	
	51-60h/wk: 48	51-60h/week: OR 0.9 (95% CI 0.4-2.0)			
	>+61 h/wk: 90	>60hweek OR 1.6 (95% CI 0.8-5.3)			

For the meta-analysis we pooled the data of all eight cohort-studies and three case control studies comparing women working more than 40 hours per week during their pregnancy versus fewer weekly working hours. The summary estimate OR was 1.25 (95% CI 1.01-1.54) (p=0.23, I^2=62%) showing a marginally significant association between long working hours and PTB (Figure 3). The forest-plot of this meta-analysis shows little homogeneity because one study reported the exposure to be significantly beneficial which yielded an I^2 of 62%.

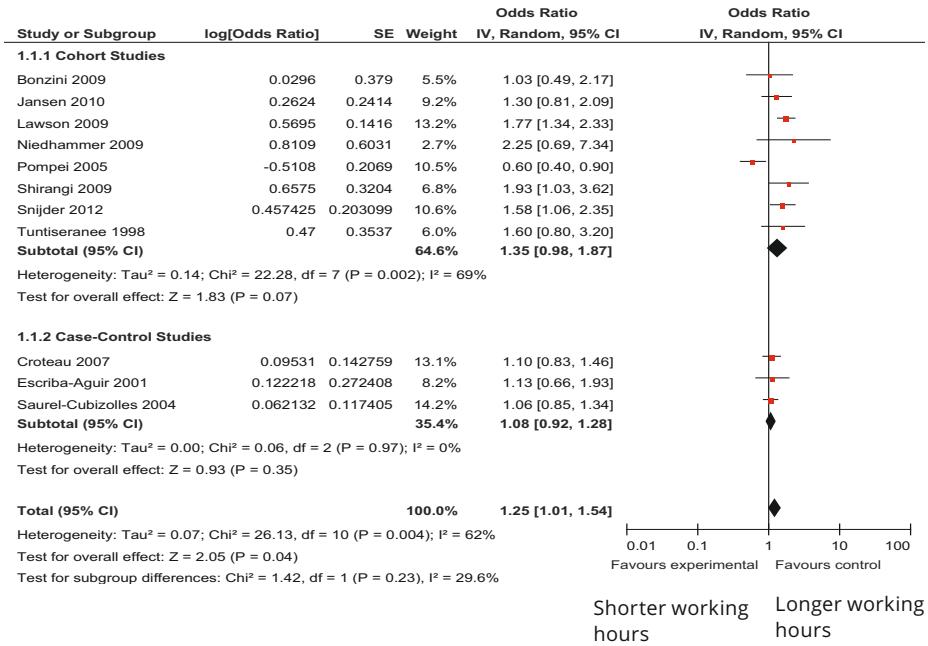

Figure 3. Forest plot of comparison longer working hours (> 40 h/week) versus shorter working hours

Discussion

In this systematic review eight high quality studies and eight moderate quality studies were included. Of all the selected studies for this review four [4, 14, 19, 23] presented statistically significant results concerning an association between PTB and working in shifts or long working hours per week. All four studies were of moderate quality. Pooling of the data in meta-analyses revealed that the overall summary estimates of the odds ratio's showed no statistically significant associations between shift work and PTB and an only marginally significant association between long working hours and PTB. In the case of long working hours, a positive association with PTB was seen in most of the

included studies, resulting in a summary estimated OR of 1.25. Because of a substantial heterogeneity in this meta-analysis this conclusion has to be taken with caution. The results of our meta-analyses are comparable with results from earlier reviews [1, 3, 15, 18] although in some of these reviews statistically significant but small associations were found.

Luke et al. (1995) and Pompeii et al. (2005) show that working night shifts during the whole pregnancy make women more at risk for PTB. Both et al. (2010), meanwhile, report that pregnant women working night shifts during the third trimester are less at risk for PTB. In case of long working hours, Luke et al. (1995) conclude that working long hours is a risk for PTB, where Pompeii et al. (2005) conclude otherwise.

'Preventive effects' from exposure to shift work or long working hours on the risk of PTB have been seen earlier in several studies [4, 11, 12, 19]Pompeii et al. 2005). This might be caused by the 'healthy worker effect': pregnant women who feel healthy are more likely to work shifts or long working hours a week in the last trimester. And because of their 'healthy pregnancy' their risk of delivering preterm is small a priori. This may be of influence on the data in all the selected studies. It will be difficult to retrieve unbiased data with regards to the healthy worker effect. It seems that the best trimester for avoiding the healthy pregnancy effect is the first trimester. But then again, some first trimester pregnancy symptoms, for example nausea and fatigue, can be hampering a pregnant woman's health causing changes in her working conditions, where the second and third trimester can go by relatively uncomplicated for her.

Three studies [9, 11, 21] restricted themselves to the first trimester. One study was restricted to the second trimester [25] and two studies [4, 26] observed exposure in two different trimesters. Nine studies [2, 5, 6, 11, 14, 19, 23, 24, 28] evaluated working conditions in the whole pregnancy. Therefore it is hard to compare the results of all studies together because different trimesters can have a different impact on the working conditions during that trimester. Also, because of the very few studies that distinguished an Odds Ratio per trimester it was not possible for us to produce a summary estimate Odds Ratio per trimester.

Strengths and limitations of this review

A strength of this review is the focus on pregnant women in the working population. The previous reviews included articles that also compared pregnant women with exposure to shift work or long working hours with women that were unemployed. This may introduce risk of bias. Women in paid employment will have other kinds of conditions in which they exert physical activities than women who are unemployed. Our assumption is that women with paid employment have comparable lifestyles. To prevent bias as much as possible, we therefore only included studies that included women with paid employment in the exposure group as well as in the control group.

Another strength of this review is that detailed information is gathered about the exposure in our quality assessment (e.g. minimal duration, period or trimester of exposure, measured at different moments, timing and reason of reduced exposure) of the included studies. Five studies scored on three of the four items [6, 12, 19, 24, 26]. Eight studies scored on two items [2, 4-6, 9, 11, 21, 25, 28]. The timing of exposure mostly occurred at moments during the whole pregnancy (8 studies).

This criterion together with the other quality criteria applied by us, proved to be a hurdle for a number of cross-sectional studies that were included in previous reviews. All of the studies included in our review were cohort studies or case control studies.

All studies show a decrease in number of women exposed to shift work or long working hours as pregnancy progresses. In general this leads to a decline in study population size in the second but especially in the third trimester. Consequently it will be harder to find data that give significant results regarding work-related risks for the pregnancy. Moreover, it is likely that because of perceived physical discomforts due to pregnancy, many women did not feel themselves capable anyhow of working the whole pregnancy. In general this will lead to a decrease in the number of working pregnant employees in the third trimester. This will influence the statistical power of many of the studies as it will be harder to get significant results. In our review, nine of the sixteen studies considered the third trimester in their study. Only two studies [2, 26] stated the exact amount of working pregnant women in the third trimester. Tuntiseranee et al (1998) and Bonzini et al. (2009) showed that respectively 59% and 60% of their study population who worked during the first trimester still worked at the third trimester [2, 26]. Due to the scarcity of high quality studies, especially high quality studies that focus on the third trimester, a firm conclusion regarding the risk of working shifts or long working hours cannot be drawn and the obtained results of this review have to be interpreted with caution.

As the number and type of the confounders considered per study were different, this could have had implications for the study results. Therefore, we checked whether the strongest associations between shift work or longer work hours and PTB were found among the studies with the least rigid statistical controlling for potential confounders. For shift work, the studies by Stinson and Lee (2003) and Pompeii et al (2005) and for long working hours, the studies by Niedhammer et al (2009), Shirangi et al (2009) and Lawson et al (2009) found the strongest associations. In all these studies, however, adjustment was made for the most relevant confounders.

Compared to other reviews about working conditions and pregnancy outcome [1, 3, 15] we constrained ourselves to studies that collected their data after 1990. We deliberately choose this restriction because we wanted to focus on more recent data for several reasons. First, the female participation rate in the working population is increasing in the last decades leading to more pregnant employees. We expected that more recent

studies would have a higher probability of including larger populations, resulting in more reliable study results and a better confidence of the data. Second, also the working conditions have changed for female employees. In several countries the medical system accomplished working benefits, or restrictions, for pregnant employees. When focussing on more recent studies the effect of introducing such benefits could be evaluated. The major features of the different reviews are summarized in Table 4.

Table 4. Comparison of differences and overlap between systematic reviews on the relationship between shift work and long working hours and preterm delivery

First author	Number of included studies	Publication period of studies	Overlap in included studies with review by van Melick et al.
Mozurkewich 2000	13	1983-1998	3
Bonzini 2007	22	1984-2005	5
Bonzini 2011	17	1984-2009	8
Van Melick 2013	16	1990-2012	16

A limitation of the study is the definition of long working hours. Five studies considered working more than 40 hours per week as long working hours, four studies set the definition at working more than 35 hours per week, one study set the limit at more than 46 hours, one study set the limit at more than 50 hours per week and also one study defined long working hours as working more than 25 hours per week. This contributes to heterogeneity in our meta-analysis resulting in less reliable results.

Another limitation is that most data concerning the amount of working hours or performing shift work was extracted from observational studies. Retrospective studies in particular can be susceptible for recall bias, especially when the timing of exposure can be years ago. Of the sixteen included studies five studies were a retrospective cohort study. Only one of those was a high quality study [25].

A third limitation of our review may be the fact that we did not consider any work leave policies. Saurel-Cubizolles et al. (2004) analysed the relation between PTD and working conditions in Europe to test whether employment related risks varied by country of residence. There were stronger links in countries with a lower overall level of perinatal health and a common practice of long prenatal leaves. Unfortunately most studies lacked of reliable data concerning work leave policies so this aspect could not be included in this review.

Recommendations

What advice, based on the results of our review, can be given to pregnant employees in daily practice? In earlier reviews by Mozurkewich et al. (2000) and Bonzini et al. (2007 and 2011) different recommendations were given. These reviews were used in the development of two evidence based guidelines on pregnancy and work in the

Netherlands (Dutch Society of Occupational Medicine (NVAB) 2007) and in the UK (NHS Plus 2009). The difference in conclusion of Mozurkewich et al. 2000 and Bonzini et al. 2007 is reflected in the recommendations of these guidelines, regarding working hours and shift work. The recommendation of the Dutch Guideline is to avoid shift work and more than 40 weekly working hours after the 20th week of pregnancy (Dutch Society of Occupational Medicine (NVAB) 2007). The English guideline indicates that there is insufficient evidence of a risk to pregnant women to make recommendations to restrict shift work, including rotating shifts or night/evening work. Concerning long working hours the English guideline indicates that employers should reduce long working hours for pregnant workers where possible, particularly in late pregnancy. Working hours should be limited as far as possible to a standard working week of approximate 40 hours per week. However, if a pregnant worker who has been informed of the possible risks wishes to continue, then there are insufficient grounds upon which to impose restrictions against her will [16]. These differences in recommendations reflect the advices given in daily practice. At the end it is the expert-based opinion, based on several personal and occupational items, that is leading in giving advice to pregnant employees.

Conclusion

In conclusion the data presented in the studies included in this review do not permit a clear conclusion whether shift work or long working hours are risk factors for preterm birth. The meta-analysis performed shows no statistically significant associations between shift work and PTB. For long working hours, a marginally statistically significant relationship with PTB was found but it reflects a slightly elevated risk. However, due to the lack of high quality studies in this meta-analysis that focused on all trimesters, in particular the third trimester, these results have to be interpreted with caution. Further research is needed by performing more high quality prospective cohort studies and intervention studies focussing on the risks per trimester to get data which present a more valid and reliable answer.

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Conflict of interest The authors declare that they have no conflict of interest.

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Working conditions in low risk nulliparous women in the netherlands: are legislation and guidelines a guarantee for a healthy working environment? A cohort study.

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Abstract

Objective: Hazardous working conditions increase the risk of adverse pregnancy outcomes. In this study we examine adherence to legislation and guidelines aimed at improving working conditions in pregnancy.

Methods: Between 2014 and 2016 we recruited a prospective cohort of low risk nulliparous pregnant women in paid employment or self-employed in 16 community midwifery practices in The Netherlands. Participants completed two questionnaires concerning demographics, education, general health and working conditions between 10-16 and 20-24 weeks of pregnancy. We calculated the proportion of participants with work-related risk factors not in accordance with legislation and/or guidelines.

Results: Of 269 participants included, 214 (80%) completed both questionnaires. At 10-16 weeks 110 (41%) participants and at 20-24 weeks 129 (63%) participants continued to work under circumstances that did not meet recommendations. Employers provided mandated information on work adjustment to 37 (15%) participants and 96 (38%) participants received no information about the potential hazards while working with biological and chemical hazards. Participants with lower educational attainment (aOR 2.2 95%CI 1.3-3.9), or employment in healthcare (aOR 4.5, 95%CI 2.2-9.0), education/ childcare & social service (aOR 2.6, 95%CI 1.1-6.0 2), , catering (aOR 3.6, 95%CI 1.1-12) and industry, construction and cleaning (aOR 3.3, 95%CI 1.1-10.3) more often continued work which did not meet recommendations.

Conclusion: There is poor adherence to national legislation and guidelines for safe working in pregnancy in The Netherlands: 50% of the pregnant women worked under hazardous conditions. Given the impact on adverse pregnancy outcomes as well as on the public purse, action to improve compliance must be taken by all stakeholders.

Keywords:
Employment; Maternity protection, Occupational Exposure; Pregnancy; Protective legislation; Preterm Birth

Introduction

Many women continue their paid job during pregnancy. In the US, 66% of mothers who gave birth to their first child between 2006 and 2008 worked during their pregnancy [1]. Hazardous working conditions, including physically demanding work, long working hours and high job strain, may increase the risk of adverse pregnancy outcomes such as miscarriage [2-5], hypertensive disorders [2, 3, 6, 7], fetal growth restriction [2, 3, 6, 8-11], preterm birth (PTB) [2-4, 12-14] and fetal abnormalities [15-18] (Supplement A). Two systematic reviews, including 80 observational studies on work related adverse pregnancy outcomes, show that various types of physically demanding work, shift work and working > 40 hours per week increased the odds of PTB by 10 to 31%. Furthermore, lifting> 10 kg, fixed night shifts and working >40 hours per week increased the odds of miscarriage by 35%, 23% and 38%, respectively [2, 3]. These adverse pregnancy outcomes can be prevented by work adjustment. Elimination of harmful work-related exposures before 24 weeks of pregnancy through implementation of legal measures was shown to result in a 30 to 50% reduction in risks for PTB [19] and fetal growth restriction [20].

Maternity protection legislation (MPL) and evidence based guidelines on working conditions in pregnancy are available in many countries [21-23]. Recommendation in MPL include restricted work time (night work and overtime) and provisions on hazardous work, and are generally aimed at prevention of adverse pregnancy outcomes. Common principles pertaining to the topic of work and pregnancy were recorded by The International Labour Organisation (ILO) with information derived from 111 countries. These principles include: (1) risk assessment and providing pregnant employees with information about these risks; (2) workplace adjustments or temporary assignment of pregnant employees to a job without risk for pregnancy complications; (3) temporary leave, preferably with retention of financial compensation for the employee [22, 23]. The implementation of MPL is lacking in most countries [21] and pregnant women continue to work in a hazardous workplace or resort to sick leave.

In The Netherlands, nine in 10 women are in paid employment and continue to work in their first pregnancy [24]. Legislation and guidelines are available to ensure a safe workplace for pregnant women. European Union law requires employers to perform an occupational risk assessment regarding pregnancy, according to Council Directive 92/85 / EEC [25]. Employers are required to provide their employees, who wish to become or are pregnant, with information on work adjustment and enable them to continue work in a safe environment. In addition to European legislation, occupational physicians from The Netherlands Society of Occupational Medicine (NVAB) in collaboration with other experts in the field have developed an evidence-based guideline '*Pregnancy, Postpartum Period and Work'*. This guideline includes recommendations regarding various work-related risk factors enabling occupational physicians to advise pregnant employees (with or

without pre-existing health problems or pregnancy complications) and their employers on work adjustment [26]. Finally, the Dutch Social and Economic Council (SER) has drawn up a '*Guide to Occupational Health and Safety Measures Pregnancy & Work*' for employers and employees to make the workplace safer and healthier for pregnant women within individual organizations [27]. To date, the implementation of legislation and guidance on working conditions and the effect on pregnancy is unknown.

The aim of this study was to examine whether the Dutch MPL and guidelines have been implemented and if not, which work-related risk factors are involved in adverse pregnancy outcomes.

Methods

Design

We used data from the PROPELLOR (PRevention Of PrEterm Labor in LOw Risk women) study, a cohort study in a population of low risk nulliparous women to identify risk factors associated with spontaneous PTB between 16 and 37 weeks of pregnancy. Pregnant women were recruited at 16 midwifery practices in the region North-West Netherlands between February 2014 and December 2016. The study was approved by the Medical Ethics Committee of the Amsterdam University Medical Centre, location Amsterdam Medical Centre (registration number NL43414.018.13).

Legislation and Guidelines

We used the guideline *'Pregnancy, Postpartum Period and Work'* [17] and the '*Guide to Occupational Health and Safety Measures Pregnancy & Work*' [27], both of which include legislation. We distinguished work-related risk factors for adverse pregnancy outcomes before 20 weeks of pregnancy and from 20 weeks onwards; we defined these work-related risk factors as > 40 hours/week, ≥ 4-6 hours/day standing and walking, lifting >5 kg >10-50 times/day, very physically demanding regularly/ often, bending regularly/ often, squatting regularly/often, high work pressure regularly/often, working in noise and work at night. The exact limits of these risk factors before and after 20 weeks pregnancy are listed in Table 1.

Table 1. Risk factors in work that exceed the limit values of guidelines and legislation (from The Netherlands Society of Occupational Medicine and Social Economic Council)

< 20 week pregnancy	≥ 20 weeks pregnancy
1. >40 hours/week	1. >40 hours/week
2. ≥ 6 hours/day standing + walking/day + rarely/never possible to sit	2. ≥ 4 hours/day standing + walking
3. Lifting >10 kg >50 times/day	3. Lifting >5 kg >10 times/day
4. Very physically demanding: often	4. Very physically demanding: regularly/ often
5. Bending down: often	5. Bending down: regularly/often
6. Squatting: often	6. Squatting: regularly/often
7. Problems with the pressure: regularly/ often	7. Problems with the pressure: regularly/ often
8. Working in noise: often	8. Working in noise: often
	9. Work at night

We constructed a cumulative work risk variable, with which we compared 'working in accordance with legislation and guidelines' (score = 0 risk factors) with 'working in the presence of ≥1 risk factors' (score = 1-8 at 10-16 weeks of pregnancy and score = 1-9 at 20-24 weeks of pregnancy).

Participants

The PROPELLOR study included nulliparous adult women with a low-risk pregnancy, being healthy women with no co-morbidity at antenatal booking between 8 and 12 weeks of pregnancy. Women were followed-up until delivery. For the present study, only participants with paid employment or self-employment, and who had completed at least the first of two questionnaires were eligible. All participants provided written informed consent.

Data collection

All participants were asked to complete two questionnaires: a questionnaire between 10-16 weeks and a questionnaire between 20-24 weeks of pregnancy. Questionnaires were either completed on paper or online via a website developed for the PROPELLOR study. All data were collected on web based electronic case report forms, and were stored in an anonymised database.

The first trimester questionnaire between 10-16 weeks of pregnancy collected data including demographics, education, general health, lifestyle and current pregnancy. In addition, we used questions from a validated questionnaire about psychosocial job strain and physically demanding work [10] supplemented with questions about other working conditions (e.g. (irregular) working times, chemical, biological and physical factors (noise, climate)). Information on biological agents was retrieved from questions about working with ill/small children, sick adults, blood and other bodily fluids and/ or stools. Furthermore, we asked whether the participant came into contact with chemical substances: cleaning supplies, solvents, anaesthetic gasses, cancer-inhibitory medication, pesticides and/or heavy metals. Finally, we asked whether the employer had

provided advice on how to adjust her work while pregnant. To determine the influence of private factors on health and work capacity, the last part of the questionnaire concerned commuting, sports, hobbies, and household characteristics.

The second trimester questionnaire between 20-24 weeks of pregnancy was used to collect work status and adjustment, working conditions, recommendations regarding work and physical and/or obstetrical complaints.

We collected participants' antenatal files retrospectively via the midwifery and hospital practices. Medical records were used to collect data on miscarriage and/or termination of pregnancy and medical history. The socio-economic status (SES), was estimated on the postal code of residence and the status scores from The Netherlands Institute for Social Research.

Outcome measurements

The primary outcome was the proportion of pregnant women exposed to work related risk factors that exceed the limit values of legislation and guidelines. We distinguished between the periods before and after 20 weeks of pregnancy. Secondary outcome was the proportion of pregnant women with work related exposure to biological and chemical agents without advice from the employer concerning safety measures.

Statistical analysis

Baseline characteristics are presented as absolute numbers and percentages for categorical variables and means with standard deviation or median with range for continuous variables. To address the potential non-response bias, we compared baseline characteristics of responders to those of non-responders.

Work-related risk factors, as defined in Table 1, were participant-reported and retrieved from the questionnaires (supplement B). These categorical and numerical variables were converted into binary variables. The risk factor 'standing and walking' was constructed from two questions (hours standing and walking per day and possibility to sit), while other risk factors were based on one question each. We constructed a cumulative work risk variable, which scored a point for each work-related risk factor present (Table 1), and otherwise was scored zero if working conditions were all in accordance with the guidelines. The cumulative work risk variable was dichotomised, comparing no risk factors present (cumulative work risk variable = 0) to ≥1 risk factors present (cumulative work risk variable 1 to 8 at 10-16 weeks of pregnancy and 0 versus 1 to 9 at 20-24 weeks of pregnancy).

The missing values of the risk factors were imputed based on job, employment sector and the answer to the question "possibility to sit". In the missing values of the second trimester questionnaire, the answers from the first trimester questionnaire were

included, if available. Missing data on one or more of the work-related factors were imputed in 13 (first trimester questionnaire) and 18 participants (second trimester questionnaire). After imputation, in both questionnaires, five work-related risk factors remained missing in two and three participants, respectively. Since these participants all had a cumulative risk score of ≥ 1 risk factors, without the missing data, they were included in the analyses.

We determined the association between the cumulative work risk score and the variables educational level, number of employees in the company and employment sector, by calculating the crude odds ratio (OR) and 95% confidence intervals (CI). P-values were calculated using a chi-squared test. A p-value < 0.05 was considered statistically significant. Using logistic regression ORs were adjusted for SES (low or middle/high), education (primary or secondary school, lower professional versus university or higher vocational education), age (< 30 versus ≥30), and ethnicity (non-white European versus white European). These variables were chosen as representative for several risk factors associated with sociodemographic features. The employment sector with the lowest number of risk factors, government, business services and culture & recreation', was chosen as reference.

Data were analysed using IBM SPSS Statistics 25 (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) for Windows.

Results

A total of 363 participants were enrolled in the PROPELLOR study, the first-trimester questionnaire was completed by 308 participants, of whom 39 without paid work. In this study, we included a total of 269 women with paid employment or self-employed, of whom 214 (80%) completed both questionnaires (Figure 1).

Mean maternal age was 29 (SD 4.2) years, the median body mass index (BMI) was 23.7 (SD 4.1) kg/m^2, 208 (77%) women were white European, 82 (31.3%) had a low SES, 173 women (64%) had completed tertiary or higher vocational education. Ten (4%) women were single, six (2%) cared for other children and nine (3%) had a previous medical disease (Table 2).

Almost one third (n=78, 29%) worked in healthcare, one quarter (n=66, 25%) in business services, nearly 10% (n=25) in education and 8% (n=22) in retail. The average travel time commuting was 57 (± 41) minutes, 140 (52%) travelled by the car. Before pregnancy, 20 (7%) women had adjusted their work because of health problems or illnesses.

Of the 55 participants who did not complete Questionnaire 1, data retrieved from the participants' antenatal files demonstrated that 9 had no paid work (Supplement C). The other 46 participants who did have paid work (but did not complete Questionnaire 1), were comparable to the study population in age (29) and BMI (23.6 vs. 23.7), the number with a Low SES score was lower in the non-response group (20% vs. 31%) (Supplement C).

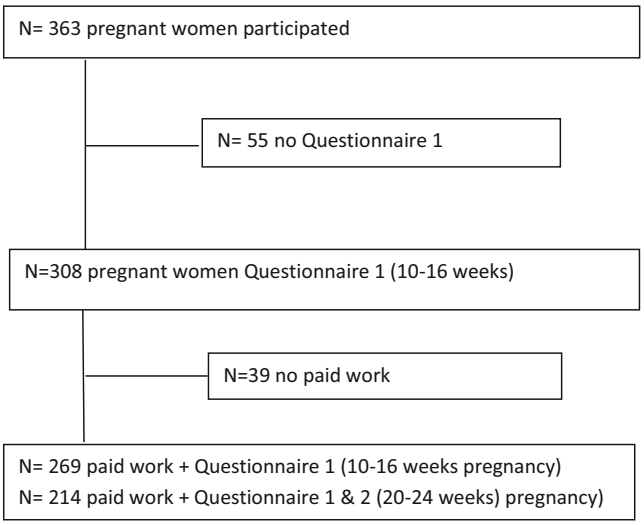

Figure 1. Flow chart PROPELLOR Study

Before 20 weeks of pregnancy, 110 (41%) women continued to work under circumstances that were not in accordance with the Dutch guidelines and legislation. From 20 weeks of pregnancy , this number was 129 (63%) (Table 3).

Table 2. Baseline characteristics study population: of nulliparous working women with a low risk pregnancy at 10-16 weeks

Demographics and general health	**N=269**	**Work: General aspects**	
Age (years)	29.1 (4.2)*	Paid work from start of the pregnancy	264 (98.1%)
Age < 30 (versus ≥30)	138 (51%)	Paid work from x weeks pregnancy	5 (1.9%) x= 8.8 (4-13%)
Body Mass Index (kg/m2)	23.7 (4.1)*	Working in sector:	
Ethnic origin: White European	208 (77%)	- Health care	78 (29%)
University or higher vocational education	173 (64.3%)	- Business services	66 (24.5%)
Low SES score	82 (31.3%)[a]	- Education	25 (9.3%)
Smoking during pregnancy	12 (4.5%)	- Retail	22 (8.2%)
Someone smoked at work last 30 days	36 (13.4%)	- Culture, recreation	16 (5.9%)
Alcohol during pregnancy	2 (0.7%)	- Government	16 (5.9%)
Drugs during pregnancy	5 (1.9%)	- Social service and child care	15 (5.6%)
Physical activity during pregnancy (sports)	118 (43.9%)	- Hospitality and Catering	15 (5.6%)
Medical history: No previous disease	253 (96.6%)[b]	- Industry/ construction	10 (3.7%)
Medication prescribed by physician	38 (14.1%)	- Cleaning	5 (1.9%)
Health complaints before pregnancy limit work	20 (7.4%)	Number of employees in the company	
Pregnancy characteristics		- 1-10	48 (17.9%)
Previous pregnancy:		- 11-50	66 (24.5%)
miscarriage and/or abortion: 55/262	55 (21%)[b]	- 51-100	19 (7.1%)
Increase in complaints from current pregnancy that limit work	108 (40%)	- >100	135 (50.4%)
- Fatigue	89 (33%)	- Self-employed	14 (5.2%)
- Nausea/vomiting	54 (20%)	**Commuting**	
- Headaches	30 (11%)	Travel distance commuting (m/km) *	35 (37)
Stomach aches	24 (8.9%)	Travel time commuting (min/hours) *	57 (41)
Private conditions		Travel time commuting (min/hours) **	0-300
Marital status: Single	10 (3.7%)	Means of travelling/ transport	
Care for other children living at home	6 (2.2%)	- Car	140 (52%)
Housekeeping: Largely doing by participant herself	70 (26%)	- Public transport	68 (25.4%)
Household help	42 (15.6%)	- By bicycle/scooter	44 (16.4%)
		- Walking	15 (5.6%)

**Mean (SD), ** min-max, all other variables mentioned as N (%)*
a: 8 missing, b: 7 missing

Table 3. Number of work-related risk factors in the work of pregnant women, that exceeds the limit values of guidelines and legislation (from The Netherlands Society of Occupational Medicine and Social Economic Council)

Risk factors*	< 20 weeks pregnancy N= 269	≥ 20 weeks pregnancy N= 214, 205 at work
no	159 (59%)	76 (37%)
yes	110 (41%)[a]	129 (63%)[b]
1	56 (21%)	44 (22%)
2	27 (10%)	24 (12%)
3	13 (5%)	23 (11%)
4	10 (4%)	15 (7%)
5	3 (1%)	15 (7%)
6	1 (0.4%)	6 (3%)
7		2 (1%)

** all variables mentioned as N (%)*
a: missing n=5 work-related risk factors of n=2 participants, both with ≥1 risk factors
b: missing n=5 work-related risk factors of n=3 participants, all with ≥1 risk factors

Specification of the risk factors that exceeded the limit values of guidelines and legislation is shown in Table 4. Frequent bending down (n= 44, 17%) and problems with job strain (n = 43, 16%) were the most frequently exceeded risk factors before 20 weeks of pregnancy. From 20 weeks of pregnancy standing and/or walking ≥ 4 hours a day was the most frequently observed risk factor in excess of guideline, occurring in 88 (43%) women followed by bending regularly in 65 (32%) and very physically demanding work in 47 (23%).

Table 4. Specification of risk factors in the work of pregnant women, that exceeds the limit values of guidelines and legislation (from Netherlands Society of Occupational Medicine and Social Economic Council)

< 20 weeks pregnancy N= 269, all at work[a]		≥ 20 weeks pregnancy N= 214, 205 at work[b]	
>40 hours/week	19 (7%)	>40 hours/week	16 (8%)
Very physically demanding: often	32 (12%)	Very physically demanding: regularly/ often	47 (23%)
≥ 6 hours standing + walking/day and rarely/never possible to sit	25 (8%)	≥ 4 hours standing + walking/day	88 (43%)
Bending down often	44 (17%)	Bending down regularly/often	65 (32%)
Squatting often	32 (12%)	Squatting regularly/often	45 (22%)
Lifting >10 kg >50 times/day	6 (2%)	Lifting >5 kg >10 times/day	41 (20%)
Problems with job strain: regularly/ often	43 (16%)	Problems with job strain: regularly/ often	33 (16%)
Working in noise: often	14 (5%)	Working in noise: often	8 (4%)
		Work at night	7 (3%)

** all variables mentioned as N (%)*
a: missing n=5 work-related risk factors
b: missing n=5 work-related risk factor

Table 5. Biological and chemical exposure and advice to adjust work, from pregnant workers < 20 weeks pregnancy and/or ≥20 weeks pregnancy, n= 269

Biological and chemical exposure*	N= 269
Exposure	127/269 (47.2%)
Exposure + in employment	117/255 (46%)
Exposure + self-employed	10/14 (71%)
Advice to adjust work*	
Advice to adjust work from:	
- employer/ supervisor[a]	37/255 (14.5%)
- midwife/ obstetrician	22/269 (8.2%)
Biological and chemical exposure + advice from management[a]	21/255 (8.2%)
Biological and chemical exposure without advice from management[a]	96/255 (37.6%)

**. all variables mentioned as N (%)*
a. participants in employment, self-employed women excluded.

Exposure to biological or chemical agents occurred in 127 out of 269 (47%) women of whom 117 were in employment and 10 were self-employed (Table 5). Of women in employment, 37 (15%) were informed about work adjustments by their employers and 22 (8%) by their obstetric healthcare provider. There was lack of information about biological and chemical exposure provided by the employer in 96 (38%) cases.

The association between the cumulative work risk score and the variables SES, educational level, age, ethnicity, number of employees in the company, employment and sector is shown in Table 6; effect estimates have been adjusted for SES, educational level, age, and ethnicity. In the first trimester, participants with lower educational level more often had a cumulative work risk score from 1-8, than those with higher educational level (aOR 2.2 95%CI 1.3 to 3.9), meaning they more frequently continued to work under circumstances that were not in accordance with the Dutch legislation and guidelines. Also participants with an age < 30 (versus ≥ 30 years) more often had a cumulative work risk score 1-8 (OR 1.9, 1.2 to 3.2), after adjustment this association was not significant. Neither SES, ethnicity, the number of employees in a company nor being self-employed impacted the cumulative work risk score.

A cumulative work risk score of 1-8 was more often present in women working in healthcare (OR 4.5, 95%CI 2.3 to 8.6), education, childcare and social service (OR 2.3, 95%CI 1.04 to 5.1) retail (OR 3.5, 95%CI 1.3 to 9.0), hospitality and catering (OR 5.2, 95% CI 1.7 to 16.2), and industry, construction and cleaning (OR 3.5 95% CI 1.2 to 10.3) compared to the reference employment sector 'government, business services and culture & recreation' (Table 6). Adjusting did not substantially change these associations for the sector healthcare (aOR 4.5, 95%CI 2.2 to 9.0), education, childcare and social service (aOR 2.6, 95%CI 1.1 to 6.0), hospitality and catering (aOR 3.6, 95%CI 1.1-12), and industry, construction and cleaning (aOR 3.3, 95%CI 1.1-10.3). After adjustment, the association between the cumulative work risk score for the sector retail was no longer statistically significant.

Table 6. Logistic regression Cumulative work risk score 1-8 vs 0, in the work of pregnant women with educational level, number of employees in the company, employment and sectora

Participants : 10-16 weeks pregnancy N= 269, all at work	Cum. work risk score: 1-8	OR	(95% CI)	P value	aOR	(95%CI)	P value
SES							
Low	32 (39%)	0.87	0.51-1.48	0.601			
Middle and High (ref.)	76 (43 %)						
Education							
Primary or secondary school, lower professional	54 (56%)	2.67	1.61-4.49	0.000	2.2	1.26-3.91	0.006
Higher vocational or University (ref.)	56 (32%)						
Age							
< 30	67 (49%)	1.93	1.18-3.17	0.009	1.5	0.85-2.65	0.157
≥ 30 (ref.)	43 (33%)						
Ethnicity		1.36	0.76-2.44	0.301			
Non-white European	28 (48%)						
White European (ref.)	81 (40%)						
Number of employees in the company							
1-50 employees	53 (47%)	1.52	0.93-2.49	0.096			
> 50 employees (ref.)	56 (36%)						
Employment							
Self-employment	6 (43%)	1.09	0.37-3.32	0.88			
In company (ref.)	104 (57%)						
Sector							
Government, business services, culture & recreation	22 (22%)	Ref.			Ref.		
Health	44 56%)	4.47	2.33-8.59	0.000	4.53	2.28-9.0	0.000
Education, child care and social service	16 (40%)	2.3	1.04-5.08	0.039	2.62	1.14-6.04	0.024
Retail	11 (50%)	3.46	1.32-9.03	0.011	2.25	0.82-6.149	0.226
Hospitality and Catering	9 (60%)	5.18	1.66-16.15	0.005	3.63	1.10-11.97	0.034
Other, Industry, construction, cleaning	8 (50%)	3.46	1.16-10.26	0.026	3.34	1.08-10.34	0.036

** all variables mentioned as N (%)*

a: Cumulative work risk score: 1-8 risk factors versus 0 risk factors

aOR: odds ratio adjusted for socio-economic status, education, age, and ethnicity. Ref.: Reference group

Discussion

In this study we found that between 41% to 63% of pregnant women continued to work under conditions that were not in accordance with the Dutch legislation and guidelines. In addition, 38% of women worked in an environment with infectious diseases or chemical exposure without receiving advice from the employer on safe working conditions. Only 15% of employers fulfilled their legal obligation to correctly inform their pregnant employees about work adjustments. Women with lower educational attainment, or those who worked in healthcare, education, childcare & social service, catering and industry, construction and cleaning sectors were at particular risk of continuing work in accordance with Dutch legislation and guidelines.

The strength of our study is the representative sample: we recruited a multi-ethnic sample of healthy nulliparous pregnant women with a wide range of education and SES backgrounds. Their employment was in a variety of sectors, with a wide range of working conditions. Professions and sectors in which participants were employed were reflective of national Dutch figures [28]. Although the sample size with 269 participants is limited, the response rate is high with 80% of recruited women completing both questionnaires. As the results of the baseline characters of non-responders were comparable to those of the participants of our study, we do not expect this to affect the results of the study.

A limitation of our study is that self-employed pregnant women were underrepresented (5.2%). In The Netherlands, there are no extra legal or financial provisions for these women except for a limited maternity leave benefit, which makes them even more vulnerable to compliance with MPL. Another limitation is that women completed the first questionnaire between 10-16 weeks of pregnancy. It is possible that employers were not yet informed of the pregnancy of their employee and therefore had not given any information about work adjustment. However, the fact that adherence to guidelines was even lower in the second trimester compared to the first trimester points to a more systematic lack of implementation of MPL. Moreover, risk of exposure to chemical, biological or radioactive agents obliges the employer to provide information about necessary measures to any of his/her employees of childbearing age who may be considering pregnancy, upon entering employment. The fact that this has not been discussed by the time of the established pregnancy indicates that employers have not adhered to this recommendations at a much earlier point in time.

Despite being prospectively collected, the data on exposure to risk factors at work are self-reported by the working pregnant women. It is therefore not entirely certain whether this reflects the actual exposure. In this study we focussed on the implementation of Dutch guidelines for working pregnant women and did not describe whether insufficient adherence to guidelines on the topic of work and pregnancy led to an actual increase in adverse outcomes including preterm birth of fetal growth restriction. Only for a limited

number of individual risk factors a reliable value of the association with some adverse outcomes has been given [2-4, 10, 12, 14]. The risk probably also differs per trimester [12] and many women also have to deal with multiple exposure (walking and lifting, work stress and night shifts). It is not known whether the magnitude of the risk is the sum of the individual risk factors.

Our findings are similar to what is reported in other European studies. In a British study, 19% of 3254 mothers said that they had identified health hazards while their employer did not [29]. In a Swiss online survey, comprising 2809 women who gave birth, 53% reported adjustments or change of their work but 20% did not, and only 6% received preventive leave [30]. Surveys in Poland and Norway show that 60% and 30% of working pregnant women, respectively, felt that they had not received the right job adjustment [31, 32]. Concerning risk analysis, in a report of the British government nearly all employers (98%) claimed they undertook health and safety risk assessments for all workers and specific for pregnant women, whereas 49% of women said they were informed by their employer about risks for themselves or their baby [33]. Another Swiss study, comprising 2809 postpartum women, reports that only 26% of women felt that their employer had fully informed them about the risks in their work [30]. Implementation of legislation and guidelines appears suboptimal in several European countries, but implementation in The Netherlands displays a number of additional shortcomings in comparisons to other European countries. The prevailing standard in The Netherlands is that women are primarily responsible for caring for children, and that men are responsible for income [24, 34]. Pregnancy- and maternity leave is just 16 weeks in total (20 weeks for multiple pregnancy) and a large proportion of (up to 75%) women work part-time. Mothers' earnings are 46% lower compared to their pre-birth earnings trajectory, whereas fathers' earnings are unaffected by childbirth. This gender stereotyping and gender norms may hamper implementation of MPL, it is not taken for granted and stakeholders are unaware of the importance.

Our study shows there is poor adherence to legislation and guidelines for safe working in pregnancy in The Netherlands. Creating greater awareness by identifying women 'at risk' and adjusting their work can prevent health care costs due to complications including PTB. This saves expenses for health insurers and benefits the society as a whole. However, companies and organisations responsible for risk analysis and work adjustment do not benefit from this 'profit'. The same applies to the costs of absenteeism due to pregnancy and childbirth, which are reimbursed to employers in The Netherlands by the Employee Insurance Agency (UWV). Reduction of these costs benefits the UWV. The lack of financial incentives for employers appears to be an important barrier to implementation as well [35].

The SER identified similar bottlenecks in work-related care in general: insufficient access to occupational healthcare and attention to prevention and insufficient cooperation with

regular care. Reason to start the project "Arbozorg Nieuwe Stijl" (Health and Safety New Style), an innovative form of financing and implementation of work-related care in the installation technology sector [36]. This project led to new (financing) agreements between the various stake holders and the introduction of a preventive consultation for employees. This project offers opportunities for innovative work-related care for pregnant women, in which health insurers, (regular) obstetrical and occupational health care can work together. Health insurers and society in particular benefit from the implementation of MPL, which is why they should bear the costs and responsibility for implementation together with employers. They could start organising and reimbursing the preventive consultation for working pregnant women, together with representatives from obstetrical and occupational care. An international approach within the EU (or ILO), as part of work-life balance policy, will ensure that sufficient progress is achieved in all Member States [37].

The occupational physician can act as an interface between employers, health care professionals and pregnant women to improve the coordination of preventive counselling for pregnant women about their work. In 2007, the NVAB introduced the 'preventive consultation' with the occupational physician for all workers before or during the first trimester of pregnancy in the Guideline 'Pregnancy, postpartum period and work [26]. Revision of this guideline in 2018 showed that the preventive consultation has added value, but implementation from the preventive consultation is lagging behind, which, like financing, depends on employers [38].

Future research is needed into innovative forms of financing and work-related care for pregnant working women in collaboration with prenatal care. A preventive consultation for all working pregnant women should be the start. The mHealth application 'Pregnancy and work' can serve as a tool especially for pregnant women at high risk for adverse pregnancy outcomes [39].

Conclusion

We found that among healthy low risk pregnant nulliparous women in The Netherlands 50% worked under hazardous conditions, putting them at increased risk of adverse pregnancy outcomes. Only 15% of the employers provided information to their pregnant employees, despite being legally obliged to do so. The legislation and guidelines are adequate, drawn up jointly by all stakeholders, but are not enforced. Given the great impact on pregnancy outcomes as well as on the public purse, action must be taken by all stakeholders to improve compliance. Health insurers and society, in addition to employers, should also bear the costs and responsibility for the implementation of legislation and guidelines for safe working in pregnancy. The joint organisation and reimbursement of a preventive consultation for all working pregnant women, together with obstetrical and occupational care could be a practical and effective way to get started.

Declarations

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Competing interests No potential competing interest is reported by the authors.

Availability of data The data are available on request.

Contributors Study concept and design: PH, MK, MP, MvB. Acquisition of data: MP, MS, HS. Analysis and interpretation of data: MvB, MK, RP, PH, RD. Drafting the manuscript: MvB. Critical revision of the manuscript for important intellectual content: MK, RP, PH, HS, MS, TB, MP, RD.

Ethics approval The study was approved by the Medical Ethics Committee of the Amsterdam University Medical Centre, location Amsterdam Medical Centre (registration number NL43414.018.13).

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SUPPLEMENT A. Reported adverse pregnancy outcomes associated with working conditions

Adverse pregnancy outcomes	Working condition	Reference
Miscarriage	Lifting objects ≥ 10kg, ≥10x/day	[2-5]
	(Fixed) Night shifts	
	Long working hours (> 40 hours/week)	
Pregnancy hypertension and/or Pre-eclampsia	Lifting objects > 10 kg	[2, 6, 7]
	High job strain	
	Rotating shifts	[3]
Low birth weight (LBW) and/ or Small for gestational age (SGA)	Lifting (≥100 kg/day)	[2]
	Prolonged standing	
	Heavy physical workload	
	Rotating shifts	[3]
	Long working hours (> 40 hours/week)	[3]
	High job strain	[6, 8-10]
	Full-time exposure to high levels of noise	[11]
	Cumulative workload	[10, 20]
Preterm birth (PTB)	Physically demanding work/ heavy physical workload	[2, 4, 12, 14]
	Standing and walking (> 3 hours/day) and prolonged standing	
	Lifting (loads > 5 or ≥ 10 kg, ≥100 kg/day, ≥10x/day	
	Work in strenuous postures	
	Long working hours (> 40 hours/week)	[3, 13]
	Rotating shifts, fixed night shifts	[3]
	Cumulative workload	[12, 19]
Fetal abnormalities	Chemical exposure	[15, 16]
	Biological exposure	[17, 18]

Abbreviation: kg= kilogram, ns = nightshift

SUPPLEMENT B. Questions used for information about risk factors (see **Table 1)**

Questions used for information about risk factors:

- 10-16 weeks pregnancy: nr. 1, 3-9
- 20-24 weeks pregnancy: nr. 1-9

1 How many hours per week do you currently work on average? ..... hours a week

2 Do you work in irregular shifts?

- ☐ No
- ☐ Yes

If Yes:

How many of your working hours do you on average spend on these shifts a week?

……. hours a week in day shifts

……. hours a week in evening shifts (until 23:00)

……. hours a week in night shifts

3a During your work, how many hours a day do you have to:

- ☐ Walk ..... hours a day
- ☐ Stand ……hours a day
- ☐ Sit .....hours a day

3b If you have to walk or stand, do you have the opportunity to sometimes sit down for a while:

- ☐ Always
- ☐ Sometimes
- ☐ Rarely
- ☐ Never

4 In the table below you can fill in how much weight you lift and how often this occurs. More than one answer is possible. If you are lifting loads or people heavier than 20kg, please fill in how much kg they weigh on average.

	Less than 5 kg	5-10 kg	10-20 kg	More than 20 kg
1-10 times a day (once an hour)	☐	☐	☐	☐ .....kg
10-25 times a day (2 or 3 times an hour)	☐	☐	☐	☐.....kg
25-50 times a day (4 to 6 times an hour)	☐	☐	☐	☐.....kg
50-100 times a day (7 to 12 times an hour)	☐	☐	☐	☐.....kg
More than 100 times a day (13 times an hour)	☐	☐	☐	☐..... kg

For the next couple of questions, please indicate every time how often certain things occur at the moment.
You can choose between the following answers: never, sometimes, regularly, often.

	Never	Sometimes	Regularly	Often
5 Do you think your work is very physically demanding?	☐	☐	☐	☐
6 Do you have to bend over during work?	☐	☐	☐	☐
7 Do you have to squat during work?	☐	☐	☐	☐
8 Do you have problems with the pressure of work?	☐	☐	☐	☐
9 During your work, are you often exposed to Noise?	☐	☐	☐	☐

SUPPLEMENT C. Baseline characteristics of cohort members responding to Questionnaire 1 compared to Non responders: no Questionnaire 1, with paid work

Nulliparous working women with low risk pregnancy at 10-16 weeks, participating in the study	Study group	Non responders Questionnaire 1
N	269	55 (no questionnaire) – 9 [no paid work] = 46 (paid work
Age (years)	29.1 (4.2)*	29.1(4.1)*
Body Mass Index (kg/m2)	23.7 (4.1)*	23.6(4.2)*
Low SES score	82 (31.3%)a	9 (19.6%)

*Mean (SD), all other variables mentioned as N (%)
a: 8 missing

Working conditions in women with multiple pregnancy, adherence to guidelines and the impact on preterm birth - a prospective cohort study

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Abstract

Background: Women with multiple pregnancies are at risk for maternal complications, such as preterm birth. Hazardous working conditions, e.g. physically demanding work and long and irregular working hours , might increase the risk of preterm birth.

Objective: The primary objective of this study is to evaluate whether the working conditions of Dutch women with multiple pregnancy have been adjusted to the guidelines of the Netherlands Society of Occupational Medicine (NVAB). The secondary objective is to determine whether certain working conditions up to 20 weeks of pregnancy increase the risk of preterm birth in multiple pregnancies.

Study design: We performed a prospective cohort study alongside the ProTWIN trial, a multicentre randomised controlled trial that assessed whether a cervical pessary could effectively prevent preterm birth. Women, with paid work > 8 hours a week, completed questionnaires concerning general health and working conditions between 16-20 weeks of pregnancy. We calculated the proportion of women that showed work-related factors not in accordance with guidelines. Univariable and multivariable logistic regression analyses were performed to identify work-related factors associated with preterm birth (32-36 weeks' gestation) and very preterm birth (< 32 weeks' gestation). We analysed a subgroup of participants who worked more than half a week (> 28 hours).

Results: We studied 383 women, of whom 168 (44%) had been randomised to pessary, 142 (37%) to care as usual and 73 (19%) did not participate in the randomised part of the study. Before 20 weeks of pregnancy, 224 (58.5%) women with multiple pregnancy continued to work under circumstances that were not in accordance with the guidelines.

After adjusting for confounding variables working hours >28 hours was associated with very preterm birth (aOR 3.0, 95%CI 1.1-8.1), irregular working times with PTB (aOR 2.0, 95%CI 1.0-4.1) and very PTB (aOR 2.7, 95%CI 1.0-7.3). Within a subgroup of 213 participants working > 28 hours per week, multivariable analysis showed that irregular working times (aOR 3.5, 95%CI 1.2-10.1) and no/little freedom in performance tasks (aOR 3.0, 95%CI 1.3-7.3) were associated with preterm birth. Irregular working times (aOR 3.4, 95%CI 1.0-11.1), requiring physical strength (aOR 5.3, 95%CI 1.6-17.8), high physical workload (aOR 3.9, 95%CI 1.1-13.9) and no/little freedom in performing tasks (aOR 3.2, 95%CI 1.1-9.6) were associated with very preterm birth.

Conclusion: In our cohort study, nearly 60% of women with multiple pregnancy, continued to work under circumstances not in accordance with the guidelines to avoid physical and job strain, and long and irregular working hours. Long and irregular hours were associated with very preterm birth, long hours with preterm birth.

Keywords:
Physical workload, working hours, shift work, job strain, occupational exposure, maternity protection legislation.

Key findings

Why was this study conducted?
This study aimed to evaluate if working conditions of Dutch women with multiple pregnancy have been adjusted to the guidelines and whether working conditions increase the risk of preterm birth.

Key findings
Nearly 60% of women with multiple pregnancy continued to work not in accordance with the guidelines. Working >28 hours/week was associated with very preterm birth, irregular times with preterm birth. In a subgroup of participants working >28 hours/week, irregular working times and limited freedom in tasks performance was associated with (very) preterm birth, high physical workload and physical strength with very preterm birth.

What does this add to what is known?
Following the guidelines to avoid physical and job strain, and long and irregular working times throughout pregnancy can prevent (very) preterm birth.

Introduction

Many women continue to work during pregnancy [1, 2]. Working conditions can lead to adverse pregnancy outcomes, including preterm birth (PTB [3-10]). Babies born preterm are at higher risk of mortality and morbidity [11,12]. In 2015, 12 per 1,000 births worldwide were twins [13], in the Netherlands 15 out of 1,000 births in 2020 involved a multiple pregnancy [14].

Women with multiple pregnancies have an increased risk for PTB: 6 to 10-fold higher than that observed in singleton gestation [15,16]. In the USA 60% of women with multiple pregnancy deliver before 37 weeks gestation [17]. In the Netherlands 45% of women with a multiple pregnancy deliver between 32 and 36 weeks gestation (PTB) and almost 10% before 32 weeks gestation (very PTB). These rates are comparable with other European countries [12].

In the Netherlands, occupational physicians together with midwives and obstetricians have developed an evidence-based guideline to guide working pregnant women: *Pregnancy, Postpartum Period and* Work [18]. Based on an increased risk for PTB, growth restriction and pre-eclampsia, this guideline provides advice to women with multiple pregnancy to 'avoid physical and job strain, and long and irregular working times throughout pregnancy, from 20-24 weeks limit work to four hours per day, stop working at 26-30 weeks'. The authors point out that there is hardly any research into the impact of working conditions in multiple pregnancy.

Determining whether adjustment of working conditions in multiple pregnancies reduces the risk on PTB, can support preventive measures. Therefore, the first aim of this study is to evaluate if the working conditions from Dutch women with a multiple pregnancy have been adjusted in accordance with the guidelines. The second aim is to identify whether certain working conditions up to 20 weeks gestation increase the risk on PTB in multiple pregnancies.

Materials and Methods

Study design

We performed a cohort study alongside the ProTWIN-trial, a multicenter, open-label randomised controlled trial that assessed a cervical pessary as a preventive measure for PTB in women with a multiple pregnancy. The study protocol and trial report have been published elsewhere [19, 20]. Women with multiple pregnancy, between 12-20 weeks of gestation, eligible for the ProTWIN trial were asked to participate in this sub-study. Disregarding women's decision on participating in the trial, women could participate in this sub-study. All women participating provided written informed consent. In addition

to approval of the ProTWIN trial, this additional cohort study on work-related factors in pregnancy was approved by the research ethics committee of Amsterdam UMC, location AMC (MEC 09-107,) and by the boards of each of the 40 participating hospitals. The trial was registered in the Dutch trial register (NTR1858).

Guidelines

We used the recommendations from the Dutch guideline '*Pregnancy, Postpartum Period and Work on multiple pregnancy*' [18] (Figure 1). We defined work-related risk factors > 40 hours/week, irregular working times, ≥ 16 hours/week standing and walking, physical strain, and problems with job strain. The exact definitions of these risk factors are listed in Table 1. We constructed a composite work risk variable, with which we compared 'working in accordance with guidelines' (score 0 on risk factors) with 'working in the presence of ≥1 risk factors' (score 1-5).

Figure 1: Recommendations multiple pregnancy and work according to the Guideline 'Pregnancy, Postpartum period and Work' from the Netherlands Society of Occupational Medicine (NVAB).

Multiple pregnancy	Recommendations
	➢ Advice, throughout pregnancy: - avoid physical and job strain - regular working times - working hours: · < 20 weeks: ≤ 40 hours per week · 20-24 weeks: ≤ 4 per day; · 26-30 weeks: stop work* ➢ Consider consulting with gynaecologist ➢ Follow-up consultation around 20 weeks to check whether the adjustments have been made and work is not a risk * for multiple pregnancies: since 1-4-2016 maternity leave from 30 weeks of pregnancy. (for single pregnancy from 34-36 weeks).

From: NVAB. Practice guideline - Pregnancy, Postpartum period and Work. Advice and guidance by the occupational physician. NVAB, the Netherlands Society of Occupational Medicine: Recommendations multiple pregnancy and work.

Table 1. Work related factors that exceed the limit values of guidelines in multiple pregnancy (< 20 weeks)

1.	Working times > 40 hours/week
2.	Irregular working times (working in the evening and/ or at night)
3.	Standing + walking ≥ 16 hours/week
4.	Physical strain*
5.	Problems with the pressure: often/always

*= sum score from 6 questions: bending, squatting, reach high, requiring physical strength, physically demanding, uncomfortable or strenuous postures.

Data collection

We used a validated questionnaire on psychosocial job strain and physically demanding work [8], supplemented with questions on other working conditions, e.g. (irregular) working times, chemical, biological and physical factors, work adjustments, leisure time and household characteristics.

Data on the gestational age at delivery, as well as other outcomes related to delivery and maternal and perinatal morbidity, were retrieved from patient files by local research nurses or midwives.

Procedure

From May 2010 until March 2012 every woman eligible for the ProTWIN-study received a questionnaire (in Dutch language), at 16, 24 and 32 weeks gestation, handed out by the attending research nurse, midwife or obstetrician. The first questionnaires had to be completed before 20 weeks gestation, the second before 28 weeks and the third at 34 weeks gestation. Completed questionnaires were received, checked, and digitalized.

Participants

The study focused on women with a multiple pregnancy, 12-20 weeks of gestation, eligible for the ProTWIN trial and with paid employment or self-employed, defined as paid work for at least 8 hours per week during women's first trimester.

Outcome measurements

The main outcome of this study was the proportion of women with multiple pregnancy who are exposed to work-related risk factors, as defined in Table 1 (participant-reported and retrieved from the questionnaires, supplement A), that exceed the recommendations from the guideline '*Pregnancy, Postpartum Period and Work*' concerning multiple pregnancy, up to 20 weeks. Gestational age at delivery was a secondary outcome.

Statistical analysis

Baseline characteristics were presented as absolute numbers with percentages for categorical variables, and means with standard deviation or median with interquartile range for continuous variables.

The analysis of the main outcome measure, a constructed composite work-related variable, was based on work-related factors, as defined in Table 1. They were measured as categorical and numerical variables, and dichotomized. Three factors were based on one question each: '*working > 40 hours/week*', '*irregular working times*' and '*problems with job strain often/always*'. The factor '*standing and walking ≥ 16 hours/week'* was constructed from two questions (working hours per week, and percentage standing and walking). The factor '*physical strain*' was the sum score of 6 questions concerning physical work. Scale reliability (Cronbach's alpha) was 0.87. These questions were dichotomized: 'never sometimes' (score 0) versus 'often always' (score 1), then the sum score was calculated. A score of 1-6 was classified as *'physical strain'*.

The constructed composite work-related variable, was made up of one point for each work-related factor present (Table 1). Participants who's working conditions complied with guideline recommendations scored zero. The composite work-related variable was dichotomized, comparing no risk factors present (score 0) to ≥ 1 risk factors present (score 1-5).

The analysis of the secondary outcome measure, PTB, was performed using logistic regression to estimate crude (OR) and adjusted odds ratios (aOR) with 95% confidence intervals (CI). We determined the association between women with PTB (32-36 weeks gestation) and very PTB (< 32 weeks gestation) compared to women with delivery at term (≥37 weeks gestation). Demographic, pregnancy characteristics and working conditions at 16-20 weeks gestation, were used as explanatory variables. ORs were adjusted for a set of predetermined risk factors known to be associated with risks for preterm birth (age, BMI, level of education, parity) as well as factors with significant baseline differences between groups (parity, assisted conception, ethnicity). A subgroup analysis for the association between gestational age and working conditions in the group of participants working >28 hours per week was performed by stratification. We opted for a cut-off of > 28 hours because the women then work for more than half a week (> 3.5 days/week) and the work-related factors are an important part of their daily lives.

A sum score 'physical workload' was calculated based on 4 questions concerning physical work. Scale reliability (Cronbach's) was 0.83. For analysis, these questions were dichotomized: 'never sometimes' (score 0) versus 'often always' (score 1), then the sum score was calculated. The sum score physical workload was dichotomized into: 'high' (score3-4) versus 'low-moderate' (≤2).

Missing baseline values of demographic and pregnancy characteristics (BMI, race, education, smoking, parity, previous PTB, triplets, chorionicity, cervical length, and gestational age) used in multivariable models were imputed using multiple imputation under the missing at random assumption. Data was missing for 18% of patients on one or more variables of interest. Ethnicity, BMI and level of education were most commonly missing (11% and both 9%). Data of work-related questionnaires was less commonly missing (>91% complete). Imputation was conducted using SAS 9.4, with fully conditional specification creating 25 imputation datasets [21]. Both data measured directly, as well as derived variables were included in the models. The continuous variables BMI and gestational age were categorized and imputed using dummy variables. Additional variables (pregnancy characteristics, gestational age) were included in the model as predictors of missingness. Model convergence was evidenced by plots. Values after imputation were plausible for the variables concerned. Weighing and pooling of results over imputation sets was done using Rubin's rules [21]

Analyses were performed using IBM SPSS Statistics for Windows, Version 27.0 (2020) Armonk, NY. P-values < 0.05 were considered statistically significant.

Results

Between May 2010 and March 2012, 996 women met the cohort's inclusion criteria, of which 813 women had been recruited in the ProTWIN trial. Because questionnaires on workload were introduced later during the trial, 324 participants did not receive the questionnaires. Of the 672 women (68%) who received a questionnaire, 449 (67%) returned a completed one. Of these 449 women, 61 women (16%) did not have a paid employment, 5 women (1%) worked <8 hours/week and were excluded, while 383 (85%) had a paid employment status and were suitable for our analysis (Figure 2). The analysis population of this study consisted of these 383 women, of whom 189 (49%) delivered at term (≥37 weeks gestation), 152 (40%) delivered between 32-36 weeks and 42 women (11%) delivered < 32 weeks.

Baseline characteristics are outlined in Table 2. Mean maternal age at inclusion was 32 (sd 4.1) years and the mean BMI was 25 (IQR: 21.3 – 26.3). Most women were Caucasian (n= 358, 93%) and had completed a higher professional education or university (n= 260, 68%). Of the included women 223 (58%) were nulliparous and 160 (42%) multiparous, of whom 9 (6%) had a history of PTB. Almost one third of the participants (31%) worked in the healthcare sector, 62% in a company with more than 50 employees. 168 (44%) women had been randomised to pessary use, 142 (37%) women had been randomised for control and 73 (19%) did not participate in the randomised part of the study.

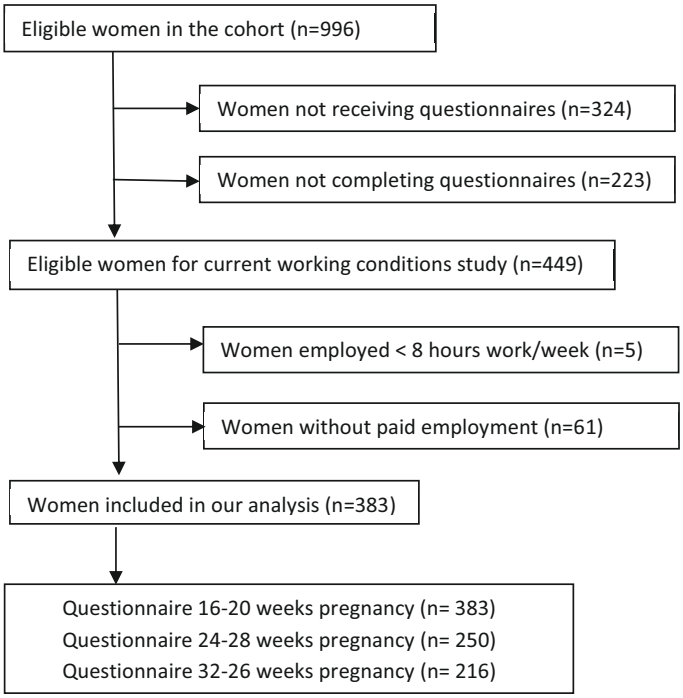

Figure 2. Selection of the study cohort

Table 2. Baseline characteristics study population*

N=383	After imputation
Demographics and general health	
Maternal age[a] (years) (Mean, SD) (IQR)	32 (4.1) (30-35)
- ≤35	298 (77.8%)
- >35	83 (21.7%)
BMI (Body Mass Index) (Mean, SD)(IQR)	25 (5) (21 – 26)
- < 18.5	11 (3%)
- 18.5-25.0	249 (65%)
- > 25.0	122 (32%)
Ethnic origin:	
- white European	358 (93%)
- non-white European	25 (7%)
Highest educational level	
- Primary or secondary school or Lower professional education	123 (32%)
- Higher professional education or University	260 (68%)
Smoking during pregnancy	21 (6%)
Physical activity (sports) during pregnancy	118 (31%)

Table 2. Continued.

N=383	After imputation	
Pregnancy characteristics		
Nulliparous	223 (58%)	
Multiparous	160 (42%)	
Multiparous, previous preterm birth	9 (6%, from 160)	
Cervical length (20 weeks) – ≤ 25 mm	19 (5 %)	
Conception[b]		
- Spontaneous conception – no. (%)	231 (60%)	
- Assisted conception	135 (35%)	
Triplets	11 (3%)	
Monochorionic	82 (21%)	
Pessary[c]	168 (44%)	
Gestation		
- < 32 weeks pregnancy	43 (11%)	
- 32- < 37 weeks pregnancy	152 (40%)	
- ≥ 37 weeks pregnancy	189 (49%)	
Work: General aspects	*n* (%)	
Employment sector		
- Health care	118 (31%)	
- Financial & business services	70 (18%)	
- Education, child care and welfare	67 (17%)	
- Government	46 (12%)	
- Retail & hospitality industry	37 (10%)	
- Industry/ transport	25 (6%)	
- Culture, recreation	14 (4%)	
- Other or unknown	6 (2%)	
Number of employees in the company >50	239 (62%)	
Travel distance commuting - km (mean, sd) (IQR)	33 (±37) (6-48)	
Travel time commuting - min/hours (mean, sd) (IQR)	53 (±40) (25-60)	
Household conditions		
Care for children (living at home): Yes	162 (42%)	
	1 kid	*2 kids*
• 0-4 years	143 (37%)	11 (3%)
• > 5 years	50 (13%)	19 (5%)
No half-day eq. childcare (mean, sd) (min-max) (n=152)	5 (±2) (1-10)	
Housekeeping largely doing by participant herself	87 (23%)	

* all variables mentioned as N (%)
SD: standard deviation. IQR: interquartile ranges,
a. missing: 2 (0.5%)
b. missing: 17 (5%)
c. not participating in randomised part of study: 73 (19%)

Adherence to guidelines

From 16-20 weeks of pregnancy, 224 (58.5%) women with multiple pregnancy continued to work under circumstances that were not in accordance with the guidelines (Table 3).

An overview of risk factors contributing to exceeding the limits on work during pregnancy of guidelines and legislation is shown in Table 3. Physical strain (sum score of 6 questions concerning physical work) (166; 43%) and prolonged standing and walking (119; 31%) were the risk factors most frequently exceeded before 20 weeks of pregnancy.

Table 3. Number and specification of work-related risk factors that exceeds the limit values of guidelines*

Work-related risk factors that exceeds the limit values of guidelines (N=383)			
Number of Risk factors	***16- 20 weeks pregnancy***	***Specification of Risk factors***	***16- 20 weeks pregnancy***
none	159 (42%)	> 40 hours/week	16 (4%)
one or more	224 (59%)	Irregular working times	57 (15%)
1	97 (25%)	≥ 16 hours standing + walking/ week	119 (31%)
2	78 (20%)	Physical strain**	166 (43%)
3	44 (12%)	Problems with job strain often/ always	48 (13%)
4	5 (1%)		

* Numbers are N (%)

** Sum score of 6 questions on: bending, squatting, reach high, requiring physical strength, physically demanding, uncomfortable, or strenuous postures.

Associations between working conditions and gestational age

Results of univariable analysis with demographic and pregnancy characteristics are listed in Table 4. PTB occurred more frequently among participants with ethnic origin 'other than Caucasian' (OR 3.5, 95% CI 1.1-11.4) and nulliparity (OR 1.8, 95% CI 1.2-2.9). Nulliparity (OR 4.8, 95% CI 2.0-11.2) and assisted conception (OR 2.1, 95% CI 1.1-4.2) were associated with very PTB.

Table 4. Univariable associations between women with preterm birth and very preterm birth compared to women with delivery at term: Demographic and pregnancy characteristics, total study population

Participants 16- 20 weeks pregnancy Total study population	**Total**	**≥37 weeks**	**32-36 weeks**	**< 32 weeks**	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	383	**189 (49%)**	**152 (40%)**	**42 (11%)**						
	N (%)	**%**	**%**	**%**	**OR**	**(95%C)**	**P value**	**OR**	**(95%C)**	**P value**
Age > 35 *vs ≤ 35*	83 (21.8%)	23.4	20.3	19.6	0.83	0.49-1.41	0.499	0.8	0.34-1.85	0.594
• **BMI 3 groups**										
• **BMI 18.5-25 ref**	249 (65%)	62	70.1	59.5			1			1
• **BMI ≤ 18.5** *vs 18.5-25*	11 (3%)	3.2	3.2	1	0.85	0.17-4.13	0.836	0.00	0.0-0.0	0.999
• **BMI >25** *vs 18.5-25*	123 (32%)	34.7	26.8	39.5	0.68	0.42-1.12	0.130	1.18	0.57-2.44	0.647
Education low-middle versus high	123 (32%)	30.3	35.4	27.5	1.25	0.77-2.04	0.360	0.74	0.40-1.91	0.735
Ethnic origin other *vs white European*	25 (7%)	3.3	10.3	7.5	3.50	1.07-11.44	0.039*	2.33	0.46-11.80	0.306
Parity 0 *vs > 0 (ref)*	223 (58%)	48.7	63.3	81.9	1.83	1.16-2.86	0.009*	4.77	2.03-11.20	< .001*
Previous PTB yes *vs no*	9 (2%)	2.4	2.2	2.8	1.34	0.29-6.11	0.708	3.90	0.37-41.53	0.259
Twin Monochorionic *vs Dichorionic*	82 (21%)	17.8	26.2	24.3	1.64	0.94-2.87	0.083	1.49	0.64- 3.44	0.353
Cervical length ≤ 25 mm *vs > 25 mm*	19 (5%)	3.6	6.6	5.6	2.04	0.44-9.38	0.359	1.70	0.23-12.69	0.604
Assisted conception	135 (37%)	34.4	35.8	52.5	1.07	0.67-1.69	0.789	2.11	1.06- 4.22	0.034*

CI: confidence interval, vs: versus, ref: reference

Table 5A and supplement D show the results of univariable analyses with working conditions and PTB within the total population. Working hours >28 hours at 16 to 20 weeks gestational age (OR 3.3, 95% CI 1.5-7.2) and performing irregular working times (OR 2.5, 95% CI 1.1-5.7) were associated with very PTB.

In the subgroup of participants working >28 hours per week, irregular working times (OR 2.8, 95%CI 1.1-6.9) and no/little freedom in performance tasks (OR 2.4, 95%CI 1.1-5.1) were associated with PTB (Table 5B and supplement E). Furthermore, the following work-related factors were associated with very PTB: irregular working times (OR 4.2, 95%CI 1.5-12.0), requiring physical strength (OR 4.2, 95CI% 1.5-12.1), high physical workload (sum score of 4 questions concerning physical work) (OR 4.0, 95CI% 1.2-13.0) and no/little freedom in performance tasks (OR 2.6, 95%CI 1.02-6.7) (Table 5B and supplement E).

Table 5. Univariable associations working conditions between women with preterm birth and very preterm birth compared to women with delivery at term:

5.A Total study population

Participants 16- 20 weeks pregnancy Total study population	**Total**	**≥37 weeks**	**32-36 weeks**	**< 32 weeks**	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	383	**189 (49%)**	**152 (40%)**	**42 (11%)**						
	%	**%**	**%**	**%**	**OR**	**(95%C)**	**P value**	**OR**	**(95%C)**	**P value**
Working hours >28 hours/week vs ≤ 28 (ref)	56	52	54	78	1.06	0.69-1.63	0.796	3.26	1.48-7.18	0.003*
Irregular working times: yes vs no	15	11	17	24	1.65	0.89-3.08	0.112	2.46	1.06-5.72	0.036*
Standing/ walking ≥ 15 hours/week	31	28	35	36	1.21	0.94-1.54	0.149	1.47	0.72-2.99	0.294
High physical workload[a]	12	9	14	19	1.66	0.84-3.30	0.174	2.41	0.93-5.81	0.061
Job strain										
Problems with pressure[b]	13	11	13	19	1.14	0.59-2.20	0.707	1.84	0.752-4.50	0.182
Freedom in performance tasks[c]	29	25	34	29	1.56	0.97-2.52	0.070	1.24	0.57-2.64	0.570
Influence on pace[b]	47	44	50	52	1.32	0.86-2.04	0.209	1.43	0.73-2.80	0.299

5.B Subgroup participants working >28 hours/ week

Participants 16-20 weeks pregnancy Subgroup working hours >28 hours/ week	**Total**	**≥37 weeks**	**32-36 weeks**	**< 32 weeks**	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	213	**99 (46%)**	**81 (38%)**	**33 (16%)**						
	%	**%**	**%**	**%**	**OR**	**(95%C)**	**P value**	**OR**	**(95%C)**	**P value**
Irregular working times: yes vs no	16	8	20	27	2.78	1.12-6.88	0.028*	4.22	1.47-12.10	0.007*
Standing/ walking ≥ 15 hours/week	34	29	39	34	1.56	0.83-2.96	0.169	1.38	0.60-3.18	0.455
Requiring physical strength[a]	14	8	16	27	2.16	0.85-5.50	0.108	4.22	1.47-12.10	0.007*
High physical workload[c]	10	6	11	21	1.87	0.64-5.49	0.254	4.02	1.24-13.00	0.020*
Job strain										
Problems with pressure[a]	15	15	21	16	0.97	0.42-2.20	0.932	1.49	0.55-4.05	0.434
Freedom in performance tasks[b]	22	14	28	30	2.37	1.10-5.11	0.028*	2.63	1.02-6.74	0.045*
Influence on pace[b]	45	39	49	54	1.54	0.84-2.82	0.159	1.90	0.86-4.23	0.114

CI: confidence interval, vs: versus, ref: reference

a: Sum score Physical workload high versus low-moderate: sum of 4 variables: lifting, physically very demanding, requiring physical strength, strenuous postures

b: often-always versus never-sometimes (ref)

c: never-sometimes versus often-always (ref)

Results of the multivariate analysis between working conditions and PTB are shown in Table 6. In the analyses within the total study population. Working hours >28 hours was associated with very PTB (aOR 3.02, 95%CI 1.1-8.1), irregular working times with PTB (aOR 2.0, 95%CI 1.01-4.1) and very PTB (aOR 2.7, 95%CI 1.0-7.3) (Table 6.A).

In the subgroup analyses with participants working >28 hours per week, irregular working times (aOR 3.5, 95%CI 1.2-10.1) and with no/little freedom in performance tasks (aOR 3.0, 95%CI 1.3-7.3) were associated with PTB (Table 6B). Within this subgroup, irregular working times (aOR 3.4, 95%CI 1.02-11.1), requiring physical strength (aOR 5.3, 95%CI 1.6-17.8), high physical workload (aOR 3.9, 95%CI 1.1-13.9) and no /little freedom in performing tasks (aOR 3.2, 95%CI 1.1-9.6) were associated with very PTB.

Table 6. Multivariable associations working conditions between women with preterm birth and very preterm birth compared to women with delivery at term:

6.A Total study population

Participants 16-20 weeks pregnancy Total study population n=383	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	aOR[d]	**(95%C)**	**P value**	**aOR[d]**	**(95%C)**	**P value**
Working hours >28 hours/week vs ≤ 28 (ref)	0.95	0.57-1.58	0.677	3.02	1.13-8.07	0.028*
Irregular working times	2.03	1.01-4.07	0.047*	2.7	1.00-7.28	0.050*
Physical work						
Requiring physical strength[a]	1.56	0.82-3.03	0.190	2.12	0.8-5.63	0.131
High physical workload[c]	1.67	0.77-3.6	0.192	2.12	0.71-6.31	0.180

6.B Subgroup participants working >28 hours/week

Participants 16-20 weeks pregnancy Subgroup working hours >28 hours/week n=213	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	aOR[d]	**(95%C)**	**P value**	**aOR[e]**	**(95%C)**	**P value**
Irregular working times	3.5	1.23-10.05	0.019*	3.36	1.02-11.06	0.046*
Physical work						
Requiring physical strength[a]	1.99	0.66-6.0	0.223	5.31	1.59-17.78	0.007*
High physical workload[c]	1.94	0.6 -6.23	0.266	3.87	1.08-13.94	0.038*
Job strain						
Freedom in performance tasks[b]	3.02	1.25-7.25	0.014*	3.21	1.08-9.56	0.037*

CI: confidence interval, vs: versus, ref: reference
a: often-always versus never-sometimes (ref)
b: never-sometimes versus often-always (ref)
c: Sum score Physical workload high versus low- moderate: sum of 4 variables: lifting, physically very demanding, requiring physical strength, strenuous postures
d: aOR: adjusted Odds Ratio: adjusted for parity, assisted conception, ethnicity, age, BMI, age, education
e: aOR: adjusted Odds Ratio: adjusted for parity, assisted conception, age, BMI, education (ethnicity= to sparse)

Comments

Principal findings

In this study we found that before 20 weeks of pregnancy, nearly 60% of women with multiple pregnancy continued to work under circumstances not in accordance with the guidelines of the Netherlands Society of Occupational Medicine[18]. Physical strain (43%) and prolonged standing and walking (31%) were the most frequently exceeded risk factors.

Working hours >28 hours and performing irregular working times were associated with very PTB (< 32 weeks gestations), working hours >28 hours with PTB. In the subgroup of participants working >28 hours per week, irregular working times and with no/little freedom in performing tasks were associated with PTB (32-36 weeks gestation) and very PTB. Requiring physical strength and high physical workload were associated with very PTB.

Results in the context of what is known

Our findings that nearly 60% of women with multiple pregnancy continued to work under circumstances not in accordance with the guidelines are higher than those in groups of women with low-risk pregnancies (40% before 20 weeks gestation) [22]. There are only a few guidelines (accessible and in English) on multiple pregnancy, with recommendations on working conditions, mostly limited to general advice [23-25]. It is unknown whether they are followed.

There are no previous studies into the impact of working conditions on PTB in multiple pregnancies, they are excluded due to their risk on PTB. Two recent meta-analyses showed that long working hours, rotating shifts and high physical workload were associated with PTB in singleton pregnancies6[6,7]. The difference between singleton and multiple pregnancies, with higher risk of complications, may explain why the ORs are somewat higher in our study.

Strengths and limitations

In this study, we prospectively and accurately identified various work-related risk factors of women with multiple pregnancies at different periods of pregnancy.

This is the first study examining the impact of working conditions in multiple pregnancies and provides direct evidence for the recommendations of the NVAB guideline. These have been drawn up in accordance with (weighting of the strength of) scientific evidence, based on the increased risk of preterm birth, growth restriction and preeclampsia in multiple pregnancies.

To prevent bias, we only included pregnant women with paid work, because employment during pregnancy is associated with a reduction in the risk of PTB [26]. Compared to the baseline characteristics of a recent RCT (n=13,520) in a low-risk pregnancy population in the Netherlands, BMI and age were comparable, however the highly educated, Caucasian, nulliparous and non-smoking women are overrepresented in our study [27]. The sectors in which the participants worked are a reflection of the national Dutch figures [28]. In our study nullipara were overrepresented. As in our study, they have a higher risk of PTB than multiparous without a history of PTB [29]. Probably because of the low number of multipara with previous PTB (6%), their risk of PTB was not increased in our study. Therefore, we only adjusted for the variable 'parity'.

The number of participants that gave birth between 32-36 weeks gestation was lower than the average in the Netherlands (40 versus 45%), while the number that gave birth before 32 weeks gestation was slightly higher (11 versus 10%)[12]. The rate of monochorionic pregnancies, with a higher risk of PTB than dichorionic, was comparable to the mean incidence (21% versus 20%) [30]. To minimize the impact of demographic and pregnancy-related factors on the outcome of PTB, we adjusted for the risk factors that significantly increased the risk of PTB (parity, ethnicity, and assisted conception).

The association between the composite work-related variable (working according to guideline as measured using various separate working conditions) and gestational age did not clearly reveal the value of independent components for this score, therefore we chose not to present these results.

Missing values of demographic and pregnancy characteristics can have caused bias of the results, despite imputation. Data was mainly missing from women eligible for participating in the ProTWIN trial who refused randomization and did allow their pregnancy outcomes to be recorded.

Implications for research and practice

Adverse pregnancy outcomes, like PTB, have an enormous impact on well-being of parents and children [12]. No guideline identified an effective strategy for women with multiple pregnancies to prevent PTB [31]. This study confirms that avoiding physical and job strain and long and irregular working hours throughout pregnancy, can prevent (very) PTB. Because there are hardly any evidence-based guidelines for working women with other medically complicated pregnancies, it is worth considering applying these recommendations to them as well.

The experience during the corona pandemic seems to support these recommendations. During periods of strict restrictive measures to prevent the transmission of the coronavirus (SARS-CoV-2), the number of PTB has fallen in several countries. In Australia, this reduction was higher in women with a previous PTB, who may have benefited from restrictive measures, such as cessation of working [32].

Further research is needed in working women with multiple pregnancy and other medically complicated pregnancies, with lower educational level and ethnicity other than Caucasian. In addition to PTB, also focusing on adverse outcomes like growth restriction and preeclampsia, may evaluate the cost-effectiveness of work adjustment early in pregnancy for working pregnant women with high-risk pregnancies.

Conclusion

Before 20 weeks gestations, nearly 60% of women with multiple pregnancy, continued to work under circumstances not in accordance with the guidelines of the Netherlands Society of Occupational Medicine (NVAB). Long (>28 hours per week) and irregular working hours were associated with very PTB (< 32 weeks gestation), long hours with PTB (32-36 weeks gestation). In the group participants working >28 hours per week, irregular working hours and with little or no freedom in performance tasks were associated with PTB and very PTB, and working with high physical strain with very PTB. Adjustment of working conditions according to the recommendations of the NVAB guideline on multiple pregnancies, to avoid physical and job strain and long and irregular working hours throughout pregnancy, can prevent (very) PTB.

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Trial registration: The original ProTWIN trial was registered at the Netherlands Trial Registry (clinical trial Identification number NTR1858). NTR (trialregister.nl) at 2009-09-01. Date of initial participant enrolment: May 2010 until March 2012.

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Contribution statement: MvB, MvM, RD, ES, SL, MS, MF, MK, BWM: concept, design and/or coordination. MvM, AvdW: data collection. MvB, RD analysis and interpretation of the data. MvB: first draft of the report. All authors critically revised the manuscript for important intellectual content and approved the submitted version.

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Supplement A. Questions used for information about risk factors (see **Table 1)**

1 How many hours per week do you currently work on average? ..... hours a week

2 Do you work in irregular shifts?

□ No

□ Yes

If Yes:

How many of your working hours do you on average spend on these shifts a week?

..... % in day shifts

..... % in evening shifts (until 23:00)

..... % in night shifts

3 During your work, how many hours a day do you have to:

□ Walk? ..... %

□ Stand? .....%

□ Sit? .....%

For the next couple of questions, please indicate every time how often certain things occur at the moment.

You can choose between the following answers: **never, sometimes, often, always.**

	Never	**Sometimes**	**Often**	**Always**
4 Do you have to bend over during work?	□	□	□	□
5 Do you have to squat during work?	□	□	□	□
6 Do you have to reach high during work?	□	□	□	□
7 Do you think your work is requiring physical strength?	□	□	□	□
8 Do you think your work is very physically demanding	□	□	□	□
9 Do you work in an uncomfortable or strenuous position?	□	□	□	□
10 Do you have problems with the pressure of work?	□	□	□	□

Supplement B. **Work status and working conditions**	**16-20 weeks pregnancy** **N=383**	**24-28 weeks pregnancy** **N=333**	**32-36 weeks pregnancy** **N=216**
Current work status			
Usual working hours	284 (74%)	141 (42%)	32 (15%)
Less than usual due to illness	99 (26%)	109 (33%)	29 (13%)
No work due to illness	0	75 (23%)	114 (53%)
Pregnancy leave	0	8 (2%)	41 (19%)
At work	**n= 383 (100%)**	**n= 250 (75%)**	**n= 61 (28%)**
Working hours			
Hours/ week*	29 (±9) (8-70)	24 (±10) (4-50)	23 (±11) (4-42)
Irregular working times (yes)	58 (15%)	11 (4%)	1 (2%)
Hours/ week per shift			
• Day shifts *	18 (±9) (0-42)	21 (±8) (6-34)	
• Evening shifts *	10 (±7) (0-30) *(n=57)*	5 (±2) (2-9) *(n=11)*	*n=1 10 hrs/wk*
• Nightshifts *	2 (±4) (0-18) *(n=14)*	*n=1 6 hrs/wk*	
Physical work			
Work posture (hours/week)		NA*[2]	NA*[2]
• Walking *	7 (±6) (0-30)		
• Standing *	5 (±6) (0-40)		
• Sitting *	18 (±12) (0-70)		
Physical work (often/ always)			
Lifting/carrying	68 (18%)	14 (6%)	1 (2%)
Bending	122 (32%)	39 (15%)	3 (5%)
Reach high	29 (8%)	13 (5%)	2 (3%)
Repetitive motion	142 (37%)	79 (33%)	15 (25%)
Physically demanding	82 (21%)	35 (14%)	8 (14%)
Requiring physical strength	68 (18%)	20 (8%)	4 (7%)
Uncomfortable or strenuous postures	50 (13%)	20 (8%)	4 (7%)
On a strenuous machine or assembly line	3 (1%)	1 (0%)	0

Continued.

Supplement B. Work status and working conditions	16-20 weeks pregnancy N=383	24-28 weeks pregnancy N=333	32-36 weeks pregnancy N=216
Job strain (often/ always)			
Problems with work pace	9 (2%)	12 (5%)	4 (7%)
Problems with the pressure	48 (13%)	25 (10%)	8 (13%)
Like to take things a little easier	77 (21%)	51 (22%)	10 (16%)
Freedom in performance of tasks	273 (71%)	201 (80%)	52 (86%)
Influence on the pace	202 (53%)	164 (66%)	46 (77%)
Planning own work	237 (62%)	183 (73%)	52 (86%)
Support from manager	260 (68%)	182 (73%)	46 (76%)
Support colleagues	309 (81%)	214 (86%)	51 (44%)
Varied work	289 (75%)	192 (77%)	49 (80%)
freedom planning working times	143 (37)	143 (57%)	43 (71%)
Physical factors (yes)		NA*[2]	NA*[2]
Heat	24 (6%)		
Cold	19 (5%)		
Noise	46 (13%)		
Biological agents	147 (38%)	NA*[2]	NA*[2]
Small and/ or sick children	77 (20%)		
Sick adults	73 (19%)		
Blood or other bodily fluids	59 (15%)		
Animals, raw meat, waste (-water)	25 (&%)		
Stool	64 (17%)		
Nature (forests, gardens)	5 (1%)		
Chemical agents (yes) (more options)	78 (20%)	NA*[2]	NA*[2]
Cleaning supplies	49 (13%)		
Solvents (paint, lacquer, glue, detergents	16 (4%)		
Anesthetic gases	5 (1%)		

Continued.

Supplement B. Work status and working conditions	16-20 weeks pregnancy N=383	24-28 weeks pregnancy N=333	32-36 weeks pregnancy N=216
Cancer inhibitory medication	10 (3%)		
Pesticides	3 (1%)		
Heavy metals/ metallic compounds	5 (15)		
Other 'medication'	6 (2)		
Hair dye/ Nail polish remover	4 (1)		

* (mean, SD) (min-max), all other variables mentioned as N (%)

NA*[1]= Not applicable: participants not working excluded, NA*[2]= Not applicable: not in questionnaire

Supplement C Work advice and adjustments *	16-20 weeks pregnancy n= 383	24-28 weeks pregnancy n= 333	32-36 weeks pregnancy n= 216
At work	**383 (100%)**	**250 (75%)**	**61 (28%)**
Work adjustment because of current pregnancy	**143 (37%)**	**169 (68%)**	**52 (85%)**
• Less physically demanding work	55 (15%)	59 (24%)	10 (16%)
• Other working hours	41 (11%)	41 (16.5%)	13 (21%)
• Less hours a day	90 (24%)	120 (48%)	34 (56%)
• Plan work yourself	44 (12%)	57 (23%) (0)1	20 (335)
• Other (less work, slower work pace)	83 (22%)	105 (42%)	19 (31%)
Advice to adjust work from:			
• Own initiative	43 (16%)	95 (38%	38 (62%)
• Obstetrician	NA*[1]	104 (42%)	24 (40%)
• Occupational physician	2 (1%)	53 (21%)	10 (16%)
• Manager	25 (9%)	45 (18%)	14 (23%)
• Other (partner, colleague, obstetrician (=1st questionnaire)	9 (2%)	23 (9%)	6 (10%)

* All variables mentioned as N (%)

NA*[1]= Not Applicable: not in questionnaire

Supplement D. Univariable associations between women with preterm birth and very preterm birth compared to women with delivery at term: Working conditions, total study population

Participants 16-20 weeks pregnancy Total study population	**Total**	**≥ 37 weeks**	**32-36 weeks**	**< 32 weeks**	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
	383	**189 (49%)**	**152 (40%)**	**42 (11%)**	**OR**	**(95%C)**	**P value**	**OR**	**(95%C)**	**P value**
	%	%	%	%						
Working hours >28 hours/week vs ≤ 28 (ref)	56	52	54	78	1.06	0.69-1.63	0.80	3.26	1.48-7.18	0.003*
Irregular working times: yes vs no	15	11	17	24	1.65	0.89-3.08	0.11	2.46	1.06-5.72	0.036*
Physical work										
Standing/ walking ≥ 15 hours/week	31	286	35	36	1.21	0.94-1.54	0.15	1.47	0.72-2.99	0.294
a. lifting[a]	18	16	19	22	1.21	0.68-2.13	0.52	1.43	0.62-3.30	0.407
b. Physically very demanding[a]	21	20	22	26	1.15	0.68-1.95	0.61	1.45	0.67-3.15	0.346
c. Requiring physical strength[a]	18	15	21	26	1.54	0.88-2.73	0.13	2.11	0.95-4.70	0.067
d. Strenuous postures[a]	13	11	14	19	1.28	0.67-2.45	0.46	1.89	0.77-4.64	0.165
Sum score a-d high vs low - moderate	12	9	14	19	1.66	0.84-3.30	0.17	2.41	0.93-5.81	0.061
Job strain										
Problems with pressure[a]	13	11	13	19	1.14	0.59-2.20	0.71	1.84	0.75-4.50	0.182
Freedom in performance tasks[b]	29	25	34	29	1.56	0.97-2.52	0.07	1.24	0.59-2.64	0.570
Influence on pace[b]	47	44	50	52	1.32	0.86-2.04	0.21	1.43	0.73-2.80	0.299

CI: confidence interval, vs: versus, ref: reference

a: often-always versus never-sometimes (ref)

b: never-sometimes versus often-always (ref)

c: Sum score Physical workload high versus low- moderate: sum of 4 variables: lifting[a], physically very demanding[a], requiring physical strength[a], strenuous postures[a]

Supplement E. Univariable associations between women with preterm birth and very preterm birth compared to women with delivery at term: Working conditions, subgroup participants working >28 hours/ week

Participants 16-20 weeks pregnancy Subgroup working hours >28 hours/week	**Total**	**≥ 37 weeks**	**32-36 weeks**	**< 32 weeks**	**32-36 weeks versus ≥ 37 weeks**			**< 32 weeks versus ≥37 weeks**		
total	**213**	**99 (46%)**	**81 (38%)**	**33 (16%)**	**OR**	**(95%C)**	**P value**	**OR**	**(95%C)**	**P value**
	%	%	%	%						
Irregular working times: yes vs no	16	8	20	27	2.78	1.12-6.88	0.028*	4.22	1.47-12.1	0.007*
Physical work										
Standing/ walking ≥ 15 hours/week	34	29	39	34	1.57	0.83-2.96	0.169	1.38	0.60-3.18	0.455
a. lifting[a]	17	15	17	21	1.11	0.49-2.53	0.801	1.51	0.55-4.13	0.420
b. Physically very demanding[a]	16	13	16	27	1.25	0.55-2.88	0.596	2.45	0.94-6.43	0.068
c. Requiring physical strength[a]	14	8	16	27	2.16	0.85-5.50	0.108	4.22	1.47-12.1	0.007*
d. Strenuous postures[a]	12	10	11	22	1.11	0.43-2.87	0.837	2.44	0.84-7.06	0.101
Sum score a-d high vs low-moderate	10	6	11	21	1.87	0.64-5.49	0.254	4.02	1.24-13.0	0.020*
Job strain										
Problems with pressure[a]	15	15	21	16	0.97	0.42-2.20	0.932	1.49	0.55-4.05	0.434
Freedom in performance tasks[b]	22	14	28	30	2.37	1.10-5.11	0.028*	2.63	1.02-6.74	0.045*
Influence on pace[b]	45	39	49	54	1.54	0.85-2.82	0.159	1.90	0.86-4.23	0.114

CI: confidence interval, vs: versus, ref: reference

a: often-always versus never-sometimes (ref)

b: never-sometimes versus often-always (ref)

c: Sum score Physical workload high versus low- moderate: sum of 4 variables: lifting[a], physically very demanding[a], requiring physical strength[a], strenuous postures[a]

Barriers and facilitators for the use of a medical mobile application to prevent work related risks in pregnancy: a qualitative analysis

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6

Abstract

Background: The number of women participating on the labor market in Europe has increased over the last decades. At the same time, there is growing evidence that certain conditions in employment during pregnancy may have a negative influence on pregnancy outcomes. In order to better inform pregnant women, we aim to develop an app to help assess the health risk as a result of personal and work related factors, and to provide personal advice for these women and their health care providers.

Objective: The aim of this study was to compose a thematic overview of the perceived facilitators and barriers according to pregnant women, medical professionals, and employers for the use of a mobile app in obstetrical care to prevent occupational-related pregnancy complications

Methods: Two multidisciplinary focus group meetings, with in total 14 participants, were conducted with pregnant women, occupational physicians, general practitioners, midwifes, obstetricians and representatives of trade unions and employers' organizations; Transcripts were analyzed through qualitatively coding procedures and constant comparative methods.

Results: We identified 24 potential facilitators and 12 potential barriers for the use of the app in four categories: content of the app, the app as a mean for providing information, ease of use and external factors. The 3 main facilitators are the need for a good interaction between the app and the user, they are viewed as a more practical source of information and the information should be understandable, according to the existing guidelines, and well-dosed. The 2 main barriers are extensive battery and memory use of the smartphone and sending frequent 'push-notifications'.

Conclusion: The results of this study are important considerations in the developing process of a medical app implementing a guideline or evidence based information in practice.

Keywords:
Qualitative research; Mobile application; Smartphone; Pregnancy; Work; Occupation; Exposure; eHealth; mHealth

Introduction

Currently the employment rate among women between 20-64 years old is 64% in Europe [1]. Around 57% of women of the labor force in the Netherlands are of childbearing age [2]. At the same time, there is growing evidence that certain conditions in employment during pregnancy may have a negative influence on pregnancy outcomes. For instance working long hours a day or working night shifts, physically demanding work, stress and chemical pharmaceutical or biological exposure can potentially cause preterm birth, low birthweight, spontaneous abortion, stillbirth and fetal abnormalities [3-9].

Pregnant women are often unaware of potential work related risks for their pregnancy [10]. Estimations are that still only 25% of the employed pregnant women receive adequate counseling on work related risks during their pregnancy [11]. Furthermore van Beukering et al. concludes in a literature study that around 25% of pregnant women in the Netherlands come in contact with above mentioned work related risks [12].

If however pregnant women would receive more information about potential risks in their work situation, this could lead to better work adjustments and thereby might prevent negative pregnancy outcomes. In the Netherlands, occupational physicians developed a guideline for healthy working conditions during pregnancy and the postpartum period [13] This guideline provides clear advice on necessary adjustments to potential harmful working conditions. With these work adjustments, a healthy working environment can be created and prevent negative pregnancy outcomes in certain cases. Mobile health (mHealth) was defined by the World Health Organization (WHO) as the use of mobile devices (mobile phones, patient monitoring devices and personal digital assistants) for medical and public health practice [14]. The benefits of mHealth interventions include that they can be delivered anywhere at any time, and they provide opportunities for interactivity and tailoring to specific groups [15]. Mobile applications (Apps) and smartphones are increasingly used in healthcare by both health care workers and the general public. In 2015, about 94% of the population in the age category of 25-45 years old owned a smartphone with internet access in the Netherlands [16]. Although these data were not specified by gender it is likely that the use of smartphones is comparable between men and women in this age category. The promising research results of apps in health care, combined with the fact that smartphones are widely used by many women of childbearing age, gives smartphones the potential to further improve maternity care as an addition to the traditional healthcare system [17].

In pregnancy several mHealth interventions or apps are developed for the care of diabetes [18-21], achieving less gestational weight gain [22-24], and support for smoking cessation [25-27]. The effectiveness of these interventions show promising results although most of these studies do not show significant outcomes mainly due to small sample sizes [18-23, 25, 27]. Moreover, a recent large study in the Netherlands does

show significant improvement of nutrition and lifestyle in 603 pregnant women and 1275 couples contemplating pregnancy due to an mHealth platform [28].

Previous research has shown that the user satisfaction of an app or mHealth intervention is high among active users and are mostly viewed as helpful, useful and convenient [25, 27, 29-31] However continued use lags behind and drop-out rates were high [22, 32, 33]. For instance in a large nationwide email based health promotion program for pregnant women in the Netherlands 45% ceased participating or never opened an email. Only 16% opened all emails received and were considered very active [32]. Therefor it is important to evaluate potential facilitators and barriers for the use of an app during development to achieve good continued use of an app.

In order to better inform pregnant women, we wanted to develop an app to help assess the health risk as a result of personal and work related factors, and to provide personal advice for these women and their health care providers. In doing so we wished to create awareness on work related risks, and empower pregnant women to discuss necessary work adjustments with their supervisor and potentially prevent negative pregnancy outcomes. To the authors' knowledge there is no evidence regarding the use of an app to provide personal advice for pregnant women on their work related risks

and necessary work adjustments.

This study was the first phase of a three phased pilot study. After this phase the prototype of the app will be tested for usability during a think aloud study among pregnant women. The third phase will consist of a powered study comparing the app as an addition to standard care with standard care alone. These phases are based on research on models for developing new tools by Elwyn et al. and Shorten et al. [34, 35].

The aim of this study was to compose a thematic overview of the perceived facilitators and barriers by pregnant women, professionals and employers for the use of an app in obstetrical care in order to reduce occupational related pregnancy complications.

Methods

Overview

We performed a qualitative research by conducting two multidisciplinary focus group meetings with in total 14 participants. We decided to conduct multidisciplinary focus groups to involve all the stakeholders and thereby evaluate the variety of opinions of both the end-users and professionals. The methods and results were reported according to the consolidated criteria for reporting qualitative research (COREQ) [36]. The ethics

board of the Academic Medical Center confirmed that the Medical Research Involved Human Subjects Act did not apply to this study.

Participants

Participants were selected by purposive sampling of stakeholders involved in occupational health and obstetrical care and contacted by e-mail and telephone. The inclusion criteria were that the participants were either pregnant women, occupational physicians, general practitioners, midwifes, obstetricians and representatives of trade unions and employers' organizations. Participants who did not speak the Dutch language fluently were excluded. In total, we invited 30 potential candidates, between 4-6 of each stakeholder category, to ensure an adequate number and variety of stakeholders in both focus groups. The invitations were only declined because of previous engagements, not because of unwillingness to participate.

Procedure

Two focus group meetings were conducted in 2015 to identify potential facilitators and barriers for the use of an app for pregnant women to prevent work related risks during pregnancy. Prior to the meeting confidentiality was assured and the process of the focus group was explained to the participants. All participants signed an informed consent form. Both meetings were audio taped and fully transcribed afterwards. The focus group meetings were both facilitated by FS (female, occupational physician and senior researcher at a Dutch academic medical center, MD, experienced in facilitating focus group). MvB (female, researcher on this project and occupational physician, MD) and SD (female, coordinator of the regional network of birth care, BSc) took field notes. The duration of both meetings were planned for two hours, and were conducted in Dutch.

During the first part of the meeting, participants were briefly introduced to the background and aims of the project. Next, the participants were asked to respond to several questions about their knowledge and experience with pregnancy and work. We also asked about their knowledge of the Dutch guideline on pregnancy and work [13], and about experiences with health apps, mainly focused on lifestyle adjustments, in general. Subsequently, several examples of existing health apps were presented, followed by a discussion based on five predetermined statements *(All questions, topics and statements are shown in appendix 1)*.

Data analysis

The transcriptions of the focus groups were structured and analyzed with MAXQDA (VERBI GmbH, Marburg, Germany), a software program to assist qualitative data analysis. For the analyses of focus group transcripts, coding procedures and constant comparative method as developed by Strauss were used [37]. It divides coding in three phases starting with open coding, axial coding and selective coding. This is a frequently used inductive,

bottom-up method for analyzing qualitative data without a predetermined theoretical framework [38].

First, each of the two researchers (AV, MvB) started with an open coding process by examining the transcripts of the focus groups, in order to assign a series of codes, which were then grouped into similar concepts [39]. To ensure consistency and inter-coder reliability, the two focus group transcripts were independently coded by two researchers. Discussions between the two researchers resulted in a consensus list of preliminary codes. In case of discussion on the interpretation of the codes a third researcher (FS) was involved in the process. Second, according to the axial coding process, recurrent themes within the transcripts were selected, and text fragments were sorted according to the thematic framework that appeared during the axial coding process, divided in main and sub codes. All codes were analyzed for influencing the use of the app, either in a positive way by stimulating the usage of the app coded as a facilitator, or in a negative way coded as a barrier. Some citations could be interpreted as both a facilitator and a barrier. Consensus meetings between researchers led to the final categorization of themes as described in the results section below.

Results

Overview

Each focus groups consisted of seven participants. The basic demographics of the participants are shown in Table 1. We successfully achieved the aim that in both meetings all different stakeholders were represented.

During the focus group meetings the participants identified 24 potential facilitators, 12 potential barriers for the use of our app which were classified into four main themes: content of the app, the app as a mean for providing information, the ease of use and external factors of influence. The barriers and facilitators in each main theme will be discussed below and the overview of the results is shown in Table *2*.

Table 1 Basic demographics

Participants (N=14)	N	%
Gender:		
Male	2	14%
Female	12	86%
Occupation:		
Midwife	2	14%
Obstetricians	1	7%
Occupational physicians	3	21%
General Practitioners	2	14%
Employers	2	14%
Labor union (FNV)	1	7%
Physician at employee Insurances Agency (UWV)*	1	7%
Pregnant women	2	14%

* Employee insurance agency

Theme 1: Content of the app

The facilitators and barriers regarding content of the app can be divided in two subcategories: the content of provided information and provided advice, and the added value of the app compared to existing apps. The two categories given most value by the participants are the content of the provided information and advice. Both categories can also be subdivided in personal information and advice specified to the individual user based on her previous responses about her work situation, and a more general information and advice which applies to every working pregnant woman.

Content of the provided information and advice

Participants agreed on the fact that facilitators related to general information and advice content are keeping the advices clear and simple and to mainly indicate the urgency or importance to follow the advice, instead of going into too many details and background.

All the information should be easily understandable for all users, and the information and advice should be in line with the existing guideline [13].

A second strong facilitator is the ability to provide specific personal information and advice by using 'selective questions'. This way, it is possible to determine if the user is at risk for a certain complication, and secondly to synchronize the advice with the gestational age.

FG 2: MB(Insurance physician): 'You wanted a start question, how did you call it, a selective question? '[...]'Do you work in one of the following occupations, you should do that.'

FG 1: MH(Employer and pregnant women): 'You should actually be able to turn off information that is irrelevant for you. I do not work with toxic agents, so everything about that is irrelevant to me [...] I tune out if there are, say, two pages about that'

Informing the pregnant woman about the changes in her body and the development of the fetus, will improve her understanding the effects the pregnancy may have on her work situation and vice versa. Possible adverse outcomes of the pregnancy are also important to mention in the app. Women with a high risk pregnancy could particularly benefit from specific and more personalized advice for their situation.

A potential barrier is the risk of users interpreting the information themselves without seeking further professional advice. One participant pointed out that a risk profile based on a questionnaire in the app cannot be compared with an actual conversation between a physician and the pregnant woman, because the app only works with the input of the user herself. This makes the reliability of personal advice difficult to interpret and could become a barrier related to the content of the app.

FG 1:FM(Occupational physician): 'Refer really fast to a gynecologist or midwife, or indeed the occupational physician. Otherwise you will indeed risk that the pregnant woman herself will interpret medical information or interpret risk factors.'

Added value of the app compared to existing apps
Participants considered it as a facilitator if the new app has added value with respect to other existing apps. Examples mentioned in the focus groups to create added value are: 1. To develop an app that is based on medical knowledge and guidelines. 2. To not cover solely the pregnancy period, but also add the preconception and postpartum period. 3. The app should not be commercial.

Theme 2: App as a mean for providing information
In this category the focus groups reported mainly facilitators in relation to the app, most importantly the practical aspects. Moreover, apps are viewed as faster and easier in searching for information and the information is available at every place and every time.

FG 1:AR(Labor union): 'Always at hand. Since that is the power of an app. You always have it on you. You can consult it anytime.'

The fact that pregnant women already receive a large amount of information regarding their pregnancy can be interpreted both as a facilitator and as a barrier for the app. One point of view, as reported by the participants, is that the app is more easily accessible than written information, and therefore a facilitator for the use. On the other hand, a few participants mentioned that the app is providing more information whereas there is already enough information available.

Theme 3: Ease of use

The facilitators and barriers for the ease of use of the app can be divided in three subcategories, the technical aspects of the app, feedback and interaction between app and user, and reaching the target users by the mode of delivering the information to the user.

Technical aspects

Participants described as facilitators that games or a quiz make an app more fun to use. Another important facilitator for the use of the app is that it is only applicable for a set period of time and you can delete it after nine months because apps that are not used frequently will be deleted according to our participants. Potential barriers that should be kept in mind are that there are numerous existing operating systems, apps that use a lot of battery and memory are unpopular, and the information provided should be readable on a smartphone.

FG2: FS(Facilitator): 'What kind of apps do you delete? HB(General Practitioner):'Lots of memory, lots of power. Apps that are very active, in that case your battery goes down…'

Feedback and interaction between app and user

Overall consensus was that interaction between the user and the app strongly stimulates the use of an app. But the opinions on interaction also showed some inconsistencies between participants, and sometimes within participants their opinion seemed to vary. Several participants emphasized that messages about the development of the fetus and the changes in the female pregnant body are informative and entertaining and facilitate the use of the app. Also reminders of specific personalized advice based on an earlier risk analysis in the app were evaluated as helpful and welcome.

On the other hand, every participant criticized 'push notifications' defined as frequent uncalled-for messages. One participant also brought under attention that these 'push notifications' can be risky when users have an adverse pregnancy outcome. Suggested solutions to this issue is to offer the option to sign out of the app in case of adverse pregnancy outcome, or to only show new general notifications when the user opens the app itself.

FG 1:DD(Pregnant woman): 'I fully recognize that. Because I do not have an app, but I do receive emails from an organization. And then you see the changes in your body and of the baby week by week, and say, and those of the baby. So in that respect I think receiving it through an app is useful. So you see the growth, and like, we are now in week 34; this is happening with your child. And you should adjust your health to your work etcetera. So I believe that would be very good.

FG 1:FS(Facilitator): 'But do you delete apps that for instance send very much push notifications?'
CvW (Employer): 'Yes, I always turn them of immediately.'
MP (Gynecologist): 'Those are very irritating.'
AR(Labor union): 'Yes, those are very irritating.'

Reaching target users by the mode of delivering the information
Three main facilitators were identified related to the mode of delivering information; the content of the app must be understandable, the information should be well-ordered and the information should be supplemented with illustrations, video fragments and icons to improve clarification.

FG 2:CdG(Pregnant woman): 'If you reduce the text and do not use extensive amounts of text and work with icons that already helps.'

The comprehensiveness of the app was considered an important facilitator, and as such subject of long debate. Several advises were given to achieve a comprehensive app on pregnancy and work. For instance participants felt that offering the app in multiple languages (Dutch, English, Spanish, Polish were named as important, Moroccan and Turkish were questioned if they are still necessary), using plain language, and having a 'read-out' function can improve accessibility of the app for all users.

Providing too much information is viewed as a barrier by the participants risking less usage of the app. Options to avoid this barrier could be to create a hyperlink in the app for further information and give users the possibility to read more if desired. On the other hand you have to prevent making the app needlessly complicated by providing too much hyperlinks.

Theme 4: External factors
The external facilitators and barriers of influence for the app can be divided in three different factors; the obstetrical caregivers, the employer, supervisor or company, and the government.

Obstetrical caregivers
he obstetrical caregivers such as the gynecologist and midwives are facilitators by supporting the app according to the participants. They work according to the occupational physicians practice guideline [13] and believe in screening for work related risks as part of the standard care. For it to become standard care this knowledge should be implemented in the education for midwifes. A second option could be to actively involve the obstetrical caregivers or create an extra app for the caregivers to use.

Employer, supervisor or company

The employers can potentially be very strong facilitators for the use of the app. Unfortunately the participants in the focus groups mainly identified barriers for the app. The participants thought that employers may have a negative prejudice about work adjustments for pregnant women. Work adjustments can be seen as more bothersome than sick leave, and the entire organization - for instance colleagues - might not understand fully the need for adjustments. Employers have little knowledge about work related risk factors for pregnant women, and many may not see that it is in their own best interest to implement well-timed work adjustment which could lower the risk of sick leave. Therefore they may not stimulate the use of the app. Participants also pointed out that the app might cause disturbance in the relation between a pregnant employee and her employer. To prevent occupational conflicts, the advice in the app should be formulated cautiously and should emphasize to stimulate a constructive dialogue.

> *FG 1: CvW (employer): Yes, I have experienced that myself, so to speak. That I basically did not dare to step up to my employer, when the last two weeks were quite heavy. I was aware that I was entitled to extra breaks etcetera, but somehow I was afraid to speak up. So I do understand the story you just told, that when an employee shows up with solely an app, and the employer is not informed that this situation might give some, well, disruption, so to speak.'*

A significant factor in preventing these barriers is informing and involving the employers and organizations. If employers see the usefulness of the app itself and the importance of sustainable work during pregnancy, they may become more involved as a facilitator for the use of the app by their employees.

The fact that there is a large variety between the type and size of employers or companies, is neither a facilitator nor a barrier for the use of the app. A footnote was placed by some participants that the app should be developed irrespective of the willingness of employers to participate. It cannot be expected that an app will change the entire culture of companies.

Government

One participant suggested that a television commercial from the ministry of health might facilitate the use of the app.

Table 2. Development of a mobile application: thematic overview of facilitators and barriers

Theme and subcategory	Facilitators	Barriers
Theme 1: Content of the app		
Content of the provided information and advice		
	Understandable information (general)	
	Information and advice according to the existing guidelines (general)	
	Keeping advice clear and simple (general)	
	Showing only relevant and personal information to the user(personal)	Reliable personal advise is difficult when the risk profile is based only on a questionnaire (personal)
	Providing information on the changes in the pregnant body and development of the baby to better understand the impact on her work situation (personal)	It's important to provide some general advices to every user, the app shouldn't become to personal (personal)
	Using a 'selective question' to determine if the user is at risk for a certain risk factor(personal)	
	Synchronizing the advice with the gestational age (personal)	
	Providing specific advice in case of adverse pregnancy outcome as well (personal)	
Added value compared to existing mobile applications		
	App should be based on medical knowledge and the guideline	
	Cover the preconception and postpartum periods in addition to the pregnancy period	
	Make the app noncommercial	
Theme 2: App as a mean for providing information		
Practical aspects		
	The app is easier and faster for searching for information and is always available	
Pregnant women already receive a lot of information regarding their pregnancy		
	App is more accessible than printed information	App provides even more information when there is already enough
Theme 3: Ease of use		
Technical aspects		
	Games and quizzes make the app more fun to use	There are several different operating system

Table 2. Continued.

Theme and subcategory	Facilitators	Barriers
	The app is only useful for 9 months and can be deleted afterwards	Creating an app that uses a lot of battery and memory of the smartphone Information should be readable in a smartphone; no pdf documents
Feedback and interaction between app and user		
	Content of the app should be understandable for every user Information should be well-ordered Illustration, icons, and videos can provide clarification Offer the possibility of linking to more information if desired	Providing too much information
Theme 4: External factors		
Obstetrical caregivers		
	Obstetrical caregivers support the app	
Employer, supervisor, or company		
	Employers are important for the app to succeed	Employers have little knowledge about work-related risk factors for pregnant women and don't see the benefit for themselves Employers might have a negative prejudice about work adjustments for pregnant women App can cause disturbance
Government		
	A television commercial might stimulate the app	

Discussion

Principal results

In this study we aimed to compose a thematic overview for pregnant women', professionals' and employers' facilitators and barriers for the use of a mobile application (app) in obstetrical care in order to reduce occupational related pregnancy complications.

We identified 24 facilitators and 12 barriers within four categorical themes of which we identified 3 main facilitators and t2 main barriers for the successful implementation of our app in obstetrical care to reduce occupational related pregnancy complications. The most important facilitator, in the opinion of our participants, is the need for a good interaction between the app and the user to make the app personal to the user. The second facilitator is the fact that apps are viewed as a more practical source of information compared to traditional written information. The third main facilitator is that the information should be understandable, according to the existing guidelines, and well-dosed. To do so it was recommended to offer the possibility of a hyperlink to additional information.

As barriers several technical aspects may have negative influence on the use of the app according to our participants. Especially extensive battery and memory use of the smartphone are considered barriers. The second important barrier mentioned by the participants is sending frequent 'push-notifications'.

Comparison with prior work

Previous qualitative health studies on mHealth and eHealth in obstetrical healthcare mainly investigate (personalized) text messages [27, 40-42], or internet based programs [35,43]. Most of our findings are comparable to these studies, especially the interactive and personalized aspects; our participants emphasize that a personalized tool which provides only relevant and specific information for the user, is a very strong facilitator for the use of the tool [35, 40-43]. Tripp et al. also showed that apps with interaction between the app and the user where shown to be the most popular category of apps in obstetrical care [17]. Furthermore, findings from the qualitative research of Naughton et al. on attitudes towards SMS text message smoking cessation support, suggests that maximizing personalization and personal relevance can increase the value of text message support and reduce the risk of disengagement [27].

Since the main purpose of our app is to provide detailed information and advice on work adjustments in certain specific work related risks in pregnancy, the personal and interactive aspects of the app could be of strong positive influence for our app. The fact that apps are viewed as faster and easier in searching for information and the information is always available at every place and every time has been pointed out in previous research as well [41, 44].

Feedback from the app to the user is a complex outcome in our results since it can potentially be a strong facilitator, however there exists a delicate balance between important stimulating reminders of advice, and frequent uncalled for 'push notifications' which can be experienced as a barrier. This delicate balance is also seen in previous studies. Two studies reported that text messages could stimulate positive behavioral changes [40, 42], and one study reported that even more frequent messages would be

appreciated [30]. On the other hand, our participants expressed frequent messages as a point of concern. These concerns are in line with the results in the study by Dennison et al in 2013 [44]. Reminders of advice are well accepted and considered useful which is also supported by other studies [30, 40, 42, 44]. For example the mixed method qualitative study of Knight-Agarwall in 2015 showed participants using an app to monitor gestational weight gain desired pop-up messages as a reminder to undertake certain activities [30].

Strengths and limitations

A strength of our study is the proper qualitative health method we used for the focus group meetings and the analysis of the data. Furthermore both focus group meetings where facilitated by the same experienced facilitator. All meetings were audio taped and fully transcribed and were independently coded by two researchers, resulting in negligible inter-coder variance. In case of discussion on the interpretation of the codes a third researcher (FS) was involved in the process.

Other strengths of our study are that in both focus group meetings all different stakeholders were represented, which created the aimed interaction between stakeholders and we have reached consensus on important issues [45].

In line with previous literature on qualitative health research our number of participants is considered sufficient [46]. Besides the sufficient number of participants the results in both meetings were comparable and we therefore believe we have achieved data saturation.

A disadvantage of conducting focus group meetings with different stakeholders together, may result in reluctance to be completely honest because of possible hierarchy between the different participants. Therefore this method might lead to potential loss of important information. The fact that in our study we chose to mix professionals and pregnant women this could be considered a limitation to our study. Since the discussed subject in our study, the development of an app, is not a delicate matter, and is in the best interest of all the participants we decided that this risk was small and therefore acceptable. The active participation of all participants during the meetings also indicated no reluctance of participants to share their opinions and experiences.

Conclusion

We have identified clear facilitators and barriers for the use of an app in obstetrical care. The correct content and dosage of interaction with the end user is a complex aspect to consider in the development of an app. These outcomes will contribute to the further developmental phases of an app. The results of this study are especially of interest to

medical professionals, in several medical areas, who aim to develop an app implementing a guideline or evidence based information in practice.

In future research we aim to evaluate the usability of the app in a think aloud study among pregnant women. Subsequently we aim to evaluate the effectiveness of the app in a controlled trial.

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Appendix 1 – Topics and statements of the focus group meetings

Part one: Introduction.
Use of smartphone and apps. Introduction of the objective of our app.

- What is your experience with the topic Pregnancy and Work?
- What are the bottlenecks you experience?
- Are you familiar with the guideline 'pregnancy, postpartum period and work'? Do you work by the guideline regularly?
- Would you appreciate support for using the guideline?
- Do you use a smartphone for health apps? What are your experiences with the health apps?
- Which apps do you use more frequent? When do you follow the provided advice and when do you not follow the advice?
- Which apps do you delete and why do you delete them?
- Which factors are of influence for pregnant users to follow the provided advice in our app?
- What are important aspects which stimulate the use of the app?
- What could potentially work as a disadvantage and frustrate the pregnant user for the use of the app?

Part two: Discussion on the basis of statements after a short presentation with examples of existing apps[1].

- Topic 1: The app as a tool to reach pregnant women:
  Statement 1: The app is the designated mean to reach all employed pregnant women. When employers and occupational health professionals do not provide the correct information we will have to provide it with an app.

- Topic 2: Content of the app and the advices:
  Statement 2: Providing a lot information or a lot of options will lead to less usage of the app. Details of the influence of for instance all the different toxins and infectious diseases do not belong in this app.

- Topic 3: Effect of the app on adjustments of the work situation:
  Statement 3: When a pregnant shop assistant receives the advice from the app to not stand more than three hours during her work, because it could be harmful for her child, it is very likely that she will arrange work changes with her supervisor.

- Topic 4: The app and health care professionals:
  Statement 4.1: Healthcare professionals in the primary care like midwifes, general practitioners and maternity nurses should stimulate the use of the app. How would that work in your opinion?
  Statement 4.2: Healthcare professionals in the secondary care like obstetricians should stimulate the use of the app. How would that work in your opinion?

- Topic 5: The app and the working environment:
  Statement 5: The working environment (employer, supervisor, human resource advisors, occupational healthcare professionals) should stimulate the use of the app. How could that be done?

- Topic 6: Reinforcing:
  Statement 6: Additionally to the provided advice the app should send encouraging messages that emphasize that the pregnant user is doing well by discussing the advice with her supervisor or occupational healthcare professional.

[1] App Werk en zwangerschap FNV (Pregnancy and work, of a trade union) ; App versterk je Enkel (Veiligheid.nl) (Strengthen your ankle (safety.nl) ; App Owise about breast cancer ; One sheet with pictures of random apps about food, weight loss and exercises.

Usability and usefulness of a mobile health app for pregnancy-related work advice: mixed-methods approach.

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JMIR Mhealth Uhealth 2019 May 9;7(5):e11442.

7

Abstract

Background: Pregnant women are often unaware of potential risks that working conditions can cause to them and their unborn child. A mobile health (mHealth) app, the *Pregnancy and Work* (P and W) app, developed by a multidisciplinary team and based on an evidence-based guideline for occupational physicians, aims to provide advice on work adjustment during pregnancy.

Objective: This study evaluates the usability of the mHealth P and W app and the perceived usefulness of the *work advice*, the main goal of the app, by potential end users.

Methods: A total of 12 working pregnant women participated in think aloud (TA) usability sessions and performed 9 tasks. All TA sessions were recorded, transcribed, and coanalyzed. The usability problems were rated for their severity in accordance with Nielsen severity scale. The completion rates and time taken for completion of tasks were registered. In addition, participants were questioned on demographics and user characteristics and were asked to evaluate the value of the app by filling in the Intrinsic Motivation Inventory (IMI) score and the System Usability Scale (SUS) questionnaire.

Results: In total, 82 usability problems with a severity ≥1 were identified, of which 40 had severity ≥3. The main usability problems concerned the interpretation of terminology used in the app's questionnaires and difficulties in finding and understanding the work advice. Furthermore, 10 out of 12 participants were able to open the work advice page in the app. Only 7 out of these 10 participants understood and intended to follow the work advice. The overall mean IMI score was relatively high (5 out of 7), indicating that the participants did indeed value the use of the app. This IMI score corresponded to the overall mean SUS score (68 out of 100) and the mean grade given to the P and W app (7 out of 10).

Conclusions: This TA usability study showed that the information provided in the P and W app was considered valuable by the end users, working pregnant women, and it meets their needs; however, usability issues severely impacted the perceived usefulness of the work advice given in the app.

Keywords
mHealth; eHealth; mobile phone; pregnancy; work; occupation; occupational exposure; qualitative research

Introduction

Background

Many women continue to work during their pregnancy. In the United States, more than 65% of pregnant women work, whereas in the Netherlands, around 80% [1, 2]. During pregnancy, exposure to certain working conditions, such as physically demanding work, long working hours, working in night shifts, and stress, are associated with preterm birth, low birth weight, and fetal abnormalities [3-12]. As pregnant women are often not aware of these risks, they do not adjust their working conditions [13].

Mobile health (mHealth) apps can offer a suitable solution to this problem as women of reproductive age who are expecting a child are frequent consumers of Web-based health information [14-17]. mHealth, defined as the use of mobile devices for medical and public health practice [18], could therefore inform pregnant working women about work-related pregnancy risks, to increase their awareness of these risks and their associated need for change in working conditions.

However, evidence on the effectiveness of mHealth apps in general is limited [17, 19]. Prior studies provide little information as to how best to design them [20-24]. Adequate consideration of the needs of their intended users is necessary so that they are easy to use and perceived as useful [25, 26]. *The extent to which a product can be used by specified users to achieve specified goals with effectiveness, efficiency, and satisfaction in a specified context of use* is the definition for applied usability, based on the International Standardization Organization [27]. To assess and improve upon the usability of mHealth apps, a wide range of usability evaluation methods (UEMs) is available to detect problems in the user-system interaction. UEMs thus assess human interaction with a system for the purpose of identifying those facets of this interaction which can be improved [28]. Ideally, the design process of any health-related product is conducted in an iterative fashion to better fit with the end user population. Utilizing UEMs in such an iterative design process in the health care domain is especially important as the poor design and usability of medical products can lead to harmful consequences [29, 30]. Therefore, the utilization of UEMs during the development and testing process of health apps is widely recommended throughout research [31,32].

In this study, we developed an mHealth solution, the Pregnancy and Work (P and W) app that aimed to provide information and advice about work-related pregnancy risks [33]. With this advice, pregnant women can adjust their work. The P and W app content is based on the evidence-based guideline for occupational physicians, *pregnancy, postpartum period, and work* [34]. In a prior study, the results of 2 multidisciplinary focus group meetings provided content and design instructions for the development of the P and W app [35].

Objectives

Think aloud (TA), an UEM method, was chosen in this study to assess the usability of the P and W app with potential end users to reveal cognitive processes in the app's user interaction that result in user-interaction problems. The TA method requires participants to talk aloud (ie, verbalize their thoughts) while performing or solving a task to reveal their cognitive processes while interacting with the app, which may result in user-interaction problems [36, 38, 39]. In this way, the TA helps to understand how pregnant woman think—or believe they think—the P and W app works (ie, their mental model) [39]. Mismatches in the end users' mental model of an app and the app's design can severely influence its usability and subsequently its use in practice. This study therefore evaluated the usability of the P and W app and also how potential end users experienced the usefulness of the work advice; this was the main goal of the app.

Methods

Participant recruitment

A total of 2 obstetric care facilities, representing a broad variety of patient groups, participated in this study. Posters and flyers were distributed in both locations. The inclusion criteria were drawn up by an obstetrician and occupational physician. If patients met the inclusion criteria, they were invited to participate in the study. The inclusion criteria were Dutch working women, who were less than 20 weeks pregnant. The criterion of being less than 20 weeks pregnant was deliberately stated as the work advice for pregnant women under 20 weeks of pregnancy can be different than that for those after 20 weeks of pregnancy. Eligible participants were recruited in the waiting area of the physician's office. Recruitment of participants continued until a total of 12 female patients agreed to participate in the TA sessions and evaluate the app; this was the first time they used the P and W app. All participants included in the study were offered a gift card worth €15. An app for this research was submitted to the ethical board of the Amsterdam University Medical Center. The board confirmed that the Medical Research Involving Human Subjects Act did not apply to this study. All data from the 12 participants were anonymously processed. Informed consent was obtained from all participants, allowing us to use the data for analysis.

P and W Pregnancy and Work App and study Flow

The P and W app (Dutch and English) was created as a Web-based app, accessible from every type of mobile browser, with an adaptive design for desktop and mobile phone use.

The P and W app requires the user to create an account to gain access to its content. After creating an account, a user needs to complete a questionnaire about her pregnancy-related medical and work conditions (Figure 1). When completing this questionnaire, the user will be directed to the home page of the app, from where she can navigate to all other

pages. On the home page, users can view monthly pregnancy- and work-related advice messages, which are also sent by email. In addition, the app provides messages about the growth of the unborn baby as the weeks pass. Next to the baby messages, a video with tips and information about pregnancy-related work advice can be viewed on the home page. Participants were given access to a Dutch beta test version of the P and W app.

Welcome page, Questionnaire page, Workadvice page

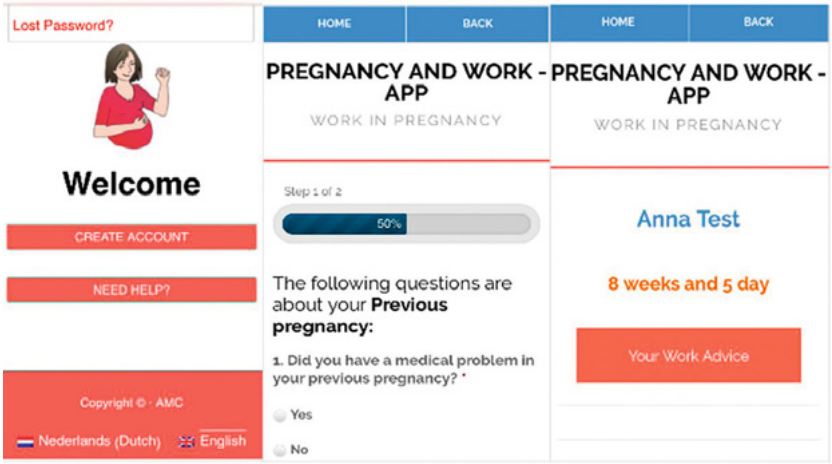

Figure 1. Examples of screenshots of Pregnancy and Work App

Phase 1: Preparation

Participants were informed about how the TA session would be performed; see Figure 2 for the full study setup.

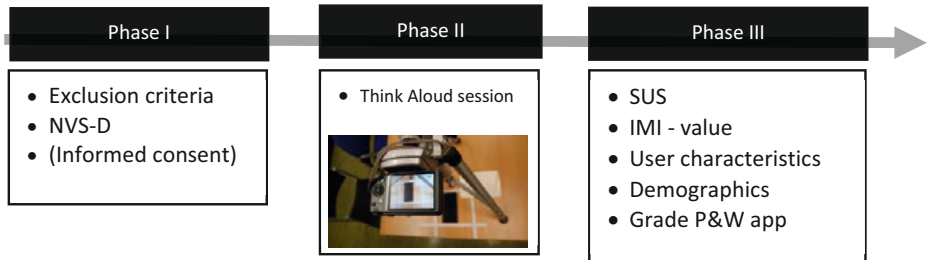

Figure 2. Overview of study setup.

After a 2-week reflection period, a condition for participation in the research, an appointment was made with those women who wanted to participate in the study. The

TA session then took place at their next visit (follow-up consultation) to the obstetrics department. After signing an informed consent form, the participant completed a short survey, the validated health literacy (HL) assessment tool—*the Newest Vital Sign*, translated to Dutch—to analyze its potential influence on the TA outcomes (Stage I, Multimedia Appendix 1 [40, 41].

Phase II: Think Aloud Usability Testing

Participants started with practice tasks on how to *think aloud* (Multimedia Appendix 2). Each participant was informed that the researcher (LvdB) was solely interested in the app's performance and would only interrupt the participant to provide new tasks and to encourage her to keep talking to break silences longer than 5 seconds [42]. A participant had to complete 9 tasks in total that were centered around the core purpose of the app (Multimedia Appendix 3). Tasks were developed in collaboration with the developer and project supervisors of the P and W project. All TA sessions were recorded via video camera. Voice and screen (of their mobile phone) were also recorded (Figure 3).

Figure 3. Set-up TA session

Phase III: Usability and Motivation Questionnaires

After the TA test was finished, the SUS survey was given to the participant to assess the perceived usability of the P and W app [43] (Multimedia Appendix 4). The SUS comprises 10 statements which the participant had to rate on a scale from 1 (strongly disagree) to 5 (strongly agree) to indicate the extent to which she agreed. Then, a short survey selection of the Intrinsic Motivation Inventory (IMI) was given to assess a self-reported evaluation on how much the participant valued the P and W app [44] (Multimedia Appendix 4). The IMI value subscale comprised 7 statements which the participant had to rate on a scale from 1 (do not agree) to 7 (strongly agree) to indicate the extent to which she agreed. An additional short survey was developed to gain more insight into participants' demographics, medical history related to pregnancy, prior experience with (pregnancy-related) mobile apps, and working hours (Multimedia Appendix 4). We asked all participants whether they had received and would follow the work advice (Multimedia

Appendix 4). Finally, participants were asked to give the P and W app a grade on a scale from 1 to 10, where 1 was the lowest and 10 the highest grade.

Data Collection and Analysis

The TA sessions were videotaped, reviewed multiple times, and transcribed to verbal protocols by 2 researchers (LvdB and LP). To gain insight into the effectiveness and efficiency of the participants in performing tasks, each TA session transcription comprised text spoken by the participant and included task completion time stamps and time taken for task completion. To analyze the usability problems participants encountered in more detail, we performed a thematic analysis for which a coding scheme was developed bottom-up in 3 iterative cycles as described by Jaspers [37]. We analyzed 2 TA sessions in-depth to develop a raw coding scheme (first cycle). Usability issues encountered by participants were then given a specific description. We subsequently discussed the resulting codes and grouped them to determine the main themes in the data (second cycle). The developed coding scheme was then applied to code and analyze all verbalizations, this was performed by LvdB and checked by LP. All new issues were discussed to determine whether they were within the branches of the coding tree or if a new main theme had emerged. Usability problems were rated on severity in accordance with Nielsen severity scale [45]. Nielsen severity scale is a rating scale from 0 to 4 (Textbox 1), that allows for the prioritization of usability problems that need to be revised in the development process. The questionnaires were completed on paper and put in a database for data analysis.

Textbox 1. Nielsen's severity scale

0–I do not agree that this is a usability problem at all.
1–Cosmetic problem only: need not to be fixed unless extra time is available on project.
2–Minor usability problem: fixing this should be given low priority.
3–Major usability problem: important to fix, so should be given high priority.
4–Usability catastrophe: imperative to fix this before product can be released.

All data filled in by the participants in the P and W app during the TA sessions were specifically transcribed into a different file to test for task efficacy in relation to the IMI-given work advice by the system. Verbalizations of task 6 in the TA sessions (*find the work advice*) were assessed to analyze whether participants would follow the work advice. These results were compared with the results of the IMI on participant level and the questions about the work advice from questionnaire 3 (Multimedia Appendix 4). Finally, the SUS was used to assess the perceived usability of the P and W app.

Results

Participant Characteristics

The TA sessions with the participants (N=12) took place between April and June 2017. Most participants scored high (=adequate) HL. All participants had paid jobs and used a mobile phone. The average gestational age of the participants was 15 weeks and 50% (6/12) of the participants were pregnant for the first time (Table 1).

Table 1. Participants' basic demographics and characteristics (N=12).

Characteristics	Statistics
Age (years), mean (SD)	33 (3.8)
Education (secondary school), n	
Higher education	8
Intermediate vocational education	4
Health literacy, n	
High	11
Low	1
Paid job, n	12
Working time (hours per week), mean (SD)	37 (6.15)
Gestational age (weeks), mean (SD)	15 (3)
Previous pregnancy, n	6
Children, n	5
Mobile phone (operating system), n	
Android	7
iPhone	5

Task Completion

The effectiveness and efficiency of the participants in performing tasks were measured by completion rates and times and the usability problems. The completion rates and times can be found in Table 2. The average duration of a TA session was 19 min 55 seconds (SD 5 min 25 seconds). Task 1, *create an account*, had a much higher completion time than the other tasks. Tasks 2, 3, 5, and 9 were completed by all participants. Tasks 1, 4, 6, 7, and 8 were not completed by all participants. The first 3 tasks took, on average, the longest time to complete, ranging from 1.5 min to 4 min. Task 9 had the fastest mean completion rate of 4 seconds.

Table 2. Completion rates and time taken per task (N=9) by participants.

Task	Completion rate	Time taken for completion (seconds), mean (SD)
1. Create an account	10/12	240 (83)
2. Fill in a questionnaire	12/12	179 (101)
3. Adjust answers to the questionnaire	12/12	96 (74)[a]
4. Find *your rights and tips for consultation* page	11/12	31 (38)
5. Find *baby message(s)*	12/12	16 (10)
6. Find the *your work advice* page	10/12	10 (8)
7. Find the *print/save* button	10/12	9 (9)
8. Find the goal of the Pregnancy and Work P and W app	11/12	32 (18)
9. Log out of the app	12/12	4 (4)

[a]A total of 2 participants initially did not understand this task.

Usability Problems

The TA study identified a total of 101 usability issues, 82 of which were considered *real* usability problems (ie, severity ≥1), whereas 40 usability problems were rated with a severity of 3 (major) or 4 (catastrophic). In addition, the participants encountered 11 unique bugs when using the P and W app. An overview of the most severe usability problems can be found in Table 3. The high completion time with *create an account* (Table 1) seemed to have a connection with the many usability problems in this area (Table 3). None of the participants experienced (severe) usability problems when completing tasks 5, 7, and 9. In the following section, we give an in-depth analysis of the severe usability problems detected regarding *terminology interpretation* and *finding and understanding the work advice* that directly impacted the participants' perceived usefulness of the advice given in the app.

Table 3. Overview of severe usability problems per main problem type.

Usability problem[a]	Frequency	Severity	Source of main problem
Unclear buttons	12	2 to 4	Create account
Functionality with layout	11	4	Create account/home page
Terminology interpretation problems	8	4	Create account/home page
Finding and understanding work advice	8	4	Home page/work advice

[a]*Multimedia Appendix 5 shows an overview of all the usability problems.*

Qualitative Assessment

Terminology Interpretation Problems

Participants had to complete a questionnaire about their pregnancy-related medical conditions, previous pregnancy (if relevant), and work conditions using the app. Several terminology interpretation problems arose during the TA study, which consequently

prevented the participants from receiving accurate personal work advice. For example, when asked whether problems had been experienced during the previous pregnancy, participants were unsure whether *previous pregnancy* implied the immediate previous pregnancy or also the pregnancies before that. One participant who had not experienced problems during her previous pregnancy, but did experience issues during the pregnancy before that, assumed it implied her direct previous pregnancy. Her confusion in answering the question correctly affected the outcome of the work advice, as relevant information was missing:

> *Okay. Um. "Did you have a medical problem in your previous pregnancy?" This is about my last pregnancy, I think, and not the pregnancies before. So, I'm assuming that. And then it's a no.* [Participant 5]

Problems were also prevalent when, in closed-ended questions, the participant did not find the answer that applied to her within the limited selection of possibilities of medical disorders. When given a list of potential problems during a previous pregnancy, participants experienced troubles in selecting the best suited option to describe their problem:

> *...But I do not know if that should be put under "deceased child" or "child born before a gestational age of 37 weeks"? You know what I mean?* [Participant 3]

Another example of a terminology interpretation problem that affected the outcome of the work advice was related to the question of *being exposed to any chemical agents in the work environment*, followed by a list of examples. Several participants did not notice the list of examples and answered *no*. Furthermore, 2 other participants did not know whether an agent that they worked with should be considered chemical, as it was not on the list of examples:

> *...Yes, with hair dye. Is that chemical?* [Participant 9]
> *...I'm having doubts. I work with laughing gas. That's not very chemical, but...I don't know whether I should answer yes or no.* [Participant 11]

Finding and Understanding the Work Advice

Participants also experienced problems in understanding the work advice because of central design problems in the interface. One of the first issues encountered was that the participants expected the app to show them something different than what it actually did. Participants expected the app to show their work advice directly on the homepage, as they perceived this to be the essential goal of the app. They did not expect to have to search for it in the interface or take any other action to find it. For example, participant 6 did not understand that the *your work advice* button was clickable and therefore sought work advice elsewhere or stated that she could not find it (Figure 4):

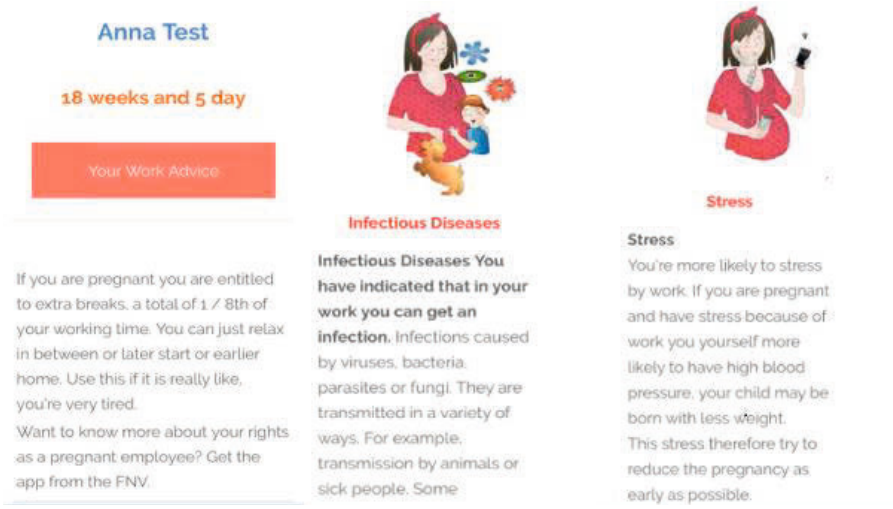

Figure 4. Your work advice

...Oh, let's see if that is somewhere. No idea. [Scrolls down and up] Have a look. Here is my work advice. Uh... [Scrolls up and down, multiple times] No, I have no idea. [Participant 6]

A different example related to the participants stating that they saw their work advice depicted on the home page. However, the home page only provided a small section with tips and information about pregnancy-related work advice, which some clearly interpreted as the entire personal work advice. A total of 2 participants thought this was the case; therefore, both of them missed the actual content of the *your work advice* page:

...I've just seen my work advice. [Scrolls up and down. Scrolls to top of the page. Taps the back button. Loads page] Yes, your work advice. I have already read it. So, it is here. [Participant 8]

Another usability issue was related to the fixed structure in which the work advice was presented in the mobile interface. Depending on the answers given in the questionnaire, specific information followed on the work advice page. The resulting advice therefore included some sections without advice and some sections with the advice, spread over the mobile interface. One participant did not get work advice below the *work header*; however, she did receive work advice with regard to issues during her previous pregnancy, but this would only have become visible if she had scrolled the page down. She therefore missed the advice given:

None? That's easy. I don't need to make any work adjustments. I don't think so either, because I have an office job. [Participant 1]

User Evaluation: Intrinsic Motivation Inventory and System Usability Scale

The task efficacy of task 6, *find the "your work advice" page*, was analyzed in relation to the detected usability problems in *finding and understanding the work advice* and combined with the results of the IMI, SUS, and questions about the work advice from questionnaire 3 (Multimedia Appendix 4). Some participants never reached the work advice page on the app (17%) but thought they did, whereas 3 out of 12 participants (25%) were convinced that they had not received this advice (Table 4). However, all participants did actually receive some form of pregnancy-related work advice. Among the 9 participants who stated that they had received work advice, 2 indicated that they would not follow it.

Using the IMI, we assessed the self-reported evaluation of how much the participants valued the P and W app; the overall mean IMI value score was 5 (SD 0.9) out of 7. The perceived usability of the P and W app was stated by the SUS. The overall mean SUS was 68 (SD 11). Finally, the participants were tasked to give the P and W app a grade on a scale from 1 to 10; the mean grade given to the P and W app was a 7 (SD 0.89; Table 4).

Table 4. User evaluation based on the use of work advice, Intrinsic Motivation Inventory (IMI), System Usability Scale (SUS), and grade.

Participant number	Did you receive work advice from the app?[a]	If so, do you intend to do something with this work advice?[b]	IMI[c]	SUS[d]	Grade
1	No[e]	N/A[f]	5.57	85	8
2	No	N/A	4.29	77.5	7
3	Yes	Yes	3.71	55	5
4	Yes	Yes	5.00	77.5	7
5	Yes	Yes	5.14	65	8
6	Yes	No	4.43	77.5	6
7	Yes	Yes	5.57	57.5	7
8	Yes	No	3.00	70	7
9	No	N/A	4.29	75	7
10	Yes	Yes	6.29	55	6
11	Yes	Yes	5.29	50	6
12	Yes	Yes	4.86	72.5	6

[a]*Multimedia Appendix 4-III Questionnaire 3, Question 1.*

[b]*Multimedia Appendix 4-III Questionnaire 3, Question 2.*

[c]*IMI score; 1=not at all true to 7=very true.*

[d]*SUS score; 1=strongly disagree to 5=strongly agree.*

[p]*participants 1, 2, and 9 were convinced that they had not received work advice; however, all participants did receive work advice.*

[f]*N/A: not applicable as the participant indicated that she did not receive work advice.*

Discussion

Principal Findings

The overall effectiveness and efficiency of the 12 participants in performing tasks in the TA sessions are gauged by the completion times and rates and the usability problems. The TA study identified 82 usability problems with a severity ≥1, of which 40 had severity ≥3. The high completion time of the task to create an account seemed to be connected to the many usability problems that participants experienced in this task. As *creating an account* in an mHealth app is not usually part of the core, there is a chance that the design of this first part of the app may be neglected. Design errors in *creating an account*, however, increase the risk of participants dropping out quickly.

We performed an in-depth analysis of the severe usability problems detected regarding *terminology interpretation* and *finding and understanding the work advice* as these issues directly impacted the usefulness of the app. As participants were unable to correctly interpret the terminology in the questionnaire about previous pregnancies, medical disorders, and chemical agents, they did not understand how to complete the questionnaires corresponding to their personal situation. They thus did not receive the correct personal work advice for their circumstances.

Participants also had a different expectation of what the app would show them. Their mental model, the way information is represented in the mind of the end user, affected how they acted in the system in filtering the relevant information. The mental model of the participants did not match how the designer developed the system, as the designer had based it on his own mental model of how future end users would act on the information presented. The mental model of end users, which encompasses values, beliefs, and knowledge, creates perspectives for filtering information and guiding problem solving [46] and has the ability to affect how a person acts [47], differed from that of the designers. The users therefore also experienced problems with understanding the work advice, as their expectations did not match how the designer developed the system (based on his mental model of how future end users should act on information).

Due to the usability problems in its design, 10 out of 12 participants were able to open the work advice page. Only 7 out of these 10 participants understood and intended to follow the work advice given in the app, which was the main goal of the app.

The overall mean IMI score was relatively high (5 out of 7), indicating that the participants did indeed value the use of the app. This corresponded to the overall mean SUS score (68 out of 100) and the mean grade given to the P and W app (7 out of 10).

Comparison With Prior Work

Our main results indicated the effect of the app's navigational structure and screen design on the ability of a specific group of participants—pregnant working women—to find work advice and their intention to follow it thereafter. Other studies in mHealth and electronic health that have applied the TA method have demonstrated that although participants *think* that they have achieved the main goal of using the apps, in reality its intended objective was not reached [48, 49]. In one study the researchers observed that the majority of participants, older cancer patients, were not able to find the requested information although the participants themselves frequently commented during testing that it was easy for them to find it [48]. In a different study, patients with rheumatic diseases were enthusiastic about the possibilities of interactive apps such as peer support forums and online consultations; however, nearly all participants experienced difficulties and were not able to complete all the usability evaluation tasks while interacting with the system [49].

As in our study, other researchers and designers have underlined the importance of an iterative approach in designing mHealth apps to understand the needs of end users as well as improve app usability and feasibility [36, 50]. The importance of performing usability studies on mHealth apps to be used in a clinical and patient setting therefore needs serious attention. User testing is an essential part of developing mHealth apps, especially when aiming to effectively change actual patient behavior and/or affect patient outcomes.

Strengths and Limitations

A limitation is that the TA sessions took place in a laboratory setting. In their own home, participants may have taken more time to take a look at the app again. One of the strengths of this study is that the sample size is adequate for obtaining usability problems and that we used a mixed-methods approach— we combined the results of a TA test with the results of questionnaires on demographics, user characteristics, SUS, perceived value (IMI), and evaluation of the app. Another strength of our study is that it was performed by a multidisciplinary team and that the TA study is part of a process in developing an mHealth app, which started with 2 multidisciplinary focus group meetings [29].

Due to a lack of variety in HL levels, we were unable to analyze its potential influence on the TA outcomes. However, the recruitment of only 1 out of 12 participants with limited HL is in line with the estimations of HL prevalence levels in the Netherlands [51]; this certainly applies to a working population.

It is possible that the intention to follow the work advice could change according to the end user's job. However, as a significant proportion of the participants was not able to open the work advice page in the app, and/or understand the work advice or intend to follow it, we think that the influence of profession is limited in this study. For the next study, we would advise asking participants about their job.

To human factor specialists, it is well known that end users should be involved from the beginning when developing an mHealth app. However, those who are well informed about a particular health domain, but less so about medical informatics, should be aware that an iterative multidisciplinary approach with the involvement of the target group from the start by using UEM research in the project is essential and can be very valuable.

The mixed-methods approach provides an insight into the cognitive process of a specific user group—pregnant working women—and their intention to use the P and W app. The TA results, in combination with the questionnaires on the perceived usability and value and the evaluation of the app, showed that incorrect interpretation of terminologies in the system prevented the end users from receiving the correct work advice. They also experienced problems with understanding the work advice because of central design problems in the interface. Despite many usability problems, the participants were relatively positive about the P and W app; the information provided in the app is considered valuable to the end users and meets their needs. The usability findings of this research could then be used to drive recommendations for developers for the next iteration of the P AND W app aimed at pregnant working women.

Conclusions

The overall conclusion of this study is that the information provided in the P and W app was considered valuable to the end users, working pregnant women, and meets their needs; however, the usability issues severely impacted the perceived usefulness of the work advice given in the app. The results of this study draw attention to the relation between effective health apps and how their design might hamper their effectiveness in changing patients' behavior. An iterative UEM multidisciplinary approach, with the involvement of the target group from the beginning, is therefore essential for the development of health apps.

The mHealth app will be redesigned and tested in an intervention study, a survey on the effect of the app on actual work adjustment by pregnant women. A future version of the P and W app will be a valuable tool for informing pregnant women about pregnancy-related work risks.

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Conflicts of Interest None declared.

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Multimedia appendix I. Questionnaire before think aloud sessions & nvs-d

(NVS-D can be requested)
Dear Mrs,

Thank you for your interest in this research. Before we can invite you to test the 'Pregnancy and Work' App, we would like to ask you to fill in a number of questions. We use these questions to divide participants into groups.
Your answers will be anonymized and used for scientific purposes only.
If you wish to discontinue this questionnaire, you may do so at any time. You are not obliged to give a reason why you want to stop.
If you have any further questions, you can ask the researcher.

Thanks in advance.

Sincerely,
The research team

Questionnaire

1) **How many weeks are you pregnant?**
   …… weeks
2) **Do you have a job?** (Tick what applies to you)
   - □ Yes
   - □ No
3) **Do you own a mobile phone?** (Tick what applies to you)
   - □ No (continue to the *Assignment)*
   - □ Yes, a mobile phone with internet (iPhone / smartphone)
   - □ Yes, a mobile phone (for example a Nokia)
4) **How often do you use your mobile phone?** (Tick what applies to you)
   - □ Almost never, just to be reachable
   - □ 1x a day or less
   - □ Several hours a day

Assignment and questionnaire NVS-D can be requested

Contact

If you are allowed to participate in the study, how can we best reach you?
Name: …… ……
E-mail address: …… ……
Phone number …… ……
End of the questionnaire.

Multimedia appendix II – think aloud session protocol

Protocol TA Sessions 'Zwangerschap en Werk' App

Researcher: L. A. van den Berg
Participants: 5-8 per HL group; ≥ 15 participants
Duration: Estimated +/- 30 minutes

Preparation:

1. Check/print enough informed consent forms.
2. Check/print enough HL forms and post TA session questionnaires.
3. Check if the correct equipment is set up and functions accordingly:
   - □ Laptop
   - □ Camera (on tripod)
   - □ Pen
   - □ Power Bank
4. Check if there is enough battery life and memory space on equipment:
   - □ Laptop
   - □ Camera (on tripod)
5. Print out list of possible participants for that day.
6. Start recruiting participants. Ask potential participants whether they match the inclusion criteria (pregnant <20 weeks, working, native speaker) and whether they are willing to participate.

HL assessment:

7. Explain the procedure of the session. "Thank you for participating in the research. Within this research we are going to look at the user friendliness of a new app, the 'zwangerschap en werk' app. During this sessions I will give you a number of questionnaires and I will let you test the app on your own telephone. When you'll test the app on your phone I'll record the screen of the phone with this camera. Is everything clear? Do you have any questions? Great, then I would like to ask you to fill in this informed consent first."
8. Give **informed consent form** and let the participant fill it in.
9. "We will start with a short list of questions. On this page you'll find a food label. The questions on the other page are all referring to the food label. Fill in all the questions and take as long as you like".
10. Give the **NVS-D**.
    - □ NVS-D (duration: 3-5 minutes)
11. If the participants asks to use a calculator, she is allowed to do so. But you cannot offer a calculator without her asking.

TA session:

12. "Now we will start testing the application on your own phone. We are going to move to this part of the table where you can see a square marked with tape." Coordinate the participant to the camera set-up.
13. "Before we start the actual testing of the app I am going to explain how the procedure is going to work. You are going to do a so-called Think Aloud test. During this test you need to keep talking about what you are doing and thing whilst using the app." Provide participant with example on the researcher's phone. "So before we start we are going to practice this with a small task. Can you show what the weather will be for tomorrow on your phone and whilst doing that keep talking? Let's give it a try."
14. Start practice round TA session. "Well done."
15. "We are almost ready to start our session. During this session I will give you a number of task to do before and in the app. When you are testing the app, let me know what you see and what you find interesting. It is important that you keep your phone as close to the table as possible and within the taped square. Any questions?"
16. Press start on camera.
17. Let participant perform the following tasks:
    - □ Create an account (provide user with study number).
    - □ Fill in the (<20 weeks) questionnaire.
    - □ Adjust questionnaire.
    - □ Find "rights and how to discuss these with your employee" page
    - □ Find baby messages
    - □ Recover (personal) advice.
    - □ Print your advice.
    - □ Go to more information page / Find the goal of the app
    - □ Log out
18. "Great, that's it."
19. Stop camera.

Post TA session questionnaires

20. "Okay now I'm going to ask you to fill in a few more questionnaires and that's the final part of this research. Do this as carefully and truthfully as possible."
21. Give participant the following questionnaires:
    - □ SUS (duration: 2 min)
    - □ IMI (duration: 1 min)
    - □ Characteristics/Miscellaneous (duration: 2 min)
22. "That was it. Thank you for participating and have a nice day."
23. Give the participant the VVV gift certificate and show her the way out.

24. Import video file to laptop and delete file on memory card.

Multimedia appendix III – participant tasks think aloud: description, achievement, and inclusion motivation

	Task	Achieved when	Inclusion motivation
1	Create an account.	Participant successfully created an account and can therefore utilise the app.	In order for the end-user to utilise the app she needs to be able to make an account.
2	Fill in the questionnaire.	Participant successfully filled in the two pages of questionnaires (mandatory) and gains access to the home page.	In order to use the app and receive work advice, the end-user needs to fill in the questionnaire.
3	Adjust answers questionnaire.	Participant was able to adjust one of the answers in the aforementioned questionnaire.	The work advice provided in the Z&W app is based on the answers given in the questionnaires. If there is a change in either of these answers the user should be able to easily adjust her answers.
4	Find 'Your rights and tips for consultation' page.	Successfully found the 'Your rights and tips for consultation' page.	The 'Your rights and tips for consultation' page provides, what is considered by the project supervisor, essential information.
5	Find 'baby message(s)'.	Either located the 'baby message' on the home page or finds the 'All baby messages' page.	The baby messages were added by the developers to stimulate recurrent visits by the user.
6	Find the 'Your work advice' page.	Participant reached the 'Your work advice' page.	The main aim of the Z&W app is to provide end users with pregnancy related work advice. Finding this page is therefore vital for achieving this goal.
7	Find the 'PRINT/SAVE' button.	Participant located the 'PRINT/SAVE' button on the 'Your work advice' page.	The end-user should be able to print and save their work advice. This documentation can potentially be used for future discussion with an employer or care giver.
8	Find the goal of the Z&W app.	Participant located the goal of the app on the 'About us' or 'About this app' page.	End-users will not use the app in a research setting, where the goal is explained beforehand. The end-user should therefore be able to locate the goal of the app on the app itself.
9	Log out of the app.	Participant successfully logged out of the app.	Whether the participant can log out was added to simulate a normal session and to check whether users could find the log out button.

Appendix IV questionnaires after think aloud session

Appendix IV-I questionnaire 1 (SUS= system usability scale)

All statements below are about the app you just tested. Please indicate to what extent you agree with the following statements.

	Strongly disagree				**Strongly agree**
	1	2	3	4	5
1. I think that I would like to use this system frequently					
2. I found the system unnecessarily complex					
3. I thought the system was easy to use					
4. I think that I would need the support of a technical person to be able to use this system					
5. I found the various functions in this system were well integrated					
6. I thought there was too much inconsistency in this system					
7. I would imagine that most people would learn to use this system very quickly					
8. I found the system very cumbersome to use					
9. I felt very confident using the system					
10. I needed to learn a lot of things before I could get going with this system					

Appendix IV-II questionnaire 2 (IMI= intrinsic motivation inventory)

All statements below are about the app you just tested. Please indicate to what extent you agree with the following statements.

	Not all true			**Somewhat true**			**Very true**
	1	2	3	4	5	6	7
I believe this activity could be of some value to me							
I think that the app is useful							
I think this the use of the app is important							
I would be willing to use the app again because it has some value to me.							
I think doing using the app could help me to							
I believe using the app could be beneficial to me.							
I think the app is a important.							

Appendix IV-III questionnaire 3

This is the last questionnaire. Below are some questions about yourself. As mentioned before, this information will not be shared with anyone.

Question 1. Did you receive work advice from the app? *(Tick what applies to you)*

□ Yes (go to question 2)

□ No (go to question 3)

Question 2. If yes, do you plan to do something with this work advice? *(Tick what applies to you)*

□ Yes

□ No

Question 3. How old are you?

.....

Question 4. Have you been pregnant before? *(Tick what applies to you)*

□ Yes

□ No

Question 5. Do you already have children? *(Tick what applies to you)*
□ Yes
□ No

Question 6. What is your highest level of education? *(what is the highest level of education you have completed)*
(Tick what applies to you)
□ **Elementary School**
□ **Pre-vocational secondary education.**
□ **Senior general secondary education**
□ **Pre-university education**
□ **Secondary vocational education.**
□ **University of applied sciences**
□ **University**
□ **Other, namely: .....**

Question 7. How many hours do you work on average per week? ..... hours

Question 8. Which of the apps below do you sometimes use?
(Check what applies to you and circle how often you use this app.)

□ WhatsApp	several times a day / daily / weekly / monthly
□ Facebook	several times a day / daily / weekly / monthly
□ Instagram	several times a day / daily / weekly / monthly
□ Twitter	several times a day / daily / weekly / monthly
□ Snapchat	several times a day / daily / weekly / monthly
□ YouTube	several times a day / daily / weekly / monthly
□ Pokémon GO	several times a day / daily / weekly / monthly
□ Google Maps	several times a day / daily / weekly / monthly
□ App for your e-mails	several times a day / daily / weekly / monthly
□ None of the apps above	several times a day / daily / weekly / monthly

Question 9. Do you use 'pregnancy' apps on your phone or tablet? (Examples: Prénatal App, Zwanger en Zo, Pregnancy Tracker, etc.)
□ Yes
□ No

Question 10. What rating would you give the app?
(Tick what applies to you)

1	2	3	4	5	6	7	8	9	10

End of the questionnaire

Evaluation of a blended care program for caregivers and working pregnant women to prevent adverse pregnancy outcomes: an intervention study

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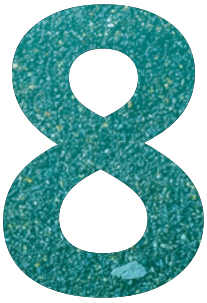

Abstract

Objective: Work-related activities can be a risk factor for pregnancy complications such as preterm birth.

This study evaluates the effectiveness of a blended care program, Pregnancy and Work, that provides pregnant workers and their obstetrical caregivers with advice on work adjustment.

Methods: Women less than 20 weeks gestation, in paid employment or self-employed, in the care of four participating hospitals and their referring midwifery practices in The Netherlands received either the blended care program (n=119), consisting of a training for professionals and a mobile health application, or care as usual (n=122) in a controlled intervention study with a follow-up in intervention and control populations. All participants completed three questionnaires concerning health and working conditions at 16, 24 and 32 weeks pregnancy. Primary outcome was the percentage of women who received advice from their obstetrical caregiver about work adjustment. Secondary outcomes were work status, realised work adjustment and working conditions. Groups were compared using univariate and multivariate regression analyses.

Results: A total of 188 (78%) completed all three questionnaires. In the blended care group, women received more advice from obstetrical caregivers to adjust their work, than in the control group, 41 (39%) versus 21 (18%) (aRR 2.2, 95%CI 1.4-3.4), but less from their employer (aRR 0.29, 95%CI 0.14-0.61). There were no significant differences in realised work adjustments. At 24 weeks, 30% of the pregnant women in both groups continued to work in hazardous workplaces.

Conclusion: Among working pregnant women, the blended-care intervention increases advice on work adjustment given by midwives and obstetricians, but does not lead to more work adjustments.

Keywords
mHealth; Blended Care; Pregnancy; Work; Employment; Employer; Return to Work; Occupational Exposure; Intervention; Legislation;

Key messages

1. What is already known about this subject:

- Exposure to certain working conditions during pregnancy is associated with adverse pregnancy outcomes.
- Working pregnant women and their health care professionals are often unaware of these risks and of maternity protection legislation.
- Pregnant women continue to work in a hazardous workplace or decide to withdraw from work using sick leave or preventive pregnancy leave schemes.

2. What are the new findings:

- We developed a blended care program called 'Pregnancy and Work', which consists of a training session for professionals and a mobile health application (the P&W app), to provide pregnant women and their obstetrical caregivers with personalised advice on work adjustment.
- Among working pregnant women, the blended-care intervention increases advice on work adjustments given by midwives and obstetricians, but less from their employer, not leading to more work adjustments.
- Only a few employers inform their pregnant employees about rights and risks, despite there being a legal obligation to do so. At 24 weeks of pregnancy, almost a third of the women in both groups continued to work in hazardous workplaces.

3. How might this impact on policy or clinical practice in the foreseeable future:

- Improving the design of the P&W app for working pregnant women, obstetrical caregivers and employers, could increase the effectiveness of the blended care 'Pregnancy and work' intervention and lead to a safer workplace for pregnant employees.
- Obstetrical caregivers can play a role in advising pregnant women on topics related to their health in their working environment and work together with occupational physicians.
- To prevent adverse pregnancy outcomes, attention should be paid to safe working conditions earlier in pregnancy.

Introduction

Many women with a paid job continue working during their pregnancy. In the United States, more than 65% of pregnant women work while in The Netherlands, nine in ten women have a paid job and continue occupational activities during their first pregnancy [1, 2]. Exposure to certain working conditions during pregnancy is associated with adverse pregnancy outcomes (preterm birth, low birth weight, foetal abnormalities) and pregnancy complications (hypertension, eclampsia, miscarriage) [3-13]. Many working pregnant women, their health care professionals and employers are unaware of these risks and legal measures concerning maternity protection in the workplace. In the European Union, including The Netherlands, employers are responsible to provide work adjustments of pregnant employees where necessary. However, due to a lack of implementation of the legislation, some of the pregnant women continue to work in a hazardous workplace or decide to withdraw from work using sick leave or preventive pregnancy leave schemes [14, 15].

Providing pregnant women with information about the required work adjustment can encourage them to realise this in their own work and thus prevent the adverse effects of poor working conditions on pregnancy or withdrawal from work on sick leave. As women of childbearing age are frequent consumers of online health information [16], mHealth application, defined as the use of mobile devices for medical and public health practice [17], have the potential to serve as a practical source of information, provided that such information is understandable and well-dosed, with a good interaction between app and user and meets existing guidelines [18]. Although most mHealth lifestyle and medical apps for pregnant women seem to be feasible and acceptable, the evidence on effectiveness is limited, and most intervention studies have evaluated small study populations [19]. An iterative multidisciplinary approach with involvement of end users from the start is important for the development of applications [20].

A step-wise approach was employed to develop a mHealth application, the Pregnancy and Work app (P&W app), based on the evidence-based guideline for occupational physicians: *Pregnancy, Postpartum Period and Work* [21]. This app provides pregnant workers, in paid employment or self-employment with personalised advice to adjust their work, adapted to their individual working conditions and health. Prior studies providing content and design instructions for the development of the P&W app [18] considered the app to be valuable and able to meet the needs of end users [22]. All stakeholders (pregnant women, occupational physicians, general practitioners, midwives, obstetricians and representatives of trade unions and employers' organizations) were involved in the developmental process. Blending face-to-face guidance with online support improves client-therapist connection and adherence [23] and may increase the coverage, quality and efficiency of occupational and safety health education [24]. Successful examples are interactive e-learning modules such as that concerning occupational asthma for health

care professionals which resulted in greater use and awareness of national occupational asthma guidelines [25]. Occupational hygiene e-courses for students were evaluated positively on effectiveness in a blended application [26].

Therefore, we developed the blended care 'Pregnancy and Work' program, consisting of a training session for professionals and a mobile health application to provide pregnant women and their obstetrical caregivers with advice on work adjustment.

The aim of this study was to evaluate whether this blended care program leads to more advice about work adjustment from obstetrical caregivers to their clients (1) and whether these pregnant women realise more work adjustments than those receiving care as usual (2).

Methods

Design

We evaluated the effectiveness of the blended care P&W program, in a controlled intervention study with a follow-up study of the intervention and control populations.

In The Netherlands prenatal care is supervised by midwives in primary care and by obstetricians in secondary care. Midwives take care of low-risk pregnancies. If specialised care is needed, midwives refer to an obstetrician in an affiliated hospital. We will refer to this stratified care model as a 'cluster', meaning a hospital including all surrounding midwifery practices [27].

Participating clusters were followed during two consecutive time-periods. The first period covered January 2016 to April 2017, and the second period covered May 2017 to August 2018. Between the two time periods the training of health care professionals took place as part of the intervention. During the second time-period patients were also offered the mobile phone (P&W) app. Selection of participants was not consecutive but depended upon availability of a trained health care professional and the available time at the prenatal visit.

Participants

Women, > 17 years, less than 20 weeks pregnant in paid employment or self-employed, visiting one of 24 obstetric care facilities in four clusters in the North West region of The Netherlands were eligible for the study.

Intervention

The blended care program consisted of a training session for midwives and obstetricians about the Netherlands Society of Occupational Medicine (NVAB) [21] *Pregnancy,*

postpartum period and work guidelines and the use of the P&W app. The training aimed to equip participants with the skills necessary to be able to work with the advice generated by the P&W app to guide their clients. After the training session, these midwives and obstetricians gave their clients access to the P&W app.

The P&W app (in Dutch and English) was developed as a Web-based app, accessible from every type of mobile browser, with an adaptive design for desktop and mobile phone use. The content is based on the evidence-based guideline for occupational physicians and provides end users with personalised advice on possible work adjustments [21]. The P&W app is described in more detail in our previous study [22] and in Supplement A. The control group received care as usual.

Procedure

Obstetrical caregivers in participating clusters provided verbal and written study information to eligible clients. After digital informed consent was given women received access to the questionnaires and P&W app if applicable.

Obstetrical caregivers (midwives and obstetricians) of the four participating clusters started including for the control group from January 2016 to April 2017 (step 1). Between March and April 2017, obstetrical caregivers of the same four participating clusters followed a multidisciplinary training session together with occupational physicians [21]. Subsequently, from May 2017 to August 2018, these obstetrical caregivers recruited participants for the intervention group (step 2). All participants received access to the online questionnaires at 16,24 and 32 weeks of pregnancy. Some participants completed the questionnaire after receiving a reminder, which was sent 2-3 weeks after the first request. Participants in the intervention group received access to the P&W app after registration.

Outcome measurements

The primary outcome was the percentage of pregnant women who received advice about their work from their midwife or obstetrician. Secondary outcomes were work status (still at work or on sick leave), work advice (from whom) and complaints of health and pregnancy, realised work adjustments and working conditions. The intervention was considered effective if pregnant women in the intervention group received advice statistically significant more often from their midwife or obstetrician to adjust their work and realised work adjustments in their work more often than women in the control group.

Data collection

All participants (both control and intervention group) received emails to complete three different online questionnaires at 16, 24, and 32 weeks of pregnancy. The first questionnaire included baseline characteristics such as data on educational level,

general health and lifestyle, and medical problems in current and former pregnancies. In addition, questions from a validated questionnaire about psychosocial job strain and physically demanding work [7] supplemented with questions about other working conditions (e.g. (irregular) working times, and chemical, biological and physical factors (noise, climate) were used. To determine the influence of private factors on the health and work capacity of pregnant women, the last part of the questionnaire concerned commuting, sports, and household characteristics. The questionnaires at 24 and 32 weeks of pregnancy concerned work status (normal working hours, sick leave or pregnancy leave), working conditions, health complaints and (advice on/ realised) work adjustment, and leisure and household characteristics in the second and third trimester. Sick leave was defined as (permitted) absence from work because of illness. We distinguished two types of leave in the period granted to mothers in connection with pregnancy and childbirth: pregnancy leave (prior to childbirth) and maternity leave (after childbirth). Data were collected on web-based electronic case report forms and were stored in anonymised form in a database.

Statistical analysis

General descriptive statistics are given for baseline characteristics as frequencies with percentages, means with standard deviation, or medians with interquartile ranges.

Tests of univariate analyses were Chi-squared or Fisher exact tests, the Mann Whitney tests, or t-tests. Multivariate models for adjusted analysis were done using generalised linear models, with log link and binomial distribution to estimate adjusted relative risks [28]. Relative risk estimates for received advices to adjust work and for achieved work adjustments were adjusted for those variables which differed significant between intervention and control group: working conditions concerning job strain and information from employer, when reporting pregnancy about work adjustment.

Outcomes on changes in work at 24 and 32 weeks of pregnancy were analysed as cumulative changes (any changes during follow-up). Therefore, these outcomes represent data that were analysed without the use of a mixed model or generalised estimating equations. Effects of hierarchical clustering of intervention effects or heterogeneity of outcomes due to hierarchical ordering of data (i.e. centre effects) were assessed using cluster analysis, as well as by stratification of outcomes by centre, with visual and statistical assessment. A cut-off value for statistical significance for heterogeneity was not prespecified as the limited sample size was considered to preclude formal statistical inference. Data were analysed using IBM SPSS Statistics 24.0.

Results

A total of 57 obstetric caregivers employed at one of the four participating clusters, together with 32 occupational physicians, followed one of the four multidisciplinary trainings sessions on the guideline and the use of P&W app (Table 1). Most of the participants rated the training as valuable (98%, n=88) and would recommend the app to their patients (94%, n=85) and use it (87%, n=78).

Table 1. Results of multidisciplinary training session for healthcare providers on NVAB 'Pregnancy, postpartum period and work' guidelines and P&W app

Characteristics participants	**90 (100%)**	
Profession		
Midwife	47 (53%)	
Obstetrician	10 (11%)	
Occupational physician	32 (36%)	
Work experience (years)		
< 10	20 (22%)	
10-25	35 (39%)	
>25	35 (39%)	
Knew about the NVAB 'Pregnancy, postpartum period and work' guideline		
No	27 (30%)	
Yes	25 (28%)	
Yes and uses it	36 (40%)	
The training	**Yes**	**Neutral**
The training was valuable to me	88 (98%)	1 (2%)
The training is in line with my knowledge	83 (92%)	7 (8%)
I will recommend the app to my patients	85 (94%)	5 (6%)
I'm going to use the P&W app	78 (87%)	12 (13%)

All variables mentioned as N (%)
Abbreviations: NVAB: The Netherlands Society of Occupational Medicine, P&W app: app pregnancy and work

A total of 241 women were included in the study: 122 in the control- and 119 in the intervention group. Of this number 188 (78%) women completed all three questionnaires: 101 in the control group and 87 in the intervention group. Supplement B shows the study flowchart.

Baseline characteristics, demographics, education, general health, general working and private conditions, were comparable in both groups (Table 2). A large majority of participating women were Caucasian and well educated.

Table 2. Baseline characteristics of pregnant workers participating in the study, in control and intervention group at 16 weeks of pregnancy [a]

Variable	Intervention group N=119	Control group N=122	P value
Demographics and general health			
Age, years *	32 (5)	33 (4)	0.251
Ethnic origin: Caucasian [b]	102 (86%)	110 (90%)	0.288
Educational level			
• University education or higher academic education	69 (58%)	68 (56%)	ref
• Higher professional education	35 (29%)	33 (27%)	0.881
• Senior secondary vocational education	15 (13%)	21 (17%)	0.354
Body Mass Index (kg/m^2) > 25	22 (19%)	14 (12%)	0.172
Health complaints/ chronic illness before pregnancy	10 (8%)	10 (8%)	0.954
Medication prescribed by physician	18 (15%)	17 (14%)	0.480
Smoking during pregnancy	0	2 (2%)	0.498
Drinking alcohol during pregnancy	4 (3%)	2 (2%)	0.442
Drugs: quit before pregnancy or earlier	21 (18%)	14 (12%)	0.174
Current pregnancy			
With a fertility treatment	9 (8%)	9 (7%)	0.985
Twins or triplet	3 (3%)	4 (3%)	1.000
Parity ≥1	52 (44%)	62 (51%)	0.268
Medical problems in former pregnancies?	9/52 (17%)	12/62 (19%)	0.532
Medical problems before current pregnancy?	10 (8%)	10 (8%)	0.954
Increase in complaints because of current pregnancy?	37 (31%)	39 (32%)	0.884
Work			
Paid work from start of the pregnancy	119 (100%)	122 (100%)	1.000
Employment sector			
• Health care	34 (29%)	32 (26%)	ref
• Business services & research	31 (26%)	37 (30%)	0.473
• Education, welfare and child care	20 (17%)	18 (15%)	0.913
• Retail & hospitality and catering industry	14 (12%)	16 (13%)	0.660
• Government & culture, recreation	13 (11%)	11 (9%)	0.823
• Other (industry/NGO's/ transport)	6 (5%)	8 (7%)	0.756
Number of employees in the company >50	81 (68%)	85 (70%)	0.715
Self-employed [c]	6/105 (6%)	8/117 (7%)	0.615
Commuting: Travel distance > 10 km	71 (60%)	73 (59%)	0.980
Travel time > 1 hour/day (min/hours)	50 (42%)	49 (40%)	0.768
Private conditions			
Sport	66 (56%)	57 (47%)	0.195
Times spent on hobby spending > 5 hours/week	9 (8%)	9 (7%)	0.985
Children (living at home): Yes	41 (35%)	48 (39%)	0.375
Housework largely done by participant herself	23 (19%)	22 (18%)	0.820

**Mean (SD), all other variables mentioned as N (%). Abbreviations: NS not significant, ref=Reference a: complete results in supplement C b: non Caucasian includes: Turkish, Moroccan, Afro/ American, Asian, Mixed and 'other non-Western' c: Based on second questionnaire (not in first questionnaire)..*

The primary outcome, the percentage of women receiving advice from their midwife or obstetrician to adjust their work, was 9% in the intervention group versus 2% in the control group at 16 weeks of pregnancy (RR 5.64), and 39% versus 18% at 24 weeks of pregnancy (RR 2.18) (Table 3).

The secondary outcome concerning work status shows that there were no significant differences at 16 and 24 weeks of pregnancy between both groups (Table 3). From 32 weeks of pregnancy, significantly fewer participants in the intervention group were on pregnancy leave (RR 0.42). During pregnancy, the participants in both groups reported an increasing number of complaints due to pregnancy, which restricted them in their work: more than 30% at 16 weeks, around 40% at 24 weeks and around 50% at 32 weeks of pregnancy (Table 3).

Table 3 shows that among pregnancy women in the 'in employment' group (that is, excluding participants who were self-employed), participants in the intervention group received information from their employer, when reporting pregnant, significantly less often at 24 weeks (RR 0.55), and at 32 weeks of pregnancy (RR 0.41). This difference concerned advice on the required work adjustments: 6% in the intervention group versus 18% in the control group at 24 weeks, 6% versus 21% at 32 weeks and on pregnancy and maternity leave (14% versus 30%;) at 32 weeks.

Table 3. Pregnant workers' work status, work advice and adjustments at 16-, 24-, and 32-weeks of pregnancy [a]

	16 weeks of pregnancy					24 weeks of pregnancy					32 weeks pregnancy				
	Intervention group N=119	Control group N= 122	*RR*	*95% CI*	*P*	Intervention group N= 105	Control group N=117	*RR*	*95% CI*	*P*	Intervention Group N=87	Control group N=101	RR	*95% CI*	*P*
Current work status														x	
Normal working hours	118 (99%)[b]	122 (100%)[b]			ref	89 (85%)	100 (86%)			ref	59 (68%)	56 (55%)			ref
Part-time due to illness	1 (1%)[b]	0[b]			0.897	8 (8%)	8 (7%)			0.822	8 (9%)	9 (9%)			0.744
No work due to illness	0	0				7 (7%)	5 (4%)			0.431	11 (13%)	10 (10%)			0.928
Pregnancy leave	0	0				1 (1%)	4 (3%)			0.261	9 (10%)	26 (26%)	0.42	0.21-0.83	0.010
Increase complaints	37 (31%)	39 (32%)			0.884	44 (42%)	45 (39%)			0.601	52 (52%)	42 (42%)			0.780
Information from employer when reporting pregnant															
Yes [c]	*NA*	*NA*				17/99 (17%)	34/117 (31%)	0.55	0.33-0.92	0.019	12/84 (14%)	33/98 (35%)	0.41	0.23-0.74	0.001
Information about [c]:															
Work adjustments	*NA*	*NA*				6/99 (6%)	20/117 (18%)	0.33	0.14-0.79	0.007	5/87 (6%)	20/101 (21%)	0.28	0.11-0.71	0.003
Pregnancy/maternity leave	*NA*	*NA*				16/99 (16%)	27/117 (25%)			0.126	12/87 (14%)	28/101 (30%)	0.48	0.26-0.88	0.013
Advice to adjust work from															
Midwife & Obstetrician	11 (9%)	2 (2%)	5.64	1.28-24.9	0.010	41 (39%)	21 (18%)	2.18	1.38-3.43	0.001	36 (41%)	29 (29%)			0.069
Occupational physician	2 (2%)	0			0.243	6 (6%)	11 (9%)			0.208	11 (13%)	12 (12%)			0.874
Manager or staff advisor	2 (2%)	6 (5%)			0.281	6 (6%)	14 (12%)			0.104	10 (11%)	17 (17%)			0.284
Own initiative	11 (9%)	16 (13%)			0.498	21 (20%)	30 (26%)			0.318	31 (36%)	29 (29%)			0.310
Realized work adjustments	17 (14%)	22 (18%)			0.430	22 (21%)	37 (32%)			0.078	32 (37%)	45 (45%)			0.280
Less physically demanding	4 (3%)	7 (6%))			0.377	2 (2%)	9 (8%)			0.184	10 (12%)	13 (13%)			0.774
Less standing or walking	4 (3%)	9 (7%)			0.168	6 (6%)	6 (5%)			0.847	11 (13%)	11 (11%)			0.709
Fewer hours per day	5 (4%)	6 (5%)			0.726	8 (8%)	12 (10%)			0.783	19 (22%)	15 (15%)			0.215
More working from home	5 (4%)	7 (6%)			0.524	3 (3%)	10 (9%)			0.334	8 (9%)	10 (10%)			0.870

NA= Not applicable, not in Questionnaire 1 (16 weeks of pregnancy)

a: complete results in supplement C. b: at start of pregnancy. c: participants self-employed excluded: 24 weeks N=13 (6%), 32 weeks N= 10 (5%)

At 16, 24 and 32 weeks of pregnancy there is a consistent, although not significant trend of difference in realised work adjustments, 14% versus 18%, 21% versus 32% and 37 versus 45% respectively (Table 3). In both groups, pregnant women adjusted mostly physically demanding work (less standing and walking, lifting and carrying) and working hours (fewer hours and night shifts). Both groups also worked from home more often.

Intervention and control group were comparable in most working conditions (Table 4). Before 20 weeks of pregnancy, participants in the intervention group experienced less pressure at work (RR 0.55) and had less need to slow down (RR 0.62). They enjoyed their work less often (RR 0.86) and were less often satisfied with their work (RR 0.84). After 24 weeks of pregnancy participants in the intervention group experienced less freedom in performing tasks (RR 0.56). They enjoyed their work less often (RR 0.34) and were less often satisfied with their work (RR 0.37).

At 24 weeks of pregnancy, about 30 % of the pregnant workers, whether in paid employment or self-employment, reported physically demanding work and exposure to biological agents and noise. Of the respondents 16 % reported 'physically very demanding work'.

Table 5 shows that, when adjusted for the working conditions in which both groups differed significantly, women in the intervention group more often received advice from their midwife and/or obstetrician (aRR 2.22), but less often advice and/or information from their employer (aRR 0.29). Although at 24 weeks of pregnancy, the frequency of realised work adjustments was higher in the control than in the intervention group, these differences were not significant, nor when adjusted for the variables in which the intervention and control group differed significantly (working conditions concerning job strain and information the employee received from employer when she reports being pregnant about the required work adjustments). Analyses for hierarchical clustering of data for participating centres, or heterogeneity of intervention effects on the primary outcomes did not indicate centre effects.

Table 4. Working conditions from pregnant workers at 16- and 24-weeks of pregnancy [a]

	16 weeks pregnancy					24 weeks pregnancy				
	Intervention group n=119	Control group n=122	*RR*	*95% CI*	*P*	Intervention group n=97	Control group n=108	*RR*	*95% CI*	*P*
Working times										
hrs/wk *	34.4 (7.4) (6-50)	33.4 (9.1) (8-50)			0.382	33.6 (8.6) (4-48)	32.1 (9.5) (6-60)			0.590
days/wk *	4.3 (0.8) (2-6)	4.1 (1) (1-7)			0.184	4.4 (0.1) (0-6)	4.2 (0.8) (0-6)			0.400
Irregular working times	17 (14%)	18 (15%)			0.897	12 (12%)	17 (16%)			0.489
Evening shifts **	17 (12.4) (10.6)	17 (6.7) (12.3)			0.902	11 (22.3 (3.2)	14 (19.9 (2.2)			0.723
Nightshifts **	18 (9) (7.5)	18 (3) (6.3)			0.957	2 (2.2 (1.9)	4 (2.7 (1.5)			0.686
Physical work:										
Standing/ walking ≥ 4 hrs/day	37 (32%)	41 (35%)			0.678	32 (32%)	33 (34%)			0.833
Lifting/ carrying loads or people	33 (28%)	31 (25%)			0.712	18 (19%)	20 (19%)			0.994
Physical work: regularly/ often										
Bending	28 (24%)	25 (21%)			0.592	19 (20%)	26 (24%)			0.438
Physically very demanding	24 (19%)	17 (14%)			0.351	15 (16%)	17 (16%)			0.957
Requiring physical strength	19 (16%)	14 (12%)			0.323	14 (14%)	10 (9%)			0.250
Job strain: often/always										
Problems with pressure	17 (14%)	32 (26%)	0.55	0.32-0.91	0.021	11 (11%)	17 (16%)			0.360
Like to take things a little easier	23 (19%)	38 (31%)	0.62	0.40-0.98	0.035	23 (24%)	28 (26%)			0.714
Freedom in performance of tasks	83 (70%)	93 (76%)			0.257	61 (63%)	85 (79%)	0.57	0.37-0.90	0.013
Influence on the pace to work	57 (48%)	67 (55%)			0.303	50 (52%)	60 (58%)			0.359
Planning own work	75 (63%)	77 (63%)			0.975	59 (61%)	70 (65%)			0.555
Support from manager	66 (56%)	80 (66%)			0.091	55 (57%)	67 (62%)			0.437
Enjoy working	93 (78%)	111 (91%)	0.86	0.77-0.96	0.006	76 (79%)	100 (93%)	0.34	0.16-0.74	0.003
Finds work satisfying	93 (78%)	113 (93%)	0.84	0.76-0.94	0.001	73 (75%)	98 (91%)	0.37	0.19-0.74	0.003
Exposed to biological agents	36 (30%)	33 (27%)			0.610	24 (35%)	29 (27%)			0.200
Exposed to chemical agents	9 (8%)	7 (6%)			0.581	9 (9%)	7 (7%)			0.456
Noise	40 (34%)	32 (26%)			0.226	32 (33%)	31 (29%)			0.507

**: Mean (SD) (Min-max) **: N, mean hrs/wk (SD) all other variables mentioned as N (%)*

Abbreviations: NS not significant, ref=Reference.

a: complete results in supplement C.

Table 5. Advice/information to adjust work and realised work adjustments N=222, 24 weeks pregnancy, multivariable analysis

	Intervention group n=105	Control group n=107	Univariate analysis			Multivariate analysis		
			RR	95% CI	P	aRR[a]	95% CI	P
Advice/information to adjust work								
- From Midwife and/or Obstetrician (Advice to adjust work)	41 (39%)	21 (18%)	2.18	1.38-3.43	0.001	2.22	1.44-3.43	0.000
- From Employer (Advice to adjust work and/or Information about work adjustments when reporting pregnancy)	8 (8%)	31 (28%)	0.28	0.14-0.59	0.001	0.29	0.14-0.61	0.001
			RR	**95% CI**	**P**	**aRR[b]**	**95% CI**	**P**
Realised work adjustments because of pregnancy	22 (21%)	37 (32%)	0.66	0.42-1.05	0.078	0.66	0.41-1.08	0.101

All variables mentioned as N (%)

a: Association with working conditions: Like to take things a little easier, enjoy work, work satisfying

b: Association with working conditions: Like to take things a little easier, enjoy work, work satisfying and information from employer, about work adjustment, when reporting pregnant.

Discussion

This study shows that pregnant women, either in paid employment or self-employed, received more frequently advice from their obstetrical caregiver to adjust their work after a blended care intervention. However, they received less often advice and/or information from their employer. Although at 16, 24 and 32 weeks pregnancy, the frequency of realised work adjustments was higher in the control than in the intervention group, these differences were not significant. At 24 weeks of pregnancy, almost a third of the pregnant women in both groups continued to work in hazardous workplaces.

Considering the long-term consequences of pregnancy complications such as preterm birth and low birth weight, awareness of work-associated risk factors is important and can have a substantial effect on the health of the offspring and on medical costs associated with complications. This study investigated the added value of a relatively cheap blended care intervention of training of obstetrical professionals, subsequent counselling of women as well the mHealth application ('app' for short) with easily accessible reliable information about pregnancy and work to achieve higher levels of work adjustment during pregnancy. We have carefully developed and tested this mHealth application (the *P&W* app). The app allows all working women participating in the study, whether in employment or self-employed, to determine work and personal risk factors and to adjust their work according to the recommendations given in the app. When designing mHealth applications, an iterative approach is important to meet the needs of end users[29]. The application under study was designed by a multidisciplinary team. During the development phase, all stakeholders were involved in focus groups and a usability study was performed [18, 22]. In addition, women received advice from their obstetrical caregiver (midwives, obstetricians), who followed a multidisciplinary training session, as part of the intervention.

Previous studies have shown the importance of using text messaging or interactive and individual coaching to improve the lifestyles of pregnant women [16, 30]. Blending face-to-face guidance with online support is more effective and increases client-therapist connection and adherence [23, 24]. In this study we combined individual access to the P&W app with counselling by professionals trained to work with the advice generated by the app, thus extending the already personalised advice provided by regular emails with updated work advice during pregnancy. Obstetrical caregivers have little awareness of the guidelines, risks and legal measures concerning maternity protection [14]. By providing midwives and obstetricians with easily accessible information, we expected them to better inform pregnant workers about the risks at work.

Data were prospectively collected at several times during pregnancy, as the working capacity of pregnant women changes over time. This allowed for longitudinal follow-up by which we could assess changes during the course of pregnancy.

The intervention and control groups were comparable in baseline characteristics and the differences in working conditions are few, but stable over time: the control group reported enjoying their job more commonly, this group also reported more freedom in performing their job, though with more working pressure. The lack of differences shown between the populations in terms of working times, and physical, biological and chemical working conditions, excludes a potential for confounding bias stemming from these conditions.

In our study however, there may have been selection bias due to differences in participants in the intervention group compared to the control group. Women in the intervention group received significantly less information about the necessary work adjustment from their employers when they reported their pregnancy. Possibly this lack motivated them to participate in the study, in order to receive information about work adjustment via the P&W app. A limitation of our study is that we have no information on how many women in both groups were on temporary employment. Women with a temporary contract are at a much higher risk of pregnancy discrimination. In The Netherlands, almost half (49%) of all women with a temporary contract were not renewed or converted to a permanent contract because of their pregnancy or new motherhood [31]. They are reluctant to report their pregnancy to their employer.

Furthermore, compared to the general population there seems to be an overrepresentation in both intervention and control group of highly educated, Caucasian, non- smoking women with low intake of alcohol during pregnancy. Compared to the baseline characteristics of a recently published large RCT (n=13.520) in a low risk pregnancy population in The Netherlands, the incidence of Caucasian ethnicity and high education were comparable [32]. However BMI, alcohol consumption and smoking were lower in our cohort. This might be explained by the phenomenon that the decision to participate in a study can correlate with social, educational and health conditions [33]. In our study, this may be related to the demographics of the participating practices, to language issues or availability of electronic devices in certain populations and even with selection by the obstetrical caregiver. However, as these baseline characteristics were comparable in both groups we do not expect this had an effect on the primary and secondary outcomes of our study.

Although the professionals are trained and the app provides personalised advice based on individual work- and health-related risks, it is uncertain whether the advice that clients received from their obstetrical caregiver was correct and also whether the pregnant women adjusted their work adequately. Another limitation of this study is the number of lost to follow-up after the second questionnaire: only 78% of the participants completed all three questionnaires, possibly due to tiredness as a result of progressing pregnancy or completing work before starting pregnancy leave. However, because 92% of the participants completed the second questionnaire, we have insight in the

(adjustments of) the working conditions of pregnant women up to the third trimester (28 weeks), that is during the longest period of pregnancy for which pregnant Dutch women continue to work (up to 34 weeks).

Because this study uses three large questionnaires, multiple testing is involved, with the risk of false significance. However, the primary outcome measures, which are the most important results, have p values of < 0.01 or 0.001 suggesting a low risk of a type I error.

The finding that the intervention population has fewer pregnant workers on pregnancy leave in the period 32 weeks of pregnancy could be a positive result, indicating more/better contact between obstetric caregivers and workers on work adjustments in the intervention population (24 weeks), which prevented a number of pregnant workers from withdrawing from work using pregnancy leave. Another explanation may be that the employer provided information on maternity leave more often at 32 weeks.

The low score given to advice offered by occupational physicians in both groups is remarkable. National guidelines advise employers to give all their pregnant employees access to a preventive consultation with the occupational physician; however, in practice, this seems to happen less frequently than expected.

Our study has similarities with a stepped-wedge approach [34]. Due to the effect of the intervention, randomisation at the individual level is not possible: the effect is not limited to individuals. Midwives and obstetricians can share information and knowledge from the training session and P&W app with other healthcare providers and clients. Clients can share information from the P&W app with other pregnant women. Furthermore, the intra-cluster correlation was anticipated to be high: the clients of midwifery hospital partnerships can differ in ethnicity and social economic status, depending on, for example, location. The study design leaves larger uncertainty about non-causal reasons for the observed treatment effects than that of an individually randomised trial. Differences in patient characteristics and their baseline prognosis between the two treatment periods have, however, been adjusted for in the multivariable analyses. Nonetheless, structural residual confounding, due to unobserved factors remains possible. A larger number of patients and a full stepped-wedge or cluster randomised design would be needed to account for such effects. Such large-scale study however, was not feasible at this stage. Finally, the intervention motivated the professionals to participate in the study; thus, a stepped introduction of the intervention would ensure that all participating professionals and their future clients would benefit from the training session and P&W app.

In the European Union, including The Netherlands, according to Council Directive 92/85/EEC it is the employer's responsibility to evaluate the potential risks facing pregnant employees and to subsequently take the necessary protective measures.

Lack of knowledge about legal obligations of employers can cause deficiencies in the implementation of maternity protection legislation. Often no risk analysis is carried out and employers fail to give pregnant workers sufficient information about their rights and risks [14, 15]. A negative attitude of employers towards their pregnancy is one of the most common stressors among working women [35]. Moreover, in our study fewer than 25% of the employers provided information to their pregnant employees about their rights, and only 12% about risks and required work adjustments even though this is a legal obligation. We do not know whether employers were aware of this legal obligation or the fact that less exposure to risks at work will reduce absenteeism among pregnant employees [36, 37].

Working pregnant women, both in paid employment and self-employment are often unaware of the risks and legal measures concerning maternity protection in the workplace, they continue to work in a hazardous workplace or decide to withdraw from work using sick leave or preventive pregnancy leave [14, 38]. This study shows that overall work is not sufficiently adjusted: after 24 weeks of pregnancy, 20% to 30% of the participants in both groups still performed physically demanding work (prolonged standing (33%), lifting (19%), bending (22%)), they worked in an environment with a lot of noise (30%), or on which was cold (18%), hot (18%) or entailed exposure to chemicals (7%) and infectious diseases (26%). The question remains whether there has been a proper evaluation of the working conditions of these pregnant women.

In future research, it is essential to include employers, more participants with lower education and non-Caucasian ethnicity, and information about temporary or permanent employment of participants. It is important to redesign the P&W app to meet the needs of different user groups: employers, their employees and caregivers. We expect that interaction in multidisciplinary training on the P&W app for caregivers and employers will encourage employers to pay more attention to (the working conditions of) their pregnant employees and use the advice from the P&W app to adjust the workplace [39, 40]. A follow-up study can evaluate whether the advice clients have received from their caregiver was correct and whether the pregnant women have adjusted their work adequately. In addition, government support is important to achieve better and more effective implementation of legislation concerning working conditions during pregnancy [24]. A comprehensive follow-up study focussing on health outcomes can demonstrate whether this blended care program, including pregnant workers, obstetrical caregivers and employers, is effective in preventing adverse pregnancy outcomes.

Conclusion

The results of our study show that a blended care intervention, which consists of a training session for obstetrical caregivers and the personalised advice provided by a

specifically developed mHealth application, increases the percentage of advices on work adjustments given by midwives and obstetricians to pregnant workers, but they received less often advice from their employer. However, it did not lead to more work adjustment. Improving the design of the P&W app, by including employers in its development, could increase the effectiveness of the intervention.

Contributors MvB, MFD and MK took part in the planning, design and funding acquisition of the study. MvB, AV, LS and MK conducted the study, MvB, AV and LS monitored data collection. MvB and MK provided the training. MvB and RD performed the statistical analyses. MvB wrote the first draft of the manuscript. All authors contributed to the interpretation of the results, revision of the manuscript and final approval of the manuscript.

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Ethics approval The ethical board of the Amsterdam University Medical Center, location AMC, confirmed that the Medical Research Involving Human Subjects Act was not applicable to this study (METC W15-102 150121).

Competing interests None declared.

Data availability statement Data are available on reasonable request.

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Supplement A

Infectious Diseases

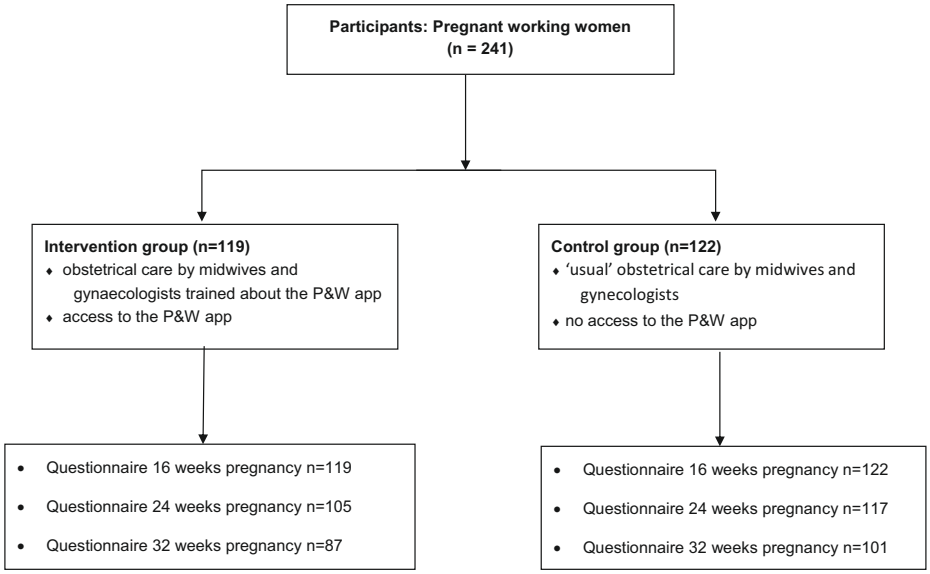
Infectious Diseases You have indicated that in your work you can get an infection. Infections caused by viruses, bacteria, parasites or fungi. They are transmitted in a variety of ways. For example, transmission by animals or sick people. Some

Stress

Stress

You're more likely to stress by work. If you are pregnant and have stress because of work you yourself more likely to have high blood pressure, your child may be born with less weight. This stress therefore try to reduce the pregnancy as early as possible.

Supplement B. Flow chart of study population



Supplement C. Complete results of Table 2, 3 and 4.

Table 2 (complete results). Baseline characteristics

	Intervention group n (%)	Control group n (%)	P
N	**119**	**122**	
General details			
Age, years (mean, sd)	32 (5)	33 (4)	NS
Ethnic origin			
• Caucasian	102 (86)	110 (90)	NS
• Other	17 (14)	12 (10)	NS
Educational level			
• University education or higher academic education	69 (58)	68 (56)	ref
• Higher professional education	35 (29)	33 (27)	NS
• Senior secondary vocational education	15 (13)	21 (17)	NS
Language Questionnaires English	0	4 (3)	NS
General Health, lifestyle			
Weight kg (mean, sd) *(* 1 unknown)*	66.97 (SD 10.49)*	65,64 (SD 11.03)	NS
Length/ weight cm (mean, sd)	170,6 (SD 6.49)	168.93 (SD 7.28)	NS
Body Mass Index (kg/m2; mean, sd) *(* 1 unknown)*	23 (3.7) *	22.9 (SD 3.1)	NS
Body Mass Index (kg/m^2) > 25	22 (19%)	14 (12%)	NS
Health complaints/ chronic illness before pregnancy: Yes	10 (8)	10 (8)	NS
Medication			
• No	92 (77)	100 (82)	ref
• Yes, medication prescribed by physician	18 (15)	17 (14)	NS
• Yes, not prescribed by physician	9 (8)	5 (4)	NS
Smoking			
• non-smoker	75 (63)	85 (69)	NS
• quitted before pregnancy	33 (28)	25 (21)	ref
• quitted because of pregnancy	11 (9)	10 (8)	NS
• current	0	2 (2)	NS
Alcohol			
• no	33 (28)	38 (31)	ref
• sometimes	82 (69)	82 (67)	NS
• ≤1/day	4 (3)	1 (1)	NS
• yes, 1-5	0	1 (1)	NS
Drugs			
• no	98 (82)	108 (88)	NS
• quitted before pregnancy or earlier	21 (18)	14 (12)	NS
Current and former pregnancies			
Current pregnancy			
• Naturally (spontaneously, without medical treatment)	110 (92)	113 (93)	NS
• With a fertility treatment	9 (8)	9 (7)	NS
• Singleton	116 (98)	118 (97)	NS

Table 2. Continued.

	Intervention group n (%)	Control group n (%)	P
N	**119**	**122**	
• Twin of triplet	3 (3)	4 (3)	NS
Parity			
• 0	67 (56)	60 (49)	NS
• ≥1	52 (44)	62 (51)	NS
Medical problems in former pregnancies?	9/52 (17)	12/62 (19)	NS
• High blood pressure, preeclampsia or Hellp syndrome	2 (2)	2 (2)	NS
• Preterm birth (before 37 weeks of pregnancy)	7 (6)	10 (8)	NS
• Low birth weight	1 (1)	0	NS
• Stillbirth	2 (2)	2 (2)	NS
• Miscarriage	18 (15)	15 (12)	NS
Medical problems before current pregnancy?	8 (7)	8 (7)	NS
Increase in complaints because of current pregnancy?	37 (31)	39 (32)	NS
• Complaints of fatigue	34 (29)	33 (27)	NS
• Headaches	15 (13)	11 (9)	NS
• Pain in the back, pelvis and/or legs	19 (16)	18 (15)	NS
• Nausea/vomiting	16 (13)	18 (15)	NS
• Stomach aches	9 (8)	1 (1)	**
Work: General aspects			
Paid work			
• Yes from start of the pregnancy	119 (100)	122 (100)	NS
• Yes from ... weeks pregnancy	1 (1) (13 weeks)		NS
Working in sector			
• Health care	34 (29)	32 (26)	NS
• Business services & research	31 (26)	37 (30)	NS
• Education, Welfare and child care	20 (17)	18 (15)	NS
• Retail & Hotel and catering industry	14 (12)	16 (13)	NS
• Government & Culture, recreation	13 (11)	11 (9)	NS
• Other (Industry/NGO's/ transport)	6 (5)	8 (7)	NS
Number of employees in the company			
• 1-10	16 (13)	17 (14)	NS
• 11-50	22 (19)	19 (16)	NS
• 51-100	11 (9)	14 (12)	NS
• More than 100	70 (59)	71 (58)	NS
Commuting			
Travel distance commuting (m/km)	*1 unknown*	*1 unknown*	
• <5 km	19 (16)	22 (18)	ref
• 5-10 km	28 (24)	26 (21)	NS
• 10-25 km	34 (29)	31 (25)	NS
• >25 km	37 (31)	42 (34)	NS
Travel time commuting (min/hours)			
• <1 hour/day	68 (57)	72 (59)	ref
• 1-2 hours/day	40 (34)	38 (31)	NS

Table 2. Continued.

	Intervention group n (%)	Control group n (%)	P
N	**119**	**122**	
• >2 hours/day	10 (8)	11 (9)	NS
Means of travelling/ transport	*1 unknown*	*1 unknown*	
• Walking	2 (2)	2 (2)	NS
• By bicycle/scooter	40 (34)	39 (32)	ref
• Public transport	28 (24)	25 (21)	NS
• Car	48 (40)	55 (45)	NS
Private circumstances/conditions			
Spare time			
Physical activity: sports		*1 unknown*	
• normally not participating in sports	27 (23)	40 (33)	NS
• stopped sports when pregnant	26 (22)	24 (20)	ref
• sport (hours/week)	66 (56)	57 (47)	NS
• <2 hours/week	35 (29)	33 (27)	NS
• >2 hours/week	31 (26)	24 (20)	NS
Hobby spending > 5 hours/week	9 (8)	7 (6)	NS
Domestic situation			
Children (living at home): Yes	41 (35)	48 (39)	NS
• 1 child	36 (30)	38 (31)	NS
• ≥ 2 children	5 (4)	10 (8)	NS
Housekeeping			
• Largely doing by participant herself	23 (19)	22 (18)	ref
• together with partner/someone else	84 (71)	88 (72)	NS
• partner/someone else does most of it	12 (10)	11 (9)	NS
Household help: Yes	39 (33)	43 (35)	NS

** P or FE <0.01NS= Non significant
ref=Reference

Table 3 (complete results). Univariate analysis Work status, workadvice and adjustments

	16 weeks pregnancy					24 weeks pregnancy					32 weeks pregnancy				
	Intervention group N=119	**Control group N= 122**	***RR***	***95% CI***	***P***	**Intervention group N= 105**	**Control group N=117**	***RR***	***95% CI***	***P***	**Intervention Group N=87**	**Control group N=101**	**RR**	***95% CI***	***P***
Current work status														**x**	
Normal working hours	118 (99)	122 (98)			NS	89 (85)	100 (86)	ref			59 (68)	56 (55)	ref		
Part time due to illness	1 (1)	0				8 (8)	8 (7)			NS	8 (9)	9 (9)			NS
No work due to illness	0	0				7 (7)	5 (4)			NS	11 (13)	10 (10)			NS
Pregnancy leave	0	0				1 (1)	4 (3)			NS	9 (10)	26 (26)	0.42	0.21-0.83	**
Increase complaints	37 (31)	39 (32)			NS	44 (42)	45 (39)			NS	52 (52)	42 (48)			NS
Advice to adjust work from:															
Midwife & Gynecologist	11 (9)	2 (2)	5.64	1.28-24.9	**	41 (39)	21 (18)	2.18	1.38-3.43	***	36 (41)	29 (29)			NS
Occupational physician	2 (2)	0			NS	6 (6)	11 (9)			NS	11 (13)	12 (12)			NS
General practitioner	0	0				3 (3)	1 (1)			NS	6 (7)	1 (1)			NS
Manager	2 (2)	4 (3)			NS	5 (5)	12 (10)			NS	8 (9)	15 (15)			NS
Staff advisor	0	2 (2)			NS	1 (1)	2 (2)			NS	2 (2)	4 (4)			NS
Own initiative	11 (9)	16 (13)			NS	21 (20)	30 (26)			NS	31 (36)	29 (29)			NS
Other	0	5 (4)			NS	6 (6)	4 (4)			NS	9 (9)	2 (2)			NS
Work adjustments?	17 (14)	22 (18)			NS	22 (21)	37 (32)			NS	32 (37)	45 (45)			NS
Less physically demanding work	4 (3)	7 (6)			NS	2 (2)	9 (8)			NS	10 (12)	13 (13)			NS
Less standing or walking	4 (3)	9 (7))			NS	6 (6)	6 (5)			NS	11 (13)	11 (11)			NS
Lifting or carrying less	5 (4)	7 (5)			NS	6 (6)	8 (7)			NS	9 (10)	9 (9)			NS
Slower work pace	2 (2)	1 (1)			NS	4 (4)	2 (2)			NS	6 (7)	7 (7)			NS
Less work	3 (3)	1 (1)			NS	4 (4)	5 (4)			NS	9 (10)	8 (8)			NS
Other working hours	3 (2)	5 (4)			NS	2(2)	5(4)			NS	8 (9)	5 (5)			NS
Less hours a day	5 (4)	6 (5)			NS	8 (8)	12 (10)			NS	19 (22)	15 (15)			NS
No more night shifts	2 (2)	4 (3)			NS	2 (2)	7 (6)			NS	4 (5)	8 (8)			NS
Plan work yourself	3 (3)	2 (2)			NS	1 (1)	2 (2)			NS	4 (5)	4 (4)			NS
More working from home	5 (4)	7 (6)			NS	3 (3)	10 (9)			NS	8 (9)	10 (10)			NS

** P or FE < 0.05, ** P or FE <0.01, *** P <0.001.*

NS= Non significant

NA= not applicable, not in Questionnaire 1 (16 weeks pregnancy)

Table 4 (Complete results). Univariate analysis Working

	16 weeks pregnancy					24 weeks pregnancy				
	Intervention group n=119	**Control group n=122**	***RR***	***95% CI***	***P***	**Intervention Group n=97**	**Control group n=108**	***RR***	***95% CI***	***P***
Working times										
hrs/wk [a]	34.4 (7.4) (6-50)	33.4 (9.1) (8-50)			NS	33.6 (8.6) (4-48)	32.1 (9.5) (6-60)			NS
days/wk [a]	4.3 (0.8) (2-6)	4.1 (1) (1-7)			NS	4.4 (0.1) (0-6)	4.2 (0.8) (0-6)			NS
Irregular working times	17 (14)	18 (15)			NS	12 (12)	17 (16)			NS
Evening shifts [b]	17 (12.4) (10.6)	17 (6.7) (12.3)			NS	11 (22.3 (3.2))	14 (19.9 (2.2))			NS
Nightshifts [b]	18 (9) (7.5)	18 (3) (6.3)			NS	2 (2.2 (1.9))	4 (2.7 (1.5))			NS
Physical work:										
Standing/ walking ≥ 4 hrs/day	37 (32)	41 (35)			NS	32 (32)	33 (34)			NS
Lifting/ carrying loads or people	33 (28)	31 (25)			NS	18 (19)	20 (19)			NS
Physical work: regularly/ often										
Bending	28 (24)	25 (21)			NS	19 (20)	26 (24)			NS
Squatting	22 (19)	23 (19)			NS	17 (18)	16 (15)			NS
Repetitive motion	40 (34)	43 (35)			NS	27 (28)	25 (23)			NS
Very physically demanding	24 (19)	17 (14)			NS	15 (16)	17 (16)			NS
Requiring physical strength	19 (16)	14 (12)			NS	14 (14)	10 (9)			NS
Uncomfortable postures	17 (14)	9 (7)			NS	8 (10)	8 (9)			NS
Job Strain: often/always										
Problems with the pressure	17 (14)	32 (26)	0.55	0.32-0.91	*	11 (11)	17 (16)			NS
Like to take things a little easier	23 (19)	38 (31)	0.62	0.4-0.98	*	23 (24)	28 (26)			NS
Freedom in performance of tasks	83 (70)	93 (76)			NS	61 (63)	85 (79)	0.57	0.37-0.9	*
Influence on the pace	57 (48)	67 (55)			NS	50 (52)	60 (58)			NS
Planning own work	75 (63)	77 (63)			NS	59 (61)	70 (65)			NS
Support from manager	66 (56)	80 (66)			NS	55 (57)	67 (62)			NS
Support colleagues	87 (73)	98 (80)			NS	81 (84)	90 (84)			NS
Enjoy working	93 (78)	111 (91)	0.86	0.77-0.96	**	76 (79)	100 (93)	0.34	0.16-0.74	**
Work satisfying	93 (78)	113 (93)	0.84	0.76-0.94	***	73 (75)	98 (91)	0.37	0.19-0.74	**

Table 4. Continued.

	16 weeks pregnancy					24 weeks pregnancy				
	Intervention group n=119	**Control group n=122**	***RR***	***95% CI***	***P***	**Intervention Group n=97**	**Control group n=108**	***RR***	***95% CI***	***P***
Biological agents	36 (30)	33 (27)			NS	24 (35)	29 (27)			NS
- Small and/ or sick children	22 (16)	18 (15)			NS	20 (21)	13 (12)			NS
- Sick adults	21 (18)	18 (15			NS	19 (8)	17 (16)			NS
- Blood or other bodily fluids	13 (11)	14 (12)			NS	11 (11)	10 (9)			NS
Chemical agents	9 (8)	7 (6)			NS	9 (9)	7 (7)			NS
Physical workload										
- Heat	22 (19)	22 (18)			NS	19 (20)	17 (16)			NS
- Cold	26 (22)	17 (14)			NS	15 (16)	11 (10)			NS
- Noise	40 (34)	32 (26)			NS	32 (33)	31 (29)			NS

** P or FE < 0.05, ** P or FE <0.01, *** P <0.001.*

[a] Mean (SD) (Min-max), [b] N, mean hrs/wk (SD)all other variables mentioned as N (%)

Abbreviations: NS not significant, ref=Reference

General discussion and implications for research and practice

Main findings

Physically demanding work, working times and preterm birth
In **Part 1** of this thesis, our aim was to identify both the effect of individual forms of physically demanding work and the combination of (multiple forms of) physically demanding work with other occupational exposures and with shift work and/or long working hours on preterm birth, differentiated per trimester, in two meta-analyses.

Standing and walking, lifting and carrying, physical effort, a job with ≥ 2 tasks with physical effort or an 'Occupational Fatigue Score' ≥ 2 showed moderate significant associations with preterm birth. As we expected, the effect of the combination of ≥ 2 tasks with physical load or another exposure, was lower than the sum of the effects of the individual risk factors. Exposure to physically demanding work occurred most during the first trimester. As pregnancy progressed, the number of women exposed to physically demanding work decreased significantly.

Long working hours (more than 40 hours a week) were associated with a moderate increased risk of preterm birth. Working in shifts or in night shifts during pregnancy did not show a statistically significant relationship.

Implementation of Maternity Protective Legislation (MPL) and guidelines
In **Part 2,** we examined whether the Dutch MPL and guidelines from the Netherlands Society of Occupational Medicine (NVAB) [1] and the Social Economic (SER) Council [2] have been implemented for both low-risk pregnant women and women with a multiple pregnancy in two prospective cohort studies.

In the first cohort of 269 working women with a low-risk pregnancy before 20 weeks gestation, 41% of the participants (and after 20 weeks gestation 63%) continued to work under circumstances that did not meet recommendations. These circumstances mostly concerned physically demanding work, job strain, long and irregular working hours and noise. Women with a lower education and a job in the sectors of healthcare, education/childcare & social services, catering, hospitality, construction and cleaning were more at risk of work without adherence to recommendations. Only 15% of employers informed their pregnant employees about risks and necessary work adjustments, with the result that 38% of their pregnant employees did not know whether they were at risk in their work with biological and chemical exposure and how to avoid these risks.

In a cohort of 383 women with multiple pregnancy, 59% did not work according to NVAB guidelines [1]. Many of these women with multiple pregnancies had to deal with high physical workload, prolonged standing and walking, irregular working hours and job strain.

In this group of working women with a multiple pregnancy, we found a significant association between long (> 28 hours/week) and irregular working hours with preterm birth < 32 weeks gestation, and irregular working times with PTB (32-36 weeks gestation). We examined the combination of longer working hours (>28 hours/week) with other risk factors in a subgroup. In this subgroup, limited freedom in task performance and irregular working times were associated with (very) preterm birth, physical strength and high physical workload with very preterm birth.

Blended care 'Pregnancy and Work' (P&W)

In **Part 3** of this thesis, we developed a blended care program called 'Pregnancy and Work' and evaluated whether this program led to more advice and realisation of work adjustment in working pregnant women.

Two multidisciplinary focus group meetings showed the importance of good interaction between the mHealth application and the user, and the use of understandable, well-dosed information, according to existing guidelines and without frequent push notifications. Based on these results and the recommendations from the evidence-based NVAB guideline, we developed the Pregnancy and Work application (P&W app), with the intention of providing pregnant working women with personalized information and advice on work-related pregnancy risks. Despite several usability issues, the pregnant women were satisfied with the application and it met their needs.

The effect of the blended care intervention was evaluated using a questionnaire survey among working pregnant women. The intervention consisted of training for professionals (midwives, obstetricians and occupational physicians) and access to the P&W application for working pregnant women and their obstetric care providers. Working pregnant women (n=119) in the intervention group with access to the blended care intervention received advice about work adjustment from their obstetric care providers more often, but less often from their employer than the group of pregnant women with 'care as usual' (n=122). Ultimately, this did not lead to further work adjustment.

Methodological strengths and weaknesses

Part 1: Physically demanding work, shift work, long working hours and preterm birth

The results of the two meta-analyses on physically demanding work, shift work, long working hours and preterm birth are in line with those of three recent meta-analysis [3-5] and a prospective cohort study [6].

They show similar moderate associations between preterm birth and walking and standing more than four hours/day or 30 hours/week, lifting more than 100 kg/day

and lifting heavy (or ≥10 kg) loads often (or ≥10x/day,) high physical and cumulative workload and working more than 40 hours/week. Unlike in our study, a survey with 62 observational studies (196,989 women), working in rotating shifts and in fixed night shifts, showed moderate significance with preterm birth [4]. The three meta-analyses [3-5] were all the first to be performed after our studies (since 2014). As with our studies, all involved a large, diverse sample of workers from many, albeit mainly developed countries. All three included more studies because they did not apply a lower time limit, while we only included studies from 1990 onwards. The studies also included only working women in the exposure and control groups.

Similarly, these studies relied on observational data, as no randomized controlled trials (RCTs) were available. Research into the impact of working conditions on pregnancy outcomes, such as preterm birth, is usually based on observational studies in which women self-report their workload via questionnaires or by interviewers (usually trained nurses or experts) who provide opportunities to go into more detail. Knowing that these working conditions can be potentially harmful to pregnancy outcome, it is unethical to conduct a randomized controlled trial (RCT), in which the pregnancy outcomes of two groups of women, whether or not they were exposed to certain working conditions during pregnancy, can be compared. To mitigate this risk of bias and confounders as much as possible, in our meta-analyses we performed a risk assessment and scored each article on items related to the clarity of information on the population, exposure, outcome and the quality of the study design and analysis, based on the methodology used in a UK guideline on physical and shift work during pregnancy [7]. In addition, we eliminated as many possible intrinsic differences between exposed and unexposed women, by including only studies with 'working' women in both the control and the exposed groups. In the absence of results from RCTs, it is possible to use other features from observational studies that suggest a causal relationship, such as consistency of the association, dose-response relationship and biological plausibility [8, 9]. Based on these characteristics, Mozurkewich points out that the meta-analysis by Cai et al. shows consistent evidence for the relationship between occupational exposure and adverse pregnancy outcomes.

Differently, the recent studies analysed outcomes other than preterm birth (miscarriage, small for gestational age, hypertensive disorders) and did not distinguish between trimesters. The trimester exposure analyses did not reveal different associations, but they did show that the proportion of pregnant women exposed to physically demanding work and shift work or long working hours decreased significantly as pregnancy progressed. This is likely due to an increase in physical discomfort as pregnancy progresses, which makes many women feel less able to continue physically demanding work or long and irregular working hours. In all studies, the number of exposed women decreased as pregnancy progressed, limiting the opportunity of significant results regarding work-

related risks to pregnancy. Therefore, the effects of exposure in the third trimester in particular should be interpreted with caution.

A limitation related to research on the impact of working conditions on preterm birth is the definition of risk factor. Defining the 'number of hours standing and walking' can be based on hours per day or per week. Unlike in many other countries, in the Netherlands many women work part-time, often three to four days a week, compared to five days in many other countries [10]. When calculating summary estimates, this difference can reduce homogeneity and reliability. The studies included in the meta-analysis mentioned above do not consider whether the ability to alternate standing and walking with regular sitting can reduce the risk of preterm birth.

Some studies consider more than 40 hours/week to be 'long working hours', while others use this definition for working more than 25, 35 or even 46 or 50 hours a week. This does not benefit the homogeneity and results in less reliable results. Therefore, we advise agreeing on the thresholds for work-related risk factors during pregnancy, in consultation with other researchers in the field of pregnancy and work.

In her research on occupational lifting and adverse pregnancy outcome, Croteau [5] accurately formulated different groups in terms of load and calculated risk estimates from higher validity studies, making the results more homogeneous and reliable and allowing effective and specific recommendations. Because (in contrast to Croteau) we also examined other forms of physical load, we limited ourselves to the groups lifting and carrying > 5 kg versus ≤ 5 kg. However, in some studies this was actually > 10 or >20 kg.

The meta-analysis on lifting and carrying > 5 kg , 'job requires physical effort or physical exertion', women working in rotating shifts or night shifts showed little or no heterogeneity, representing a relatively homogeneous group of studies. The forest plot of studies on 'women working during their pregnancy in jobs with a combination of two or more tasks with physical effort' or an 'Occupational Fatigue Score' showed moderate heterogeneity. Little homogeneity showed summary estimates of studies on 'standing and walking more than three hours a day' and 'working more than 40 hours/week versus less', the last because one of eleven studies reported the exposure to be beneficial which yielded an I^2 (inconsistency test) of 62%. The three recent meta-analysis on physically demanding work, shift work, long working hours and preterm birth also showed good evidence strength with results on (heavy) lifting [3, 5] and moderate homogeneity in other risk factors [3, 4].

Furthermore, Cai et al. [3, 4] conducted a dose-response analysis in both reviews. Pregnant women who stand at work more than two and a half hours/day (versus 0), or who work more than 56 versus 40 hours/week, were 10% more likely to have preterm birth.

The previous reviews have not yet included the results of a recent study with a large prospective cohort of more than 7,500 working pregnant women on the impact of physically demanding work on both spontaneous and iatrogenic preterm births: high physical workload was associated with an increased risk of iatrogenic, but not spontaneous preterm birth [6]. They mention that their results suggest that Pregnancy Induced Hypertension (PIH) is a 'risk enhancer': high physical workload has a greater impact on preterm birth in the presence of PIH).

Part 2: Implementation legislation and guidelines

Implementation of MPL and guidelines is important because, through work adjustment, this leads to a decrease in preterm birth, fewer infants who are small for their gestational age [3-5, 11, 12] and a decrease in sickness absence during pregnancy [13].

Because the NVAB guideline sets concrete and evidence-based limits, we were able to compare these with detailed data on risk factors at work of women with low-risk and multiple pregnancies, prospectively collected during pregnancy.

In the study of low-risk pregnant women (chapter 4), there was a representative sample: their personal and work-related factors were reflections of national Dutch figures [10]. In the study of multiple pregnant women (chapter 5), highly educated, white, nulliparous and non-smoking women were overrepresented. On the one hand, women who are pregnant for the first time may be less aware of risks at work than women who have worked during a previous pregnancy. On the other hand, women with a lower education level, in particular, run the risk on employment not in accordance with MPL and guidelines (Chapter 4). We assume that this did not significantly affect the results.

The results of our studies are comparable to those of several European countries [14-17]. 20 to 70% of working pregnant women in England, Norway, Switzerland and Poland received no information about the work-related risks from their employer. Pregnant women in England (20%), Norway (30%) and Poland (60%) indicated that they did not receive the correct work adjustment. In a recent Dutch survey of more than 300 women working in primary education, a small majority were aware of the possibility of visiting the occupational physician during pregnancy [18]. A limited number of women (21%) had been informed by the employer about the risks in their work and the necessary adjustment to work and the possibility and value of a preventive consultation.

What could explain the lack of compliance with MPL and the guidelines in our research? Adherence to (clinical and professional) guidelines benefits from consistent leadership, communication, training and participation and commitment of all employees or team members [19, 20]. On the other hand, a lack of knowledge, time, clarity and credibility in the evidence and limited financial resources hinder implementation. The implementation of health and safety legislation is a complex process influenced by political, economic

and organizational factors and requires more than communication and training [21]. We discuss whether these factors hinder the implementation of the Dutch MPL and guidelines, as shown by our studies.

First of all, Figure 1 shows that several actors are involved in (health) care and the realization of a healthy workplace for working pregnant women: obstetric and occupational health services, employers, health insurers and the government. The diversity of these stakeholders and their interests makes the successful implementation of MPL and guidelines challenging.

Figure 1 illustrates three barriers to implementation:
First: the access to healthcare for working pregnant women:

a) Most women receive counselling from an obstetrician or midwife early in pregnancy [22], but they have no knowledge or awareness of MPL and guidelines [23, 24].
b) However, in occupational healthcare, which has this knowledge of MPL and guidelines, there is a lack of coverage for all working pregnant women (Figure 1) [24-26].

The solution seems obvious: retrain the midwives and obstetricians and give them a role in prevention for their working clients, and/or improve access to occupational healthcare. However, in the Netherlands there is a major shortage of occupational physicians. As a result, pregnant women only receive guidance if they call in sick for a long time, or by staff who are not qualified and who are not familiar with the MPL and the guidelines [27]. Due to a major shortage in Switzerland, limited access to (preventive) occupational healthcare is also an issue in Switzerland [25].

While MPL has internationally comparable principles [28, 29], there are substantial differences in the division of roles in the guidance of working pregnant women per country. In contrast to the Netherlands, in Switzerland, Poland, Belgium and Sweden, the obstetrician has an official role in guiding and advising working pregnant women [30-33]. Research shows that Swedish and Swiss obstetricians, who can prescribe (preventive) leave to their clients, often consider themselves incapable of assessing the working conditions and fitness for work of pregnant women[33, 34]. Regular conflicts arose with their other role as the patient's confidant.

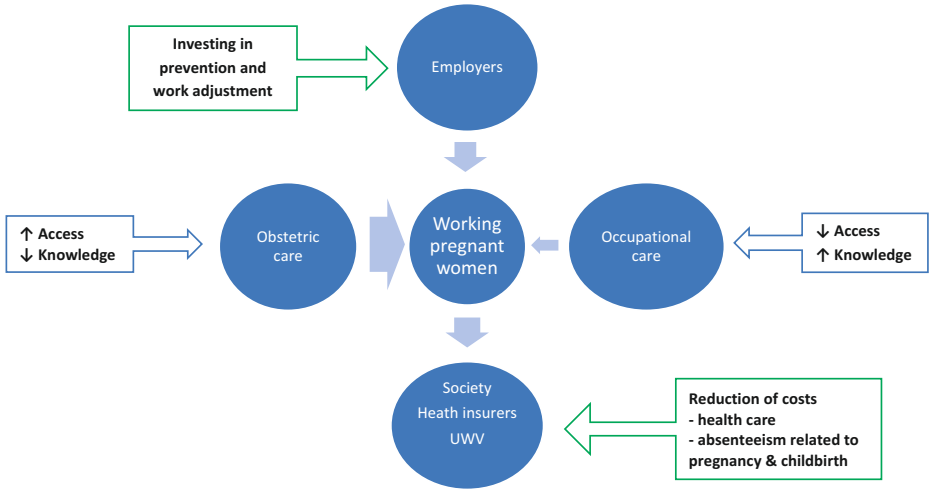


Figure 1. Incentives from implementation of Maternity Protective Legislation (MPL) and guidelines and access to (occupational health-) care for pregnant women

Various actors are involved in the implementation of MPL and guidelines: working pregnant women themselves, obstetric and occupational health services, employers, health insurers and the government. Two mechanisms are important for implementation:

1. The vertical arrows show that, if employers fulfil their legal obligation to invest in prevention and work adjustment for working pregnant women, this leads to:

a) *fewer abnormalities in mother and child and therefore saves costs for health insurers*

b) *decrease in absenteeism, which benefits UWV = government*

2. The horizontal arrows show access to health care for working pregnant women:

a) *Most women receive counselling from a midwife or obstetrician early in pregnancy, but the obstetrical care had no knowledge or awareness of MPL and guidelines.*

b) *However, in occupational health care, which does have this knowledge of MPL and guidelines, there is a lack of coverage for all working pregnant women.*

Abderhalden et al. [25] distinguished in her study practices of obstetricians that act 'in line with legislation (MPL)' versus 'limited in line with legislation (MPL)'. This was related to the obstetricians' knowledge of MPL obstetricians: the more knowledge, the more their practice matched the MPL. A significantly higher proportion of these obstetricians applying MPL in their practice had received training. While in the first group, 83% refer their patients to occupational physicians when they suspect an occupational risk, this number in the group obstetricians of practices 'limited in line with MPL' was 0%. Furthermore, the majority of obstetricians whose application of MPL was limited in their practice considered the provisions too burdensome for employers. No research has been done, but it is likely that these differences between the practices of obstetricians and midwives also exist in the Netherlands.

Second: Incentives for employers: if they fulfil their legal obligation to invest in prevention and work adjustment for working pregnant women, this leads to fewer abnormalities in mother and child and decrease in costs of absenteeism. Like the financial benefits of other occupational safety and health interventions, those for working pregnant women also seem promising [35, 36]. However, it mainly saves costs for health insurers (healthcare costs) and the Employee Insurance Agency (UWV= government), which reimburses employers in the Netherlands for the costs of absenteeism due to pregnancy and childbirth. Sometimes employers benefit more from their pregnant employee reporting sick than from work adjustment. A project by the SER shows that things can be done differently. Insufficient access, no attention to prevention and insufficient cooperation with regular care are also bottlenecks in work-related care in general. The SER started a project with an innovative form of financing and implementation of work-related care in installation technology: 'Arbozorg Nieuwe Stijl' [37]. The result of this project, new (financing) agreements between the various stakeholders and preventive consultation hours for employees, offers opportunities for health insurers, obstetrical and occupational healthcare in guiding working pregnant women.

Interestingly a tight labor market can be an incentive for employers to know that pregnant women feel safer at work if their supervisors are committed to their safety and if there are formal procedures within the organization for employees to supervise pregnant women [38].

Third: commitment from and communication with all parties involved. In the Netherlands, guidelines have been developed jointly with all stakeholders (Figure 1) [1, 2]. However, this concerns a limited group of representatives. Although both guidelines have been communicated via national websites, this does not lead to awareness and participation of most employers, employees and obstetric care providers. Only for occupational physicians and a limited number of midwives and obstetricians have training courses been organized to guide working pregnant women (and their employers), according to the NVAB guideline. A tailored intervention targeting perceived barriers in occupational physicians, with peer learning groups and eight meetings spread over a year, led to better compliance with NVAB mental health guidelines [39]. Given the challenge faced by occupational physicians, it is worth applying this intervention to the NVAB 'Pregnancy, postpartum period and work' guideline, as well.

Finally: two other factors that can hinder implementation of the Dutch MPL and guidelines. On the one hand, 'lack of time' has already proven to be a barrier for occupational physicians in a preventive (lifestyle) intervention [36, 40]. Another kind of barrier could be gender stereotyping. The Netherlands, together with several European countries, ranks at the top of healthcare quality; however, it seems to be at the bottom of the list in terms of MPL implementation and guidance of pregnant working women, compared to European countries [41]. It is possible that in the Netherlands, gender

stereotyping (that is, that women are primarily responsible for childcare and men for income [42, 43]) causes stakeholders to be unaware of the importance of MPL and hinders the implementation of MPL.

Part 3: Blended care 'Pregnancy and Work' (P&W)

There are many mHealth applications for pregnant women available, they use them frequently during their pregnancy [44, 45] and consider them useful [46]. MHealth applications can be widely used to improve maternal wellbeing [47], but few of these mHealth applications for pregnant women are evidence-based, and often no professional is involved in the development [48]. The exception is a number of mHealth applications for pregnant women, which, as in our studies, were developed for scientific research. This concerns studies with applications aimed at lifestyle or medical interventions during pregnancy [49-53]. Evaluation of these applications shows that pregnant women often need reliable and frequently accessible information, with options for personalization and monitoring [46].

The usability of mHealth applications improves by taking an iterative approach and starting from the needs of the user group 'pregnant women' and the care providers involved in counselling their clients [48, 54-56]. Interaction between healthcare providers and their clients can increase effectiveness [44, 46]. The effectiveness of mHealth applications, aimed at lifestyle or medical interventions during pregnancy, is often limited because study populations are too small or long-term follow-up is lacking [48, 50].

The blended care program, Pregnancy and Work (P&W) broadly met these conditions: the P&W application was based on an evidence-based guideline (NVAB) and developed and evaluated in a iterative process. End users (pregnant working women), caregivers (obstetricians and midwives) and other stakeholders (occupational physicians, general practitioners and representatives of trade unions and employers' organizations) were involved in the development in a focus group- and think aloud study. The design of the P&W application has been (somewhat) modified based on the results of the think aloud study. Caregivers are trained in the use of the P&W application and in advising their clients at their work.

However, an important limitation in our study is that we did not apply a protocol-based stepwise approach such as intervention mapping [57] or user-centred design [49]. When launching this project, we had already determined our goal (work advice and work adjustment by working pregnant women) and tool (mHealth app) in advance, without an accurate need analysis or problem analysis to determine what needs to change and for whom. As a result, the P&W application may not sufficiently match the questions, problems and needs of the target group: working pregnant women. They aren't interested in well-intentioned advice, or they can't find the advice they are looking for. Ultimately, they will not use the app.

Second, we did not involve end users (working pregnant women) and human factor specialists from the start of the study, with as a result many usability problems of the P&W app. Furthermore, it is possible that the P&W application would be more effective if different versions were developed for different end users. Working pregnant women differ in education, ethnicity and SES, in contract, be it (temporary) employment or self-employed, in working conditions and in health. A recent systematic review [51] recommends taking into account ethnically specific dietary recommendations to improve the effectiveness of digital tools to support the dietary self-management of gestational diabetes mellitus. Derksen et al. [49] developed an mHealth application with social and game support elements, to support pregnant socioeconomically disadvantaged young women to quit smoking. She showed that these women have unique usability problems.

The end users of the P&W app, 'working pregnant women', participated in the multidisciplinary focus groups; however, their needs will probably be addressed more in a group with only working pregnant women. For this reason, in their research on maternity care, Laureij et al. [58] organized three separate focus groups among (1) parents of new-borns, (2) caregivers and (3) other stakeholders. In the presence of experts and employers, working pregnant women may have had less opportunity to express their opinions and experiences. This may ultimately have resulted in the app's design being more tailored to the needs of experts and less suitable for working pregnant women.

Finally, in the intervention study, there may have been selection bias, despite the intervention and control groups being similar in baseline characteristics and working conditions. A new analysis (after publication) showed that in eight (out of twenty-four) midwifery practices and their affiliated hospitals, there was a large difference in the number of participants in the intervention and control groups. Three practices had primarily participants in the intervention group, while in five practices the participants were mainly in the control group, representing 45% (n=109) of the total number of participants (Table 1). In the other sixteen practices, the participants were (fairly) evenly distributed between both groups.

Table 1. Distribution participants per practise between intervention- and control group.

Participating practise	***Intervention group***	***Control group***	***Total***
Mainly participants in control group n=3	9	40	49 (20.3%)
Mainly participants in intervention group n=5	54	6	60 (24.9%)
Participants equally divided n=16	56	76	132 (54.8%)
Total	119	122	241 (100%)

On the one hand, this may be the result of the procedure that midwives and obstetricians of the participating practices first started including for the control group and later, after following a multidisciplinary training, the obstetric caregivers of the same practices recruited participants for the intervention group. On the other hand, demographic differences between practices may have resulted in more participants in the control group than in the intervention group, with employers providing information on risks at work and job adjustment during pregnancy. Also, the lack of information may have motivated participants in the intervention group to participate in the study, expecting to receive information on work adjustment through the P&W app. Because in our study no distinction was made in the practice to which the client belonged when collecting data, this can no longer be traced.

Finally, we answer the research questions and hypotheses of this thesis, as formulated in the Introduction, using the Core Concept 'Pregnancy and Work' (see Chapter 1, Figure 6).

Part 1- The results of this thesis confirm our hypotheses that *work-related risk factors* 'physically demanding work and long working hours' showed moderate significant associations with preterm birth. Contrary to our study, an update in a recent review showed moderate significance between 'irregular working hours' and preterm birth [4]. In pregnancies with working women with a *personal risk factor related to birth,* such as multiple births, the risk of preterm birth is even greater and also applies to 'irregular work and job strain'.

Part 2- Work adjustments can prevent these adverse outcomes and are laid down in *legislation and (medical) guidelines*. As assumed, a significant part of working pregnant women with low-risk (50%) and multiple pregnancies (59%) continued to work not in accordance with legislation and guidelines, comparable with other European countries. The failure of implementation of MPL and guidelines (SER and NVAB) is a challenge and seems the result of problems at different levels: little or no knowledge and communication with working pregnant women and their obstetrical caregivers about the risks and work adjustment, lack of access to occupational healthcare and absence of financial incentives for employers, while health insurers and governments, which do benefit, do not contribute to implementation (according to current regulations).

Part 3 - In the context of *prevention*, we have developed the blended care program 'Pregnancy and Work'. The results of our study confirmed the hypothesis that this preventive intervention led to more 'work advice' from obstetric care providers in the blended care group of working pregnant women than in the control group, but less often from their employers, with ultimately no difference in realising work adjustment between the two groups. The lack of a protocol-based step-by-step approach, in which end users and human factor specialists are involved from the beginning, and selection

bias between control and intervention groups may explain that the blended P&W care program was only partially effective.

Implications for practice, policy and jurisdiction

Application in guidelines, training and practice
The results of our research have already been applied into guidelines and folders for professionals and working pregnant women and used in jurisdiction.

In 2018, the results of both meta-analyses have been used in the revision of the SER and NVAB guidelines for recommendations regarding physical workload and (irregular) working times (Figure 2). These results have also been incorporated in *a brochure from the National Institute for Public Health and the Environment (RIVM)* [59] for working pregnant women and professionals about physically demanding work during pregnancy.

Emphasizing to employers and working pregnant women that the guidelines are based on scientific research can motivate them to follow the recommendations. However, the results of earlier studies show that there is no guarantee that people will simply trust and follow the recommendations based on scientific research [60]. During the pandemic, 'trust in science' increased because scientists were considered competent and committed, they were more visible and there was information on how researchers work [60, 61]. Occupational health professionals could take this as an example and discuss the need for preventive measures at work with employers and working pregnant women more often. In their training, (young) occupational physicians practice guiding their pregnant clients, with the results of our research in mind, and discussing the 'drafting and implementation of pregnancy policy' with employers (SGBO Radboud UMC). This could be expanded in the form of multidisciplinary training for as many obstetric and occupational healthcare providers as possible. Tailor-made training, with peer learning groups with occupational physicians, aimed at perceived barriers, can improve compliance with the guidelines [39].

Results Chapter 2 and 3 applied in guidelines and brochure

Physical workload

- **Lifting ≤ 10 kg**
- **Standing/walking ≥ 20 weeks ≤ 3 hours/day**
- **High risk pregnancy: no physical strain**

Periode van de zwangerschap	Het is verboden om te:
gehele zwangerschap	meer te tillen dan 10 kilogram in één handeling;
Vanaf de twintigste week	meer dan 10 keer per dag gewichten van meer dan 5 kilogram te tillen;
Vanaf de dertigste week	meer dan 5 keer per dag gewichten van meer dan 5 kilogram te tillen;
De laatste 3 maanden	dagelijks meer dan eenmaal per uur te hurken, knielen, bukken of staande voetpedalen te bedienen.

Er bestaat veel wetenschappelijk bewijs voor het schadelijke effect van fysieke belasting op de zwangerschap en het ongeboren kind. Als grenswaarden wordt daarom naast bovengenoemde verboden aanbevolen:

Periode van zwangerschap	Richtlijnen
gehele zwangerschap	Zo veel als mogelijk voorkomen om: · met de hand gewichten tetillen; · te bukken, hurken ofknielen; lang te staan en te lopen
Vanaf de twintigste week	Zo veel als mogelijk voorkomen om: Langer dan 3 uur per dag te staan en lopen
Vanaf de dertigste week	Zo veel als mogelijk voorkomen om: Langer dan 2 uur per dag te staan en lopen

De Arbowet en de richtlijn van bedrijfsartsen (NVAB) geven de volgende grenzen voor lichamelijk zwaar werk:

Gehele zwangerschap	• Bukken, hurken en knielen: zo weinig mogelijk; • Tillen: zo weinig mogelijk, maximaal 10 kg, • Staan: zoveel mogelijk vermijden, vooral in de laatste 3 maanden van de zwangerschap
Vanaf de 20e week	• Tillen: per dag niet meer dan 5 maal 10 kg tillen
Vanaf de 30e week	• Tillen: per dag niet meer dan 5 maal 5 kg tillen • Bukken, hurken, knielen of staand een voetpedaal bedienen: niet meer dan 1 keer per uur

TABEL 2A FYSIEKE WERKBELASTING EN INTERVENTIES

Interventie(s)

Zwaar tillen en dragen

Adviseer zo weinig mogelijk te tillen/dragen gedurende de gehele zwangerschap (maximaal gewichten van 10 kg, vanaf 20e week max. 5x10 kg per dag, vanaf 30e week max. 5x5 kg per dag).

Langdurig staan en lopen

- ➢ Adviseer lang staan gedurende de gehele zwangerschap zoveel mogelijk te vermijden.
- ➢ Adviseer het staan af te wisselen met lopen en zitten.
- ➢ Adviseer vanaf 20e zwangerschapsweek max. 3 uur staan en lopen, vanaf 30e zwangerschapsweek max. 2 uur staan en lopen per werkdag.

Bukken, hurken en knielen

- ➢ Adviseer zo weinig mogelijk te bukken/hurken/knielen gedurende de gehele zwangerschap (max. 25x per dag, vanaf 30e week max. 1x per uur).

(Irregular) working times

- **≤ 40 hrs/week**
- **No night work ≥ 20 weeks**
- **High risk pregnancy: no irregular work**

TABEL 2B ONREGELMATIGE WERKTIJDEN EN PLOEGENDIENST

Interventie(s)

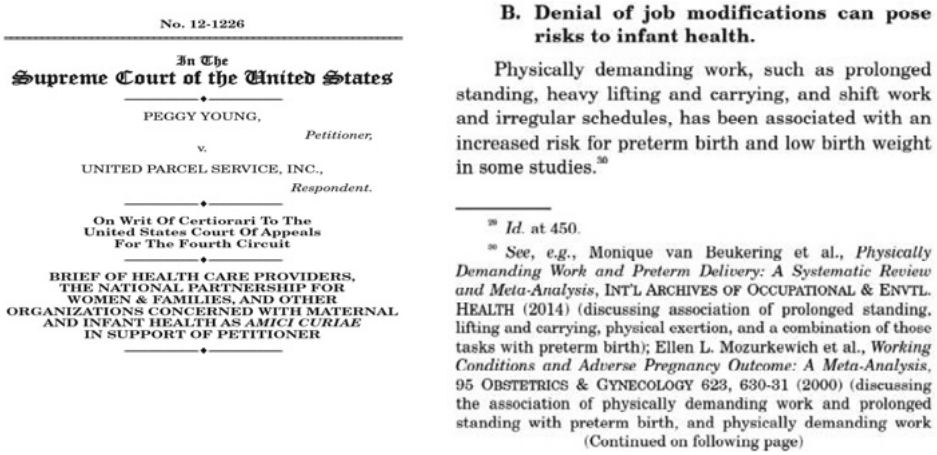
- ➢ Adviseer gedurende de zwangerschap en gedurende de postpartumperiode (tot 6 maanden na de bevalling):
- vanaf de 20e week geen nachtdiensten te draaien (geen werk tussen 23.00 en 07.00 uur).
- als de zwangere dat zelf vóór de 20e week wenst: geen nachtdiensten te draaien.
- regelmatige werktijden met 12 uur hersteltijd ertussen om te reizen, te eten en te slapen.
- geen overwerk te verrichten.
- maximaal 9 uur per dag te werken en max. 40 uur per week.
- geen vaste nachtdiensten te draaien gedurende gehele zwangerschap.
- ➢ Informeer betrokkene over haar wettelijk recht:
- dat zij zo nodig een achtste van de werktijd extra rusttijd of pauzes mag nemen.
- dat zij een kwart van werktijd aan voeden/kolven mag besteden (tot het kind 9 maanden oud is).

Figure 2 Results of both meta-analysis used in the revision of the Guidelines from SER and NVAB and brochure RIVM 'Physically demanding work …. during pregnancy' for working pregnant women and professionals.
Source:

- *Social economic Council (SER): 'Guide to Occupational Health and Safety Measures Pregnancy & Work' (2018)*
- *Netherlands Society of Occupational Medicine (NVAB): 'Guideline Pregnancy, Postpartum Period and Work' (2018)*
- *National Institute for Public Health and the Environment (RIVM): Brochure 'Physically demanding work …. during pregnancy' for working pregnant women and professionals.*

Multiple and other medically complicated pregnancies and work
This study provides evidence that adjusting work according to the NVAB guidelines can prevent (very) preterm birth in multiple pregnancies: avoid physically demanding work or job strain, as well as long or irregular working hours. This evidence can also provide guidance for working women with other high-risk pregnancies, such as a previous preterm birth.

Jurisdiction
While it's best not to get to that point, one of the implications of this thesis could be a warning to employers. In the USA, an employer forced his pregnant employee to choose between her healthcare provider's advice 'to stop lifting' and her job (Figure 3). That choice could risk compromising her health and the health of her unborn child. After eight years of litigation, she finally won the lawsuit at the US Supreme Court. The 'Attorneys for amici curiae' partly based their defence on the results of the meta-analysis regarding physically demanding work (Chapter 2) [62].



No. 12-1226

In The
Supreme Court of the United States

PEGGY YOUNG,
Petitioner,
v.
UNITED PARCEL SERVICE, INC.,
Respondent.

On Writ Of Certiorari To The
United States Court Of Appeals
For The Fourth Circuit

BRIEF OF HEALTH CARE PROVIDERS, THE NATIONAL PARTNERSHIP FOR WOMEN & FAMILIES, AND OTHER ORGANIZATIONS CONCERNED WITH MATERNAL AND INFANT HEALTH AS *AMICI CURIAE* IN SUPPORT OF PETITIONER

B. Denial of job modifications can pose risks to infant health.

Physically demanding work, such as prolonged standing, heavy lifting and carrying, and shift work and irregular schedules, has been associated with an increased risk for preterm birth and low birth weight in some studies.[30]

[29] *Id.* at 450.

[30] *See, e.g.*, Monique van Beukering et al., *Physically Demanding Work and Preterm Delivery: A Systematic Review and Meta-Analysis*, INT'L ARCHIVES OF OCCUPATIONAL & ENVTL. HEALTH (2014) (discussing association of prolonged standing, lifting and carrying, physical exertion, and a combination of those tasks with preterm birth); Ellen L. Mozurkewich et al., *Working Conditions and Adverse Pregnancy Outcome: A Meta-Analysis*, 95 OBSTETRICS & GYNECOLOGY 623, 630-31 (2000) (discussing the association of physically demanding work and prolonged standing with preterm birth, and physically demanding work

(Continued on following page)

Figure 3. *US Supreme court Statement Peggy Young versus UPS, page 13.*

Recommendations for future research, policy and practice

Recommendations for future research
A cost-effectiveness study, including an economic evaluation of productivity, health and safety, can provide information on the impact of preventive measures on pregnant women in work [35]. A rough estimate from 2014 showed that prevention in the Netherlands saves at least 11 to 28 million euros annually in medical costs (treatment

of mother and child up to 1 year) and 5 to 11 million euros in avoidable absenteeism due to illness [63]. However, it was assumed that 10% and 25%, respectively, of all pregnant women from a certain sector were exposed to risks appropriate to their work/sector. Based on the results and discussion in this thesis, we can more accurately determine how much working pregnant women are exposed in certain sectors (chapters 4 and 5), what working conditions they are exposed to, and then estimate their risk of PTB and other adverse pregnancy outcomes (chapters 2 and 3). We expect that, in reality, the costs and thus the savings will be much higher.

In addition to this quantitative research, qualitative research on employers' barriers and facilitators can provide insight into their needs and incentives in implementing MPL. Examples of best practice from employers who have policies in line with legislation (MPL) can help persuade others to adopt a 'pregnancy policy' as well.

Research into redefining the roles of midwives, obstetricians and occupational physicians in the care of working pregnant women can reveal the added value of cooperation. Officially, in the Netherlands, midwives and obstetricians do not have a role to play in guiding their pregnant clients in advising them about working conditions. However, because they play a central role in the care of pregnant women, working conditions are often discussed during counseling [64]. They need to know about risks on the job and want to advise their clients to a limited extent [Chapter 8, 65]. Schonewille et al. [65] developed a short training for midwives and obstetricians on work-related risks during pregnancy, and a screening list with which working pregnant women could screen themselves for occupational risks in the waiting room of the practice. During the intake, they discussed the results of this screening with their midwife or obstetrician. All women appreciated this screening and discussing the results with the midwives or obstetrician. In our study, the P&W increased advice on work adjustments provided by trained midwives and obstetricians (Chapter 8).

With the results of this thesis and those of Schonewille et al., qualitative research (e.g. a focus group with representatives of obstetric and occupational healthcare), can provide insight into the possibilities for effective cooperation and tools, such as an e-learning or an Mhealth application. While access to occupational physicians is limited, pregnant women all receive obstetric care. In 2020, 162,687 women gave birth of whom 26.9% in primary care and 69.2% in secondary care (Volksgezondheidzorg.info). If midwives and obstetricians perform the first screening and advice on work adjustment, occupational physicians, used to advise employers, can focus on a limited group of working pregnant women with more complex work-related or personal risks.

Lack of implementation in MPL occurs in several European countries. An inventory of international differences and similarities in incentives for employers and the division of

roles in care for working pregnant women, for example, within the EU, can provide insight into bottlenecks, and countries can learn from each other's best practices.

In further *research on the impact of occupational activities and pregnancy outcomes*, it is important to take into account the following implications:

- Distinguish spontaneous and induced preterm birth: high physical workload was associated with an increased risk of iatrogenic, but not with spontaneous preterm birth [6].
- Especially for prolonged standing and walking, long working hours and cumulative workload: to improve the homogeneity distinguish different categories of workload [5].
- Because pregnancy-induced hypertension (PIH) is considered a 'risk enhancer', as high physical workload had a greater impact on PTB in the presence of PIH [6], include data on PIH from participants. In addition, vice versa, when researching PIH, it is important to include data on the (physical) workload of the participants.
- To limit bias in the survey due to participants self-reporting their workload, involve trained interviewers to complete questions about workload and pregnancy outcomes.
- Distinguish between workloads during the different periods of pregnancy, as workloads tend to decrease over the course of pregnancy, preferably in three trimesters or before and after 20 weeks of pregnancy.
- Adjustment of working conditions, according to the recommendations of the NVAB guideline on multiple pregnancies, can prevent preterm birth. We recommend investigating whether the advice of the NVAB guideline is also effective for working women with other medically complicated pregnancies.

Finally, in their research on adverse pregnancy outcomes such as preterm birth, midwives and obstetricians focus on personal, demographic and pregnancy characteristics, but hardly on working conditions [66]. It is recommended to also include the impact of working conditions (i.e. physical load, (irregular) working hours) in research on pregnancy outcomes.

Communication and training of the recommendations of the NVAB and SER guidelines should be aimed at different stakeholders. Clear communication and credibility in the evidence supports implementation.

An improved design *of the blended care program 'Pregnancy and Work'* can be a tool to implement the recommendations of the MPL and guidelines. Redesigning the P&W application requires a protocolled step-by-step approach involving end users and human factor specialists from the start. Specific target groups must be taken into account: working pregnant women differ in education, ethnicity and SES, in contract ((temporary) employment or self-employed), in working conditions and in health. Priority in development should be given to groups of women more at risk of work, without

adherence to recommendations, with a lower education and a job in the sectors of healthcare, education/childcare & social services, retail catering, hospitality, construction and cleaning (Chapter 4). This also applies to women with pregnancy complications or a higher risk of adverse outcomes, such as multiple pregnancies (Chapter 5). Also, professionals should realize that mHealth applications will increasingly be used in counselling pregnant women [48, 55].

Stakeholders in occupational and obstetric healthcare for working pregnant women together can take advantage of this accessible, relatively cheap way to reach many people. It is important that the information is unambiguous, trustworthy and preferably part of a guideline, and should be updated regularly. The P&W application as part of the blended care program is a promising tool, after redesign based on the findings of this thesis, as discussed above. The development of different versions of the P&W application or an interactive website, for working pregnant women, (obstetric) healthcare professionals and employers, could increase the effectiveness of the blended care intervention 'Pregnancy and Work' intervention. And finally, in the redesign, involving experts in medical informatics from the beginning is essential.

Recommendations for working pregnant women, employers and healthcare professionals

The previous recommendations are largely related to the long term and require time and money. However, working women who are now pregnant cannot wait for that. With the following implications, pregnant women, employers and organizations and healthcare providers can get started right away.

- *Pregnant working women*: half of the women work under conditions that can be harmful to your pregnancy, think of physically demanding or standing work, lifting, long and irregular working hours, job strain and work with infectious diseases or toxic substances. Ask your employer if he or she is aware how you can adjust your working conditions and continue to work safely. Visit your occupational physician (this can be done anonymously), or if you don't have one, your midwife or obstetrician for reliable advice on work adjustment.
- *Employers:* Make sure you belong to the better half of the employers in the Netherlands and create a safe working environment for your pregnant employees. Comply with your legal duty and create an RIE (Risk Inventory and Evaluation) for pregnant women. Use the SER's Guide to Working Conditions Pregnancy & Work. The occupational health service can provide support in developing a 'pregnancy policy'. Advise your pregnant employees to visit the occupational physician for a preventive consultation. This guarantees adequate work advice. UWV reimburses if the wage costs fall as a result of these adjustments. This leads to less absenteeism, better pregnancy outcomes and better employment relations, which is relevant in a tight labor market.

- *Midwives and obstetricians:* This thesis confirms that physically demanding work and long and irregular working hours can lead to a higher chance of preterm birth, up to 25-50% higher in low-risk pregnancies and up to three times higher in high-risk pregnancies. Half of women work in conditions that can be harmful to the pregnant woman and her unborn child. Refer all your clients to the employer to discuss whether their work needs to be adjusted, or as recommended in the NVAB guideline: to the occupational physician for a 'preventive consultation'. This can be done anonymously, without the employer's knowledge. Or, if this is not possible, consult the NVAB guideline to give yourself reliable advice on working adjustment.
- *Occupational healthcare*: Ask companies and organizations whether they are sure that their pregnant employees can work safely. Motivate and support them in implementing a 'pregnancy policy', using the SER and NVAB guidelines.

Conclusions

Physical and job strain and long and irregular working hours increase the risk of preterm birth in multiple pregnancies. In low-risk pregnancies, physically demanding work and long working hours have a moderately increased risk of preterm birth.

Legislation and evidence-based guidelines on pregnancy and work have been jointly drafted and recognized by relevant stakeholders, but their implementation in practice is not forthcoming. Half of pregnant women with a low-risk pregnancy and almost 60% of women with multiple pregnancies work in unsafe conditions. This seems to be the result of little or no knowledge and communication with working pregnant women and their obstetrical caregivers about the risks and work adjustment, lack of access to occupational healthcare and absence of financial incentives for employers. Redefining the roles between midwives, obstetricians and occupational physicians can improve the quality and coverage of occupational healthcare for all working pregnant women. Involving health insurers and the government can promote implementation, because they benefit from a preventive approach.

The blended care intervention 'Pregnancy and Work' can be a tool for realizing implementation. Further improvement of the design of the 'Pregnancy and Work' application aimed at different groups of working pregnant women, their obstetric care providers and also for their employers can increase the effectiveness of the blended care intervention and may lead to a safe workplace for pregnant women.

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Summary

10

This thesis concerns working pregnant women: the impact of working conditions on their pregnancy and unborn child, the implementation of Maternity Protective Legislation (MPL) and the guidelines and opportunities for prevention of adverse pregnancy outcomes.

In this chapter, we summarise and discuss the findings of our research and the implications for (clinical) practice, policy and future perspectives to improve 'healthy work in pregnancy'.

The introduction (**Chapter 1**) provides an overview of the history and current participation in the labour market of (pregnant) women. Based on the core concept 'Pregnancy and Work', we explore the research opportunities and present the objectives of this thesis.

Worldwide, more than half of women aged 15 to 65 years have paid work. In the Netherlands, 82% of women of childbearing age are employed or in self-employment. Although unlike in other countries, many women work part-time, 'work' is an important part of the daily life of Dutch pregnant women: nine out of ten pregnant women work an average of 30 hours a week during their first pregnancy, often in the health and social services sectors, in pedagogical and service (health and welfare) professions. In recent years, the Netherlands Institute for Human Rights has drawn attention to the vulnerability of working pregnant women in various campaigns. More than 40% of working women with a child have experienced discrimination due to pregnancy or recent motherhood, including with respect to work conditions.

The core concept 'Pregnancy and Work' shows that during pregnancy there are two types of risk to consider in the workplace: work-related and personal risk factors. Adjustment of working conditions, according to legislation (MPL) and guidelines from the Netherlands Society of Occupational Medicine (NVAB) and the Social Economic Council (SER), can prevent disorders in mothers and children. Based on the core concept, we explored the gaps in the following three themes: impact on working conditions, implementation of MPL and guidelines and prevention of adverse outcomes.

The evaluation of research on the impact of physically demanding work and (irregular) working hours for working pregnant women at preterm birth shows that little is known about the difference per trimester and about the impact of the combination of different risk factors related to work (multiple workload).

In the Netherlands, there are two up-to-date guidelines on MPL and guidance for pregnant employees (NVAB and SER), but what is known so far is reason to doubt the implementation. In addition to recommendations for adjusting work for low-risk pregnancies, the NVAB guideline provides advice for the guidance of working women with high-risk pregnancies, such as a multiple pregnancy. Due to a lack of scientific research, the recommendations for working women with a multiple pregnancy are based on expert opinion.

Until now, there are hardly any preventive interventions for working pregnant women. Mobile health applications (mHealth apps) are promising tools in the care of pregnant women. They may be able to support working pregnant women and their caregivers with (realisation of) work adjustment.

The aim of this thesis is to identify the impact of physically demanding work and (irregular) working hours on preterm birth in low-risk pregnant women and, in particular, with multiple pregnancies. We then investigate whether the Dutch MPL and guidelines have been implemented, and finally we want to develop a preventive intervention to advise pregnant women and their obstetric caregivers about work adjustment.

This thesis consists of three parts, with the following research questions:

Part 1- The impact of working conditions on preterm birth

1. Do pregnant workers in paid employment or self-employed who are exposed to different kinds of physically demanding work during the pregnancy have a higher risk of preterm birth, defined as delivery before 37 weeks gestations, compared to their colleagues who are not exposed or to a lesser extent exposed to physically demanding work (Chapter 2)?
2. Do pregnant workers in paid employment or self-employed with shift work or long working hours have a higher risk of preterm birth compared to their colleagues who are not exposed or to a lesser extent exposed (Chapter 3)?

Part 2 - Implementation of legislation and guidelines for working pregnant women

3. Are pregnant employees informed about the risks at work and necessary work adjustments, and have any work adjustments been made, according to the Dutch MPL and guidelines, in a low-risk group on the one hand (Chapter 4) and a group with a personal risk factor on the other, that being women with a multiple pregnancy (Chapter 5)?
4. What working conditions contribute to an increased risk of preterm birth in multiple pregnancies up to 20 weeks of gestation (Chapter 5)?

Part 3- Intervention: blended care Pregnancy and Work

5. What are the perceived facilitators and barriers according to pregnant women, medical professionals and employers for the use of a mobile application in obstetric care to prevent occupational-related pregnancy complications (Chapter 6)?
6. What is the usability of the mHealth Pregnancy and Work application (P&W app) and the perceived usefulness of the work advice of the P&W application by potential end users (Chapter 7)?
7. Does the blended care program Pregnancy and Work, which consists of a training session for professionals and access to a mobile health (mHealth) application (the P&W app), lead to more advice about work adjustment from obstetric caregivers to their clients, and do these pregnant women realise more work adjustments than those receiving care as usual (Chapter 8)?

Part 1- The impact of working conditions on preterm birth

In Part 1 in two meta-analyses, we have identified both the effect of individual forms of physical workload and the combination of (multiple forms of) physical workload with other occupational exposures (routine work or tasks without mental stimulation, noise, cold temperature, wet atmosphere or manipulation of chemical substances) and with irregular and/or long working hours on preterm birth, differentiated per trimester.

Various forms of physically demanding work (standing and walking, lifting and carrying, physical effort, a job with ≥ 2 tasks with physical effort or an 'Occupational Fatigue Score' ≥ 2 and demanding posture) showed moderate significant associations with preterm birth (Odds ratios: 1.3-1.5) **(Chapter 2).** Odds Ratios were higher with a multiple workload, but lower than the sum of each risk factor separately. The trimester exposure analyses showed no difference in associations. During the first trimester, exposure to physically demanding work was most frequent and decreased as pregnancy progressed.

Long working hours, more than 40 hours per week, showed a moderately significant association with preterm birth **(Chapter 3).** Irregular work hours or night shifts during pregnancy were not associated with an increased risk of preterm birth. For these risk factors, it was not possible to make a summary of the estimated odds ratio per trimester because only a few studies distinguished the exposure per trimester. In the absence of high-quality studies focusing on the risks per trimester, most in the third trimester, the results should be interpreted with caution.

Part 2 - Implementation of maternity protective legislation and guidelines for working pregnant women

In Part 2, in two prospective cohort studies, we examined whether the Dutch MPL and guidelines from the Netherlands Society of Occupational Medicine (NVAB) and the Social Economic Council (SER) have been implemented and the impact of working conditions in multiple pregnancies on preterm birth.

The first was a cohort of 269 working women with a low-risk pregnancy. Of the participants, 41% worked before 20 weeks of pregnancy, and 63% after 20 weeks of pregnancy, under conditions that did not meet the recommendations **(Chapter 4)**. Many of these women had to deal with (a combination of) physical workload (prolonged standing and walking, lifting, bending), job strain, long and irregular working hours and noise. Women with a lower education and a job in the sectors of health care, education/ childcare & social services, catering, hospitality, construction and cleaning were less

likely to work according to recommendations. In addition to the above risk factors, 47% of the participants worked with potential biological and chemical exposure. Despite a legal obligation, only 15% of employers informed their pregnant employees of the risks and necessary work adjustments. For 38% of the participants, this meant that they were unaware of whether they were at risk of biological and chemical exposure during their work and how these risks could be avoided.

In the second cohort with 383 women with a multiple pregnancy, 59% of the participants did not work under conditions that met the guidelines (NVAB) **(Chapter 5)**. Despite the recommendations, physical workload, prolonged standing and walking, irregular working hours and job strain were common among these participants. In this cohort of 383 working women with a multiple pregnancy, long (>28 hours) and irregular work hours were associated with preterm birth < 32 weeks of gestation and irregular work times with preterm birth between 32 and 36 weeks of gestation. In a subgroup of this cohort, with 213 women working more than 28 hours per week, irregular working hours and tasks with little/no freedom were significantly associated with preterm birth, both before 32 and between 32 and 36 weeks of gestation. Requiring physical strength and high physical strain were associated with preterm birth < 32 weeks gestation **(Chapter 5)**.

Part 3- Intervention: blended care pregnancy and work

In Part 3, we developed an intervention through two qualitative studies and evaluated it in an intervention study. This intervention, 'blended care Pregnancy and Work' (P&W), intended to provide pregnant women and their obstetrical caregivers with personalised advice on work adjustment.

The result of the first study, with two multidisciplinary focus group meetings, provided insight into characteristics that impact the use of a mobile health application (mHealth app) **(Chapter 6)**. The three most important facilitators were 1) good interaction between application and user, 2) a practical source of information and 3) understandable information, well-dosed and according to existing guidelines. The two main barriers were 1) extensive battery and memory use of the smartphone and 2) sending frequent push notifications.

We then developed a mHealth application, the Pregnancy and Work application (P&W app), based on the results of the focus group study (Chapter 6) and the recommendations from the evidence-based guideline from the Netherlands Society of Occupational Medicine (NVAB) 'Pregnancy, postpartum period and work'. The purpose of this application was to provide pregnant working women with personalised information and advice on work-related pregnancy risks.

In the second qualitative study, twelve working pregnant women evaluated the usability and the value of the P&W app, through think-aloud sessions, supplemented with questionnaires (Intrinsic Motivation Inventory and System Usability Scale) **(Chapter 7)**. Despite 82 usability issues, the pregnant women were satisfied with the application and it met their needs.

Chapter 8 describes an intervention study in which we evaluated the effect of the blended care intervention 'Pregnancy and Work' on (advice on) adjustment of working conditions, through a questionnaire survey among 269 working pregnant women. We developed a training for professionals (midwives, obstetricians and occupational physicians) about the recommendations from the NVAB guideline and the P&W app. Most obstetric caregivers (n = 57) who participated in the training rated the training as valuable and would use the P&W application and recommend the application to their clients. The blended care intervention included this training for professionals and access to the (slightly modified) 'P&W' application for working pregnant women and their obstetric care providers.

After the blended care intervention, pregnant working women in the intervention group (n=119, with access to the blended care intervention), received advice on work adjustment from midwives or obstetricians more often than women in the control group (n=122, with care as usual): 41 (39%) versus 21 (18%). However, these women in the intervention group less often received advice and/or information from their employer than women in the control group: 8 (8%) versus 31 (28%). In the end, this did not lead to a difference in work adjustment between the two groups.

Conclusions, implications and recommendations of research and practice

In **Chapter 9,** we evaluated the results of this thesis and discuss implications for future research and practice.

Evaluation of results

The findings of our two meta-analyses are similar to the results of other recent studies. This did not apply to 'irregular working hours', which in a recent extended meta-analysis showed a moderately significant association with preterm birth. These associations were higher in our study in working women with multiple pregnancies. Following the recommendations of the NVAB guideline to adapt work conditions in multiple pregnancies can prevent (extreme) preterm birth. The need to adapt work, especially among working women at risk, is confirmed by the decrease in preterm birth as a result of the involuntary worldwide experiment caused by the Corona pandemic: many pregnant women stopped working temporarily, or they worked fewer hours or from home.

Successfully implementing MPL and guidelines is a challenge, given the diversity of stakeholders and their interests. The absence of financial incentives for employers, limited access to occupational health care for all working pregnant women and the lack of knowledge and communication about the importance of work adjustment among working pregnant women and their obstetric healthcare providers appear to be the main cause of poor adherence to MPL and guidelines.

Although the P&W application was based on an evidence-based guideline and was developed and evaluated in an iterative process with all stakeholders, we did not use a protocolled step-by-step approach, involving end users and human factor specialists from the start. And while the blended care group in the intervention study was comparable to the group receiving usual care in terms of baseline characteristics and working conditions, demographic differences between obstetric practices appear to have led to selection bias. As a result, participants in the intervention group received less information and work adjustment from their employers. In the end, despite more advice from their midwife and obstetrician, participants did not adjust their work more often than the participants in the control group.

Implications

The *NVAB and SER guidelines* have adjusted their recommendations in a revised version based on the results of our research on physically demanding work and working hours. The Dutch government has incorporated these results into *brochures for professionals and working pregnant women*. Finally, the lawyers of a working pregnant woman have used them, with success, in defence of the US Supreme Court.

The results of our thesis provide a scientific justification for the recommendations of the NVAB guideline on multiple pregnancies. We recommend giving the same advice to working women with other high-risk pregnancies.

Future research

We provide recommendations for further research. First, we recommend a cost-effectiveness study on the impact of preventive measures on working pregnant women and a qualitative study on facilitators and barriers for employers when implementing 'pregnancy policy'.

Next, we suggest investigating redefining the role of midwives, obstetricians and occupational physicians in the care of working pregnant women. We then recommend evaluating whether the advice of the NVAB guideline is also effective for working women with other medically complicated pregnancies.

Finally, we suggest redesigning the P&W app. This requires a protocolled step-by-step approach involving end users and human factor specialists from the start.

Advice for daily practice
Women who are pregnant now or in the near future cannot wait for the results of future research. That is why we end this thesis with *practical advice:*

- *For working pregnant women*: to ask their employer or occupational physician how to continue to work safely until their maternity leave
- *For employers:* to create a safe working environment for their pregnant employees using the guideline from the SER and/or NVAB
- *For midwives and obstetricians:* to refer all clients to the employer and/or occupational physician to discuss whether their work needs to be adjusted or, if necessary, to give advice themselves, based on the NVAB guideline
- *Occupational health care*: to actively motivate companies and organisations to implement a 'pregnancy policy', using the guidelines of the SER and NVAB

Conclusions

In low-risk pregnancies, various forms of physically demanding work and long working hours have a moderately increased risk of preterm birth. Physical and job strain and long and irregular working hours increase the risk of preterm birth in multiple pregnancies. 50% of working pregnant women with low-risk pregnancies and nearly 60% of women with multiple pregnancies continue to work not in accordance with legislation and guidelines, even though these have been drawn jointly with all stakeholders. This puts mother and child at risk of adverse outcomes and seems the result of little knowledge of working pregnant women and their obstetric caregivers about risks in the workplace, lack of access to occupational health care and absence of financial incentives for employers. To improve working conditions for pregnant women, this thesis recommends further research on the redefinition of roles in the care of pregnant women and on employers' incentives and barriers to implementation. In particular, it is recommended to involve health insurers and the government, as they benefit from implementation.

We conclude that the blended care intervention 'Pregnancy and Work' can be further developed into an effective tool. This includes new designs of the 'Pregnancy and Work' app, aimed at working pregnant women on the one hand, their midwives and obstetricians on the other, and finally at their employers. Ultimately, this can lead to a safe work environment for pregnant women.

Samenvatting

Dit proefschrift gaat over werkende zwangeren in Nederland. Het beschrijft allereerst de invloed van arbeidsomstandigheden op de zwangerschap en het ongeboren kind, vervolgens de implementatie van bestaande wetgeving en richtlijnen rondom arbeid en zwangerschap, en tot slot de mogelijkheden voor preventie van nadelige zwangerschapsuitkomsten.

In dit hoofdstuk vatten we de bevindingen van ons onderzoek samen en bespreken we de implicaties voor de (klinische) praktijk, het beleid en de mogelijkheden voor verder onderzoek, met als doel de bevordering van gezond werken tijdens de zwangerschap in de toekomst.

De inleiding (**hoofdstuk 1**) geeft een overzicht van de historische en de huidige arbeidsparticipatie van (zwangere) vrouwen. Op basis van het concept 'zwangerschap en werk' verkennen we de onderzoeksmogelijkheden en presenteren we de doelstellingen van dit proefschrift.

Wereldwijd verricht meer dan de helft van de vrouwen van betaald werk. In Nederland werkt 82% van de vrouwen in de vruchtbare leeftijd, in loondienst of als zelfstandige. Hoewel vergeleken bij andere landen in Nederland veel vrouwen in deeltijd werken, is 'werk' een belangrijk onderdeel van het dagelijks leven van Nederlandse zwangeren: 9 van de 10 zwangere vrouwen werken tijdens hun eerste zwangerschap, gemiddeld 30 uur per week. Ze werken het meest in functies in zorg en welzijn, gevolgd door pedagogische en dienstverlenende beroepen. Het College voor de Rechten van de Mens heeft de afgelopen jaren in verschillende campagnes aandacht besteed aan de kwetsbaarheid van werkende zwangeren op de arbeidsmarkt. Meer dan 40% van de werkende vrouwen met een kind heeft te maken gehad met discriminatie vanwege zwangerschap of recent moederschap, ook wat betreft hun arbeidsomstandigheden.

Het concept 'zwangerschap en werk' gaat uit van twee soorten risico's tijdens de zwangerschap: werkgerelateerde en persoonlijke risicofactoren. Aanpassing van arbeidsomstandigheden volgens de wettelijke regels en richtlijnen van de Nederlandse Vereniging voor Arbeids- en Bedrijfsgeneeskunde (NVAB) en de Sociaal Economische Raad (SER) kan afwijkingen bij moeders en kinderen voorkomen. We zijn op zoek gegaan naar hiaten op de volgende drie gebieden: impact van arbeidsomstandigheden op vroeggeboorte, implementatie van bestaande wetgeving en richtlijnen op het gebied van zwangerschap en werk, en preventie van nadelige uitkomsten zoals vroeggeboorte.

Uit de evaluatie van onderzoek naar de impact van lichamelijk zwaar werk en (onregelmatige) werktijden voor werkende zwangeren op vroeggeboorte blijkt dat er weinig bekend is over het verschil van de invloed per trimester en over de impact van de combinatie van verschillende soorten werkgerelateerde risicofactoren (meervoudige belasting).

Er is nauwelijks onderzoek gedaan naar de implementatie van de NVAB- en SER-richtlijnen met betrekking tot wetgeving en advisering/begeleiding van werkenden zwangeren. Naast aanbevelingen voor het aanpassen van werk bij gezonde zwangeren (met een laag risico op complicaties), geeft de NVAB-richtlijn adviezen voor de begeleiding van werkende vrouwen met 'risicozwangerschappen' (met een verhoogd risico op complicaties), zoals een meerlingzwangerschap. Bij gebrek aan wetenschappelijk onderzoek zijn de aanbevelingen voor werkende vrouwen met een meerlingzwangerschap gebaseerd op adviezen van experts.

Tot nu toe komen preventieve interventies voor werkende zwangeren nauwelijks voor. In de zorg voor zwangere vrouwen zijn mobiele gezondheidsapplicaties (apps) veelbelovend. Zij kunnen werkende zwangeren en hun verloskundige zorgverleners ondersteunen bij (het realiseren van) werkaanpassingen.

Het doel van dit proefschrift is het onderzoeken van de impact van lichamelijk zwaar werk en (onregelmatige) werktijden op vroeggeboorte bij zwangeren met een laag risico op complicaties, in het bijzonder bij vrouwen met een meerlingzwangerschap. Vervolgens gaan we na of de Nederlandse wetgeving en richtlijnen rondom zwangerschap en werk zijn geïmplementeerd. Tot slot willen we een preventieve interventie ontwikkelen om zwangere vrouwen en hun verloskundige zorgverleners te adviseren over aanpassing(en) van werkomstandigheden met behulp van mobiele applicaties (apps). We willen onderzoeken of verloskundige zorgverleners bij deze advisering hun traditionele 'face-to-face contactmomenten' kunnen combineren met 'online zorg' in zogenoemde 'blended care'.

Dit proefschrift bestaat uit drie delen, met de volgende onderzoeksvragen:

Deel 1- De impact van arbeidsomstandigheden op vroeggeboorte

1. Lopen werkende zwangeren (in loondienst of zelfstandig) die tijdens de zwangerschap worden blootgesteld aan verschillende soorten lichamelijk zwaar werk, een hoger risico op vroeggeboorte, gedefinieerd als bevalling vóór 37 weken zwangerschap, dan hun collega's die niet of in mindere mate worden blootgesteld aan lichamelijk zwaar werk (**hoofdstuk 2**)?
2. Lopen zwangeren (in loondienst of zelfstandig) met lange en/of onregelmatige werktijden een hoger risico op vroeggeboorte dan hun collega's die niet of in mindere mate zijn blootgesteld aan lange en/of onregelmatige werktijden (**hoofdstuk 3**)?

Deel 2 - Implementatie van wetgeving en richtlijnen voor werkende zwangeren

3. Krijgen werkende zwangeren voorlichting over de risico's op het werk en de noodzakelijke werkaanpassingen? Is het werk aangepast volgens regels en aanbevelingen van de Nederlandse wetgeving en richtlijnen, enerzijds in een groep met een laag risico op complicaties (**hoofdstuk 4**) en anderzijds in een groep met

een persoonlijke risicofactor, namelijk vrouwen met een meerlingzwangerschap (**hoofdstuk 5**)?

4. Welke arbeidsomstandigheden dragen bij aan een verhoogd risico op vroeggeboorte bij vrouwen die zwanger zijn van een meerling in de eerste 20 weken van de zwangerschap (**hoofdstuk 5**)?

Deel 3- Interventie: blended care bij zwangerschap en werk

5. Wat zijn volgens zwangere vrouwen, medische professionals en werkgevers faciliterende en beperkende factoren voor het gebruik van een mobiele applicatie (smartphone-app) in de verloskundige zorg om werkgerelateerde zwangerschaps-complicaties te voorkomen (**hoofdstuk 6**)?
6. Wat is de bruikbaarheid van de mobiele Pregnancy & Work-applicatie (P&W-app) en het door potentiële eindgebruikers ervaren nut van de werkaanpassingsadviezen van de P&W-app (**hoofdstuk 7**)?
7. Leidt het blended care-programma 'Zwangerschap en werk', dat bestaat uit een training voor professionals en toegang tot de P&W-app, tot meer advies over werkaanpassing van verloskundige zorgverleners aan hun cliënten? Realiseren deze zwangere vrouwen meer aanpassingen in hun werk dan vrouwen die reguliere zorg krijgen (**hoofdstuk 8**)?

Deel 1- De impact van arbeidsomstandigheden op vroeggeboorte

In deel 1 hebben we in twee meta-analyses onderzocht wat het effect is op vroeggeboorte van zowel individuele vormen van lichamelijke belasting als de combinatie van (meerdere vormen van) lichamelijke belasting met andere risicofactoren in het werk (routinematig werk, lawaai, lage temperatuur, natte omgeving of werk met chemische stoffen) en lange en/of onregelmatige werktijden, gedifferentieerd per trimester.

Verschillende vormen van lichamelijk zwaar werk (staan en lopen, tillen en dragen, lichamelijke inspanning, werk met ≥ 2 lichamelijk belastende taken of een 'Occupational Fatigue Score' ≥ 2 en een ongemakkelijke houding) vertoonden matig significante verbanden met vroeggeboorte (odds ratio's: 1,3-1,5) (**hoofdstuk 2**). De odds ratio's waren hoger bij een meervoudige belasting, maar lager dan de som van de afzonderlijke risicofactoren. Er was geen verschil in verband per trimester. In het eerste trimester was de blootstelling aan lichamelijk zwaar werk het meest frequent, deze nam af naarmate de zwangerschap vorderde.

Lange werktijden, van meer dan 40 uur per week, vertoonden een matig significant verband met vroeggeboorte (**hoofdstuk 3**). Er was geen verband tussen onregelmatige werktijden of nachtdiensten tijdens de zwangerschap en een verhoogd risico op vroeggeboorte. Voor deze risicofactoren was het niet mogelijk om een overzicht te geven

van de geschatte odds ratio per trimester omdat slechts enkele studies de blootstelling uitsplitsten naar trimester. Vanwege het gebrek aan kwalitatief hoogwaardige studies die onderscheid maakten in de risico's per trimester, met name in het derde trimester, moeten de resultaten voorzichtig worden geïnterpreteerd.

Deel 2 - Implementatie van wetgeving en richtlijnen voor werkende zwangere vrouwen

In deel 2 hebben we in twee prospectieve cohortstudies onderzocht of de Nederlandse wetgeving en richtlijnen van de Nederlandse Vereniging voor Arbeids- en Bedrijfsgeneeskunde (NVAB) en de Sociaal Economische Raad (SER) zijn geïmplementeerd en wat de invloed is van arbeidsomstandigheden bij vrouwen met een meerlingzwangerschap op vroeggeboorte.

De eerste studie bestond uit een cohort van 269 werkende vrouwen met een laag risico op complicaties tijdens de zwangerschap. Vóór 20 weken zwangerschap bleven 110 (41%) vrouwen werken onder omstandigheden die niet in overeenstemming waren met de Nederlandse richtlijnen en wetgeving. Vanaf 20 weken zwangerschap was dit aantal 129 (63%) (**hoofdstuk 4**). Veel van deze vrouwen hadden te maken met (een combinatie van) lichamelijke belasting (langdurig staan en lopen, tillen, bukken), werkdruk, lange en onregelmatige werktijden en lawaai. Vrouwen met een lagere opleiding en een baan in de sectoren gezondheidszorg, onderwijs/kinderopvang & welzijn, horeca, bouw en schoonmaak werkten minder vaak volgens de wettelijke regels en richtlijnen. Naast de bovengenoemde risicofactoren liep 47% van de deelnemers een risico op blootstelling aan biologische agentia (infectieziekten) en chemische stoffen. Ondanks een wettelijke verplichting gaf slechts 15% van de werkgevers hun zwangere werknemers voorlichting over de risico's en noodzakelijke werkaanpassingen. Voor 38% van de deelnemers betekende dit dat ze niet wisten of ze tijdens hun werk risico liepen op biologische en chemische blootstelling en hoe ze deze risico's konden vermijden.

In de tweede studie, met een cohort van 383 vrouwen met een meerlingzwangerschap, werkte 59% van de deelnemers niet volgens de NVAB-richtlijnen (**hoofdstuk 5**). Ondanks de aanbevelingen hadden deze deelnemers vaak te maken met lichamelijke belasting, langdurig staan en lopen, onregelmatige werktijden en werkdruk. Bij deze 383 werkende vrouwen met een meerlingzwangerschap was er een significant verband tussen lange (> 28 uur) en onregelmatige werktijden en vroeggeboorte < 32 weken zwangerschap, en tussen onregelmatige werktijden en vroeggeboorte na 32-36 weken zwangerschap. In een subgroep van dit cohort, met 213 vrouwen die meer dan 28 uur per week werkten, was er een significant verband tussen onregelmatige werktijden en met weinig/geen vrijheid in uitvoering van taken en vroeggeboorte, zowel < 32, als na 32-36 weken zwangerschap. Lichamelijke krachtsinspanning en zware lichamelijke belasting

vertoonden een significant verband met vroeggeboorte < 32 weken zwangerschap (**hoofdstuk 5**).

Deel 3 - Interventie: blended care bij zwangerschap en werk

In deel 3 hebben we in twee kwalitatieve studies een interventie ontwikkeld en deze vervolgens geëvalueerd in een interventiestudie. De interventie, 'blended care bij zwangerschap en werk', een combinatie van online en offline zorg, is bedoeld om zwangere vrouwen en hun verloskundige zorgverleners persoonlijk advies te geven over de benodigde werkaanpassing.

Doel van het eerste onderzoek was het krijgen van inzicht in kenmerken die van invloed zijn op het gebruik van een mobiele gezondheidsapplicatie ('mHealth-app') door middel van twee multidisciplinaire focusgroepbijeenkomsten (**hoofdstuk 6**). De drie belangrijkste bevorderende kenmerken waren 1) goede interactie tussen applicatie en gebruiker, 2) een praktische informatiebron en 3) begrijpelijke informatie, goed gedoseerd en volgens bestaande richtlijnen. De twee belangrijkste belemmerende kenmerken waren 1) een toename van het batterij- en geheugengebruik van de smartphone en 2) het regelmatig versturen van pushberichten.

Op basis van de resultaten van het focusgroeponderzoek (**hoofdstuk 6**) en de aanbevelingen uit de evidence-based NVAB-richtlijn 'Zwangerschap, postpartumperiode en werk', hebben we vervolgens een mHealth-applicatie ontwikkeld, de Pregnancy & Work- applicatie (P&W-app). Het doel van deze applicatie was om werkende zwangeren individueel advies te geven over werkgerelateerde risico's voor de zwangerschap.

In het tweede kwalitatieve onderzoek beoordeelden 12 werkende zwangeren de bruikbaarheid en het nut van de P&W-app door middel van think aloud-sessies, aangevuld met vragenlijstonderzoek (**hoofdstuk 7**). Ondanks 82 bruikbaarheidsproblemen waren de zwangere vrouwen tevreden met de applicatie en voorzag de P&W-app in hun behoeften.

Hoofdstuk 8 beschrijft een interventiestudie waarin we het effect van de blended care-interventie 'Zwangerschap en werk' op (advisering over) aanpassing van arbeidsomstandigheden hebben geëvalueerd door middel van een vragenlijstonderzoek onder 269 werkende zwangeren. We hebben een training ontwikkeld voor professionals (verloskundigen, gynaecologen en bedrijfsartsen) over de adviezen uit de NVAB-richtlijn en de P&W-app. De meeste zorgverleners (n = 88, 98%) die deelnamen aan de training, beoordeelden deze als bruikbaar en nuttig. Ze waren van plan de P&W-app te gebruiken en deze aan te bevelen aan hun cliënten. De blended care-interventie bestond uit deze

training voor professionals en toegang tot de (iets aangepaste) P&W-applicatie voor werkende zwangeren en hun verloskundige zorgverleners.

Werkende zwangeren in de interventiegroep (n=119 (49%), met toegang tot de blended care-interventie) kregen significant vaker advies over werkaanpassing van verloskundigen of gynaecologen dan zwangeren in de controlegroep (n=122 (51%), met gangbare zorg): 41 (39%) versus 21 (18%). De vrouwen in de interventiegroep kregen echter minder vaak advies en/of voorlichting van hun werkgever dan vrouwen in de controlegroep: 8 (8%) versus 31 (28%). Dit leidde uiteindelijk niet tot een verschil in werkaanpassing tussen de twee groepen.

Aanbevelingen voor onderzoek en praktijk

In **hoofdstuk 9** hebben we de resultaten van dit promotieonderzoek geëvalueerd en de implicaties voor toekomstig onderzoek en de praktijk besproken.

De resultaten bevestigen dat de aanbevelingen in wetgeving en richtlijnen rondom zwangerschap en werk adequaat en noodzakelijk zijn. Succesvolle implementatie van deze wetgeving en richtlijnen is, gezien de diversiteit aan stakeholders en hun belangen, een uitdaging. De belangrijkste oorzaken van de gebrekkige implementatie lijken 1) de beperkte toegang tot bedrijfsgezondheidszorg voor alle werkende zwangeren, 2) het ontbreken van financiële prikkels voor werkgevers en 3) gebrek aan kennis van en communicatie over het belang van werkaanpassing onder werkende zwangeren en hun verloskundige zorgverleners. Wat betreft dit laatste punt: zowel werkende zwangeren als hun verloskundig zorgverleners hebben behoefte aan informatie en adviezen over veilig werken tijdens de zwangerschap. Blended care, een combinatie van face-to-face en online zorg, heeft de potentie om in deze behoefte te voorzien.

Toekomstig onderzoek

We doen aanbevelingen voor verder onderzoek. Dit betreft ten eerste een onderzoek naar de kosteneffectiviteit van preventieve maatregelen voor werkende zwangeren en een kwalitatief onderzoek naar faciliterende en beperkende factoren voor werkgevers bij de implementatie van zwangerschapsbeleid.

Vervolgens stellen we voor onderzoek te doen naar een alternatieve rolverdeling van verloskundigen, gynaecologen en bedrijfsartsen in de zorg voor werkende zwangeren. Daarnaast adviseren wij te evalueren of het advies van de NVAB-richtlijn voor vrouwen met een meerlingzwangerschap ook effectief is voor werkende vrouwen met andere medisch gecompliceerde zwangerschappen.

Ten slotte bevelen we aan om de P&W-app verder te ontwikkelen en het design ervan te herzien. Dit vraagt om een geprotocolleerde stapsgewijze aanpak waarbij eindgebruikers en verschillende experts vanaf het begin betrokken zijn.

Praktische adviezen
Vrouwen die nu of in de nabije toekomst zwanger zijn, kunnen niet wachten op de resultaten van toekomstig onderzoek. Daarom sluiten we dit proefschrift af met enkele *praktische adviezen*:

- Voor *werkende zwangeren*: om hun werkgever of bedrijfsarts te vragen hoe ze hun werk veilig kunnen blijven doen tot aan het zwangerschapsverlof
- Voor *werkgevers*: om een veilige werkomgeving te creëren voor hun zwangere werknemers met behulp van de richtlijnen van de SER en de NVAB
- Voor *verloskundigen en gynaecologen*: om alle cliënten te verwijzen naar de werkgever en/of bedrijfsarts om te bespreken of hun werk moet worden aangepast, of indien nodig zelf advies te geven op basis van de NVAB-richtlijnen
- *Voor de bedrijfsgezondheidszorg*: om bedrijven en organisaties actief te motiveren een 'zwangerschapsbeleid' in te voeren, gebruikmakend van de richtlijnen van de SER en de NVAB

Conclusies

Bij vrouwen met een laag risico op complicaties tijdens de zwangerschap leiden verschillende vormen van lichamelijk belastend werk en lange werktijden tot een matig verhoogd risico op vroeggeboorte. Werk met lichamelijke en mentale belasting en lange en onregelmatige werktijden verhogen het risico op vroeggeboorte bij meerlingzwangerschappen.

50% van de vrouwen met een laag risico op complicaties tijdens de zwangerschap en bijna 60% van de vrouwen met een meerlingzwangerschap werken niet volgens de wettelijke regels en richtlijnen, hoewel deze door alle belanghebbenden gezamenlijk zijn opgesteld. Hierdoor lopen moeder en kind risico op nadelige gevolgen zoals vroeggeboorte. Er zijn daarvoor drie belangrijke oorzaken: werkende zwangeren en hun verloskundige zorgverleners zijn nauwelijks op de hoogte van de risico's in het werk, werkende zwangeren hebben amper toegang tot bedrijfsgezondheidszorg en het ontbreekt aan financiële prikkels voor werkgevers om zwangerschapsbeleid te implementeren.

Om de arbeidsomstandigheden voor zwangere vrouwen te verbeteren, beveelt dit proefschrift aan verder onderzoek te doen naar een andere rolverdeling in de zorg voor zwangere vrouwen en naar datgene wat werkgevers kan stimuleren en belemmeren om zwangerschapsbeleid te implementeren. In het bijzonder raden we aan om

zorgverzekeraars en de overheid bij dit proces te betrekken, omdat ook zij baat hebben bij de implementatie.

De blended care-interventie 'Zwangerschap en werk' heeft de potentie om een effectief instrument te worden. Onderdeel ervan is de ontwikkeling van een nieuwe versie van de P&W-app, gericht op werkende zwangeren, hun verloskundigen en gynaecologen én hun werkgevers. Uiteindelijk kan dit leiden tot een veilige werkomgeving voor alle zwangere vrouwen.

Appendices

Appendix I. List of abbreviations

CI	Confidence interval
H/D	Hours a day
HL	Health literacy
ILO	International Labour Organisation
IMI	Intrinsic Motivation Inventory
kg	kilogram
mHealth app	mobile Health application
LBW	Low Birth Weight
MPL	Maternity Protection Legislation
NA	Not Applicable
NS	Nightshift
NVAB	The Netherlands Society of Occupational Medicine
OHSS	Occupational Health and safety service
OR	Odds ratio
P and W app	Pregnancy and Work app
P&W	Pregnancy and Work
PIH	Pregnancy Induced Hypertension
PTB	Preterm Birth
PTD	Preterm Delivery
Q	Questionnaire
Ref	Reference
RIVM	National Institute for Public Health and the Environment
RR	Relative Risk
aRR	adjusted Relative Risk
S	Significant
SD	Standard Deviation
SER	Social Economic Council
SES	Socioeconomic status
SGA	Small for Gestational Age
SUS	System Usability Scale
TA	Think aloud
UEM	Usability evaluation methods
UWV	Employee insurance agency
VS	Versus
ZonMw	the Netherlands Organization for Health Research and Development.

Appendix II. List of co-authors and their affiliations

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dr. A. van de Wetering, Maastricht University, Faculty of Health, Medicine and Life Sciences, Maastricht, The Netherlands.

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About the author

Curriculum vitae

Monique van Beukering was born on May 24, 1960 in Eindhoven, the Netherlands, in a family with 3 brothers and one sister. After graduation of high school in 1978 (Gymnasium at 'Augustinianum'), she studied medicine at the Catholic University Nijmegen, faculty of medicine (since 2020 Radboud UMC). During high school and medical studies, she became aware of the importance of paid work for women, which was not common at that time. Together with the possibility of preventing diseases, this led to a specialization in occupational medicine, with a particular interest in the health of working women.

Occupational physician
From 1988 to 1991 she followed the training as occupational physician, at the Faculty of Social Medicine, Catholic University Nijmegen. During 1988 to 2000 she worked as an occupational physician at the Occupational Health and Safety Service (OHSS) of the GGD Arnhem, which was taken over by Arbo Unie Midden en Zuid-Gelderland in 1996. Her clients were companies and organizations in the branches utilities, education, municipalities and industry.

From 2000 to 2016, she combined her work as an occupational physician with leading KEMA Arbo, an internal OHSS. In addition to internal clients (KEMA) she also worked for a number of external companies such as TenneT and DEKRA. Due to international takeovers of KEMA by DNV GL, it was decided to outsource their OHSS. From 2016 (and still) she works at the OHSS of Zorg van de Zaak, with clients with an academic setting: Wageningen University & Research and HAN University of Applied Sciences. In addition, together with colleagues from Zorg van de Zaak, she set up the Scientific Research Working Group, one of her tasks is to guide occupational physicians in training in their research.

Research and other activities
Since her training as an occupational physician, she has been involved in various ways with the theme 'Women, work and health'. She published various articles for manuals and magazines and was (and still is) guest lecturer for, among others, occupational and insurance physicians, often together with other experts (e.g. (the late) prof. dr. Pieter Treffers, obstetrician, Amsterdam UMC (AMC) and Wim Otto (insurance physician UWV).

After urging the NVAB, she was given the opportunity to develop the guideline 'Pregnancy, Postpartum-period and work', as project leader. This guideline (published in 2007, revised in 2018), was the result of an intensive collaboration with a multidisciplinary team, including dr. Maria Pel, obstetrician, at Amsterdam UMC, AMC. Her colleague prof. dr. Ben Willem Mol asked Monique to support them in research into 'pregnancy and work'. In 2015 this resulted in the start of a PHD trajectory 'Healthy work in pregnancy',

supervised by promotores prof. dr. Ben Willem Mol and prof. dr. Monique Frings-Dresen, and dr. Marjolein Kok and dr. Teus Brand (co-promotores).

Monique is married with Maarten Visser, together they have three children (Fleur, Judith and Niels).

Portfolio

Name PhD student: M.D.M. van Beukering
PhD period: (July) 2015- 2022
Promotores: prof. dr. B.W.J. Mol, prof. dr M.H.W. Frings-Dresen
Co-promotores: dr. M. Kok, dr. T. Brand

	Year	Workload (ECTS)
1. PHD training		
General courses		
- Basic course on Regulations and Organization for clinical investigators (BROK)	2015	1.0
- Qualitative Health Research	2016	1.9
- Scientific Writing in English	2018	1.5
- Practical Biostatistics	2018	1.1
Other		
Various courses, workshops, presentations, symposia, regarding the 're-registration' as occupational physician by the Royal Dutch Medical Association (RDMA) . • Re-registration • Visitation	2017-2022 2019	6.2 1.0
International conferences		
Third Global Summit for Improving Standards of Care for Preemies, Bulgaria.	2016	0.5
2. Teaching		
Lecturing/ oral presentations		
SBGO (Radboud University), Post academic training Occupational and Insurance physicians. 'Guideline pregnancy and work'	2015-2022	1.2
"Pregnant Now" Course for Pregnant Women. Obstetric Course Center Nijmegen, on "Pregnancy and Work"	2016-2019	0.5
Summer School Work and Health NSPOH on Pregnancy and work.	2015	0.5
Symposium Maasstad-Ikazia hospital. Pregnancy and occupational risks	2015	0.25
Third Global Summit for Improving Standards of Care for Preemies, Bulgaria.	2016	0.25
Symposium Regional Consortium South-West Netherlands, Work and Pregnancy	2016	0.25
Annual NVAB congress: on the planned revision of NVAB guidelines for Pregnancy, Postpartum Period and Work.	2016	0.25
Multidisciplinary training App healthy work in pregnancy. Midwifery hospital partnership In region North West Netherlands (5x)	2017	0.5
Symposium "Women are really different". Hoytema foundation Enschede.	2017	0.25
Progress Report Presentation, dept. Obstetrics and Gynaecology Amsterdam UMC, loc. AMC.	2018	0.25
Annual NVAB congress: on the revised NVAB guidelines for Pregnancy, Postpartum Period and Work.	2018	0.5

	Year	Workload (ECTS)
Training physicians NVAB Guideline Pregnancy, postpartum period and work. Suriname.	2018	1.0
NVAB guideline and results of the project Healthy working in pregnancy symposium Noord NL	2019	0.5
Midwifery hospital partnership Kennemerland, on guideline Pregnancy and work and results of the project healthy working in pregnancy.	2019	0.25
Occupational physicians Region Amsterdam on the NVAB guideline Pregnancy and work and the results of the project Healthy work in pregnancy.	2019	0.25
SBGO (Radboud University), Training for trainers: supervising AIOS, with Evidence-based medicine	2020	0.5
Webinar Zorg van de Zaak: Pregnancy and work	2021	0.25
Progress report presentation: Healthy work in pregnancy, Dept. Obstetrics and Gynaecology, Amsterdam UMC	2021	0.25
Tutoring, mentoring		
Mentor L. van den Berg, MSc student Medical Informatics at Scientific Research Project and master Thesis, The 'Healthy Work in Pregnancy' Application: A Study of Health Literacy, Usability Methods, and Intention to Change Behaviour	2016-2017	1.8
Community project, Bachelor students Medicine at Erasmus University, 'Risk factors on low birth weight in children of physician assistants'.	2018-2019	1.0
Occupational physicians in training guidance at their scientific research.	2019-2022	4.3
3. Other		
Project leader. Guideline 'Pregnancy, postpartum period and work'. NVAB/ Netherlands Society of Occupational Medicine.	2016-2018	4
Member Advisory Board: Project 'Work and pregnancy, make it work' Erasmus University, Rotterdam.	2015-2017	0.5
Member Committee Burger & Zielhuis-penning (NVAB)	2015-2022	1.6
Member Authorization committee (NVAB)	2015-2021	2
Member project group Reproduction and work, Netherlands Center for Occupational Diseases.	2015-2016	0.25
'Round table meeting' with parents of premature children and experts on work and pregnancy, organized by ABBVIE.	2016	0.25
Expert meeting WomenINC on Pregnancy, menopause and work. Amsterdam UMC, loc. VUMC.	2018	0.25
Hackathon on infectious diseases, pregnancy and labor. RIVM: National Institute for Public Health and the Environment. Ministry of Health, Welfare and Sport.	2019	0.25
Expert meeting Implementation PIL (Preconception Indication List) CPZ (College Perinatal Care) Utrecht	2019	0.25
Center of expertise on Women and Health, IKANED (development and expert)	2018-2019	1

	Year	Workload (ECTS)
Updating documents regarding Pregnancy and work, website RIVM: National Institute for Public Health and the Environment. Ministry of Health, Welfare and Sport.	2018	1
Updating the Guidelines on Occupational Health and Safety Measures for Pregnancy and Work. Website SER (Social and Economic Council)	2018	1
Working group Scientific Research 'Zorg van de Zaak'	2017-2022	6.1
TOTAL (28 hrs =1 ECTS)		**45.50**

List of publications

Publications in this thesis

1. **van Beukering M.D.M.**, van Melick M.J., Mol B.W., Frings-Dresen M.H., Hulshof C.T. Physically demanding work and preterm delivery: a systematic review and meta-analysis. International archives of occupational and environmental health. 2014 Nov;87(8):809-34.
2. van Melick M.J., **van Beukering M.D.**, Mol B.W., Frings-Dresen M.H., Hulshof C.T. Shift work, long working hours and preterm birth: a systematic review and meta-analysis. Int Arch Occup Environ Health. 2014 Nov;87(8):835-49.
3. **van Beukering M.D.M.**, Schuster H.J., Peelen M.J.C.S., Schonewille M.E.A., Hajenius P.J., Duijnhoven R.G., Brand T., Painter R.C., Kok M. Working conditions in low risk nulliparous women in The Netherlands: are legislation and guidelines a guarantee for a healthy working environment? A cohort study. Int Arch Occup Environ Health. 2022 Jun 16.
4. **van Beukering M.D.M.**, van Melick M.J., Duijnhoven R.G., Schuit E., Liem S., Frings-Dresen M.H., van de Wetering A., Spaanderman M.E.A., Kok M., Mol B.W. Working conditions in women with multiple pregnancy, adherence to guidelines and the impact on preterm birth - a prospective cohort study. *Submitted 2022-06-30.*
5. Velu AV, **van Beukering M.D.M.**, Schaafsma F.G, Frings-Dresen M.H.W., Mol B.W.J., van der Post J.A.M., Kok M. Barriers and Facilitators for the Use of a Medical Mobile App to Prevent Work-Related Risks in Pregnancy: A Qualitative Analysis. JMIR Res Protoc. 2017 Aug 22;6(8):e163.
6. **van Beukering M.**, Velu A., van den Berg L., Kok M., Mol B.W., Frings-Dresen M., de Leeuw R., van der Post J., Peute L. Usability and Usefulness of a Mobile Health App for Pregnancy-Related Work Advice: Mixed-Methods Approach. JMIR Mhealth Uhealth 2019 May 9;7(5):e11442.
7. **van Beukering M.**, Velu A., Schonewille L.H.N., Duijnhoven R., Mol B.W., Brand T., Frings-Dresen M., Kok M. Evaluation of a blended care programme for caregivers and working pregnant women to prevent adverse pregnancy outcomes: an intervention study. Occup Environ Med. 2021 Apr 19:oemed-2020-107191.

Other publications

1. Schuster H.J., Peelen M.JC.S., Hajenius P.J.**, van Beukering M.D.M.**, van Eekelen R., Schonewille M., Playfair H., van der Post J.A.M., Kok M., Painter M.C. Risk factors for spontaneous preterm birth among healthy nulliparous pregnant women in the Netherlands, a prospective cohort study. Health science reports. Volume5, Issue3. May 2022.
2. Overdijkink S.B., Velu A.V., Rosman A.N., **van Beukering M.D.**, Kok M., Steegers-Theunissen R.P. The Usability and Effectiveness of Mobile Health Technology–Based Lifestyle and Medical Intervention Apps Supporting Health Care During Pregnancy: Systematic Review. JMIR Mhealth Uhealth 2018;6(4):e109.

3. Kuijpers D., **van Beukering M.D.M.**, Goessens B., Smeets R. Letsel na een elektrische schok op het werk bedrijfsgeneeskundige aspecten. TBV 22/ nr. 4/ 2014.
4. **van Beukering M.D.M.**, Lebbink M., Bastiaanssen M.H.H. Samenwerking Verloskundigen- Bedrijfsartsen. Onderzoeksrapportage. Stichting NVAB, Kwaliteitsbureau NVAB. Februari 2012. In opdracht van ministeries VWS en SZW.
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