ORIGINAL ARTICLE

Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review

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Background: Occupational activities are suspected of having an adverse impact on outcomes of pregnancy.
Aim: To assess the evidence relating three major adverse outcomes (preterm delivery, low birthweight (LBW) and pre-eclampsia/gestational hypertension) to five common occupational exposures (prolonged working hours, shift work, lifting, standing and heavy physical workload).
Methods: A systematic search of Medline and Embase (1966–December 2005) using combinations of keywords and medical subject heading terms was conducted. For each relevant paper, standard details were abstracted that were then used to summarise the design features of studies, to rate their methodological quality (completeness of reporting and potential for important bias or confounding) and to provide estimates of effect. For studies with similar definitions of exposure and outcome, pooled estimates of relative risk (RR) in meta-analysis were calculated.
Results: 53 reports were identified—35 on preterm delivery, 34 on birth weight and 9 on pre-eclampsia or gestational hypertension. These included 21 cohort investigations. For pre-term delivery, extensive evidence relating to each of the exposures of interest was found. Findings were generally consistent and tended to rule out a more than moderate effect size (RR >1.4). The larger and most complete studies were less positive, and pooled estimates of risk pointed to only modest or null effects. For small-for-gestational age, the position was similar, but the evidence base was more limited. For pre-eclampsia and gestational hypertension, it was too small to allow firm conclusions.
Conclusions: The balance of evidence is not sufficiently compelling to justify mandatory restrictions on any of the activities considered in this review. However, given some uncertainties in the evidence base and the apparent absence of important beneficial effects, it may be prudent to advise against long working hours, prolonged standing and heavy physical work, particularly late in pregnancy. Our review identifies several priorities for future investigation.

In Europe, as in most parts of the world, women of reproductive age now comprise a substantial proportion of the total workforce. Current European Union legislation (directive no. 85, 1992) requires employers to assess health and safety risks to pregnant workers, and where possible to minimise them.[1] A number of reproductive hazards associated with work are well established—for example, from ionising radiation and lead—and strategies have been developed to manage the associated risks. For others, the scientific evidence is less certain.

Important among these is the possibility that physical activities at work might impact adversely on outcomes of pregnancy such as preterm delivery and LBW.[2] In theory, long working hours, prolonged standing, heavy lifting or unusual workload may pose a number of threats to the pregnant worker. For example, the high demand for uterine and placental blood flow in the third trimester could limit reserve capacity for vigorous exercise, the gravid uterus could limit venous return and cardiac output, especially in those who stand, and raised norepinephrine levels could increase uterine contractility and thereby raise the risk of preterm labour. On the other hand, marked physiological adaptations to the demands of pregnancy tend to preserve constant fetal oxygen consumption. Practical management of the pregnant worker is made more difficult because the activities of concern (especially physical exercise), although suspected of being hazardous, could also be beneficial. Thus, a precautionary approach to the uncertainty may not be ideal.

To help clarify the way forward, we conducted a systematic review of the epidemiological evidence relating three major adverse outcomes of pregnancy (preterm delivery, LBW and pre-eclampsia/gestational hypertension) to five common occupational exposures (prolonged working hours, shift work, lifting, standing and heavy physical workload). We aimed to establish what was a reasonable practical approach for employers, given the current balance of evidence, and to identify priorities for further research that could improve the formulation of policy in the future.

METHODS

Search strategy

We conducted a systematic search of the Medline and Embase electronic bibliographic databases for the period 1966 to December 2005. Medical subject heading terms and keywords were chosen to represent each of the outcomes and exposures of interest and then combined. The following medical subject heading terms were used: pregnancy, reproductive health, pre-eclampsia, infant-premature, labour-premature, birth weight, gestational age, small for gestational age, fetal growth retardation, labour complications and pregnancy complications (as outcomes); and lifting, work schedule tolerance, exercise, fatigue, work, workload, employment and occupational exposure (as exposures). We also used several simple search terms

Abbreviations: LBW, low birthweight; SGA, small for gestational age to supplement our inquiry—namely, occupational activity, standing, manual lifting, heavy lifting and shift work (as exposures). We limited our search to papers with an abstract written in English. Abstracts were examined, duplicates and irrelevant references were eliminated, and paper copies of all primary reports and reviews were obtained. We checked the references of retrieved papers for other relevant material. Papers finally included were those which, for one or more outcome–exposure combinations, compared an exposed with a less heavily exposed or an unexposed reference group and which provided estimates of effect (or the data from which these could be calculated).

These procedures and the later steps below were replicated independently by MB and KTP, and differences were resolved by consensus.

Data abstraction

For each paper that was deemed relevant, we abstracted a standard set of information, including details of the study populations, setting, timing of investigation, study design, exposure contrasts, strategies for assessment of exposure(s) and outcome(s), response rates, confounders considered and estimates of effect. For reports that provided frequencies but no estimate of relative risk (RR), we calculated odds ratios (ORs) with exact confidence intervals (95% CI) using STATA V.8 software. Similarly, for papers that presented birth weight as a continuous measure, with group means and standard deviations, we calculated the mean difference between exposure groups with a 95% CI. Where several subanalyses were presented, we focused on the exposure contrasts that were most comparable across studies. Our assessment of papers was unblinded to authorship.

Quality assessment

We rated each paper for completeness of reporting, and each exposure–outcome permutation in terms of its potential for significant confounding or ''inflationary'' bias.

The completeness of reporting was graded on a nine-point scale according to the number of the following items that were clearly defined: (1) study design; (2) sampling frame and procedures; (3) inclusion/exclusion criteria; (4) main characteristics of the study population (age, ethnicity and social class); (5) study numbers and response rates; (6) method(s) of exposure assessment; (7) method(s) of outcome assessment; (8) method(s) of analysis; and (9) measures of association with 95% CI and numbers in the analysis. Studies in which $\geqslant$3 of these items were missing/unclear were classified as poor in quality of information. The scoring scheme was based on elements proposed by Ariens *et al*[3] and van der Windt *et al*[4] but modified for purpose.

For each health outcome examined, we assessed known risk factors to identify those with important potential to confound associations with occupational activities and patterns of work. This assessment was based on the relative risk (RR) associated with the risk factor, its prevalence in the general population and the likelihood that it might vary importantly according to occupational exposures. Risk factors carrying only small RRs, with only a low prevalence, or with little potential to vary in relation to occupational exposures would be less likely to have a major confounding effect. Those that might reflect the effects of occupational exposure or that might lie on the causal pathway between exposure and health outcome were also discounted. We classified reported associations as being more susceptible to confounding if important potential confounders had not been addressed.

By inflationary bias, we implied bias that could cause important overestimation of RRs. We considered that this was most likely when exposures were self-reported retrospectively (especially if they were of a type that is more difficult to recall), and were related to outcomes that were themselves self-reported or were clearly adverse. Thus, for retrospective studies with self-reported exposures, we assigned one point for each of the following features that was present: (1) self-reported outcome; (2) outcome of pre-eclampsia, gestational hypertension or very low birthweight; and (3) exposure related to physical workload (standing, lifting or activity score). Exposure–outcome pairings were scored 0–3, and scores $\geqslant$2 were considered to indicate important potential for inflationary bias.

By these criteria, we counted exposure–outcome combinations to be of lower methodological quality if they had significant potential for confounding or bias, or were derived from studies with incomplete reporting or low effective response rates (<50%).

Meta-analysis

For studies with sufficiently similar definitions of exposure and outcome, we calculated a pooled estimate of RR, using a random effects (DerSimonian–Laird) model, and weighting log RRs or log ORs by the inverse of their variances. This method made the simplifying assumption that all measures of RR (ORs, incidence density ratios, hazards ratios and so on) were equivalent. Most comparisons were summarised as ORs, but where other measures were used, the difference is likely to have been small since outcomes were uncommon and point estimates of RR were fairly close to unity. We performed the meta-analysis using the Sharpe and Sterne STATA macro (http://bmj.bmjjournals.com/archive/7126/7126ed9.htm). We also conducted a sensitivity analysis to check the impact of excluding papers of lower quality, and explored possible publication bias using funnel plots.

RESULTS

Our search identified a total of 49 studies (53 reports)—34 (35 reports) on preterm delivery, 33 (34 reports) on birth weight and 8 (9 reports) on pre-eclampsia or gestational hypertension. Some investigations covered multiple exposures and/or outcomes. Table 1 lists the studies and their main design features. Tables 2–5 summarise quantitative relationships for specific exposure–outcome combinations.

Quality of evidence

Completeness of reporting

In general, the completeness of reporting was satisfactory across studies. As judged by our 9-point criteria, the median score was 7.5 (range 4.5–9). However, for 10 (20%) investigations, the score was $\leqslant$6,[6 12 15 17 27 42–44 50 57] the most common omission being a failure to provide a breakdown of the numbers of women included in analyses and the confidence limits associated with risk estimates.

Sample size and response rates

Sample sizes varied from small (<50) to extremely large (>35 000), but many risk estimates were based on findings from >1000 pregnancies. Response rates at baseline (cross-sectional studies) or follow-up (cohort studies) often exceeded 80% (32/49 studies) or even 90% (23/49 studies). However, in six studies, the usable response was <65%[17 24 39 46 51 57] and in eight studies,[18 25 27 29 43–45 55] it was unclear from the description provided.

Assessment of exposures

In 21 cohort investigations, exposure was ascertained prospectively during pregnancy, whereas for 28 studies (8 case–control,

Table 1 Features of the studies included in the review

First author, (year)	Location	Study period	Study design	Exposure(s)	Method of exposure assessment	Outcome(s)
Ahlborg GJ (1990)[5]	Orebro, Sweden	1980–3	Prospective cohort	Lifting	Self-administered questionnaire after delivery; exposure validated by hygienist in a subgroup	Preterm delivery (<37 weeks) LBW (<2500 g) LBW adjusted for gestational age
Axelsson G (1989)[6]	Sweden	1980–4	Cross-sectional	Shift work	Mail questionnaire	Birth weight (continuous)
Berkowitz GS (1983)[7]	New Haven, USA	1977–8	Case–control, hospital based	Working hours Standing Lifting	Expert interview after delivery	Preterm delivery (<37 wks)
Bodin L (1999)[8]	Sweden	1980–7	Cross-sectional	Working hours Shift work	Mail questionnaire	Preterm delivery (<37 weeks) LBW (<2500 g) SGA ⩽(<10th centile) Birth weight (continuous)
Brink-Henriksen T (1995)[9,10]	Denmark	1989–91	Prospective cohort	Working hours Standing Lifting	Self-administered questionnaire during pregnancy	Preterm delivery (<37 weeks) Birth weight (continuous)
Cerón-Mireles P (1996)[11]	Mexico City, Mexico	1992	Cross-sectional	Working hours Standing Physical activity	Personal interview, soon after delivery	Preterm delivery (<37 weeks) SGA (⩽10th centile)
Florack EIM (1995)[12]	The Netherlands	1987–9	Prospective cohort	Lifting Physical activity	Personal interview, before pregnancy	Gestational age (in weeks vs expected term) Birth weight (continuous)
Fortier I (1995)[13]	Quebec, Canada	1989	Cross-sectional	Working hours Shift work Standing Lifting Physical activity	Telephone interview after delivery (median 6 weeks)	Preterm delivery (<37 weeks) SGA (<10th centile)
Hanke W (1999)[14]	Lodz, Poland	1996–7	Cross-sectional	Shift work Standing Physical activity	Interview, few days after delivery	SGA (<10th centile)
Hartikainen-Sorri AL (1989)[15]	Finland	1982	Case–control, hospital based	Shift work Standing Physical activity	Mail questionnaire within 1year of delivery	Preterm delivery (<37 wks)
Hatch M (1997)[16]	USA	1987–9	Prospective cohort	Working hours Standing Lifting Physical activity	Telephone interview, mail questionnaire	LBW (⩽3000 g). Birth weight (continuous)
Hickey CA (1995)[17]	USA	1985–8	Prospective cohort	Working hours Standing Physical activity	Self-administered questionnaire during pregnancy	Preterm delivery (<37 weeks)
Homer CJ (1990)[18]	USA	1979–83	Cross-sectional	Physical activity	Derived from job title, using a validated physical effort scale	Preterm delivery (<37 weeks) LBW (<2500 g) Birth weight (continuous)
Irwin DE (1994)[19]	USA	1987–9	Cross-sectional	Standing Lifting Physical activity	Based on job title using military data of activity	Gestational hypertension and pre-eclampsia
Klebanoff MA (1990)[20]	USA	1985	Cross-sectional	Working hours	Mail questionnaire after delivery, (non-respondents contacted by telephone)	Preterm delivery (<37 weeks) SGA (<10th centile) Birth weight (continuous)
Klebanoff MA (1990)[21]	USA	1984–7	Prospective cohort	Standing Physical activity	Face-to-face interview	Preterm delivery (<37 weeks) Birth weight (continuous)
Landsbergis PA (1996)[22]	USA	1987–9	Prospective cohort	Working hours Physical activity	Telephone interview and mail update	Gestational hypertension and pre-eclampsia
Launer LJ (1990)[23]	Guatemala	1984–6	Prospective cohort	Standing Physical activity	Face-to-face interview	Preterm delivery (<37 weeks) SGA (⩽10th centile)
Luke B (1995)[24]	USA	From 1980	Case–control, population based	Working hours Shift work Standing Physical activity	Mail questionnaire	Preterm delivery (<37 weeks)

Table 1 Continued

First author, (year)	Location	Study period	Study design	Exposure(s)	Method of exposure assessment	Outcome(s)
Magann EF (1996)[25]	Australia	1989–91	Prospective cohort	Physical activity	Self-administered questionnaire	Preterm delivery (<37 weeks) Birth weight (continuous) SGA (<3rd and <10th centiles)
Magann EF (2005)[26]	San Diego, USA	Not specified	Prospective cohort	Standing Lifting	Face-to-face interview	Preterm delivery (<37 weeks) SGA (intrauterine growth retardation, undefined)
Mamelle N (1984)[27]	France	1977–78	Cross-sectional	Working hours Shift work Standing Physical activity	Face-to-face interview	Preterm delivery (<37 weeks)
Marcoux S (1999)[28]	Quebec, Canada	1984–6	Case–control, hospital based	Working hours	Face-to-face interview a few days after delivery	PIH
McDonald AD (1988)[29] and Armstrong BG (1989)[30]	Montreal, Canada	1982–4	Cross-sectional	Working hours Shift work Standing Lifting Physical activity	Interview after delivery	Preterm delivery (<37 weeks) LBW ($\leqslant$2500 g)
Meyer BA (1985)[31]	USA	1981	Case–control, population based	Standing	Based on job title according to an expert validated database	LBW (<2500 g)
Misra DP (1998)[32]	USA	1988–9	Prospective cohort	Shift work Standing Lifting	Face-to-face or telephone interview	Preterm delivery (<37 weeks)
Newman RB (2001)[33]	USA	Not specified	Prospective cohort	Standing Physical activity	Face-to-face interview	Preterm rupture of membranes (<37 weeks)
Nurminen T (1989)[34 35]	Finland	1976–82	Cross-sectional	Shift work Standing Physical activity	Face-to-face expert interview 2–4 months after delivery	Preterm delivery (<37 weeks) SGA ($\leqslant$10th centile) Gestational hypertension
Peoples-Sheps MD (1991)[36]	USA	1980	Cross-sectional	Working hours Physical activity	Derived by job title and mail interview	Preterm delivery (<37 weeks) LBW (<2500 g)
Rabkin CS (1990)[37]	London, England	1982–4	Prospective cohort	Working hours Physical activity	Face-to-face expert interview	Birth weight (continuous)
Pompeii LA (2005)[38]	North Carolina, USA	1995–2000	Prospective cohort	Working hours Shift work Standing Lifting	Telephone or face-to-face interview	Preterm delivery (<37 weeks) SGA (<10th centile)
Ramirez G (1990)[39]	USA	1981–4	Cross-sectional	Physical activity	Military records	Preterm delivery ($\leqslant$37 weeks).
Rao S (2003)[40]	Pune, India	1994–6	Prospective cohort	Physical activity	Interview before delivery	Preterm delivery (<37 weeks) Birth weight (continuous)
Saftlas AF (2004)[41]	Connecticut, USA	1988–91	Prospective cohort	Standing	Face-to-face expert interview	Gestational hypertension and pre-eclampsia
Saurel-Cubizolles MJ (1985)[42]	France	1979–81	Cross-sectional	Physical activity	Face-to-face expert interview after delivery	Preterm delivery (<36.5 weeks) LBW (<2500 g) Gestational hypertension
Saurel-Cubizolles MJ (1987)[43]	France	1981	Cross-sectional	Working hours Shift work Standing Lifting Physical activity	Face-to-face expert interview after delivery	Preterm delivery (<37 weeks) LBW (<2500 g)
Saurel-Cubizolles MJ (1991)[44]	France	1987–8	Cross-sectional	Working hours Standing Lifting Physical activity	Face-to-face expert interview after delivery	Preterm delivery (<37 weeks)

Table 1 Continued

First author, (year)	Location	Study period	Study design	Exposure(s)	Method of exposure assessment	Outcome(s)
Saurel-Cubizolles MJ (2004)[45]	16 European countries	1994–7	Case–control hospital based	Working hours Shift work Standing Lifting	Interview after delivery	Preterm delivery (<37 weeks)
Savitz DA (1996)[46]	USA	1988	Cross-sectional	Working hours	Mail or telephone questionnaire	Preterm delivery (<37 weeks) VLBW (<1500 g) MLBW (1500–2499 g) SGA (<10th centile)
Schramm WF (1996)[47]	Missouri, USA	1989–91	Case–control, population based	Standing Lifting	In-hospital interview or mail questionnaire	VLBW (<1500 g) MLBW (1500-2499 g)
Spinillo A (1995)[48]	Pavia, Italy	1990–4	Case–control study, hospital based	Physical activity	Face-to-face expert interview	Pre-eclampsia
Stinson JC (2003)[49]	USA	Not specified	Prospective cohort	Shift work Physical activity	Self-administered questionnaire during pregnancy	Preterm delivery (<37 weeks)
Tafari N (1980)[50]	Addis Ababa, Ethiopia	1976–7	Cross-sectional	Physical activity	Face-to-face interview	Birth weight (continuous)
Teitelman AM (1990)[51]	New Haven, USA	1980–2	Prospective cohort	Standing	Based on job title	Preterm delivery (<37 weeks) Gestational age (in weeks) LBW (<2500 g) Birth weight (continuous)
Tuntiseranee P (1998)[52]	S Thailand	1994–5	Prospective cohort	Working hours Standing Lifting Physical activity	Face-to-face expert interview at 17 and 32 weeks	Preterm delivery (<37 weeks) LBW (⩽2500 g) SGA (<10th centile)
Wergeland E (1997)[53] and (1998)[54]	Norway	1989	Cross-sectional	Working hours Shift work Standing Lifting	Self-administered questionnaire after delivery	LBW (<2500 g) Birth weight (continuous) pre-eclampsia
Xu X (1994)[55]	Anhui, China	1992	Prospective cohort	Shift work	Face-to-face interview	Preterm delivery (<37 weeks) LBW (<2500 g) Birth weight (continuous)
Zhu JL (2004)[56]	Denmark	2004	Prospective cohort	Shift work	Telephone interview during pregnancy	Preterm delivery (<37 weeks), LBW (<2500 g) SGA (<10th centile)
Zuckerman BS (1986)[57]	Boston, USA	1977–9	Cross-sectional	Standing	Face-to-face interview after delivery	Gestational age (weeks) Birth weight (continuous)

LBW, low birthweight; MLBW, moderately low birthweight; ref, reference; SGA, small for gestational age; VLBW, very low birthweight.

Table 2 Weekly working hours, shift work, standing and risk of preterm delivery

First author (year)	Numbers in analysis	RR (95% CI)	Exposure: Comparison	Exposure: Timing	Higher potential for: Bias	Higher potential for: Confounding	Incomplete reporting	Pooled in meta-analysis
WEEKLY WORKING HOURS								
Cohort studies								
Brink-Henriksen T (1995)[10]	927	1.87 (0.78 to 4.16)	⩾45 vs <30 h/wk	16 weeks	No	No	No	Yes
Hickey CA (1995)[17]	183	0.68 (0.12 to 2.7)	>40 vs 1–20 h/wk	24–26 weeks	No	No	Yes	Yes*
Pompeii LA (2005)[38]	1037	0.6 (0.4 to 0.9)	>46 vs 35–45 h/wk	Trimester 1	No	No	No	No
Pompeii LA (2005)[38]	1037	0.4 (0.2 to 0.8)	>46 vs 35–45 h/wk	Trimester 2	No	No	No	No
Pompeii LA (2005)[38]	1037	0.3 (0.1 to 0.7)	>46 vs 35–45 h/wk	Trimester 3	No	No	No	No
Tuntiseranee P (1998)[52]	886	1.6 (0.8 to 3.3)	⩾61 vs ⩽50 h/wk	15–28 weeks	No	No	No	No
Case–control studies								
Luke B† (1995)[24]	1470	1.6 (1.1 to 2.2)	>36 vs ⩽36 h/wk	Not stated	No	No	No	No
Saurel-Cubizolles MJ (2004)[45]	2062	1.33 (1.1 to 1.6)	⩾43 vs 30–39 h/wk	Trimester 1	No	No	Yes	Yes*
Cross-sectional studies								
Bodin L (1999)[8]	1685	1.3 (0.6 to 2.7)	⩾36 vs 21–35 h/wk	Trimester 2	No	No	No	No
Ceron-Mireles P (1996)[11]	2429	1.21 (0.9 to 1.62)	>50 vs 3–25 h/wk	Not stated	No	No	No	Yes
Fortier I (1995)[13]	1833	1.14 (0.71 to 1.82)	⩾40 vs <30 h/wk	Not stated	No	No	No	Yes
Klebanoff MA (1990)[20]	989	1.2 (0.8 to 1.7)	Residents (>100 h) vs others	Any	No	No	No	No
Mamelle N (1984)[27]	1928	1.7 (1.1 to 2.5)	>41 vs ⩽40 h/wk	Not stated	No	Yes	Yes	Yes*
McDonald AD (1988)[29]	22761	1.34, p<0.05	⩾46 vs <46 h/wk	Not stated	No	No	No	No‡
Peoples-Sheps MD (1991)[36]	1853	1.1 (0.7 to 1.8)	⩾40 vs 1–20 h/wk	Not stated	No	No	No	Yes
Saurel-Cubizolles MJ (1987)[43]	2245	0.59 (0.21 to 1.37)	⩾42 vs <42 h/wk	Trimester 1	No	Yes	Yes	No
Saurel-Cubizolles MJ (1991)[44]	873	1.0 (0.4 to 2.5)	>45 vs ⩽45 h/wk	Not stated	No	No	Yes	No
Savitz DA (1996)[46]	1015	1.1 (0.8 to 1.5)	⩾40 vs no paid work	5 months	No	No	No	Yes
SHIFT WORK								
Cohort studies								
Misra DP (1998)[32]	1166	1.0 (0.59 to 1.69)	Shifts vs none	Trimesters 1 and 2	No	No	No	Yes
Pompeii LA (2005)[38]	1796	1.5 (1.0 to 2.1)	Regular night work (yes vs no)	Trimester 1	No	No	No	—
Pompeii LA (2005)[38]	1796	1.6 (1.0 to 2.8)	Regular night work (yes vs no)	Trimester 2	No	No	No	Yes§
Pompeii LA (2005)[38]	1796	1.8 (0.8 to 3.4)	Regular night work (yes vs no)	Trimester 3	No	No	No	—
Stinson JC† (2003)[49]	359	1.8 (0.93 to 3.53)	Night vs day	22–26 weeks	No	No	No	Yes
Xu X (1994)[55]	887	2.0 (1.1 to 3.4)	Rotating shift work (yes vs no)	Not stated	No	No	No	Yes
Zhu JL (2004)[56]	35662	0.97 (0.8 to 1.17)	Rotating shift work vs daytime work	Trimesters 1 and 2	No	No	No	Yes
Case–control studies								
Hartikainen-Sorri AL (1989)[15]	358	0.86 (0.51 to 1.45)	Shift work (yes vs no)	Not stated	No	Yes	Yes	Yes*
Luke B† (1995)[24]	1470	1.5 (1.1 to 2.1)	Evening/night vs day	Not stated	Yes	No	No	Yes*
Saurel-Cubizolles MJ (2004)[45]	6309	0.97 (0.8 to 1.1)	Shift work (yes vs no)	Trimester 1	No	No	Yes	Yes
Cross-sectional studies								
Bodin L (1999)[8]	1685	5.6 (1.9 to 16.4)	Night vs day	Trimester 2	No	No	No	Yes
Fortier I (1995)[13]	4118	1.03 (0.72 to 1.48)	Shift work vs day only	Not stated	No	No	No	Yes
Mamelle N (1984)[27]	1928	1.6 (1.0 to 2.5)	Shift and night work vs none	Not stated	No	Yes	Yes	Yes*
McDonald AD (1988)[29]	22761	1.18, p>0.05	Changing shift vs not	Not stated	No	No	No	No‡
Nurminen T (1989)[34]	Unclear	0.9 (0.7 to 1.1)	Shift work (yes vs no)	Not stated	No	No	No	Yes
Saurel-Cubizolles MJ (1987)[43]	2261	0.8 (0.16 to 2.51)	Night vs day	Trimester 1	No	Yes	Yes	Yes*
STANDING								
Cohort studies								
Brink-Henriksen T (1995)[10]	4259	1.2 (0.6 to 2.4)	>5 vs 0–2 h/d	16 weeks	No	No	No	Yes
Hickey CA (1995)[17]	612	1.11 (0.61 to 2.11)	>3 vs ⩽3 h/d	24–26 weeks	No	No	Yes	Yes*
Klebanoff MA (1990)[21]	7101	1.31 (1.01 to 1.71)	⩾8 vs 0 h/d	1–5 months	No	No	No	Yes
Launer LJ (1990)[23]	4168	1.56 (1.04 to 2.6)	Standing vs sitting	Not stated	No	No	No	No
Magann EF (2005)[26]	485	1.64 (0.88 to 3.06)	⩾4 vs <4 h/d	Trimester 1	No	No	No	No
Misra DP (1998)[32]	1166	1.05 (0.63 to 1.71)	⩾3 vs <3 h/d	Trimesters 1 and 2	No	Yes	No	Yes*
Newman RB (2001)[33]	1218	1.69 (1.2 to 2.38)	>3 vs ⩽3 h/d	22–24 weeks	No	No	No	Yes
Pompeii LA (2005)[38]	977	1.2 (0.9 to 1.7)	>30 vs 6–15 h/wk	Trimester 1	No	No	Yes	—
Pompeii LA (2005)[38]	977	0.9 (0.6 to 1.2)	>30 vs 6–15 h/wk	Trimester 2	No	No	Yes	Yes§
Pompeii LA (2005)[38]	977	1.3 (0.8 to 2.3)	>30 vs 6–15 h/wk	Trimester 3	No	No	Yes	—

Table 2 Continued

First author (year)	Numbers in analysis	RR (95% CI)	Exposure		Higher potential for			
			Comparison	Timing	Bias	Confounding	Incomplete reporting	Pooled in meta-analysis
Teitelman AM (1990)[51]	708	2.72 (1.24 to 5.95)	Standing still >3 h/d vs continuous active motion	Trimester 1 (mostly)	No	No	No	Yes
Tuntiseranee P (1998)[52]	1121	0.9 (0.3 to 2.3)	⩾5 vs ⩽4 h/d	15–28 weeks	No	No	No	No
Case–control studies								
Berkowitz GS (1983)[7]	186	1.36 (0.73 to 2.55)	Most/all of the time vs none/little of the time	Not stated	No	Yes	No	Yes*
Hartikainen-Sorri AL (1989)[15]	358	1.16 (0.71 to 1.9)	Standing-moving vs not	Not stated	No	Yes	No	No
Luke B† (1995)[24]	1470	2.42 (1.37 to 4.62)	>4 vs <4 h/d	Not stated	Yes	No	No	No
Saurel-Cubizolles MJ (2004)[45]	4810	1.26 (1.1 to 1.5)	>6 vs <2 h/d	Trimester 1	No	No	Yes	Yes*
Cross-sectional studies								
Ceron-Mireles P (1996)[11]	2429	1.16 (0.89 to 1.51)	>7 vs ⩽7 h/d	Not stated	No	No	No	No
Fortier I (1995)[13]	3502	0.88 (0.59 to 1.33)	⩾6 vs <3 h/d	Not stated	No	No	No	Yes
Mamelle N (1984)[27]	1928	1.6 (1.0 to 1.9)	⩾3 vs <3 h/d	Not stated	No	Yes	Yes	Yes*
McDonald AD (1988)[29]	22761	1.07, p>0.05	Standing ⩾8 vs <8 h/d	Not stated	No	No	No‡	No
Saurel-Cubizolles MJ (1987)[43]	2269	1.29 (0.85 to 1.94)	Standing (yes vs no)	Trimester 1	No	Yes	Yes	No
Saurel-Cubizolles MJ (1991)[44]	874	1.59 (0.82 to 3.19)	Standing (often/always vs none/sometimes)	Not stated	No	No	Yes	Yes*

h/d, hours per day; h/wk, hours per week.
RR is used generically to encompass a variety of published effect measures (odds ratios, incidence density ratios, hazard ratios and so on).
*Excluded from sensitivity analysis.
†Effective response rate <50%.
‡Not pooled as a standard error could not be derived from the published data.
§Second trimester chosen for meta-analysis (being the most comparable with other studies).

19 cross-sectional and 1 retrospective cohort), information about exposure was elicited after the relevant health outcomes had occurred. The data on exposure were collected mostly through self-report (by mail, telephone or interview), but in a minority of studies[18 19 31 36 39 51] job title was used as a surrogate index of exposure. Most studies of working hours and shift work employed similar definitions of exposure, but for other exposures, non-comparability restricted the opportunity for meta-analysis—for example, definitions of lifting varied with regard to load, frequency and duration, and some reports failed to define a ''heavy load'' at all. Similarly, the components of indices that were used to score physical workload differed between studies. Issues of measurement error were seldom considered by authors, even in prospective studies with the opportunity to validate reports by direct observation. However, a few studies[12 25 40] used personal diaries to assist self-reporting of exposures. Around half of the studies did not report the timing of exposures during pregnancy.

Assessment of health outcomes

With few exceptions,[18 20 24] health outcomes were established from hospital records, registers or birth certificates.

Bias and confounding

Various strategies were used to control for possible confounding, including matching, restriction, stratification and regression modelling, but confounding was ignored altogether in a few investigations.[7 22 42] In addition, the associations in which we were interested were not always the prime focus of a paper, and sometimes the data that we were able to abstract, therefore, came only from crude preliminary tables. Tables 2–5 list the exposure–outcome pairings that carried higher potential for inflationary bias or confounding according to our prespecified criteria.

Preterm delivery

Case definition

Most, but not all,[12 33 51 57] of the reports that we identified adopted the World Health Organization definition for preterm delivery: ''the birth of a living fetus before 37 completed weeks of gestation''.

Potential confounding factors

Various maternal characteristics have been associated with an increased risk of preterm delivery, including a history of preterm delivery or fetal loss, multiple gestation, diabetes, pre-eclampsia, bacterial vaginosis, extremes of maternal age, weight, stature, ethnicity, educational level, socioeconomic status, tobacco and alcohol intake, substance misuse, parity, complications of pregnancy and maternal disease.[58–61] However, few of these factors are common and carry a high RR, whereas some were universally controlled (eg, multiple gestation) and some (eg, obstetric events in earlier pregnancies) could have arisen from previous exposures at work. Smoking and social class (or proxies of social class—eg, educational attainment or income) are believed to carry moderate RRs (1.5–2.0) and are prevalent exposures whose frequency could vary systematically by occupational activity. We deemed risk estimates that failed to take account of both these variables to have a higher potential for confounding (17 of 91 exposure–outcome combinations, as listed in tables 2 and 3).

Scope for meta-analysis

Formal meta-analysis was judged feasible for associations of preterm delivery with longer working hours, shift work and standing. For lifting and physical workload, definitions of exposure were considered too heterogeneous to be combined.

Table 3 Lifting, physical activity and risk of preterm delivery

First author (year)	Numbers in analysis	RR (95% CI)	Exposure		Higher potential for		Incomplete reporting
			Comparison	Timing	Bias	Confounding	
LIFTING							
Cohort studies							
Ahlborg GJ (1990)[5]	3389	1.29 (0.69 to 2.4)	≥12 kg >50 x/wk vs none	Not stated	No	No	No
Brink-Henriksen T (1995)[10]	3410	0.93 (0.45 to 1.75)	Lifting ≥12 kg ≥10 x/d vs never	16 weeks	No	No	No
Magann EF (2005)[26]	318	1.14 (0.32 to 3.18)	Lifting ≥11 kg >6 x/h	Trimester 1	No	No	No
Misra DP (1998)[32]	1166	1.49 (0.61 to 3.28)	Lifting heavy objects on the job (yes vs no)	Trimesters 1 and 2	No	No	No
Pompeii LA (2005)[38]	1176	1.3 (0.9 to 1.8)	Lifting ≥25 lbs ≥13 vs 0 x/wk	Trimester 1	No	No	No
Pompeii LA (2005)[38]	1176	1.3 (0.8 to 2.1)	Lifting ≥25 lbs ≥13 vs 0 x/wk	Trimester 2	No	No	No
Pompeii LA (2005)[38]	1176	1.3 (0.6 to 2.9)	Lifting ≥25 lbs ≥13 vs 0 x/wk	Trimester 3	No	No	No
Tuntiseranee P (1998)[52]	1108	0.9 (0.4 to 2.1)	>12 kg, 1–10 x/d vs none	15–28 weeks	No	No	No
Case–control studies							
Berkowitz GS (1983)[7]	231	0.81 (0.43 to 1.49)	Lifting on the job	Not stated	No	Yes	No
Saurel-Cubizolles MJ (2004)[45]	4786	1.02 (0.8 to 1.2)	Loads carried >20 kg vs none	Trimester 1	No	No	No
Cross-sectional studies							
Fortier I (1995)[13]	3078	0.87 (0.52 to 1.45)	≥10 kg vs none	Not stated	No	No	No
McDonald AD (1988)[29]	22761	1.25, p<0.01	Lifting heavy weights ≥15 vs <15 x/d	Not stated	No	No	No
Saurel-Cubizolles MJ (1987)[43]	2262	1.35 (0.77 to 2.24)	Carrying of heavy loads (yes vs no)	Trimester 1	No	Yes	No
Saurel-Cubizolles MJ (1991)[44]	874	1.31 (0.64 to 2.58)	Lifting heavy loads (often/always vs none/sometimes	Not stated	No	No	No
PHYSICAL ACTIVITY							
Cohort studies							
Hickey CA (1995)[17]	612	0.7 (0.41 to 1.18)	Occupational fatigue score (≥3 vs <3)	24–26 weeks	No	No	No
Klebanoff MA (1990)[21]	7100	1.04 (0.76 to 1.42)	Heavy work ≥4 vs 0 h/d	1–5 months	No	No	No
Launer LJ (1990)[23]	4168	1.11 (0.77 to 1.62)	Manual vs office work	Not stated	No	No	No
Magann EF (1996)[25]	531	1.26 (0.64 to 2.6)	>2900 vs <2300 kcal/d energy expenditure	16–18 weeks	No	Yes	No
Newman RB (2001)[33]	1218	1.17 (1.01 to 1.35)	Physical activity score	22–24 weeks	No	No	No
Rao S (2003)[40]	508	0.8 (0.4 to 1.6)	High vs low activity	18 weeks	No	No	No
Rao S (2003)[40]	485	1.2 (0.6 to 2.3)	High vs low activity	28 weeks	No	No	No
Stinson JC (2003)[49]	359	1.79 (0.93 to 3.44)	Fatigue score >660 (severe vs ≤660) high vs low	22–26 weeks	No	No	No
Tuntiseranee P (1998)[52]	346	1.2 (0.4 to 3.8)	High vs low	15–28 weeks	No	No	No
Case–control studies							
Hartikainen-Sorri AL (1989)[15]	358	0.81 (0.46 to 1.43)	Heavy physical loading (yes vs no)	Not stated	No	Yes	No
Luke B* (1995)[24]	1470	1.4 (1.1 to 1.9)	Occupational fatigue score (≥3 vs <3)	Not stated	Yes	No	Yes
Cross-sectional studies							
Ceron-Mireles P (1996)[11]	2429	1.25 (0.97 to 1.6)	Job requires physical effort (yes vs no)	Not stated	No	No	No
Fortier I (1995)[13]	1829	0.87 (0.49 to 1.54)	Important vs none	Not stated	No	No	No
Homer CJ (1990)[18]	773	2.0 (1.1 to 3.9)	High vs low exertion job	Not stated	No	No	No
Mamelle N (1984)[27]	1928	1.7 (1.1 to 2.0)	High vs low exertion	Not stated	No	Yes	No
McDonald AD (1988)[29]	22761	1.1, p>0.05	Great physical effort (yes vs no)	Not stated	No	No	No
Nurminen T (1989)[35]	675	1.4 (1.1 to 1.7)	Work with a moderate physical load vs sedentary	Trimester 3	No	No	No
Peoples-Sheps MD (1991)[36]	535	1.1 (0.6 to 2.1)	High vs low strength requirement	Not stated	No	No	No
Ramirez G* (1990)[39]	1960	1.75 (1.12 to 2.75)	Very heavy vs low physical demands	Not stated	No	No	Yes
Saurel-Cubizolles MJ (1985)[42]	580	4.11 (2.15 to 7.78)	Activity score (2/3 vs 0/1 strenuous items)	Not stated	No	Yes	No
Saurel-Cubizolles MJ (1987)[43]	2262	2.13 (1.16 to 3.76)	Activity score (3/4 items vs none)	Trimester 1	No	Yes	No
Saurel-Cubizolles MJ (1991)[44]	874	1.2 (0.5 to 2.5)	Activity score (2/3 vs 0/1 items)	Not stated	No	No	No

x/day, times per day; x/wk, times per week.
RR is used generically to encompass a variety of published effect measures (odds ratios, incidence density ratios, hazard ratios, etc).
*Effective response rate <50%.

Table 4 Occupational activity and risk of being small-for-gestational age at delivery

First author (year)	Numbers in analysis	RR (95% CI)	Exposure: Comparison	Exposure: Timing	Higher potential for: Bias	Higher potential for: Confounding	Incomplete reporting
WEEKLY WORKING HOURS							
Cohort studies							
Pompeii LA (2005)[38]	1037	1.1 (0.7 to 1.7)	>46 vs 35–45 h/wk	Trimester 1	No	No	No
Pompeii LA (2005)[38]	1037	1.0 (0.6 to 1.8)	>46 vs 35–45 h/wk	Trimester 2	No	No	No
Tuntiseranee P (1998)[52]	886	2.1 (0.6 to 7.0)	⩾61 vs ⩽50 h/wk	15–28 weeks	No	Yes	No
Cross-sectional studies							
Bodin L (1999)[8]	1685	1.1 (0.7 to 1.9)	⩾36 vs 21–35 h/wk	Trimester 2	No	No	No
Ceron-Mireles P (1996)[11]	2406	1.59 (1.14 to 2.22)	>50 vs 3–25 h/wk	Not stated	No	Yes	No
Fortier I (1995)[13]	1833	0.99 (0.7 to 1.39)	⩾40 vs <30 h/wk	Not stated	No	No	No
Klebanoff MA (1990)[20]	989	0.9 (0.6 to 1.3)	Residents (>100 h) vs others	Any	No	No	No
Savitz DA (1996)[46]	589	0.8 (0.6 to 1.2)	⩾40 vs no paid work	5 months	No	No	No
SHIFT WORK							
Cohort studies							
Pompeii LA (2005)[38]	1796	1.3 (0.8 to 2.2)	Regular night work (yes vs no)	Trimester 1	No	No	No
Pompeii LA (2005)[38]	1796	1.4 (0.9 to 2.4)	Regular night work (yes vs no)	Trimester 2	No	No	No
Zhu JL (2004)[56]	35 662	1.07 (0.94 to 1.21)	Rotating shift work vs daytime work	Trimesters 1 and 2	No	No	No
Cross-sectional studies							
Bodin L (1999)[8]	1685	0.8 (0.4 to 1.8)	Night vs day	Trimester 2	No	No	No
Fortier I (1995)[13]	4118	0.98 (0.75 to 1.27)	Shift work vs day only	Not stated	No	No	No
Hanke W (1999)[14]	1064	1.0 (0.19 to 3.26)	Shift work (yes vs no)	Not stated	No	No	No
Nurminen T (1989)[34]	738	1.5 (1.0 to 2.4)	Shift work (yes vs no)	Most of pregnancy	No	Yes	No
LIFTING							
Cohort studies							
Ahlborg GJ (1990)[5]	3389	0.65 (0.24 to 1.77)	⩾12 kg >50 x/wk vs none	Not stated	No	No	No
Magann EF (2005)[26]	485	0.81 (0.47 to 1.41)	⩾4 vs <4 h/d	Trimester 1	No	No	No
Pompeii LA (2005)[38]	1176	1.2 (0.7 to 2.0)	Lifting ⩾25 lbs⩾13 vs 0 x/wk	Trimester 1	No	No	No
Pompeii LA (2005)[38]	1176	1.2 (0.6 to 2.2)	Lifting ⩾25 lbs⩾13 vs 0 x/wk	Trimester 2	No	No	No
Tuntiseranee P (1998)[52]	1108	0.5 (0.1 to 1.7)	>12 kg, 1–10 x/d vs none	15–28 weeks	No	Yes	No
Cross-sectional studies							
Fortier I (1995)[13]	3078	1.03 (0.71 to 1.51)	⩾10 kg vs none	Not stated	No	No	No
STANDING							
Cohort studies							
Launer LJ (1990)[23]	5035	1.21 (1.02 to 1.44)	Standing vs sitting	Not stated	No	Yes	No
Magann EF (2005)[26]	318	0.59 (0.20 to 1.74)	Lifting ⩾11 kg >6 x/h	Trimester 1	No	No	No
Pompeii LA (2005)[38]	977	1.1 (0.7 to 1.7)	>30 vs 6–15 h/wk	Trimester 1	No	No	No
Pompeii LA (2005)[38]	977	1.0 (0.6 to 1.5)	>30 vs 6–15 h/wk	Trimester 2	No	No	No
Tuntiseranee P (1998)[52]	1121	2.0 (0.7 to 5.4)	⩾5 vs ⩽4 h/d	15–28 weeks	No	Yes	No
Cross-sectional studies							
Ceron-Mireles P (1996)[11]	2379	1.4 (1.03 to 1.91)	>7 vs ⩽7 h/d	Not stated	No	Yes	No
Fortier I (1995)[13]	3502	1.42 (1.02 to 1.95)	⩾6 vs <3 h/d	Not stated	No	No	No
Hanke W (1999)[14]	1064	0.89 (0.48 to 1.62)	Mostly standing posture at work (yes vs no)	Not stated	No	No	No
Nurminen T (1989)[35]	676	1.0 (0.4 to 2.3)	Standing work vs sedentary	Trimester 3	No	Yes	No
PHYSICAL ACTIVITY							
Cohort studies							
Launer LJ (1990)[23]	5035	1.32 (1.12 to 1.56)	Manual vs office work	Not stated	No	Yes	No
Magann EF (1996)[25]	531	0.8 (0.42 to 1.45)	>2900 vs <2300 kcal/day energy expenditure	16–18 weeks	No	Yes	No
Tuntiseranee P (1998)[52]	346	0.7 (0.20 to 3.2)	High vs low	15–28 weeks	No	Yes	No
Cross-sectional studies							
Ceron-Mireles P (1996)[11]	2379	1.4 (1.03 to 1.91)	>7 vs ⩽7 h/d	Not stated	No	Yes	No
Fortier I (1995)[13]	1829	0.87 (0.56 to 1.35)	Important vs none	Not stated	No	No	No
Hanke W (1999)[14]	1064	0.89 (0.48 to 1.62)	Mostly standing posture at work (yes vs no)	Not stated	No	No	No
Nurminen T (1989)[35]	524	2.4 (1.3 to 4.6)	Work with a moderate physical load vs sedentary	Trimester 3	No	Yes	No

h/d, hours per day; h/wk, hours per week; x/wk, times per week.
RR is used generically to encompass a variety of published effect measures (odds ratios, incidence density ratios, hazard ratios and so on).

Table 5 Occupational activity and the risks of pre-eclampsia and pregnancy-induced hypertension

First author (year)	Outcome	Numbers in analysis	RR (95% CI)	Exposure: Comparison	Exposure: Timing	Higher potential for: Bias	Higher potential for: Confounding	Incomplete reporting
WEEKLY WORKING HOURS								
Cohort studies								
Landsbergis PA (1996)[22]	PIH	575	1.1 (0.2 to 5.7)	41–49 vs <35 h/wk	Trimester 1	No	No	No
Case–control studies								
Marcoux S (1999)[28]	PIH	267	0.85 (0.48 to 1.54)	⩾35 vs ⩽21 h/wk	First 20 weeks	No	No	No
SHIFT WORK								
Cross-sectional studies								
Nurminen T (1989)[34]	PIH	890	0.9 (0.4 to 1.9)	2 or 3 shift work vs none	Most of pregnancy	No	Yes	No
Wergeland E (1997)[53]	PE	3281	1.3 (0.8 to 1.9)	Shift work (yes vs no)	Trimester 1	No	No	No
LIFTING								
Cross-sectional studies								
Irwin DE (1994)[19]	PIH	2413	1.1 (0.8 to 1.6)	⩾13.6 vs ⩽4.5 kg/d	Not stated	No	Yes	No
Irwin DE (1994)[19]	PE	2420	0.68 (0.47 to 0.98)	⩾13.6 vs ⩽4.5 kg/d	Not stated	No	Yes	No
Wergeland E (1997)[53]	PE	3284	1.7 (1.2 to 2.5)	Lifting heavy loads (10–20 kg; yes vs no)	Trimester 1	Yes	No	No
STANDING								
Cohort studies								
Saftlas AF (2004)[41]	PIH	1009	1.26 (0.83 to 1.91)	Sitting <34% vs ⩾67% of the time	Trimester 1	No	No	No
Saftlas AF (2004)[41]	PE	1009	0.72 (0.32 to 1.59)	Sitting <34% vs ⩾67% of the time	Trimester 1	No	No	No
Cross-sectional studies								
Irwin DE (1994)[19]	PIH	2882	1.0 (0.71 to 1.4)	⩾2/3 vs ⩽1/3 of time	Not stated	No	Yes	No
Nurminen T (1989)[35]	PIH	687	1.1 (0.6 to 2.0)	Standing work vs sedentary	Trimester 3	Yes	Yes	No
Irwin DE (1994)[19]	PE	2879	0.82 (0.57 to 1.2)	⩾2/3 vs ⩽1/3 of time	Not stated	No	Yes	No
Wergeland E (1997)[53]	PE	3294	0.7 (0.5 to 1.0)	Standing/walking (yes vs no)	Trimester 1	Yes	No	No
PHYSICAL ACTIVITY								
Cohort studies								
Landsbergis PA (1996)[22]	PIH	575	0.7 (0.2 to 2.5)	Physical activity score (>200 vs ⩽200)	Trimester 1	No	No	No
Landsbergis PA (1996)[22]	PE	575	0.7 (0.2 to 2.5)	Physical activity score (>200 vs ⩽200)	Trimester 1	No	No	No
Case–control studies								
Spinillo A (1995)[48]	PE	480	2.1 (1.18 to 3.75)	Activity score (moderate/high vs mild/none)	Trimester 1	Yes	No	No
Cross-sectional studies								
Irwin DE (1994)[19]	PIH	2665	1.2 (0.83 to 1.6)	⩾2/3 vs ⩽1/3 of time	Not stated	No	Yes	No
Irwin DE (1994)[19]	PE	2668	0.75 (0.52 to 1.1)	⩾2/3 vs ⩽1/3 of time	Not stated	No	Yes	No
Nurminen T (1989)[35]	PIH	529	1.1 (0.4 to 3.2)	Work with a moderate physical load vs sedentary	Trimester 3	Yes	Yes	No
Saurel-Cubizolles MJ (1985)[42]	PIH	591	3.47 (2.04 to 5.83)	Activity score (2/3 vs 0/1 strenuous items)	Not stated	Yes	Yes	Yes

h/wk, hours per week; kg/d, kilograms per day; PE, pre-eclampsia.
RR is used generically to encompass a variety of published effect measures (odds ratios, incidence density ratios, hazard ratios etc).

Working hours

The relationship of working hours with preterm delivery was considered in 16 investigations[8 10 11 13 17 20 24 27 29 36 38 43–46 52] (including four cohort studies), the high exposure group generally being women who had worked for at least 40 h per week in the first two trimesters of pregnancy. Only moderate associations were reported (table 2). Estimates of RR exceeded 1.5 in four studies,[10 24 27 52] and in two of these the increase was statistically significant. However, these positive findings were limited in one case[24] by an unusually low response rate, and in the other[27] by incomplete reporting and a higher potential for confounding. No risk estimate was as high as 2, and in the four largest studies (>2000 pregnancies analysed),[11 30 43 45] which included the 16-country EUROpean Project of Occupational risks and Pregnancy outcome case–control Study,[45] RRs lay in the range 0.59–1.34.

A pooled RR of 1.31 (95% CI 1.16 to 1.47; test of heterogeneity, $Q = 4.33$, $p = 0.74$) was derived from eight studies that compared work for at least 40 h per week with shorter hours, and for the subset of five studies judged to have higher methodological quality, the corresponding risk estimate was 1.20 (0.98 to 1.47; $Q = 1.32$, $p = 0.86$).

Shift work

We found 14 studies that considered the association of preterm delivery with shift work (usually defined as either shift or night work),[8 13 15 24 27 29 32 34 38 43 45 49 55 56] including 5 cohort investigations (table 2). In seven studies, the point estimate of RR was close to unity, but in six studies[8 24 27 38 49 55] (including four of higher quality[8 38 49 55]), the RR was >1.5. Two studies found significantly increased risks of ≥2.0.[8 55]

The positive studies tended to be small relative to others of similar design, and the four largest investigations[13 29 45 56] found little association between shift work and preterm delivery. In particular, a prospective study, based on the Danish National Birth Cohort and with record linkage to 3 national birth outcome registers, compared >32 000 women working in the daytime with 3197 women working in rotating shifts during the first 2 trimesters, and reported an adjusted OR close to unity.[56] Risk estimates from subanalyses for other shift patterns (fixed evening, fixed night, rotating shifts without night) were in the range 0.7–1.1.

The pooled estimate of risk across 13 studies with sufficient data was 1.20 (95% CI 1.01 to 1.42; $Q = 31.30$, $p = 0.002$) and for the eight studies that met our criteria for higher quality, it was 1.26 (95% CI 0.98 to 1.63; $Q = 21.83$, $p = 0.003$).

Standing

Standing and preterm delivery were considered in 20 papers,[7 10 11 13 15 17 21 23 24 26 27 29 32 33 38 43–45 51 52] including 10 based on cohort studies (table 2). ''High'' exposure was defined (or could be interpreted) as standing for at least 3 h/day in 12 of the studies. Risk estimates exceeded 1.5 in seven studies,[23 24 26 27 33 44 51] whereas in most of the remainder, they exceeded unity but were less clearly positive (OR 1.2–1.3). In the five largest studies (>4000 pregnancies), ORs lay in the range 1.07–1.56.[10 21 23 29 45]

The pooled estimate of risk across the 12 studies that compared standing for at least 3 h with lower exposures was 1.28 (95% CI 1.11 to 1.47; $Q = 16.50$, $p = 0.12$), and that for the subset of 6 studies of higher methodological quality was 1.26 (95% CI 0.96 to 1.66; $Q = 13.19$, $p = 0.02$).

Lifting

The relationship between occupational lifting and preterm delivery was examined in 12 studies,[5 7 10 13 26 29 32 38 43–45 52] including 6 of cohort design (table 3). For the most part, inquiry focused on exposures in the first trimester, but studies differed substantially in their definition of exposure. In none did the point estimate of risk exceed 1.5, although in three studies[32 43 44] (one of higher quality[32]) it was >1.3.

Physical workload

The link between physical workload and preterm delivery was investigated in 21 studies.[11 13 15 17 18 21 22–25 27 29 33 35 36 39 40 42–44 49 52] (table 3). Exposure was defined in various ways. Six studies[17 24 27 29 33 49] used an occupational fatigue score, first proposed by Mamelle *et al*,[27] and comprising several occupational factors—standing >1 h/day, work on an industrial machine, carrying loads of >10 kg, mental stress, and chemical or physical exposures in the work environment. Another common approach was based on a score of physical workload calculated after grouping certain exposures (eg, strenuous conditions and self-reported physical exertion), or according to the estimated daily energy expenditure.[11–13 15 18 23 25 33 35 36 39 40 42 43] In practice, however, exact definitions tended to vary, hindering comparison.

RR estimates close to unity (0.8–1.3) were found in about half of the studies, but for six studies they exceeded 1.5 (five statistically significant[18 27 39 42 43]), and in three studies they were at least doubled.[18 42 43] Findings differed materially by study design, however. In 7 of the 8 prospective cohort studies, RRs were <1.3, whereas in 5 of the 13 retrospective studies, they were >1.7. The two highest risk estimates (both from cross-sectional surveys of lower quality[42 43]) were derived from a crude secondary analysis of the data. Four of the five largest studies reported only modestly increased risks (OR <1.3).[11 21 23 29]

Birth weight

Case definition

The 32 investigations of LBW that we identified used 3 main approaches to characterise the outcome. Some treated birth weight as a continuous measure, some defined cases as having a birth weight less than a stated threshold (most often 2500 g), and some took as cases babies that were small for gestational age (SGA) according to a cut-point on the expected distribution (usually the 10th centile). Many papers presented results for more than one of these outcome measures, and where birth weight was adjusted for gestational age, risk estimates tended, if anything, to be lower. This suggested that associations with unadjusted birth weight in part reflected effects on gestation. Therefore, since we carried out a separate review of occupational risk factors for preterm delivery, we present findings for SGA. Supplementary tables S1 and S2 summarising results for other measures of birth weight are available online (http://oem.bmj.com/supplemental).

A total of 14 studies provided information on occupational risks of SGA[5 8 11 13 14 20 23 25 26 34 35 46 52 56] (table 4).

Potential confounders

In developed countries, four risk factors are suspected to account for most of cases of intrauterine growth retardation: cigarette smoking during pregnancy, small maternal stature, suboptimal nutrition and low maternal weight gain during pregnancy. Other less significant risk factors include race, alcohol consumption, prematurity or LBW in the mother, parity, maternal illnesses and maternal age.[62–64] Among the major risk factors, low maternal weight gain in pregnancy could lie on the causal pathway between occupational exposures and SGA, whereas socioeconomic status represents a useful proxy for poorer nutrition. We thus classified risk estimates as having a higher potential for confounding if they failed to take account of both smoking and at least one of the factors—namely, socioeconomic status, maternal height or pre-pregnancy weight (13 of the 29 exposure–outcome combinations listed in table 4).

Scope for meta-analysis

A pooled estimate of risk was calculated for the association of SGA with shift work, but data on other exposures were too sparse or too heterogeneous to warrant meta-analysis.

Working hours

Weekly working hours and SGA were considered in seven studies,[8 11 13 20 38 46 52] all but two of which were of higher quality. High exposure mostly entailed working for ⩾40 h/week in the first or second trimesters of pregnancy. The largest study found an OR of 1.59 (95% CI 1.14 to 2.22),[11] and in the one cohort study, the OR was 2.1 (95% CI 0.6 to 7).[52] The other five investigations all gave risk estimates close to unity.

Shift work

Our search retrieved six studies that reported on shift work and SGA,[8 13 14 34 38 56] all but one of which were considered to be of higher quality. In one, the estimated RR was 1.5 (95% CI 1.0 to 2.4),[34] but otherwise, risk estimates tended to be close to unity. The pooled estimate of risk from the six studies was 1.07 (95% CI 0.96 to 1.19; Q = 3.30, p = 0.51).

Lifting

Lifting was considered in five studies of SGA[5 13 26 38 52] (four of higher quality). None of the studies showed either a significant positive or a significant negative association.

Standing

Standing and SGA were analysed in eight studies,[11 13 14 23 26 35 38 52] including four of cohort design. Four of the studies[13 14 26 38] were classified as being of higher quality.

The highest risk estimate (OR 2.0, 95% CI 0.7 to 5.4, for those standing ⩾5 vs ⩽4 h/day in the second trimester) came from a cohort study in Thailand.[52] Otherwise, risk estimates were <1.5.

Physical workload

SGA and physically demanding work were considered in seven investigations,[11 13 14 23 25 35 52] including three of cohort design. As with preterm delivery, there was considerable variation in definitions of exposure. In half the studies, the timing of exposure was unstated, whereas the remainder focused mainly on the first two trimesters.

One cross-sectional study found a risk ratio of 2.4 (95% CI 1.3 to 4.6),[35] and a large cohort study indicated an OR of 1.32 (95% CI 1.12 to 1.56)[23] for manual work as compared with office work. However, only one other study[11] gave a risk estimate >1. Only two studies[13 14] were classified as being of higher quality and both these reported an OR just below unity.

Gestational hypertension and pre-eclampsia

Case definition

Pregnancy-induced hypertension is commonly subclassified as

(1) gestational hypertension (increase in blood pressure in a woman who previously had normal blood pressure, which occurs after the 20th week of gestation and resolves after delivery); and
(2) pre-eclampsia (gestational hypertension with proteinuria and oedema).

For pre-eclampsia, we found some variation in terms of the level of blood pressure and the degree of proteinuria required for diagnosis: two studies relied on routine diagnosis by the clinicians caring for subjects[19 53]; two defined pre-eclampsia as diastolic blood pressure ⩾90 mm Hg and proteinuria ⩾1 g/l on at least two separate occasions after 20 weeks of gestation and not before[22 28]; one used a different cut-point (which included systolic hypertension)[41]; and one study (two reports) was based on a rise in mean arterial blood pressure between the first and last antenatal visits.[34 35] Similarly, criteria for gestational hypertension varied importantly between studies.

Potential confounders

Epidemiological research on hypertension in pregnancy has tended to focus mainly on pre-eclampsia, but gestational hypertension may be part of the same spectrum of disease, with a similar pathogenesis and causation.

The pathogenesis of pre-eclampsia is thought to involve superficial placentation, immune maladaptation, reduced concentrations of angiogenic growth factors and increased placental debris in the maternal circulation, provoking a maternal inflammatory response that is modulated by pre-existing cardiovascular or metabolic fitness.[65] Reported risk factors include a history of chronic hypertension, previous pre-eclampsia, primiparity, obesity, diabetes, multiple gestation, extremes of age, ethnicity, family history, low calcium intake, use of barrier contraception, artificial donor insemination and donated oocyte gestation.[22 65 66] Smokers have been found to be at a lower risk of pre-eclampsia in some, but not all, studies.[66 67] The only factors we considered to be both common and to carry a substantial RR were overweight[68] and primiparity.[69] We classified risk estimates as having a higher potential for confounding if they failed to take account of both of these variables (10 of 21 exposure–outcome pairings in table 5).

Scope for meta-analysis

Because of potentially important differences in definitions of outcome from one study to another, we did not attempt meta-analysis for any occupational association with gestational hypertension or pre-eclampsia.

Associations with occupational activities

Our review identified nine unique investigations (two cohort studies) on gestational hypertension, pre-eclampsia and occupational activity—two on working hours,[22 28] two on working in shifts,[34 53] two on lifting,[19 53] four on standing,[19 35 41 53] and five on physical workload[19 22 35 42 48] (table 5). Positive associations were found with lifting of heavy loads in one study[53] and with high physical activity scores in two studies.[42 48] All three of the positive studies were retrospective, and we rated all as having higher potential for inflationary bias. In addition, one[42] was incomplete in its reporting and was assessed as having a greater potential for confounding.

Funnel plots

To check for possible publication bias, we constructed funnel plots for those associations with sufficient data to be included in meta-analyses. These plots, which are available from the authors on request, suggest a degree of publication bias in relation to shift work and preterm delivery (smaller studies increasingly more positive), but showed no clear pattern in relation to the other associations.

DISCUSSION

The health outcomes that we examined in this review are clinically important. Preterm delivery is a major determinant of perinatal mortality, and of neonatal and infant morbidity.[70] LBW is also related to infant morbidity and mortality (eg, in England and Wales during 1999, nearly two-thirds of infant deaths were in babies of LBW[71]), as well as to predicting adverse outcomes in childhood and later life, such as poorer growth and development, and higher risks of neurological and cognitive deficit, high blood pressure, non-insulin-dependent diabetes, coronary heart disease, stroke and obstructive lung disease.[72] Pregnancy-induced hypertension was associated with 16% of pregnancy-related maternal deaths in the US during 1991–7.[73]

The extent of epidemiological evidence that we identified on occupational risks varied. For some associations (eg, the relationship of preterm delivery to shift work and lifting) a substantial body of research had been published, whereas for others (eg, SGA with lifting) relatively few reports were retrieved. Although our literature search was restricted to English language publications, and did not extend beyond those in peer-reviewed journals, we think it unlikely that many important papers will have been overlooked. There is, however, a possibility of publication bias, with more complete reporting of positive than non-positive findings, especially from smaller studies, and the funnel plots that we constructed would tend to support an element of such bias.

A further limitation of the available evidence relates to the definition and ascertainment of exposures. Many of the occupational activities that have been studied are complex constructs, and cannot readily be characterised by a simple, unidimensional metric. For example, occupational lifting could be classified according to the frequency of lifting tasks in a working day, the duration of such tasks, the heaviness of the weights lifted and perhaps also the postures in which lifting is carried out. Similarly, shift work could encompass varying patterns of rotation, with or without work at night. In the absence of clear pointers to the aspects of occupational activities that are most relevant to the health outcomes under investigation, it is not obvious how exposures should best be categorised, and if the classification is suboptimal, risks may be underestimated.

One aspect of exposure that could be important for any of the occupational activities examined is its timing during pregnancy. Thus, the same activity might carry different risks if it occurred late in pregnancy as compared with only a few weeks after conception. In some reports, it was unclear exactly when during pregnancy the reported exposures occurred, but in most, the exposures analysed were in the first or second trimester. Only six papers[12 16 37 38 40 46] presented risk estimates separately for exposures in different trimesters, and these did not point to major differences. However, data on exposures late in pregnancy were generally sparse.

Ascertainment of exposures was usually by direct questioning, or by inference from job title. The accuracy of self-reported exposures is likely to differ according to their nature. For example, hours of work and night work should be relatively easy to recall, whereas frequency of lifting may be more difficult to remember accurately. Where exposures were assessed from memory after delivery (ie, in case–control and cross-sectional studies), there was a potential for differential errors of recall, with exposures perceived as hazardous being over-reported by cases or under-reported by controls. This would apply particularly if the adverse nature of the health outcome was obvious to participants (eg, pre-eclampsia) and the exposure of interest was difficult to remember reliably, and would have tended to inflate risk estimates. Thus, when reporting results, we highlighted those studies that we considered most susceptible to such bias.

Even where differential misclassification of exposure was unlikely, however, there remained the possibility of non-differential errors in exposure assessment, especially for exposures that were harder to characterise or were inferred indirectly from job title. The effects of such non-differential misclassification would normally be to bias risk estimates towards the null.

Other possible sources of error include misclassification of health outcomes, response bias and uncontrolled confounding effects, but these are probably less important. With few exceptions,[18 20 24] outcomes were determined from hospital records, registers or birth certificates, in a way that seems unlikely to have been influenced by a knowledge of exposures. Response rates frequently exceeded 80% (32 of 49 studies), and even when they were lower, there was usually no reason to expect that responders would have differed markedly from non-responders in the associations under examination. Of the known risk factors for the pregnancy outcomes studied, few are common and carry a RR >2, and even if they were quite strongly associated with occupational activities, their confounding effect would be relatively small.

Current balance of evidence

Given the above limitations, table 6 summarises our assessment of the overall strength of evidence linking occupational activities with different categories of outcomes of pregnancy.

For preterm delivery, we found extensive evidence relating to each of the exposures that we considered. Findings were generally consistent and tended to rule out a more than moderate effect size (RR >1.4). Strongly positive studies were uncommon, the larger and most complete studies tended to be less positive, and pooled estimates of risk, where feasible, pointed to only modest or null effects.

For SGA, the position is not dissimilar. Findings were generally consistent and rarely indicated more than moderate effect sizes. However, the evidence base was more limited. For example, we found only one cohort study on working hours and only one on shift work.

For pre-eclampsia and gestational hypertension, although positive findings were few in number, the evidence base is too limited to allow firm conclusions.

For none of the exposures examined was there any indication of important beneficial effects on outcomes of pregnancy.

Comparison with earlier reviews

Although there have been numerous narrative reviews on work and pregnancy outcome,[70 74–79] few systematic reviews have been published, and even fewer that contain an element of meta-analysis. The investigation closest to our own, by Mozurkewich *et al*,[2] considered several of the same papers,

Main messages

- This review considered the relationship of three adverse outcomes of pregnancy (preterm delivery, LBW and pre-eclampsia/gestational hypertension) to five occupational exposures (long working hours, shift work, lifting, standing and heavy physical workload).
- For preterm delivery, there was extensive evidence related to each exposure, and this tended to rule out more than moderate effects (RR >1.4)
- We found less evidence for the other outcomes, especially for pre-eclampsia.
- We found no evidence of benefit from these occupational exposures.

Policy implications

- On balance, the evidence does not support mandatory restriction of any of the activities considered.
- It may still be prudent to limit extremes of exposure, especially in late pregnancy.

Table 6 Summary of the main findings

Exposure	Preterm delivery	Small–for-gestational age	Pre-eclampsia/hypertension
Working hours	RR ⩽1.34 (11/16) RR⩾2.0 (0/16) Four biggest studies, RR = 0.6–1.3 Meta-analysis RR = 1.31 Extensive evidence Reasonably consistent Balance of evidence suggests a small effect and makes a large effect unlikely	RR ~1.0 (5/7) RR ⩾2.0 (1/7) Largest study, RR = 1.6 Reasonable body of evidence (but only two cohort studies) Generally consistent Balance of evidence tends to favour a no more than moderate effect More research would be prudent	PIH: RR ⩽1.1 (2/2) PE: no studies Limited evidence Consistent Favours no effect More research would be prudent
Shift work	RR ⩽1.5 (9/14) RR ⩾2.0 (2/14) Four biggest studies, RR ~1.0 Meta-RR = 1.2 Extensive evidence Reasonably consistent Balance of evidence suggests a small effect and makes a large effect unlikely	RR ~1.0 (4/6) RR 1.5 (1/6) Largest study, RR ~1.0 Reasonable body of evidence (but only two cohort studies) Generally consistent Balance of evidence tends to favour no effect, or an effect that is no more than a moderate	PIH: RR <1.0 (1/1) PE: RR = 1.3 (1/1) Very limited evidence (only two studies) No more than a moderate effect found More research would be prudent
Lifting	RR ⩽1.35 (11/12) RR ⩾1.5 (0/12) Extensive evidence Consistent Balance of evidence tends to rule out a more than moderate effect	RR ⩽1.2 (5/5) Two large studies, three cohort Limited evidence Consistent Balance of evidence tends to favour no effect However, more research would be prudent	PIH: RR = 1.1 (1/1) PE: RR = 0.7–1.7 (two studies) Very limited evidence (only three studies) More research would be prudent
Standing	RR ⩽1.5 (12/20) RR ⩾2.0 (2/20) Five biggest studies, RR 1.07–1.56 Meta-RR = 1.28 Extensive evidence Moderately consistent Balance of evidence suggests a small effect and makes a large effect unlikely	RR ⩽1.4, 7/8 RR ⩾2.0 1/8 (ns) Three biggest studies, RR = 1.2–1.4 Reasonable amount of evidence Generally consistent Balance of evidence tends to favour an effect that is no more than moderate	PIH: RR ⩽1.26 (3/3) PE: RR = <1.0 (3/3) Limited evidence Consistent Tends to favours a no more than moderate effect More research would be prudent
Physical activity	RR ⩽1.4 (15/21) RR ⩾1.7 (6/21); ⩾2 (3/21) Three biggest studies, RR ~1.0 Extensive evidence Less consistent than for other exposures and prematurity Harder to assess—outcome measure not robust or clear, and more prone to bias More research unhelpful unless better targeted	RR ⩽1.4 (6/7); <1 (4/7) RR ⩾2.0 (1/7) Two biggest studies, RR = 1.3–1.4 Reasonable amount of evidence Generally consistent Favours a no more than moderate effect More research unhelpful unless better targeted	PIH: RR ⩽1.6 (3/4); RR >3 (1/4) Biggest study, RR = 1.2, cohort = 0.6 PE: RR <1.0 (2/3); RR >2 (1/3) Biggest study, RR = 0.8, cohort = 0.7 Limited evidence Mixed findings More research would be prudent

ns, not significant at the 5% level; PE, pre-eclampsia; PIH, gestational hypertension.
The numbers in brackets represent the number of studies with the stated RR as compared with the number of all studies for the exposure–outcome combination.

but differed in certain respects. Firstly, the authors excluded many more papers than we did. Thus, our review, which also had the benefit of at least five further years of research reports, covered almost twice the number of investigations. Secondly, Mozurkewich *et al* pooled in meta-analysis several studies that we believe have fundamentally dissimilar definitions of exposure. Thirdly, our review covers some exposure–outcome combinations that were not reported by Mozurkewich *et al.* Nonetheless, where comparisons can be made, the conclusions of our two reviews are similar in most respects. Mozurkewich *et al* estimated that physically demanding work (including lifting) was significantly associated with preterm delivery (OR 1.22), SGA (OR 1.37) and hypertension or pre-eclampsia (OR 1.67), and that the risks of preterm delivery were also higher in those with prolonged standing (OR 1.26) and shift and night work (OR 1.24).[2] Among these, only the estimates for pre-eclampsia from our reading seem to be without much evidential support.

Implications for occupational health practice

Given the scientific evidence that is currently available, how should the occupational activities of pregnant mothers be managed?

We do not think that the current balance of evidence is sufficiently compelling to justify mandatory restrictions on any of the activities considered in this review, if a woman wishes to continue them through pregnancy. At the same time, however, given the uncertainties in the evidence base and the apparent absence of any important beneficial effects, it would seem prudent to advise against long working hours (>40 h per week), prolonged standing and heavy physical work, particularly late in pregnancy. Shift work does not seem to carry an important increase in risk for the health outcomes examined, and in this respect, there seems no reason to recommend its discontinuation during pregnancy. However, societal customs and expectations may dictate that a change from shift work should be permitted if requested.

Priorities for future research

Although we have identified uncertainties in relation to all the occupational activities and health outcomes examined, the potential to reduce this uncertainty by further research varies. We suggest that the highest priorities for future investigation should be the relationship of SGA to working hours and lifting, and further assessment of occupational risk factors for pre-eclampsia and gestational hypertension. In particular, there is a need for well-designed cohort studies in which relevant exposures are assessed prospectively at different stages of pregnancy and subsequent health outcomes are systematically ascertained.

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