



Work activities and risk of prematurity, low birth weight and pre-eclampsia: an updated review with meta-analysis

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ABSTRACT

Objectives We assessed the evidence relating preterm delivery (PTD), low birth weight, small for gestational age (SGA), pre-eclampsia and gestational hypertension to five occupational exposures (working hours, shift work, lifting, standing and physical workload). We conducted a systematic search in Medline and Embase (1966 to 2011), updating a previous search with a further 6 years of observations.

Methods As before, combinations of keywords and medical subject headings were used. Each relevant paper was assessed for completeness of reporting and potential for important bias or confounding, and its effect estimates abstracted. Where similar definitions of exposure and outcome existed we calculated pooled estimates of relative risk (RR) in meta-analysis.

Results Analysis was based on 86 reports (32 cohort investigations, 57 with usable data on PTD, 54 on birth weight and 11 on pre-eclampsia/gestational hypertension); 33 reports were new to this review. For PTD, findings across a substantial evidence base were generally consistent, effectively ruling out large effects (eg, RR>1.2). Larger and higher quality studies were less positive, while meta-estimates of risk were smaller than in previous analyses and best estimates pointed to modest or null effects (RR 1.04 to 1.18). For SGA, the position was similar but meta-estimates were even closer to the null (eight of nine RRs≤1.07). For pre-eclampsia/gestational hypertension the evidence base remains insufficient.

Conclusions The balance of evidence is against large effects for the associations investigated. As the evidence base has grown, estimates of risk in relation to these outcomes have become smaller.

In the UK, as in most parts of the world, women make up a substantial proportion of the workforce (50% in 2010¹). Almost 70% of women work through their reproductive years,² amounting to some 350 000 pregnant workers in any 1 year.³ The impetus and legal onus to assess health and safety risks to pregnant workers, and where possible to minimise them, is thus considerable.

As strategies have evolved to manage the risks associated with well-established but uncommon reproductive hazards (eg, ionising radiation, lead), so attention has turned to everyday occupational exposures, relating to working hours, shift work, standing, lifting and physical workload.

In theory, such common exposures could affect the outcomes of pregnancy. For example, disrupted circadian rhythms from shift working could trigger neuroendocrine changes that affect fetal growth and

What this paper adds

- In theory, physical activities at work could adversely affect outcomes of pregnancy. However, an earlier systematic review indicated that long working hours, shift work, prolonged standing, heavy lifting and high physical workload have limited impact on risks of preterm delivery and low birth weight/small for gestational age (SGA).
- This review adds 33 more reports, increases the available number of effect estimates by some 30–50%, and allows additional meta-estimates of risk.
- For preterm delivery and SGA the substantially enlarged evidence base provides greater confidence that any risks from these activities are, at most, small.
- For pre-eclampsia and gestational hypertension the available evidence remains limited.

timing of parturition, while raised noradrenaline levels from heavy physical exertion could increase uterine contractility and risks of preterm labour. Set against this, however, considerable physiological adaptations to the demands of pregnancy tend to preserve constant fetal oxygen consumption, and a growing body of evidence suggests that moderate physical exercise in pregnancy can be beneficial;^{4–7} several authoritative clinical bodies now recommend it.^{8 9}

Previously¹⁰ we reviewed the evidence (to December 2005) relating five common occupational exposures (prolonged working hours, shift work, lifting, standing, and heavy physical workload) to five clinically important adverse outcomes of pregnancy (preterm delivery, small for gestational age (SGA), low birth weight (LBW), pre-eclampsia and gestational hypertension). Subsequently, a request by the Royal College of Physicians of London to prepare national clinical guidelines on pregnancy and work afforded us the opportunity to update our search over several more years in a surprisingly active area of research inquiry. We report here on the considerably enlarged body of evidence, and present new meta-estimates of effect for exposures and outcomes of interest.

METHODS

Search strategy

Previously we conducted a systematic search in Medline and EMBASE from 1966 to December

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2005,¹⁰ with a partial update in Medline in respect of shift work to February 2010.¹¹ For this review the same search strategy was run in both databases to provide complete coverage from 1966 to 31 December 2011, adding 6 more years of data.

As before, medical subject headings and key words representing each outcome and exposure of interest were combined. The medical subject headings used were: pregnancy, reproductive health, pre-eclampsia, infant-premature, labour-premature, birth weight, gestational age, SGA, fetal growth retardation, labour complications, pregnancy complications (as outcomes); and lifting, work schedule tolerance, exercise, fatigue, work, workload, employment and occupational exposure (as exposures). Several simple search terms also supplemented the inquiry: occupational activity, standing, manual lifting, heavy lifting and shift work (as exposures). Searches were limited to papers with an abstract in English. Titles and abstracts were examined and all potentially relevant primary reports and reviews were obtained. The references of retrieved papers and a major report in the area by the Royal College of Physicians of London and NHS Plus,¹² published since our last review, were also checked for relevant material. These procedures and the steps below were replicated independently by two of us and differences were resolved by consensus. Papers finally included were those which compared an exposed with a less heavily or unexposed reference group for at least one exposure-outcome combination of interest and which provided estimates of effect or the data to calculate these.

Data abstraction

Details were abstracted from each relevant paper on the study populations, setting, timing of investigation, study design, exposure contrasts, methods for assessment of exposure(s) and outcome(s), response rates, confounders considered and estimates of effect. Where a paper provided frequencies but not estimates of relative risk (RR), ORs with exact 95% CIs were calculated using STATA software. Similarly, where birth weight was presented as a continuous measure, with group means and standard deviations, the mean difference between exposure groups was calculated with 95% CIs. Where several sub-analyses were presented, analysis focussed on exposure contrasts that were most comparable across studies.

Quality assessment

Each paper was rated for completeness of reporting and each exposure-outcome permutation for its potential for significant confounding or 'inflationary' bias, as defined previously.¹⁰ In brief, completeness of reporting was graded according to nine items that were clearly defined (study design, sampling frame and procedures, inclusion/exclusion criteria, main characteristics of the study population, numbers and response rates, method(s) of assessment of exposure and of outcome, method of analysis, measures of association with 95% CI and numbers in the analysis): studies for which three or more than three items were missing or unclear were classed as poorer in information quality. Potentially important confounders were identified from among risk factors that were reasonably prevalent, unlikely to reflect the effects of occupational exposure or lie on the causal pathway between exposure and health, and which carried a reasonable RR (the choice of confounders varied by outcome as described below). 'Inflationary' bias (bias that could cause important overestimation of RRs) was considered most likely when exposures were self-reported retrospectively (especially if of a type difficult to recall), and were being related to outcomes that were self-reported or were clearly adverse. Thus,

retrospective studies with self-reported exposures were assigned one point for each of: (1) self-reported outcome; (2) outcome of pre-eclampsia, gestational hypertension, or LBW; (3) exposure related to physical workload (standing, lifting, activity score). Exposure-outcome pairings were scored 0 to 3, and scores ≥ 2 were considered indicative for potential inflationary bias. By these criteria, exposure-outcome combinations were counted as of poorer quality if they had significant potential for confounding or bias or came from studies with incomplete reporting. In summarising findings, we also distinguished risk estimates based on >1000 deliveries from smaller analyses. (With an α of <0.05, this cut-point should provide a $\geq 95\%$ power to detect an OR in case-control studies of 2.0 for exposures such as working >40 h/week and shift work 'most of the time', and a RR in cohort studies of 2.0 for preterm delivery and SGA (details available on request)).

Meta-analysis

For studies with similar definitions of exposure and outcome, pooled estimates of RR were calculated by weighting log RRs or log ORs by the inverse of their variances. Meta-analysis was performed using the Sharp and Sterne STATA macro. A fixed effects model was chosen unless there was evidence of heterogeneity ($p < 0.1$), whereupon a random effects (DerSimonian-Laird) model was selected instead. Overall meta-estimates for possible exposure-outcome combinations were computed and also a sensitivity analysis excluding papers of lower quality. Where possible, estimates were also made for occupational exposures continuing into the second or third trimesters of pregnancy. Where studies provided estimates of effect for several trimesters, the estimate earliest in pregnancy was used for the overall analysis and that latest in pregnancy for the second and third trimester analysis.

RESULTS

Our earlier review identified 53 reports (covering 49 studies).¹³⁻⁶⁵ The updated search, together with a review of the bibliographies of published papers, identified a further 33 reports⁶⁶⁻⁹⁸ relating to 30 studies—in all, 86 reports, 57 with usable data on preterm delivery, 54 on birth weight (including SGA) and 11 concerning pre-eclampsia or gestational hypertension (some reports covered several exposures and/or outcomes). The additional material comprised 28 reports published after the index date in December 2005⁶⁶⁻⁹³ and five⁹⁴⁻⁹⁸ from before it identified from citations in papers retrieved by this search.

For reasons of parsimony, we tabulate here only a descriptive summary of risk estimates across the full material (1966 to December 2011), overall and for larger higher quality studies (table 1), and associated meta-estimates where these could be derived (table 2). Online supplementary tables S1-S7 provide a complete listing, covering the design features of all 79 studies, our assessment of their study quality, and associated risk estimates from the 86 reports, enumerated separately by pregnancy outcome. Unless otherwise stated, our description of the findings and discussion cover the entire search period.

Identified studies covered 27 countries, a third of reports coming from the USA and a third from Europe. In general, reports had satisfactory completeness of reporting by our criteria. However, for 20/79 (25%) studies the score was ≤ 6 .

Sample sizes varied from small (<50) to extremely large (>350 000), but 57% of the 353 effect estimates across both reviews (see online supplementary tables S1-S7) were based on findings from >1000 births. Response rates at baseline (cross-sectional studies) or follow-up (cohort studies) often exceeded 80-90%, but

Table 1 Descriptive summary of the associations between reviewed activities and pregnancy outcomes (1966–2011)*

Outcome/exposure	All studies				Higher quality larger studies†			
	N Studies	Median (IQR)	Range	N estimates (RR≥2.0/all estimates)	N Studies	Median (IQR)	Range	N estimates (RR≥2.0/all estimates)
Preterm delivery (RR)								
Working hours	25	1.18 (1.00 to 1.34)	0.30 to 3.69	2/30	11	1.10 (1.01 to 1.21)	0.30 to 1.60	0/15
Shift work	21	1.10 (0.67 to 1.60)	0.67 to 5.60	3/33	9	1.03 (0.94 to 1.16)	0.67 to 1.80	0/19
Standing	28	1.16 (1.00 to 1.35)	0.58 to 4.10	3/36	10	1.09 (0.92 to 1.23)	0.76 to 1.69	0/12
Lifting	17	1.12 (0.90 to 1.30)	0.55 to 2.91	1/22	11	1.02 (0.90 to 1.30)	0.55 to 1.49	0/15
Physical activity	33	1.20 (1.10 to 1.70)	0.71 to 4.10	4/35	8	1.10 (1.04 to 1.16)	0.87 to 1.25	0/9
SGA (RR)								
Working hours	14	1.10 (1.00 to 1.27)	0.80 to 2.10	1/18	6	1.10 (1.00 to 1.10)	0.99 to 1.19	0/9
Shift work	11	1.25 (0.94 to 1.49)	0.70 to 3.31	2/18	6	1.00 (0.92 to 1.25)	0.70 to 1.50	0/11
Standing	12	1.00 (0.93 to 1.26)	0.86 to 2.00	1/17	4	1.06 (0.98 to 1.24)	0.89 to 1.42	0/4
Lifting	7	1.03 (0.73 to 1.15)	0.50 to 1.20	0/11	4	1.08 (1.04 to 1.17)	0.65 to 1.20	0/6
Physical activity	13	1.00 (0.82 to 1.38)	0.70 to 2.40	2/14	5	0.88 (0.81 to 1.00)	0.76 to 1.20	0/6
Low birth weight (RR)								
Working hours	8	1.34 (1.20 to 1.65)	0.96 to 1.80	0/10	0	–	–	–
Shift work	7	1.28 (1.02 to 1.47)	0.71 to 2.10	1/9	1	–	1.02	0/1
Standing	9	1.13 (0.70 to 1.58)	0.50 to 1.92	0/13	1	–	0.5	0/1
Lifting	7	1.10 (0.70 to 1.26)	0.50 to 2.40	1/9	3	0.75 (0.73 to 1.58)	0.70 to 2.40	1/3
Physical activity	10	1.13 (1.04 to 1.80)	0.60 to 4.32	2/11	1	–	0.99 to 1.13	0/2
Birth weight (gms diff)								
Working hours	7	–60 (–74 to 7)	–84 to –32	(N=9)	3	–45 (–53 to 44)	–60 to 43	(N=3)
Shift work	6	10 (–273 to 39)	–438 to 195	(N=13)	1	37 (21 to 57)	2 to 91	(N=4)
Standing	8	–25 (–31 to 0.5)	–49 to 20	(N=11)	3	–36 (–42 to 29)	–49 to 18	(N=4)
Lifting	3	–21 (–24 to 11)	–44 to 19	(N=8)	0	–	–	–
Physical activity	8	–59 (–148 to 29)	–216 to 183	(N=14)	2	–	–21 to 51	(N=2)
Pregnancy-induced hypertension								
Working hours	5	1.10 (0.85 to 1.10)	0.76 to 1.18	0/5	1	–	0.76	0/1
Shift work	2	–	0.90 to 1.10	0/2	0	–	–	–
Standing	4	1.05 (0.93 to 1.14)	0.70 to 1.26	0/4	1	–	1.26	0/1
Lifting	2	–	1.10 to 1.10	0/2	0	–	–	–
Physical activity	4	1.15 (1.00 to 1.77)	0.70 to 3.47	1/4	0	–	–	–
Pre-eclampsia								
Working hours	2	–	0.96 to 1.20	0/2	1	–	0.96	0/1
Shift work	2	–	1.00 to 1.30	0/2	1	–	1.30	0/1
Standing	4	0.77 (0.72 to 1.34)	0.70 to 2.90	1/4	1	–	0.72	0/1
Lifting	3	1.1	0.68 to 1.70	0/3	0	–	–	–
Physical activity	3	0.75	0.70 to 2.10	1/3	0	–	–	–

*See online supplementary tables S1 to S7 for a complete listing of the reports and associated risk estimates summarised in this table.

†After excluding estimates with higher potential for bias or confounding, involving <1000 deliveries, or from incompletely reported studies.

RR, relative risk; SGA, small for gestational age

Table 2 Relationship between working hours, standing, shift work and two pregnancy outcomes (preterm delivery and small for gestational age): meta-estimates of relative risk (1966–2011)*

	Working hours (> vs <40 h/week)		Standing (>4 vs <4 h/day)		Shift work (Yes vs No)	
	N	RR (95% CI)	N	RR (95% CI)	N	RR (95% CI)
Preterm delivery						
Overall meta-estimate	17	1.23 (1.13 to 1.34)	12	1.22 (1.12 to 1.33)	19	1.14 (1.01 to 1.30)
Sensitivity analysis†	11	1.18 (1.05 to 1.33)	7	1.13 (0.99 to 1.29)	12	1.04 (0.94 to 1.15)
Later pregnancy	6	1.17 (0.94 to 1.45)	7	1.15 (0.96 to 1.37)	8	1.17 (0.86 to 1.60)
SGA						
Overall meta-estimate	8	1.04 (0.94 to 1.16)	7	1.07 (0.94 to 1.22)	10	1.01 (0.92 to 1.10)
Sensitivity analysis†	6	0.99 (0.88 to 1.11)	5	1.16 (0.97 to 1.38)	7	0.98 (0.90 to 1.08)
Later pregnancy	4	0.99 (0.83 to 1.19)	5	0.95 (0.76 to 1.20)	5	1.05 (0.94 to 1.18)

*See online supplementary tables S1 and S2 for details of the reports and risk estimates incorporated into these meta-analyses.

†Excluding studies with a higher potential for bias or confounding, or which reported incompletely.

RR, relative risk; SGA, small for gestational age

were <65% or unclear in 21 reports.^{25 26 32 34 35 37 47 51–54 59 65 79 85 87 89 90 92 93 98}

In 29 cohort investigations, occupational history was determined during pregnancy and in three others^{64 71 77} by record linkage; for the remaining studies information on work exposures was obtained after delivery, mostly through self-report, but in a minority^{26 27 39 44 47 59 77 80 82 90} using job title as a surrogate index. Issues of measurement error in exposure assessment were seldom considered, only a few studies employed personal diaries to assist self-reporting, and about 40% of studies did not report the timing of exposures during pregnancy. Most studies of working hours, standing and shift work employed similar exposure definitions. However, definitions for lifting and physical workload differed materially between studies.

With few exceptions health outcomes were established objectively (from hospital records, registers or birth certificates).

Various strategies were used to control for confounding (matching, restriction, stratification, regression modelling), but confounding was ignored altogether in some investigations. Roughly 40% of exposure-outcome pairings carried higher potential for inflationary bias or confounding according to our criteria.

Preterm delivery

Case definition

Most reports adopted the WHO definition for preterm delivery: 'the birth of a living fetus before 37 completed weeks of gestation'.

Potential confounding factors

Many maternal characteristics have been associated with an increased risk of preterm delivery (eg, previous preterm delivery, multiple gestation, diabetes, pre-eclampsia, bacterial vaginosis, extremes of maternal age), but few such factors are common and carry a high RR and some (eg, obstetric events in previous pregnancies) could have arisen from previous work exposures. Smoking and lower social class carry moderate RRs (1.5–2.0) and are prevalent exposures whose frequency could vary systematically by occupational activity. Risk estimates that failed to take account of both of these variables (or proxies of them—eg, lower educational attainment or income) were classed as having higher potential for confounding.

Scope for meta-analysis

Formal meta-analysis was feasible for associations of preterm delivery with working hours (>40 h/week vs less), shift work (Yes vs No) and standing (>4 h/day vs less). For lifting and physical workload, definitions of exposure were too heterogeneous to justify being combined.

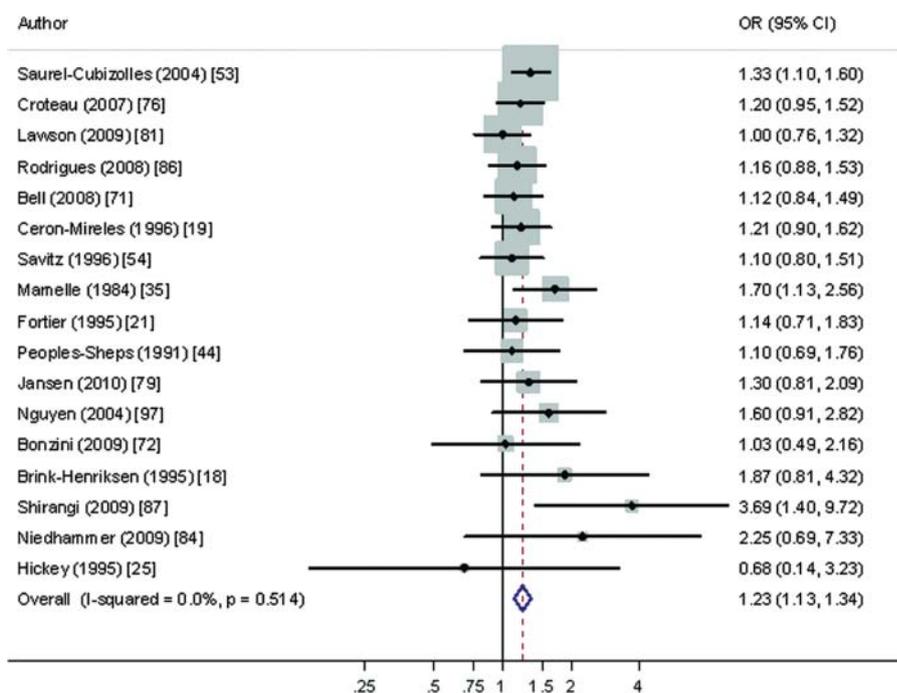
Working hours

The relation of working hours to preterm delivery was considered in 25 studies,^{16 18 19 21 25 28 32 35 37 44 45 51–54 60 71 72 76 79 81 84 86 87 97} including nine cohort investigations. These provided 30 estimates of RR, the median RR being 1.18 (and 1.10 in 11 large studies of higher quality). In only 2 of 30 estimates, was the RR ≥ 2.0 .^{84 87} One of these studies was unusual in its focus on exposure to anaesthetic gases and infective risks,⁸⁷ and both were small relative to the field (<750 births), with correspondingly wide 95% CIs. By contrast, the eight largest studies (>2000 births)^{19 37 51 53 71 76 79 81} all had RRs ≤ 1.34 . A pooled RR of 1.23 (95% CI 1.13 to 1.34) (figure 1) was derived from 17 studies that compared work for at least 40 h per week with shorter hours.^{18 19 21 25 35 44 53 54 71 72 76 79 81 84 86 87 97} For the subset of 11 studies judged of higher methodological rigour,^{18 19 21 44 54 72 76 79 81 84 87} the meta-RR was somewhat lower (1.18 (95%CI 1.05 to 1.33)), while the meta-estimate for exposure continuing into later pregnancy was close to this second value.

Shift work

Twenty-one studies^{16 21 23 32 35 37 40 42 45 51 53 57 63 64 68 70 72 73 76 81 84} were found that considered the association of preterm delivery with shift work (usually defined either as shift or night work), including nine cohort investigations. Together these provided 33 estimates of effect. In two-thirds the point estimate of RR was near or below unity, although in nine studies^{16 32 35 45 57 63 68 73 84} the RR was ≥ 1.5 and in three of these^{16 63 68} risks were elevated ≥ 2.0 . Among these, one study focussed primarily on exposure to anaesthetic gases in midwives¹⁶ and was an outlying observation. A second involved exposure to shift working and to self-reported undefined 'physical and chemical hazards'.⁶⁸ This and a third study of textile workers⁶³ were relatively small (<1000 births). Among the seven largest studies of shift working and preterm delivery,^{21 37 53 64 73 76 81} each involving >4000 births, 13 of 14 RRs were ≤ 1.18 . The median estimate of RR across all studies was 1.10, but only 1.03 in the nine larger better quality studies; the

Figure 1 Risk of preterm delivery associated with working >40 h per week during pregnancy (Forest plot ordered by study size).



meta-estimate (based on 19 studies^{16 21 23 32 35 40 42 45 51 53 57 63 64 70 72 73 76 81 84}) was 1.14 (figure 2), and that for the 12 studies that met our criteria for higher quality^{21 40 42 45 57 63 64 72 73 76 81 84} was 1.04 (95% CI 0.94 to 1.15).

Standing

Twenty-eight studies^{15 18 19 21 23 25 29 31-33 35 37 40 41 45 51-53 59 60 68 70 72 76 81 85 86 98} which considered standing and preterm delivery, including 12 of cohort design, provided 36 estimates of effect. 'High' exposure was defined as standing for ≥ 4 h/day in 12 studies.^{17 21 29 32 33 45 53 60 68 72 76 81} Risk estimates exceeded 1.5 in eight studies,^{31-33 35 41 52 59 98} of which three reported

RRs ≥ 2.0 .^{32 59 98} Of these three, two^{32 98} were of lower quality, in part because exposures were self-reported after delivery and two^{59 98} were small (<750 births). In the 10 largest studies (>2000 births),^{18 19 21 29 31 37 51 53 76 81} 10 of the 11 effect estimates were ≤ 1.31 . The overall median estimate of RR was 1.16 and 1.09 in larger and better quality studies. The meta-estimate (based on 12 studies) was 1.22 (figure 3), and that for the seven studies^{18 21 29 33 60 72 76} of higher quality was 1.13 (95% CI 0.99 to 1.29).

Lifting

The relation between occupational lifting and preterm delivery was examined in 17 studies,^{13 15 18 21 33 37 40 45 51-53}

Figure 2 Risk of preterm delivery associated with working shifts during pregnancy (Forest plot ordered by study size).

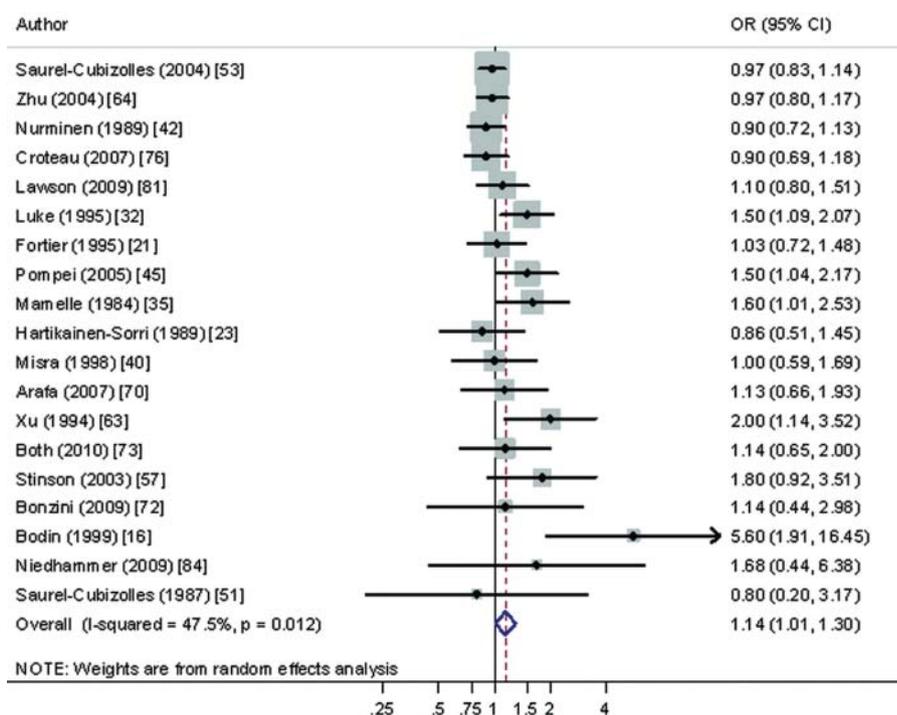
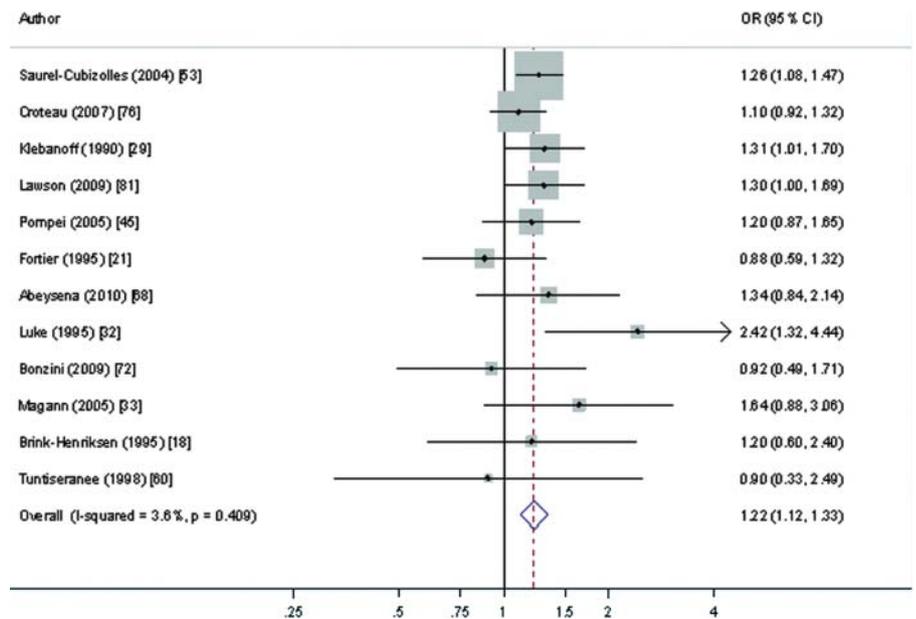


Figure 3 Risk of preterm delivery associated with standing at work for >4 h per day during pregnancy (Forest plot ordered by study size).



60 72 76 81 89 98 including eight prospective investigations. Studies differed substantially in their definition of exposure. Twenty-two effect estimates were reported, the median overall being 1.12. In only one of 22 estimates was the RR >2.0;⁹⁸ this study was rated as more susceptible to confounding and was also relatively small (<500 births). In the 11 higher quality studies with >1000 births,^{13 18 21 37 40 45 53 60 72 76 89} the median value was 1.02 (IQR 0.90–1.30).

Physical workload

Thirty-three studies,^{19 21 23 25 26 29 31 32 34 35 37 41 43 44 47 48 50–52 57 60 69 71 77 80 82–86 90 94 97} including 12 of cohort design, investigated the link between physical workload and preterm delivery and provided 35 risk estimates. Exposure was defined variously. For example, six studies^{25 32 35 37 41 57} used an occupational fatigue score proposed by Mamelle *et al*, comprising a combination of standing >1 h/day, work on a machine, carrying loads >10 kg, mental stress and chemical or physical exposures at work; while other studies used a physical workload score, calculated as an estimated daily energy expenditure or by grouping self-estimates of physical exertion.

The median effect estimate was 1.20. In 4 of 35 estimates the RR was >2.0. These came from three studies of relatively small size (<800 births),^{50 51 83} two of which were classified as having higher potential for confounding.^{50 51} In the six largest studies (>3000 births),^{29 31 37 71 77 82} the highest risk estimate was 1.16, the median value being 1.10 (IQR 1.07–1.11). Self-reporting of a subjective exposure (eg, 'heavy' workload) is more than usually susceptible to reporting bias, so ideally occupational history would be taken before pregnancy outcome. The 12 prospective studies^{25 29 31 34 41 48 57 60 71 77 84 97} gave a median RR of 1.16; but this provides only a limited guide as 7 of the 12 relevant estimates came from small studies (<650 births). The median RR for higher quality studies with >1000 births was 1.10.

Birth weight

Case definition

The 53 identified reports on LBW used three different approaches to define outcome: birth weight as a continuous measure, birth weight below a threshold (usually 2500 g), or

SGA by a cut-point on an expected distribution (usually the 10th centile). Several papers presented results for several outcomes and where birth weight was adjusted for gestational age, risk estimates tended if anything to be lower, suggesting that associations with unadjusted birth weight partly reflected effects on gestation. This account therefore focuses on the 24 studies that provided information on occupational risks of SGA,^{16 19 21 22 28 31 33 34 42 45 54 56 60 64 66 70–72 75 77 79 84 88 91} though additional results (from 38 reports) for other measures of birth weight are presented in the online supplementary tables.

Potential confounders

Major risk factors for intrauterine growth retardation in developed countries include smoking, small maternal stature, suboptimal nutrition and low maternal weight gain; but among these, poor maternal weight gain could lie on the causal pathway between occupational exposures and SGA, while lower socioeconomic status is a proxy for poorer nutrition. Risk estimates were therefore classified as having higher potential for confounding if they failed to take account of smoking and ≥ 1 of: socioeconomic status, maternal height or prepregnancy weight.

Scope for meta-analysis

A meta-estimate of risk of SGA was calculated in relation to working hours (>40 h/week vs less), standing (>4 h/day vs less) and shift work (Yes vs No); but exposure definitions for lifting and physical workload were too heterogeneous to be combined.

Working hours

Fourteen studies^{16 19 21 28 45 54 56 60 71 72 75 79 84 88} (seven of cohort design), all but three of higher quality, considered weekly working hours and SGA, providing 18 estimates of effect. The median RR was 1.10. In only one of 18 estimates was the RR ≥ 2.0 —in a relatively small study (<1000 births) with higher potential for confounding.⁶⁰ 'High' exposure mostly entailed working for ≥ 40 h/week and in eight studies^{16 19 21 51 71 72 75 79 84} with the exposure that could be combined in meta-analysis the estimated RR was 1.04 (95% CI 0.94 to 1.16) overall, and 0.99 (95% CI 0.88 to 1.11) in six

studies of higher quality. The estimated effect from this exposure continuing beyond the first trimester was below 1.0.

The median estimated RR for LBW (1.34), based on 10 estimates from eight reports,^{16 24 37 44 51 60 84 92} was somewhat higher than for SGA, but 7 of the 10 estimates derived from smaller studies (<1000 births) and the three larger studies^{16 44 51} were deemed more susceptible than average to confounding. None of the 10 estimated RRs was as much as doubled.

Online supplementary table S6 summarises the outcome in relation to birth weight measured continuously. All seven studies^{16 24 28 62 79 88 95} found a lower birth weight in women working longer (median 60 gms, range 32–84 gms). Most studies were small (four had ≤ 250 births), but in the two largest studies,^{79 88} rated of better quality and prospective birth weights were on average about 45 gm lower in women with longer working hours.

Shift work

Eleven studies^{16 21 22 42 45 64 66 70 72 75 84} (eight of higher quality) reported on shift work and SGA. The median RR overall was 1.25 and in only one study (2 of 18 estimates) was above 2.0. This study⁶⁶ was small, had a higher potential for inflationary bias, and defined exposure in terms of shift work and the presence of self-reported 'physical or chemical hazards at work'. However, the median RR for larger higher quality studies was 1.0. The pooled estimate of risk was 1.01 (95% CI 0.92 to 1.10), and 0.98 (95% CI 0.90 to 1.08) when analysis was restricted to seven studies^{21 22 45 64 72 75 84} of higher quality.

The median RR for LBW (1.28) was somewhat higher than that for SGA, but only one of nine estimates was derived from a higher quality study with >1000 births (based on a national birth cohort in Denmark⁶⁴). In this the RR was 1.01, in keeping with meta-analytic estimates. Online supplementary table S6 also summarises the outcome in relation to birth weight measured continuously. There was a large span of results in relation to shift work, from an average loss of 438 gms at one extreme to a gain of 195 gms at the other, with a median estimated gain of 19 gms. Negative findings were particularly evident in one very small study (25–67 births) of lower quality,¹⁴ and in the three largest studies (1685–>35 000 births)^{16 64 73} shift work was associated on average with a modest gain in birth weight.

Standing

Standing and SGA were analysed in 12 studies^{19 21 22 31 43 45 56 60 66 72 75 88} (five classed as higher quality) including six of cohort design. The median RR from 17 estimates of effect was 1.00 (IQR 0.93–1.26) and only one moderately sized study, from Thailand, with higher than average potential for confounding, reported a RR as high as 2.0.⁶⁰ The overall meta-estimate, assuming a cut-point of 4 h/day, was 1.07 (95% CI 0.94 to 1.22), or 1.16 in sensitivity analysis, and 0.95 for exposures at this level continuing beyond the first trimester. Four estimates came from higher quality studies analysing >1,000 births,^{21 22 66 88} with a median of 1.06 (IQR 0.98–1.24).

Thirteen estimates of RR for LBW were available, from nine studies,^{24 37 39 51 59 60 62 66 85} the median being 1.13, with no RR ≥ 2.0 ; and there were 11 estimates of birth weight analysed continuously in women who stood at work versus those that did not (eight studies^{17 24 29 59 62 65 88 94}), ranging from an average weight loss of 49 gms to a weight gain of 20 gms).

Lifting

Lifting was considered in seven studies of SGA,^{13 21 33 45 60 72 75} with a median RR overall of 1.03 (IQR 0.73–1.15) and a similar value for the four studies of higher quality. All 11 estimates of effect were ≤ 1.2 . Seven studies^{13 24 37 51 60 62 89} provided evidence on LBW (see online supplementary table S5), but only one of nine estimated RRs was ≥ 2.0 (a cross-sectional study in which exposures were self-reported after delivery⁶²). Only three studies^{20 24 62} looked at birth weight assessed continuously, with mixed results (see online supplementary table S6), ranging from a mean reduction in birth weight of 44 gms to a mean gain of 18.9 gms in women with lifting duties.

Physical workload

SGA and physical workload were considered in 13 investigations,^{19 21 22 31 34 43 56 60 71 77 84 88 91} including eight of cohort design. Exposures were defined diversely. The median RR was 1.00 (IQR 0.82–1.38) (based on 14 estimates) and 0.88 in higher quality studies. Two studies^{43 56} reported RRs ≥ 2.0 ; both were small (about 500 births) and of lower quality.

A similar median estimate of effect was found for LBW (1.13), with RRs > 2.0 in two studies, both with <800 births.^{26 84} Eight studies^{20 24 26 29 34 48 58 88} provided 14 estimates of continuously assessed birth weight, with mixed results—a median weight loss on average of 59 g, but ranging from an average loss of 216 g to an average weight gain of 183 g.

Gestational hypertension and pre-eclampsia

Case definition

Studies subclassified pregnancy-induced hypertension in the standard way, as: (1) gestational hypertension (raised blood pressure in a previously normotensive woman after the 20th week of gestation, which resolves after delivery); or (2) pre-eclampsia (gestational hypertension with proteinuria and oedema). However, variation existed in the level of blood pressure and degree of proteinuria underlying case definitions.

Potential confounders

Among many reported risk factors for pre-eclampsia, we considered only obesity and primiparity to be common and to carry substantial RRs. Risk estimates were classified as having higher potential for confounding if they failed to take account of *both* of these variables.

Scope for meta-analysis

Because of potentially important differences in outcome definition from one study to another and a small pool of studies, we did not attempt meta-analysis for occupational associations with gestational hypertension or pre-eclampsia.

Associations with occupational activities

Eleven investigations^{27 30 36 42 49 50 56 61 74 78 79} (including three cohort studies) were identified concerning gestational hypertension, pre-eclampsia and occupational activity, providing 31 estimates of effect across the five categories of work exposure. However, data were sparse when individual exposure-outcome combinations were analysed separately. For example, only two estimates of effect were found respectively for standing, shift work and lifting in relation to gestational hypertension, and only two respectively for working hours, and shift work in relation to pre-eclampsia. It may be seen, however, that median RRs, where feasible to estimate, were low (RR < 1.15) and that only three studies^{50 56 78} reported RRs ≥ 2.0 . In the study by Haelterman

*et al*⁷⁸ the exposure associated with a RR of 2.9 was standing on the spot for ≥ 1 h at a time, but no other study assessed standing in this way. The other two studies focussed on self-reported physical activity. All three, however, were retrospective in design and rated as of lower methodological quality, two of them were also small (<600 births)^{50 56} and one was incompletely reported.⁵⁰

DISCUSSION

This study updates an earlier review by providing an extra 6 years of observation. The number of available risk estimates increased over this time by 30–50%, depending on outcome, allowing additional meta-analyses (on SGA and separately for late pregnancy) that could not be justified a relatively short while ago. Twelve of 30 new studies involved >4000 deliveries, one with >350 000 births,⁷⁸ there were nine new cohort studies (in 12 reports), and eight new reports^{66–68 72 73 75 76 91} furnished risk estimates separately for different pregnancy trimesters, adding to the six^{20 24 45 46 48 54} previously identified; 40% of risk estimates were linked with a specified trimester, a much improved situation. We summarise the current evidence now as substantial for preterm delivery, reasonably large for SGA (especially when other measures of birth weight are also considered), but still small for gestational hypertension/pre-eclampsia.

Our search was restricted to publications with abstracts in English, did not extend to the ‘grey’ literature, and may therefore have not been perfectly comprehensive. However, it seems unlikely that many important papers will have been missed. On the other hand, the consistent finding that risk estimates were lower in the largest and better studies, with outliers confined to small studies, suggests that publication bias may be inflating estimates of risk.

Strengths of the evidence base, across most studies, include high response rates and ascertainment of outcomes independent of exposures (from objective sources such as birth records). Thus, response bias and non-differential misclassification of health endpoints is unlikely to have much affected findings. On the other hand, non-differential misclassification could still arise for exposures that are hard to characterise, with bias to the null.

Another continuing limitation in available evidence relates to the heterogeneity of exposure definitions, especially for lifting and physical workload. The challenge is not inconsiderable: lifting tasks, for example, may be classified according to their average daily frequency, duration, load and posture, and the optimum choice of metrics is not obvious; but there has been little move towards standardisation over time. This limitation impedes causal inference and risk communication, by precluding meta-regression and full assessment of exposure-response relationships.

One aspect of exposure that may be important is its timing during pregnancy. However, studies that presented risk estimates separately for different trimesters did not point to major differences, and in meta-analysis risks of preterm delivery and SGA from long working hours, standing and shift work in the second and third trimesters were not noticeably higher.

As previously, we have highlighted those studies considered most susceptible to confounding and inflationary bias (which may arise particularly if workers who have suffered an adverse pregnancy event relatively over-report exposures they perceive as hazardous). Meta-estimated RRs were somewhat lower in sensitivity analyses which excluded such studies, as were summary risk estimates for larger better quality studies, and we judge these estimates to be more reliable than those overall.

Most reports emanated from Europe and North America, but findings from developing countries (16 studies, 66 effect

estimates) were broadly similar to those from industrialised economies.

Current balance of evidence

Given the above strengths and limitations, we assess the balance of evidence as follows:

1. For *preterm delivery* findings across a considerable evidence base were generally consistent and effectively rule out large effect sizes (RR \geq 2.0). Well-powered, better studies were less positive than smaller, lower quality studies. Pooled estimates of risk where available pointed at most to only modest effects—for example, excess risks of 2% to 18% with analysis restricted to higher quality reports.
2. For *SGA* the position is similar. Moreover, most meta-estimates, including those from higher quality and larger studies, were close to the null value. Studies on LBW provided somewhat higher effect estimates, but these were fewer in number and lower in quality. Findings on birth weight, similarly, were reported in relatively few studies of limited quality and were mixed in their findings, but again pointing to a limited impact on fetal growth.
3. For *pre-eclampsia and gestational hypertension* the evidence base has barely grown since 2005 and remains too limited to draw firm conclusions. Nonetheless, most estimates pointed to small or null effects.

Although there have been many narrative reviews on work and pregnancy outcomes, few have been systematic and produced meta-estimates of risk. In comparison, however, our earlier analysis¹¹ estimated somewhat higher RRs for preterm delivery in relation to working hours, shift work and standing, with pooled RRs of 1.31, 1.28 and 1.20 overall, and 1.20, 1.26 and 1.26, respectively in the subsets of studies of higher methodological quality. Similarly, for preterm delivery, Mozurkewich *et al*⁹⁹ estimated an RR of 1.26 for prolonged standing and 1.24 for shift and night work.

Implications

Findings to date seem broadly reassuring. Small levels of excess risk may exist, but it is also possible (especially given the smaller estimates from bigger and better studies, and their shrinkage over time, as more data have accumulated), that much or all of these effects are explained by a combination of chance, bias and imperfectly controlled confounding. However, a degree of residual uncertainty will always surround estimation of risks at lower levels and information on risks at extremes of exposure is very limited.

The balance of evidence is against a strong effect of the reviewed activities on the reviewed pregnancy outcomes. At the same time, for none of the exposures examined was there any indication of important beneficial effects. Moreover, given the clinical importance, say, of preterm delivery, a RR of 1.18 (the meta-estimate in better quality studies for working >40 h/week) might equate to 1.2 additional cases (95% CI 0.3 to 2.2) per 100 deliveries to women with that exposure, assuming a background prevalence of singleton live preterm delivery of 6.7%¹⁰⁰ and, if truly present, would be important to avoid. Given residual uncertainties in the evidence base and the apparent absence of benefits, there may be a precautionary case for advising women against long working hours (eg, >40 h/week), prolonged standing (eg, >4 h/day), and heavy physical work, particularly late in pregnancy, at a time in any case when fatigue limits the capacity for high demand duties. This case is not strongly driven by evidence of harm, however, and care should

be taken to avoid causing undue anxiety among patients and their employers.

The need for further research is most evident for pre-eclampsia and hypertension, where studies are few, but somewhat less pressing for preterm delivery and SGA since the database has grown substantially larger over the past few years. A relatively neglected area, deserving of more attention however, concerns the impact of work activities on intrauterine growth trajectory and birth anthropometrics,⁷² given the growing evidence that poorer health in adulthood is predicted by SGA and birth weight and other markers like small head circumference, reduced abdominal girth, thinness at birth, shortness at birth and LBW relative to placental weight.¹⁰¹

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