## Concise guidance: Pregnancy - occupational aspects of management

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**Summary**

Most pregnant women are exposed to some physical activity at work. This guidance is aimed at doctors advising healthy women with uncomplicated singleton pregnancies about the risks arising from five common workplace exposures (prolonged working hours, shift work, lifting, standing and heavy physical workload). The adverse outcomes considered are: miscarriage, preterm delivery, small-for-gestational age, low birthweight, pre-eclampsia and gestational hypertension. Systematic review of the literature indicates that these exposures are unlikely to carry much of an increased risk for any of the outcomes, since small apparent effects may be explicable in terms of chance, bias, or confounding, while larger and better studies yield lower estimated risks than smaller and weaker studies.

In general, patients may be reassured that such work is associated with little, if any, adverse effect on pregnancy. Moreover, moderate physical exercise is thought to be healthy in pregnancy and most pregnant women undertake some physical work at home. The guidelines provide risk estimates and advice on counselling.

**Background**

In the UK, as in most parts of the world, women make up a substantial proportion of the modern workforce (47.6% in spring 20101), with an estimated 350,000 pregnant women working each year.2 Several reproductive hazards associated with work are well established – for example, from ionising radiation and lead – and particular strategies have been developed to manage the associated risks. However, there are other potential workplace hazards for which the scientific evidence is less certain.

Important among these is the possibility that physical activities at work might adversely affect outcomes of pregnancy.3 It has been suggested, for example, that women’s work schedules (including rotating shifts and night-work) can induce neuroendocrine changes as a consequence of sleep deprivation or disrupted circadian rhythms, affecting fetal growth and the timing of parturition. In theory, also, long working hours, prolonged standing, heavy lifting, or unusual workload may pose a number of threats to pregnant workers. The high demand for uterine and placental blood flow in the third trimester could limit reserve capacity for vigorous exercise, while raised noradrenaline levels could increase uterine contractility and thereby the risk of preterm labour. On the other hand, marked physiological adaptations to the demands of pregnancy tend to preserve constant fetal oxygen consumption.

Provision of appropriate information to the pregnant worker is made more difficult because most of the activities of concern (especially physical exertion), while suspected of being hazardous, could also be beneficial, as suggested in other contexts by a number of reviews.4-7 Thus, advice on avoiding work activity might in theory be detrimental and cause needless anxiety.

**Scope of the guidelines**

This guidance is aimed at clinicians advising healthy women with uncomplicated singleton pregnancies about the relative safety of physical factors at work. Women with co-morbidity, or with a previous adverse obstetric history, or complications in the present pregnancy, including multiple pregnancy, should seek specialist advice from their obstetrician or midwife. Further information has also been provided by the National Institute for Health and Clinical Excellence (NICE) and the National Collaborating Centre for Women’s and Children’s Health.8

*Evidence synthesis and rationale*

The evidence synthesis underpinning the present guidelines has been built on, and extends, three previous reviews on occupational activity and pregnancy outcome.3,9,10 It relates to five occupational exposures (working hours, shift work, lifting, standing, and physical workload) all of which are common among women of reproductive age. For example, in 2010, 16% of working women aged 15-39 years undertook shifts in their main job “most of the time”1 and 10% of women in full-time jobs worked more than 40 hours/week.11

The chosen outcomes (miscarriage, preterm delivery, small for gestational age (SGA), low birthweight (LBW), pre-eclampsia and gestational hypertension are important to the health of the fetus, baby and mother. Preterm birth is the most important single determinant of adverse infant outcome in terms of both survival and quality of life.12,13 LBW is a cause of infant morbidity and mortality,14as well as predicting adverse outcomes in later life (eg poorer growth and development, neurological and cognitive deficit, high blood pressure,non-insulin dependent diabetes, coronary heart disease,stroke, obstructive lung disease);15 pre-eclampsia and eclampsia were responsible for 8.4% of maternal deaths in the UK in 2006-8;16 miscarriage can cause enduring psychological distress. As well as being important, these adverse pregnancy outcomes are quite common – 6.7% of live singleton births in hospitals in England during 2010-11 were complicated by prematurity, 6.7% involved gestational hypertension and/or pre-eclampsia, and 6.6% of birthweights were <2,500 gms;17 10-14% of recognised pregnancies end in miscarriage.18

Current EU legislation (92/85, EEC) and the related Management of Health and Safety at Work Regulations 1999 and guidance from the Health and Safety Executive (HSE)19 require employers to assess health and safety risks to pregnant workers, and to control them; but currently, there is limited advice for clinicians who care for healthy pregnant workers.20

*Definitions commonly used in the research supporting these guidelines*

**Preterm delivery** – birth of a living fetus before 37 completed weeks of gestation

**Small for gestational age** – birthweight below the 10th centile on the expected distribution of birthweights by duration of gestation

**Low birthweight** – birthweight <2500 gm

**Pregnancy-induced hypertension** - gestational hypertension (elevation of blood pressure in a previously normotensive woman that occurs after the 20th week of gestation and resolves after delivery) (in the absence of proteinuria)

**Pre-eclampsia** - gestational hypertension with proteinuria and oedema

**Miscarriage** – pregnancy loss after recognition of pregnancy and before the 24th week of gestation\*

**Prolonged standing** - >4 hours/day in total (>6 hours/day for miscarriage)

**Prolonged working hours** - >40 hours/week

**Shift work** – night shift working, evening shift work, rotating shift work. **Fixed night shift work** – work always at night; **three-shift schedule** – a rotational shift pattern involving time worked in blocks, sometimes during the day, sometimes the evening and sometimes at night.

**Heavy lifting & heavy physical workload** – the evidence base in the occupational setting does not permit exact definitions. However, the RCOG advises in relation to sustained exertion that recreational exercise in pregnancy should allow the woman still to conduct a conversation, be “somewhat hard” (i.e. ‘quite an effort/feel tired, but can continue’, on the Borg scale of perceived exertion), should be in a target heart rate range defined by maternal age if aerobic (not >155 beats/minute in 20 year-olds, not >140 beats/minute in >40 year olds), should not precipitate unusual symptoms (eg dizziness, palpitations), and should include warm-up and cool-down phases.23 In relation to ‘heavy lifting’, the HSE does not give specific guidance for pregnant workers , but a "typical" load in studies that provided such detail was about 10-12 kg (a weight that is not uncommonly lifted in the home by pregnant women with toddlers).

*\* Studies used various definitions, ranging from 20 to 28 weeks*

**Guideline development**

Two systematic searches in Medline and EMBASE (January 1966 to June 13th 2012 for miscarriage, January 1966 to December 31st 2011 for other outcomes) identified 112 overlapping reports relating to these work exposures and pregnancy outcomes – 57 reports on preterm delivery, 54 on birthweight, 29 on miscarriage and 11 concerning pre-eclampsia or gestational hypertension. Eligible studies were critically assessed for their completeness of reporting and potential for bias and confounding following previously published methods,9,10 adapted in part from SIGN methodology and elements proposed by Ariens et al21 and van der Windt et al.22 For studies with similar definitions, pooled meta-estimates of relative risk (RR) were calculated, updating earlier computations.9 A multi-disciplinary stakeholders’ group, comprising representatives from obstetrics, midwifery, general practice, general medicine, occupational medicine, the RCP, the trades union movement and the public (a representative from the parents’ charity NCT), formulated these guidelines in light of the evidence. A summary of methods can be found at [**GIVE WEBLINK**].

**Appraisal of the evidence**

The evidence base is extensive for preterm delivery, LBW and SGA, more limited for miscarriage, and very limited for pre-eclampsia and gestational hypertension. It has several strengths: pregnancy outcomes were almost always confirmed from objective sources, most studies were well reported, response rates were typically high and studies were often large. On the other hand, nearly half of reports were potentially affected by confounding or bias and the exposures “occupational lifting”, “physical workload”, and even “shift work”, were not defined uniformly between studies.

Within these limitations (and strengths), findings were broadly reassuring. For preterm delivery, pooled estimates tended to indicate no more than modest elevations in risk (eg RR<1.2 or <1.3 extra case per 100 deliveries to exposed women). The larger and most complete studies reported the smallest levels of risk, suggesting that risk estimates in other studies were inflated by bias. For SGA, meta-estimates were close to the no-effect level. For miscarriage, meta-risk estimates were elevated moderately overall, but generally lower in better quality studies (RR<1.2); higher risks were implied from working fixed night shifts, but in only a small number of studies, each with individual limitations (RR 1.5). For pre-eclampsia and gestational hypertension there were insufficient data to draw firm conclusions, although risks were seldom much elevated.

A table of evidence is presented showing best estimates of the excess risk (per 100 exposed women, together with an assessment of the strength of evidence and statistical uncertainty. In summary, none of the exposures appeared likely to carry much of an increased risk for any of the outcomes. While small levels of excess risk may exist for preterm delivery, SGA, LBW, and miscarriage, it is possible that much or all of these effects arises from a combination of chance, bias and residual confounding. (As detailed in the table, even in the absence of bias or confounding, estimates of effect embrace the possibility of no effect or even a small benefit from many of the activities of interest.)

**Legal position**

Employers have an ongoing duty to assess and control risks to employees’ health and safety arising from their work. They also have a specific obligation in relation to pregnant workers (Management of Health and Safety at Work Regulations 1999), which extends where necessary and feasible to the offer of alternative work or, failing this, medical suspension with pay and job protection (Employment Rights Act 1996). This obligation may require employers to search for suitable alternative daytime work for a pregnant shift worker certified by a doctor or midwife as unfit to work nights.19 According to Directgov,23 lifting, carrying, standing, working hours and shift work bear consideration in employers’ risk assessments of pregnant workers; similarly, HSE cautions that risks can arise from working conditions, including manual handing and working hours.24

**The issues in context**

The evidence base supporting mandatory medical restriction for the work activities covered by this guideline is weak, however. Such advice should not be issued without careful consideration as some women may become anxious and unnecessary avoidance of work may ensue. By inference, also, similar physical activities outside work might seem contraindicated, whereas the Royal College of Obstetricians and Gynaecologists25 and the American College of Obstetricians and Gynaecologists26 recommendthat "all women should be encouraged to participate in aerobic and strength-conditioning exercise as part of a healthy lifestyle during their pregnancy" and that "reasonable goals” of aerobic conditioning should be maintained; these appear to confer physical and psychological benefits (eg reduced fatigue, varicosities, swelling of extremities, insomnia, stress, anxiety and depression, perhaps even length of labour and delivery complications25).

On the other hand, outcomes like preterm delivery can have important health consequences and patients will differ in their understanding and tolerance of uncertainty at apparently low levels of risk. In general the evidence base is reassuring, especially given the potential *disadvantages* of refraining from work activities. Some women may remain clinically anxious and need tailored individual counselling, or a choice, for example, of moving from fixed night working to an alternative work pattern. In any event, many women will need to reduce long working hours, prolonged standing, and heavy physical work, particularly in late pregnancy when physical stamina limits capacity for onerous duties.

**Recommendations**

In relation to healthy uncomplicated singleton pregnancies, the Guideline Development Group recommends that:

**Advising pregnant women**

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| **Grade†** | **Statement** |
| A | Pregnant women can be reassured that current evidence offers no justification for imposing *mandatory* restrictions in relation to their **working hours, shift working, lifting, standing, and physical workload at work** |
| GPP | Pregnant women can be informed that it is uncertain whether or not **long working hours, shiftwork, prolonged standing**, **lifting** and **heavy physical work** increase risks of *preterm delivery*, *SGA*, *miscarriage* and *pre-eclampsia/gestational hypertension* to a small degree. Best estimates generally suggest small increases in risk, but typically the data are also compatible with no effect (or even a small benefit) from work. There may also be *disadvantages* in refraining from work, which need to be considered (see text). Thus, advice on work avoidance should be tailored to each patient’s tolerance of uncertainty at apparently low levels of risk, and the anxiety or otherwise that this engenders. |
| GPP | In communicating risk information to pregnant women, a structured approach is recommended, covering the background level of risk in unexposed women, best estimates of any excess risk with uncertainties (both in the estimate of risk and in the quality of evidence), and any follow-on advice – see [LINK TO ADVICE LEAFLETS]. |
| GPP | Women with an adverse obstetric history or with obstetric risk factors and/or pregnancy complications need to receive individualised advice from their obstetrician or midwife. |
| GPP | Regardless of any potential risks to the fetus, the physiological demands of late pregnancy (after 28 weeks gestation) are such that women may struggle to cope with excessive work demands, such as:   * long working hours (eg >40 hours/week) * shift work * prolonged standing (eg >4 hours/day) * heavy physical work and heavy lifting¶   A good case exists for limiting them, and employers should have regard to making reasonable adjustments to the worker’s job profile. |

**Table of evidence**

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| **Grade†** | **Statement** |
| There may potentially\* be a small increased risk of *preterm delivery* and *miscarriage* from **working for more than 40 hours per week** during pregnancy. | |
| A | The potential\* risk of *preterm delivery* is estimated to be 1.2 extra cases (95%CI 0.3 to 2.2) in every 100 deliveries to women working more than 40 hours a week |
| A | Available evidence does not indicate an increase in risk in relation to *SGA* (-0.1 extra cases (95%CI -1.2 to 1.1) in every 100 deliveries to women working more than 40 hours a week) |
| B | The potential\* risk of *miscarriage* is estimated to be 2.0 extra cases (95%CI -2.4 to 8.5) in every 100 pregnancies to women working more than 40 hours a week |
| There may potentially\* be an increased risk of *miscarriage* and also a very small increased risk of *preterm delivery* from **shift working, including night shift working**. | |
| A | The potential\* risk of *preterm delivery* is estimated to be 0.3 extra cases (95%CI -0.4 to 1.0) in every 100 deliveries to women who work shifts |
| A | Available evidence does not indicate an increase in risk in relation to *SGA* (-0.2 extra cases (95%CI -1.1 to 0.8) in every 100 deliveries to women with that exposure) |
| B | The potential\* risk *of miscarriage* is estimated to be 1.4 extra cases of (95%CI -0.5 to 3.6) in every 100 pregnancies to women working a 3-shift schedule |
| C | The potential\* risk *of miscarriage* is estimated to be 6.1 extra cases (95%CI 3.2 to 9.4) in every 100 pregnancies to women with a fixed night shift schedule |
| There may potentially\* be a small increased risk of *preterm delivery,* *SGA* and of *miscarriage* from **prolonged standing at work**. | |
| A | The potential\* risk for *preterm delivery* is estimated to be 0.9 extra cases (95%CI -0.1 to 1.9) in every 100 deliveries to women undertaking prolonged standing (>4 hours/day) at work |
| A | The potential\* risk for *SGA* is estimated to be 1.6 extra cases (95%CI -0.3 to 3.8) in every 100 deliveries to women undertaking prolonged standing (>4 hours/day) at work |
| C | The potential\* risk for *miscarriage* is estimated to be 1.9 extra cases (95%CI 0.1 to 3.8) in every 100 pregnancies to women undertaking prolonged standing (>6 hours/day) at work |
| There may potentially\* be a very small increased risk of *preterm delivery*, SGA and *miscarriage* from **heavy lifting¶** at work. | |
| B | The potential\* risk is estimated to be 0.1 extra cases (IQR -0.7 to 2.0) of *preterm delivery* in every 100 deliveries to women who undertake heavy lifting at work |
| B | The potential\* risk is estimated to be 0.8 extra cases (IQR 0.4 to 1.6) of *SGA* in every 100 deliveries to women who undertake heavy lifting at work |
| B | The potential\* risk is estimated to be 0.2 extra cases (95%CI -3.2 to 5.3) of *miscarriage* in every 100 pregnancies to women lifting >100 kg per day |
| There may potentially\* be a small increased risk of *preterm delivery* and *miscarriage* among women with a **heavy physical workload¶** at work. | |
| B | The potential\* risk of *preterm delivery* is estimated to be 0.7 extra cases (IQR 0.3 to 1.1) in every 100 deliveries to women with a heavy physical workload |
| B | Available evidence does not indicate an increase in risk in relation to *SGA* (-1.2 extra cases (IQR -1.9 to 0.0) in every 100 deliveries to women with a heavy physical workload) |
| C | The potential\* risk of *miscarriage* is estimated to be 1.4 extra cases (IQR -8.2 to 2.4) in every 100 pregnancies to women with a heavy physical workload) |
| D | Pregnant women can be advised that there is insufficient evidence to draw firm conclusions about the effect of **long working hours, shift work, prolonged standing**, **lifting** and **heavy physical work**, on risks of *pre-eclampsia and gestational hypertension*, although such evidence as exists suggests that risks are probably no more than small |

*95%CI – 95% confidence intervals; IQR – interquartile range; GPP – Good practice point (as advised by the Guideline Development Group)*

\* *Uncertainty in risk estimation reflects both the amount of evidence (and play of chance) and its quality (eg vulnerability to bias or confounding). The* ***numbers*** *capture the effect of chance* ***assuming there is no bias*** *(which may not be so): where a negative number is quoted, risk estimates appear compatible with a benefit from the activity; estimates of uncertainty which straddle 0.0 at their confidence limits (or IQR) may arise by chance in the absence of a true effect. The* ***grading*** *reflects the overall weight, quality and consistency of evidence.*

† *The grading system was adapted from SIGN by the Guideline Development Group: A – a substantial and consistent body of observational evidence at roughly grade 2+, supported by one or several high quality systematic reviews with meta-estimates of effect; B – as A, but without meta-estimates of effect;* ***or*** *as A, but with a fewer, but still reasonably large number of studies; C – a small body of observational evidence at roughly grade 2+ tending in the same direction (with or without accompanying meta-analysis); D – a very small body of observational evidence.*

*Estimated numbers of excess cases per 100 deliveries to exposed women are based where available on meta-estimates from higher quality studies, with 95%CI, and otherwise on the median and IQR across all relevant studies. The estimates assume a prevalence of singleton live preterm delivery of 6.7%,17 a prevalence of SGA of 10% and a prevalence of miscarriage of 12%.27*

*¶ The evidence base does not allow exact definition of heavy lifting or physical workload, but the National Collaborating Centre for Women’s and Children’s* *Health and NICE advise that “beginning or continuing a moderate course of exercise during pregnancy is not associated with adverse outcomes”8*

**Coherence with other advice**

These recommendations are consistent with previous ones issued on behalf of the RCP and NHS Plus in 2009 in relation to the same exposures and outcomes.18 The evidence base supporting them, however, is deeper, allowing firmer conclusions to be drawn.

**Implementation**

No specific issues arise in relation to implementation, as the emphasis will largely be on allaying concerns raised by the patient, rather than some more proactive policy; and the advice recommended carries no resource implications for the advising clinician.

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**References**

1. Labour Force Survey – Quarterly Household Dataset, April – June 2010.
2. Department of Trade and Industry. Work and Parents: Competitiveness and Choice. Research and Analysis, Nov 2000 (as cited at: http://tommys.org/)
3. Mozurkewich EL, Luke B, Avni M, et al. Working conditions and adverse pregnancy outcome: A meta-analysis. Obstet Gynecol 2000;95:623-634
4. Kramer MS, McDonald SW. Aerobic exercise for women during pregnancy. Cochrane Database of Systematic Reviews 2006, Issue 3. Art. No.: CD000180. DOI: 10.1002/14651858.CD000180.pub2.
5. Chasan-Taber L, Evenson KR, Sternfeld B, et al. Assessment of recreational physical activity during pregnancy in epidemiologic studies of birthweight and length of gestation: methodologic aspects. Women Health 2007;45:85–107.
6. Schlussel MM, de Souza EB, Reichenheim ME, et al. Physical activity during pregnancy and maternal-child health outcomes: a systematic literature review. Cad Saude Publica. 2008;24(Suppl 4):531–44.
7. Lagerros YT. Physical activity—the more we measure, the more we know how to measure. Eur J Epidemiol 2009;24:119–22.
8. National Institute for Health and Clinical Excellence. Antenatal care. Routine care for the healthy pregnant woman. NICE clinical guideline 62. March 2008. <http://www.nice.org.uk/nicemedia/pdf/CG062NICEguideline.pdf>
9. Bonzini M, Coggon D, Palmer KT. Risk of prematurity, low birth weight, and pre-eclampsia in relation to working hours and physical activities: A systematic review, Occup Environ Med 2007; 64: 228-243.
10. Bonzini M, Palmer KT, Coggon D, et al. Shift work and pregnancy outcomes: a systematic review with meta-analysis of currently available epidemiological studies. BJOG 2011; 118: 1429-1437.
11. Annual Survey of Hours and Earnings, 2010 <http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-238620> (Table 1).
12. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. Lancet 2008;371:261–9.
13. Costeloe K, EPICure Study Group. EPICure: facts and figures: why preterm labour should be treated. BJOG 2006; 113 Suppl 3:10-2.
14. Moser K, Li L, Power C. Social inequalities in low birth weight in England and Wales: trends and implications for future population health. J Epidemiol Community Health 2003;57:687-91
15. Barker DJB, ed. Fetal and infant origins of adult disease. London: BMJ Publishing Group, 1992.
16. Centre for Maternal and Child Enquiries (CMACE). Saving Mothers Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom, BJOG 2011;118 (Suppl. 1) 1-203.
17. Hospital Episode Statistics 2011.Table 22: Complications recorded in the pregnancy episode, 2010-11, NHS Hospitals, England; Table 28: Singleton and multiple deliveries by birth weight and birth status, 2010-11, NHS Hospitals, England.
18. Wilcox A. Fertility and pregnancy – an epidemiological perspective. Oxford University press, 2010.
19. Health and Safety Executive. New and expectant mothers: the law. HSE. <http://www.hse.gov.uk/mothers/law.htm>
20. RCP-NHS Plus. Physical and shift work in pregnancy: Occupational aspects of management. A national guideline. RCP, 2009, ISBN 978-1-86016-353-1.
21. Ariens G, van Mechelen W, Bongers PM, et al. Physical risk factors for neck pain. Scand J Work Environ Health 2000;26:7–19.
22. Van der Windt DAWM, Thomas E, Pope DP, et al. Occupational risk factors for shoulder pain: a systematic review. Occup Environ Med 2000;57:433–42.
23. Directgov. Working when pregnant: health and safety for pregnant employees. <http://www.direct.gov.uk/en/Parents/Moneyandworkentitlements/WorkAndFamilies/Pregnancyandmaternityrights/DG_10026556>
24. Health and Safety Executive. New and expectant mothers. FAQ. http://www.hse.gov.uk/mothers/faqs.htm
25. Royal College of Obstetricians and Gynaecologists. Exercise in pregnancy. Statement No 4, January 2006. <http://www.rcog.org.uk/files/rcog-corp/Statement4-14022011.pdf>
26. Artal R, O'Toole M. Guidelines of the American College of Obstetricians and Gynaecologists for exercise during pregnancy and the postpartum period. Br J Sports Med 2003; 37:6-12.
27. Regan L, Braude PR, Trembath PL. Influence of past reproductive performance on risk of spontaneous abortion. BMJ 1989; 299:541-5.