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Occupational factors and risk of preterm birth in nurses

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Abstract

Objective—We evaluated the risk of first-trimester exposures among nurses and the risk of preterm birth among participants of the Nurses' Health Study II.

Study Design—Log binomial regression was used to estimate the relative risk (RR) for preterm birth in relation to occupational risk factors, adjusting for age, parity, work schedule, physical factors, and exposures to chemicals and x-rays.

Results—Part-time work (<= 20 hours a week) was associated with a lower risk for preterm birth [RR=0.7, 95% confidence interval (CI) = 0.6–0.9]. Self-reported exposure to sterilizing agents was associated with an increased risk (RR=1.9, 95% CI = 1.1–3.4). Other exposures, including shift work, physical factors, anesthetic gases, antineoplastic drugs, antiviral drugs, and x-ray radiation were not associated with risk of preterm birth.

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Conclusions—These data suggest that sterilizing agents may be related to preterm birth, while physically demanding work and work schedule are not strong predictors.

Keywords

Nurses; Occupational Exposure; Pregnancy; Preterm Birth; Work Schedule Tolerance

INTRODUCTION

In the United States, over 2.5 million nurses are employed and approximately half of them are women of reproductive age.[1] Nurses work in a unique occupational environment that can require rotating and night shifts, long hours, prolonged standing, heavy lifting, and exposure to chemicals and x-ray radiation. Several papers have reviewed the occupational exposures of health care workers, suggesting that reproductive health issues continue to be of concern to nurses.[2,3,4] Despite other advances in obstetric care, the rate of preterm birth in the U.S. has risen approximately 30% in the past two decades,[5] and preterm birth is one of the leading causes of neonatal morbidity and mortality.[6] We investigated the association between occupational exposures and the risk of preterm delivery among participants of the Nurses' Health Study II.

METHODS

Study Population

The Nurses' Health Study II is a national cohort study of 116,608 U.S. female nurses aged 25 to 42 at enrollment, established in 1989.[7] Follow-up questionnaires are mailed every two years. On the 2001 biennial questionnaire, participants were asked if they: 1) had a pregnancy since 1993; 2) worked as a nurse during the most recent of these pregnancies; and 3) would be willing to participate. An occupational supplement was mailed to women who answered yes to all three questions.[8]

Of 101,281 respondents to the 2001 biennial questionnaire, 11,177 (11%) had a pregnancy since 1993 during which they worked as a nurse. Of these women, 9,547 (85%) indicated willingness to participate; 645 (6%) declined; and 985 (9%) did not answer the question about the supplemental survey. Of the 9,547 women who were mailed the supplemental questionnaire, 8,461 responses were received (89%), resulting in an overall participation rate of 76%. Women were excluded if their pregnancy ended in a spontaneous (n=826) or induced (n=147) abortion, ectopic pregnancy (n=62), molar pregnancy (n=13), multiple pregnancy (n=236 twin/triplet pregnancy), or stillbirth (n=42). Pregnancies with incomplete data were also excluded, such as missing data on pregnancy outcome (n=34), the year the pregnancy ended (n=10), or the length of the pregnancy (n=22). In addition, women were excluded if they reported working less than one hour per week, on average, during the first trimester (n=54). Missing information for hours worked, lifting, and standing, that resulted in missing cells for analysis, also resulted in exclusion (n=38). In total, 1,484 women were excluded, leaving 6,977 live births available for analysis.

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Data Collection

Trimester-specific occupational exposures and activities included work schedule (days only, evenings only, nights only, rotating with nights, rotating without nights, other/didn't work); night work (none, 1–2 nights/month, 3–4 nights/month, 2–3 nights/week, 4+ nights/week); and average hours worked per week during each trimester (none, 1–20 hours/week, 21–40 hours/week, 41–60 hours/week, 61+ hours/week). Night shift was defined as most of work hours falling between midnight and 8 am. Because relatively few women worked 61 or more hours per week (n=33), we combined this group with the women who worked 41–60 hours per week. We combined the work schedule data with information about night shifts to form the following mutually exclusive categories: days only (reference), days/evenings with no nights, rotating shifts with nights, and nights only.

Other occupational data included how often during the average day the respondent lifted 25 pounds or more at work (never, 1–5 times/day, 6–15 times/day, 16–30 times/day, 31+ times/day); hours per day of standing or walking at work (< 1 hour/day, 1–4 hours/day, 5–8 hours/day, 9+ hours/day); and hours per day of exposure to anesthetic gases, antineoplastic drugs, antiviral drugs, sterilizing agents, or x-ray radiation (0, 1–4, 5–8, 9+ hours). Because first trimester exposures predated both pregnancy complications that might affect gestation length and the outcome of preterm birth, we used data from the first trimester as our primary time period of interest.

Data on risk factors for preterm birth, such as previous preterm deliveries, gestational high blood pressure or pre-eclampsia (toxemia), and trimester-specific data on smoking, caffeine, and alcohol consumption were collected. Spontaneous delivery and delivery induced after “water broke but labor didn't progress” were classified as spontaneous births. From the main biennial cohort questionnaire, data were available on maternal age, race/ethnicity, height and weight, history of spontaneous abortion, parity, and medication use.

Gestational age was collected categorically as completed weeks since last menstrual period (LMP) [less than 8; 8 to 11; 12–19; 20–23; 24–27; 28–31; 32–36; 37–41 (term); and 42 or more]. Preterm birth was defined as a pregnancy lasting less than 37 weeks from LMP.

Statistical Analysis

Age-adjusted means and prevalence of selected maternal characteristics were calculated. We examined the relationship between first-trimester work schedule, physical factors, and exposure to chemicals and x-rays and preterm birth in univariate and multivariate analyses. We first considered the associations of individual occupational exposures with risk of preterm birth, adjusted for age and parity. Our full multivariate model included all work factors adjusted for each other and age and parity. When lifestyle and other factors, such as cigarette smoking, coffee, soda, tea, and alcohol consumption, and height or BMI were included in the multivariate model, no notable variation in the point estimates of the occupational exposures was observed, so these variables were not included in the full multivariate models. For exposure variables that were missing data, including reported exposure to anesthetic gases, anticancer drugs, antiviral drugs, sterilizing agents, and x-ray radiation, a “missing” indicator was created and analyzed as a category within each variable.

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To calculate trend, the midpoint of each reporting category was used to create continuous variables.

We used log binomial regression; relative risk estimates were computed using PROC GENMOD in SAS with the binomial distribution and log link.[9,10] We modeled age as a continuous variable. Parity was defined dichotomously as ever or never having delivered a live born child. The study was approved by the Institutional Review Board of the Brigham and Women's Hospital.

RESULTS

Among 6,977 pregnancies ending in singleton live births during which the mother reported working as a nurse during the first trimester, 588 (8%) delivered before the 37th week from LMP. Of those who reported preterm birth, 524 (89%) delivered between 32 and 36 weeks from LMP, 47 (8%) between 28 and 31 weeks, 15 (3%) between 24 and 27 weeks, and 2 (0.3%) between 20–23 weeks. Delivery was induced in 40% of the study pregnancies. The prevalence of preterm birth was 9% for spontaneous births and 8% for induced births.

Table 1 shows selected characteristics of the study population during the first trimester, including occupational exposures, for pregnancies ending in preterm birth and full-term birth, standardized by maternal age. As expected, a lower percentage of preterm birth mothers were parous, and parous preterm birth mothers were more likely to have a history of preterm birth in a previous pregnancy.

Table 2 provides the estimated relative risks for preterm birth for occupational factors. In the reduced models, we analyzed each individual work factor separately, adjusting for age and parity. The full multivariate model included all work factors together, as well as age and parity. Most occupational work exposures were not associated with risk of preterm birth, with a few exceptions described below.

Working rotating shifts or nights was not associated with the risk of preterm birth. Women who reported working part-time (20 or less hours per week) during the first trimester were 30% less likely to have a preterm birth [risk ratio (RR) for the full model = 0.7, 95% confidence interval (CI) = 0.6–0.9], compared to women who worked 21–40 hours per week. Although the test for trend was statistically significant for hours worked (p=0.01), there was no association between working overtime (41+ hours per week) and risk of preterm birth. Heavy lifting and prolonged standing or walking were moderately associated with the risk of preterm birth in the reduced models, but not in the full model.

Women who reported exposure to sterilizing agents for five or more hours per day had a near doubling in risk of preterm birth compared to women exposed to less than one hour per day, even after adjusting for other occupational factors in the full model (RR =1.9, 95% CI = 1.1–3.4; test for trend p-value = 0.04)) (table 2). Self-reported exposure to anesthetic gases and x-ray radiation were not associated with preterm birth in the full model. Similarly, no association with preterm birth was observed for self-reported exposure to anti-cancer or anti-viral drugs (data not shown). Data from the 2nd and 3rd trimesters showed similar results.

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Though preterm birth can result from induction of delivery for medical reasons, restricting the analysis to the 4,068 spontaneous deliveries (table 2) did not change the results. Maternal high blood pressure / toxemia was associated with an increased risk for preterm birth (RR=2.2, 95% CI=1.8–2.6), though controlling for hypertensive disorders did not materially change the relative risks associated with the occupational factors.

A stratified analysis by history of previous preterm birth among parous women (n=5,603, after exclusions for missing data) revealed a higher percentage of preterm birth in those with a previous preterm birth (25% versus 5%), as expected (data not shown). However, associations of occupational exposures with risk of preterm birth were similar between the two groups. Although not statistically significant, the only notable difference was that women with a previous preterm birth who worked more than 40 hours per week had a 30% increased risk for current preterm birth, compared with women who worked 21–40 hours (RR=1.3, 95% CI=1.0–1.8). In contrast, parous women with no history of prior preterm birth had no increased risk associated with working long hours.

We conducted a sub-analysis of the 64 cases that were born before 32 weeks gestation, using continuous variables (the midpoint of each category) for hours worked, times lifted, and hours of exposure to standing, sterilizing agents, anesthetic gases, and x-rays. Women who reported working nights had a significant increase in risk of early preterm delivery (RR=3.0, 95% CI = 1.4–6.2), after adjusting for age, parity, and other work factors. The results showed no association with narrow confidence intervals for hours worked, lifting, and standing, and no association with wider confidence intervals for reported exposure to sterilizing agents, anesthetic gases, and x-rays (results not shown).

We did not collect information on socio-economic status at the time of the pregnancy, though adjustment for the following variables collected on the biennial questionnaires did not change our results: annual household income, husband’s or partner’s education, or whether the nurse was ever married.

COMMENT

In this large cohort of nurses, women who worked part-time had a lower risk of delivering preterm, though there was not a clear dose-response relationship with overtime hours. The risk of preterm birth was moderately associated with reported exposure to sterilizing agents, while prolonged standing and heavy lifting were weak predictors of preterm birth. The risk of preterm birth was not associated with other work exposures common to nurses, including rotating shift work, night work, x-ray radiation or other chemical exposures.

Strengths and Weaknesses

Our study is limited by the self-reported nature of our data collection. Nurses are well-educated health professionals, however, who are presumably more sensitized to health events than the general population. Moreover, the recall period was relatively short (≤ eight years). Several validation studies have shown that Nurses’ Health Study participants self-report health data accurately, including current and past body habitus, ovulatory infertility, surgical menopause, hypertension, hyperlipidemia, and other factors.[7, 11–14] There is still

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potential for recall bias due to the assessment of pregnancy outcome and occupational exposures on the same questionnaire; however, the fact that we observed associations for some, but not all exposures argues against a blanket recall bias.

Compared to the previous studies we reviewed, our study has a higher sample size than most, allowing for multivariate analyses of several exposure outcome relationships. Another strength of this study is that by examining a national sample of U.S. nurses, socioeconomic variability and differences in working conditions were minimized and the likelihood of working rotating or night shifts was increased, as compared to other studies of women working in heterogeneous occupations. One other previous study examined a national sample of U.S. nurses,[15] similar to our study in that it was a retrospective design with a self-administered questionnaire. However, their study was a case-control design, and our study had more preterm cases (588 versus 210), had a higher participation rate than their study (76% versus 42%), and we were able to adjust each occupational exposure for other correlated occupational risk factors. That study showed positive associations between preterm and shift work, hours spent standing, and long working hours; although comparison with our study is not straightforward as that study did not present adjusted results for shift work or standing.[15]

We did not collect information on the specific sterilizing agents or other chemicals to which the nurses in our study were exposed, and we have no information on what protective measures may have been used to limit exposure. The maternal age range should be noted in that these results may not be generalizable to women under the age of 29. Because of these limitations, and because there is a dearth of published studies to support our findings on sterilizing agents and other chemical exposures and preterm birth, we recommend a cautious interpretation until future studies can examine these relationships more thoroughly. A pilot study is currently underway to assess the feasibility of conducting a web-based cohort study of younger nurses that will collect detailed prenatal occupational exposure data to allow prospective examination of occupational exposures and pregnancy outcomes.

It is possible that there was a healthy worker survivor effect in our study, in that women who had healthier pregnancies were more able to perform heavy lifting or prolonged standing throughout their pregnancies. We tried to minimize this effect by analyzing data on occupational exposures during the first trimester, so that bed rest or other restrictions would be less likely to have resulted in under-reporting of occupational exposures.

The overall prevalence of preterm birth among singleton pregnancies in our study is similar to the United States national prevalence (1993 to 2001) among women of similar age and race.[16] Established risk factors related to preterm birth include infection, inflammation, multiple births, hypertension, low pre-pregnancy BMI, the extremes of maternal age, incompetent cervix, history of prior preterm birth, and cigarette smoking.[17,18] In our study we were able to account for all of these risk factors except infection, inflammation, and incompetent cervix. It seems unlikely that these factors would have varied by exposure group.

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Strengths and Weaknesses in Relation to Other Studies

The lack of a strong association between physical work demands and risk of preterm birth in this study is consistent with most previous studies, including two recent meta-analyses.[15, 19–30]. While it has been suggested that heavy lifting may provoke uterine contractions by increasing intra-abdominal pressure,[31] the evidence from our and previous studies does not support an associated increase in risk of preterm births, when adjusting for other occupational risk factors. A standing posture during the third trimester in pregnancy has been found to result in compressed pelvic vessels and a reduction in venous blood flow, resulting in uterine contractions.[32]

We saw no significant increased risk for preterm birth among women who reported working rotating shifts or nights. However, women who worked nights were at a three-fold increased risk of delivering early preterm (less than 32 weeks gestation), which is consistent with the results of our spontaneous abortion analysis.[8] Results from previously published studies are conflicting with respect to shift work. Two meta-analyses analyzing work schedule and preterm birth report modest increased risks of 20% associated with rotating shift work or night work.[19, 20] However, individual studies report widely varying results, with relative risks ranging from 0.7 to 5.6 for night or rotating shift work, possibly due to inconsistent definitions of work schedule and insufficient sample sizes in the night or shift work categories.[24, 26, 27, 29, 33, 34, 35]

In our study, women who worked part-time had a decreased risk of preterm birth, though long working hours were associated with increased risk only among parous women with a history of previous preterm birth. Though there was a statistically significant trend for working hours (p-value = 0.01), it's possible that a threshold effect occurred at 20 to 40 hours. Long working hours are related to increased stress and fatigue due to less time to recover from work.[36,37] Though the categorical definitions of hours worked per week varied, previous studies showed modest, if any, increases in risk, and most failed to show a dose-response relationship,[19–21,26–29,33] except one study of U.S. nurses.[15]

Reported exposure to sterilizing agents was associated with a 90% increase in risk of preterm birth in our study, though based on few exposed women. Our questionnaire listed glutaraldehyde, formaldehyde, and ethylene oxide as examples. These chemicals are used to sterilize medical equipment and surgical instruments. Though previous studies have examined spontaneous abortion and birth defects,[38,39] we are aware of only one study that analyzed preterm birth.[40] In that study, dental assistants exposed to ethylene oxide were at an increased risk of preterm birth (age-adjusted RR= 2.7, 95% CI 0.8–8.8). However, that study had several limitations, including few exposed pregnancies and lack of power to adjust for major confounders, such as parity, and the authors speculated that chemical exposures could disturb the feedback mechanism between mother and fetus and thus, increase preterm birth.

Our study showed no effect on preterm birth for reported exposure to anesthetic gases, antineoplastic drugs, antiviral drugs, or radiation. Many anticancer drugs are recognized genotoxic and carcinogenic chemicals,[41] and the adverse reproductive effects of cytotoxic drugs have been well-characterized.[2]

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In summary, our study found that shift work and physical factors were not strong predictors of preterm birth and part-time work was inversely associated with preterm birth. A suggestive new finding is the association between reported exposure to sterilizing agents and preterm birth. This finding, however, is based on few exposed cases, and future research is needed to confirm the association.

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Table 1

Characteristics of participants during the first trimester of pregnancy.

Characteristic	Preterm Delivery		Full-Term	
	n = 588	%[a]	n = 6,389	%[a]
Maternal age mean, range (SD)	36.5, 29–47 (3.4)		36.4, 29–50 (3.4)	
Maternal age categories				
< 30	15	2.6	170	2.7
31–35	218	37.1	2496	39.1
36–40	289	49.2	2941	46.0
40+	66	11.2	782	12.2
Mean prepregancy BMI,[b] range (SD)	24.3, 17–48 (5.0)		24.2, 15–50 (4.8)	
Mean height (inches), range (SD)	65.0, 52–72 (2.7)		65.0, 50–83 (2.6)	
Race				
Asian	13	2.3	109	1.7
African American	8	1.4	38	0.6
Caucasian	538	93.2	5939	94.6
Hispanic	10	1.8	94	1.5
Other	8	1.3	98	1.6
Parous	427	72.7	5304	83.0
Previous preterm delivery[c]	175	42.0	535	10.3
First trimester lifestyle exposures				
2+ Caffeinated coffee per day[d]	56	9.4	658	10.3
2+ Caffeinated soda or tea /day[d]	70	11.9	685	10.7
1+ Alcoholic beverage per week[e]	33	5.6	302	4.7
Smoked cigarettes	40	6.8	370	5.8
First trimester work schedule				
Shift				
Days only	409	69.4	4330	67.8
Nights only	52	8.9	544	8.5
Rotating shifts including nights	35	6.0	417	6.5
Evenings or Day / Evening rotating no nights	91	15.5	1078	16.9
Missing	1	0.2	20	0.3
Hours worked (hours / week)				

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Characteristic	**Preterm Delivery**		**Full-Term**	
	n = 588	**%[a]**	**n = 6,389**	**%[a]**
1–20	101	17.3	1665	26.1
21–40	371	63.1	3642	57.0
41+	116	19.7	1082	16.9
First trimester physical work demands				
Lifting (times / day)[f]				
<1	208	35.4	2411	37.7
1–5	239	40.7	2586	40.5
6–15	105	17.9	1126	17.6
16+	36	6.1	266	4.2
Standing (hours / day)				
0–4	168	28.6	2031	31.8
5–8	269	45.6	3035	47.5
9+	151	25.8	1323	20.7
First trimester chemical and x-ray exposures				
Anesthetic gases (hours / day)				
<1	524	89.1	5843	91.5
1–4	23	3.9	217	3.4
5+	39	6.6	312	4.9
Missing	2	0.3	17	0.3
Anti-cancer drugs (hours / day)				
<1	566	96.3	6122	96.1
1+	22	3.7	248	3.9
Anti-viral drugs (hours / day)				
<1	556	94.8	5986	94.3
1+	30	5.2	360	5.7
Sterilizing agents (hours / day)				
<1	521	88.6	5841	91.4
1–4	45	7.6	408	6.4
5+	11	1.9	50	0.8
Missing	11	1.9	90	1.4
X-ray radiation (hours / day)				
<1	486	82.8	5465	85.5
1+	96	16.2	879	13.8
Missing	6	1.0	45	0.7

[a]Percentages of all variables except for age, BMI, and height are directly standardized by year of age at pregnancy

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[b] Body Mass Index (kg/m^2) prior to the pregnancy

[c] Among women with a previous pregnancy lasting at least 20 weeks

[d] Servings of caffeinated beverages = 8 oz coffee, 12 oz soda, 8 oz hot tea, 16 oz iced tea

[e] Servings of alcoholic beverages = 12 oz beer, 6 oz wine, 1 oz liquor

[f] Lifting refers to lifting or moving a physical load of 25 pounds or more, including repositioning or transferring patients

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Table 2

Association between preterm delivery and work factors during the first trimester for participants, adjusted for age and parity

First Trimester Occupational Factors	Risk Ratio (95% Confidence Interval)		
	Reduced Models[a]	Full Model[b]	Full Model, Excluding Medically-Indicated Preterm Births[c]
Shift			
Days only (reference)	1.0	1.0	1.0
Rotating day/evening (no nights)	1.0 (0.8–1.2)	1.0 (0.8–1.3)	1.0 (0.7–1.3)
Nights only	1.1 (0.8–1.4)	1.0 (0.8–1.4)	1.1 (0.8–1.5)
Rotating shifts including nights	0.9 (0.7–1.3)	0.8 (0.6–1.2)	0.7 (0.5–1.1)
Hours worked (hours / week)			
1–20	0.7 (0.5–0.8)	0.7 (0.6–0.9)	0.7 (0.6–1.0)
21–40 (reference)	1.0	1.0	1.0
41+	1.0 (0.8–1.2)	1.0 (0.8–1.2)	1.0 (0.8–1.4)
p for trend[d]	0.003	0.01	0.04
Lifting (times / day)[e]			
<1 (reference)	1.0	1.0	1.0
1–5	1.1 (0.9–1.3)	1.0 (0.8–1.2)	1.1 (0.8–1.4)
6–15	1.1 (0.9–1.4)	1.0 (0.7–1.2)	1.0 (0.7–1.4)
16+	1.5 (1.1–2.1)	1.2 (0.9–1.7)	1.2 (0.8–2.0)
p for trend[d]	0.02	0.3	0.2
Standing or walking (hours / day)			
0–4	0.9 (0.8–1.1)	0.9 (0.8–1.2)	1.0 (0.7–1.2)
5–8 (reference)	1.0	1.0	1.0
9+	1.3 (1.0–1.5)	1.2 (1.0–1.5)	1.3 (1.0–1.7)
p for trend[d]	0.03	0.2	0.09
Anesthetic gases (hours / day)[f]			
<1 (reference)	1.0	1.0	1.0
1–4	1.2 (0.8–1.8)	1.1 (0.8–1.7)	1.2 (0.7–2.0)
5+	1.3 (1.0–1.8)	1.1 (0.8–1.6)	1.2 (0.8–1.9)
p for trend[d]	0.07	0.6	0.4
Sterilizing agents (hours / day)[f]			
<1 (reference)	1.0	1.0	1.0
1–4	1.2 (0.9–1.6)	1.1 (0.8–1.5)	1.1 (0.7–1.6)

First Trimester Occupational Factors	Risk Ratio (95% Confidence Interval)		
	Reduced Models[a]	Full Model[b]	Full Model, Excluding Medically-Indicated Preterm Births[c]
5+	2.2 (1.3–3.7)	1.9 (1.1–3.4)	1.7 (0.7–3.8)
p for trend[d]	0.003	0.04	0.2
X-ray radiation (hours / day)[f]			
<1 (reference)	1.0	1.0	1.0
1+	1.2 (1.0–1.5)	1.0 (0.8–1.3)	1.0 (0.7–1.3)
p for trend[d]	0.4	0.5	0.4

[a]These models test associations for each work factor separately, adjusted for age and parity

[b]In this model each work factor was adjusted for the remaining work factors, as well as age and parity

[c]Excluded 216 medically indicated preterm births, as well as 11 preterm births with missing information type of delivery.

[d]To test for trend in the reduced models, the work factor was modeled continuously, adjusting for age and parity. In the full model, each work factor was modeled continuously while adjusting for the remaining categorical work factors, age, and parity.

[e]Lifting refers to lifting or moving a physical load of 25 pounds or more, including repositioning or transferring patients

[f]Categories for missing data are included in the analysis for these variables; data not shown

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