

## OBSTETRICS

## Occupational factors and risk of preterm birth in nurses

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**OBJECTIVE:** We evaluated first-trimester exposures and the risk of preterm birth in the most recent pregnancy of 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, such as work schedule, physical factors, and exposures to chemicals and x-rays, adjusted for age and parity.

**RESULTS:** Part-time work ( $\leq 20$  hours a week) was associated with a lower risk of preterm birth [RR, 0.7; 95% confidence interval [CI], 0.6-0.9]. Working nights was associated only with early preterm birth

(< 32 weeks of gestation) (RR, 3.0; 95% CI, 1.4-6.2). Although based on only 11 exposed preterm cases, self-reported exposure to sterilizing agents was associated with an increased risk (RR, 1.9; 95% CI, 1.1-3.4).

**CONCLUSION:** These data suggest that night work may be related to early but not late preterm birth, whereas physically demanding work did not strongly predict risk.

**Key words:** nurses, occupational exposure, pregnancy, preterm birth, work schedule tolerance

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In the United States, more than 2.5 million registered nurses are employed, and approximately half of them are women of reproductive age.<sup>1</sup> 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

### ★ EDITORS' CHOICE ★

occupational exposures of health care workers, suggesting that reproductive health issues continue to be of concern to nurses.<sup>2-4</sup> Despite other advances in obstetric care, the rate of preterm birth in the United States has risen approximately 30% in the past 2 decades,<sup>5</sup> and

preterm birth is 1 of the leading causes of neonatal morbidity and mortality.<sup>6</sup> We investigated the association between occupational exposures and the risk of preterm delivery among participants of the Nurses' Health Study II.

### MATERIALS AND METHODS

#### Study population

The Nurses' Health Study II is a national cohort study of 116,608 US female nurses aged 25-42 years at enrollment, established in 1989.<sup>7</sup>

Follow-up questionnaires are mailed every 2 years. On the 2001 biennial questionnaire, participants were asked whether 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 3 questions to assess occupational exposures during the most recent pregnancy since 1993.<sup>8</sup>

Of 101,281 respondents to the 2001 biennial questionnaire, 11,177 (11%) had at least 1 pregnancy since 1993 during which they worked as a nurse. Of these women, 9547 (85%) indicated willingness to participate; 645 (6%) declined; and 985 (9%) did not answer the ques-

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tion about the supplemental survey. Of the 9547 women who were mailed the supplemental questionnaire, 8461 responses were received (89%), resulting in an overall participation rate of 76%. The study was conducted in California, Connecticut, Indiana, Iowa, Kentucky, Massachusetts, Michigan, Missouri, New York, North Carolina, Ohio, Pennsylvania, South Carolina, and Texas.

Women were excluded if their most recent 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 1 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 6977 women included in the analysis. Because we collected data related to the most recent pregnancy, only 1 pregnancy per woman was included.

### Data collection

Trimester-specific occupational exposures and activities included work schedule (days only, evenings only, nights only, rotating with nights, rotating without nights, other/did not work); night work (none, 1-2 nights/month, 3-4 nights/month, 2-3 nights/week,  $\geq 4$  nights/week); and average hours worked per week during each trimester (none, 1-20 hours/week, 21-40 hours/week, 41-60 hours/week,  $\geq 61$  hours/week). Night shift was defined as most of work hours falling between midnight and 8:00 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, or 31 or more times/day); hours per day of standing or walking at work (< 1 hour/day, 1-4 hours/day, 5-8 hours/day, or  $\geq 9$  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, or  $\geq 9$  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 preeclampsia (toxemia), and trimester-specific data on smoking, caffeine, and alcohol consumption were collected. Spontaneous delivery and delivery induced after "water broke but labor did not 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) (< 8; 8-11; 12-19; 20-23; 24-27; 28-31; 32-36; 37-41 [term]; and  $\geq 42$ ). Preterm birth was defined as a pregnancy ending before 37 completed weeks from LMP. These data were collected categorically, and therefore, early preterm birth was defined as 20 to less than 32 weeks' gestation.

### 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 body mass index (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. To calculate trend, the midpoint of each reporting category was used to create continuous variables.

Because the parameter of interest in these analyses is the risk ratio, we calculated the risk ratio directly using log binomial regression models, rather than using the odds ratio to approximate risk.<sup>9</sup> Relative risk estimates were computed using PROC GENMOD in SAS (SAS Institute, Cary, NC) with the binomial distribution and log link.<sup>10</sup>

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 6977 pregnancies ending in singleton live births during which the mother reported working as a nurse in 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 medically indicated in 40% of the study pregnancies. The prevalence of preterm birth was 9% for

spontaneous births and 8% for medically indicated 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 an elevated risk of preterm birth, with a few exceptions described in the following text.

Working rotating shifts or nights was not associated with the risk of preterm birth, overall. Women who reported working part time ( $\leq 20$  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 with women who worked 21-40 hours per week. Although the test for trend was statistically significant for hours worked ( $P = .01$ ), there was no association between working overtime ( $\geq 41$  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.

Although the study was based on few exposed women, nurses who reported exposure to sterilizing agents for 5 or more hours per day had a near doubling in risk of preterm birth, compared with women exposed to less than 1 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  $P = .04$ ) (**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-re-

**TABLE 1**  
**Characteristics of participants during the first trimester of pregnancy**

Characteristic	Preterm delivery		Full-term	
	n = 588	% <sup>a</sup>	n = 6389	% <sup>a</sup>
Maternal age, y, mean, range (SD)	36.5, 29-47 (3.4)		36.4, 29-50 (3.4)	
Maternal age categories, y				
$\leq 30$	15	2.6	170	2.7
31-35	218	37.1	2496	39.1
36-40	289	49.2	2941	46.0
$\geq 40$	66	11.2	782	12.2
Mean prepregnancy BMI, range (SD) <sup>b</sup>	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	91.4	5939	93.0
Hispanic	10	1.7	94	1.5
Other	8	1.3	98	1.5
Missing	11	1.9	111	1.7
Parous	427	72.7	5304	83.0
Previous preterm delivery <sup>c</sup>	175	42.0	535	10.3
First-trimester lifestyle exposures				
$\geq 2$ cups caffeinated coffee per day <sup>d</sup>	56	9.4	658	10.3
$\geq 2$ cups caffeinated soda or tea per day <sup>d</sup>	70	11.9	685	10.7
$\geq 1$ alcoholic beverage per week <sup>e</sup>	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 (h/wk)				
1-20	101	17.3	1665	26.1
21-40	371	63.1	3642	57.0
$\geq 41$	116	19.7	1082	16.9

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ported exposure to anticancer or antiviral drugs (data not shown). Data from the second and third trimesters showed similar results.

Because preterm birth can result from medically indicated delivery, we conducted a subanalysis that excluded the 227 preterm births that were not sponta-

**TABLE 1**  
**Characteristics of participants during the first trimester of pregnancy (continued)**

Characteristic	Preterm delivery		Full-term	
	n = 588	% <sup>a</sup>	n = 6389	% <sup>a</sup>
First-trimester physical work demands				
Lifting (times/d) <sup>f</sup>				
< 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 (h/d)				
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 (h/d)				
< 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
Anticancer drugs (h/d)				
< 1	566	96.3	6122	95.8
≥ 1	22	3.7	248	3.9
Missing	0	0	19	0.3
Antiviral drugs (h/d)				
< 1	556	94.5	5986	93.7
≥ 1	30	5.2	360	5.6
Missing	2	0.3	43	0.7
Sterilizing agents (h/d)				
< 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 (h/d)				
< 1	486	82.8	5465	85.5
≥ 1	96	16.2	879	13.8
Missing	6	1.0	45	0.7

<sup>a</sup> Percentages of all variables except for age, BMI, and height are directly standardized by year of age at pregnancy. <sup>b</sup> BMI (kilograms per square meter) prior to the pregnancy. <sup>c</sup> Among women with a previous pregnancy lasting at least 20 weeks.

<sup>d</sup> Servings of caffeinated beverages = 8 oz coffee, 12 oz soda, 8 oz hot tea, 16 oz iced tea. <sup>e</sup> Servings of alcoholic beverages = 12 oz beer, 6 oz wine, 1 oz liquor. <sup>f</sup> Lifting refers to lifting or moving a physical load of 25 pounds or more, including repositioning or transferring patients.

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neous deliveries (Table 2). The association between 9 or more hours of standing and risk of preterm birth was somewhat more pronounced and still of borderline statistical significance. The effect of sterilizing agents on the risk of preterm birth was attenuated, although based on only 6 exposed cases of preterm birth. All other results were similar to our main analysis.

We conducted a subanalysis 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).

Although controlling for hypertensive disorders did not materially change the relative risks associated with the occupational factors, maternal high blood pressure/toxemia was associated with an increased risk for preterm birth (RR, 2.2; 95% CI, 1.8-2.6).

A stratified analysis by history of previous preterm birth among parous women (n = 5603, after exclusions for missing data) revealed a higher percentage of preterm birth in those with a previous preterm birth (25% vs 5%), as expected (data not shown). However, associations of occupational exposures with risk of preterm birth were similar between the 2 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.

TABLE 2

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

First-trimester occupational factors	Risk ratio (95% confidence interval)		
	Reduced models <sup>a</sup>	Full model <sup>b</sup>	Full model, excluding medically indicated preterm births <sup>c</sup>
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 (h/wk)			
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)
<i>P</i> for trend <sup>d</sup>	.003	.01	.04
Lifting (times/d) <sup>e</sup>			
< 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)
<i>P</i> for trend <sup>d</sup>	.02	.3	.2
Standing or walking (h/d)			
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)
<i>P</i> for trend <sup>d</sup>	.03	.2	.09
Anesthetic gases (h/d) <sup>f</sup>			
< 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)
<i>P</i> for trend <sup>d</sup>	.07	.6	.4
Sterilizing agents (h/d) <sup>f</sup>			
< 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)
≥ 5	2.2 (1.3-3.7)	1.9 (1.1-3.4)	1.7 (0.7-3.8)
<i>P</i> for trend <sup>d</sup>	.003	.04	.2

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We did not collect information on socioeconomic status at the time of the pregnancy, although 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, although there was not a clear dose-response relationship with overtime hours. Nurses who worked night shift had a 3-fold risk of delivering early preterm (< 32 weeks) but not with later

preterm (32-36 weeks). The risk of preterm birth was moderately associated with reported exposure to sterilizing agents; however, because there were few exposed women, this finding should be interpreted cautiously. Prolonged standing and heavy lifting were weak predictors of preterm birth, whereas other

**TABLE 2****Association between first trimester work factors and preterm delivery, adjusted for age and parity (continued)**

First-trimester occupational factors	Risk ratio (95% confidence interval)		
	Reduced models <sup>a</sup>	Full model <sup>b</sup>	Full model, excluding medically indicated preterm births <sup>c</sup>
X-ray radiation (h/d) <sup>f</sup>			
< 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 <sup>d</sup>	.4	.5	.4

<sup>a</sup> These models test associations for each work factor separately, adjusted for age and parity. <sup>b</sup> In this model each work factor was adjusted for the remaining work factors as well as age and parity. <sup>c</sup> Excluded 216 medically indicated preterm births as well as 11 preterm births with missing information or type of delivery. <sup>d</sup> 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 and adjusting for the remaining categorical work factors, age, and parity. <sup>e</sup> Lifting refers to lifting or moving a physical load of 25 pounds or more, including repositioning or transferring patients. <sup>f</sup> Categories for missing data are included in the analysis for these variables; data not shown.

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work exposures common to nurses were not related, including rotating shift 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 ( $\leq 8$  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.<sup>7,11-14</sup> There is still potential for recall bias because of the assessment of pregnancy outcome and occupational exposures on the same questionnaire, particularly with regard to exposures that may be regarded as hazardous, such as sterilizing agents or antineoplastic drugs. The fact that we observed associations for some, but not all, exposures, however, argues against a blanket recall bias.

Compared with 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 US nurses, socioeconomic

variability and differences in working conditions were minimized and the likelihood of working rotating or night shifts was increased, as compared with other studies of women working in heterogeneous occupations.

One other previous study examined a national sample of US nurses,<sup>15</sup> similar to our study in that it was retrospective with a self-administered questionnaire. However, their study was a case-control design, and our study had more preterm cases (588 vs 210), had a higher participation rate than their study (76% vs 42%), and we were able to adjust each occupational exposure for other occupational risk factors. That study showed positive associations between preterm and shift work, hours spent standing, physical exertion, and long working hours, although comparison with our study is not straightforward because that study presented only unadjusted results for shift work, physical exertion, and standing, and our study combined walking and standing.<sup>15</sup>

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 years. 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 US national prevalence (1993-2001) among women of similar age and race.<sup>16</sup> Established risk factors related to preterm birth include infection, inflammation, multiple births, hypertension, low prepregnancy BMI, the extremes of maternal age, incompetent cervix, history of prior preterm birth, and cigarette smoking.<sup>17,18</sup> 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.

### 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 a recent metaanalysis.<sup>15,19-30</sup> The mechanisms by which heavy lifting and prolonged standing might increase the risk for preterm birth are unclear but may be related to increased intraabdominal pressure<sup>31</sup> or compressed pelvic vessels and a reduction in venous blood flow.<sup>32</sup>

Our finding of an increased risk of early preterm with night work is consistent with the results of our previous analysis of spontaneous abortion, in which we report a 60% increased risk of spontaneous abortion in nurses who worked nights.<sup>8</sup> Because we saw no increased risk for later preterm birth (32-36 weeks) among rotating shift or night workers, it is possible that night work affects earlier pregnancy outcomes. Results from previously published studies vary with respect to shift work, with relative risks ranging from 0.7 to 5.6 for night or rotating shift work; differences are possibly due to inconsistent definitions of work schedule and insufficient sample sizes in the night or shift work categories.<sup>24,26,27,29,33-35</sup>

Although there was a statistically significant trend for working hours ( $P = .01$ ), it is possible that a threshold effect occurred at 20-40 hours. Long working hours are related to increased stress and fatigue because of less time to recover from work.<sup>36,37</sup> Although 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,<sup>19-21,26-29,33</sup> except 1 study of US nurses.<sup>15</sup>

Our findings of an increased risk of preterm birth from reported exposure to sterilizing agents is based on few exposed women and could have been subjected to recall bias and therefore should be interpreted cautiously. Our questionnaire listed glutaraldehyde, formaldehyde, and ethylene oxide as examples of steril-

izing agents. These chemicals, in addition to orthophthalaldehyde, peracetic acid, and hydrogen peroxide, are used to sterilize medical equipment and surgical instruments.

The majority of nurses in our study who reported exposure to sterilizing agents worked as operating room/surgical nurses. In a previous 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).<sup>38</sup> That study had several limitations, however, including few exposed pregnancies and lack of power to adjust for major confounders, such as parity. Thus, the effect of sterilant exposure on preterm birth deserves more attention in future studies. Although our study showed no effect on preterm birth for reported exposure to antineoplastic drugs, these medications are recognized genotoxic and carcinogenic chemicals<sup>39</sup> with well-characterized adverse reproductive effects.<sup>2</sup>

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. Nurses who worked nights, however, had a 3-fold higher risk of delivering before 32 weeks' gestation. 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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### REFERENCES

1. United States Department of Health and Human Services (US DHHS), Health Resources and Services Administration, Division of Nursing. The national sample of registered nurses, 2000. Bethesda (MD): United States Department of Health and Human Services; 2002.
2. Vecchio D, Sasco AJ, Cann CI. Occupational risk in health care and research. *Am J Ind Med* 2003;43:369-97.
3. Shortridge-McCauley LA. Reproductive hazards: An overview of exposures to health care workers. *AAOHN J* 1995;43:614-21.
4. Figa-Talamanca I. Reproductive problems among women health care workers: epidemiologic evidence and preventive strategies. *epidemiol Rev* 2000;22:249-60.
5. Kuehn BM. Groups take aim at US preterm birth rate. *JAMA* 2006;296:2907-8.
6. MMWR. Quickstats: infant mortality rates for 10 leading causes of infant death—United States. *MMWR Wkly Rep* 2007;56:1115.
7. Rich-Edwards JW, Goldman MB, Willett WC, et al. Adolescent body mass index and ovulatory infertility. *Am J Obstet Gynecol* 1994; 171:171-7.
8. Whelan EA, Lawson CC, Grajewski B, Hibert EN, Spiegelman D, Rich-Edwards JW. Work schedule during pregnancy and spontaneous abortion. *Epidemiology* 2007;18:350-5.
9. Skov T, Deddens J, Petersen MR, Endahl L. Prevalence proportion ratios: estimation and hypothesis testing. *Int J Epidemiol* 1998; 27:91-5.
10. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol* 2005;162:199-200.
11. Colditz GA, Stampfer M, Willett WC, et al. Reproducibility and validity of self-reported menopausal status in a prospective cohort study. *Am J Epidemiol* 1987;126:319-25.
12. Colditz GA, Martin P, Stampfer MJ, et al. Validation of questionnaire information on risk factors and disease outcomes in a prospective cohort study of women. *Am J Epidemiol* 1986;123:894-900.
13. Rimm EB, Stampfer MJ, Colditz GA, Chute CG, Litin LB, Willett WC. Validity of self-reported waist and hip circumferences in men and women. *Epidemiology* 1990;1:466-73.
14. Troy LM, Hunter DJ, Manson JE, Colditz GA, Stampfer MJ, Willett WC. The validity of recalled weight among younger women. *Int J Obes Relat Metab Disord* 1995;19:570-2.
15. Luke B, Mamelle N, Keith L, et al. The association between occupational factors and preterm birth: a United States nurses' study. *Am J Obstet Gynecol* 1995;173:849-62.
16. March of Dimes. Peristats. <http://www.marchofdimes.com/peristats>.
17. Kramer MS. The epidemiology of adverse pregnancy outcomes: an overview. *J Nutr* 2003;133:1592S-6S.
18. Shennan AH, Bewley S. Editorial. Why should preterm births be rising? If a rise is confirmed, the implications are considerable. *BMJ* 2006;332:924-5.
19. Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: a meta-analysis. *Obstet Gynecol* 2000;95:623-35.
20. Bonzini M, Coggon D, Palmer KT. Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: A systematic review. *Occup Environ Med* 2007;64:228-43.
21. Brink Henriksen T, Hedegaard M, Secher NJ, Wilcox AJ. Standing at work and preterm delivery. *Br J Obstet Gynaecol* 1995;102: 198-206.

**22.** Klebanoff MA, Shiono PH, Carey JC. The effect of physical activity during pregnancy on preterm delivery and birth weight. *Am J Obstet Gynecol* 1990;163:1450-6.

**23.** Launer LJ, Villar J, Kestler E, de Onis M. The effect of maternal work on fetal growth and duration of pregnancy: a prospective study. *Br J Obstet Gynaecol* 1990;97:62-70.

**24.** Misra DP, Strobino DM, Stashinko EE, Nagey DA, Nanda J. Effects of physical activity on preterm birth. *Am J Epidemiol* 1998; 147:628-35.

**25.** Newman RB, Goldenberg RL, Moawad AH, et al. Occupational fatigue and preterm premature rupture of membranes. *Am J Obstet Gynecol* 2001;184:438-46.

**26.** Pompei LA, Savitz DA, Evenson KR, Rogers B, McMahon M. Physical exertion at work and the risk of preterm delivery and small-for-gestational-age birth. *Obstet Gynecol* 2005; 106:1279-88.

**27.** Saurel-Cubizolles MJ, Zeitlin J, Lelong N, et al. Employment, working conditions, and preterm birth: results from the Europrop case-control survey. *J Epidemiol Community Health* 2004;58:395-401.

**28.** Tuntiseranee P, Geater A, Chongsuvivatwong V, Kor-anantakul O. The effect of heavy maternal workload on fetal growth retardation and preterm delivery: a study among Southern Thai women. *J Occup Environ Med* 1998; 40:1013-21.

**29.** Fortier I, Marcoux S, Brisson J. Maternal work during pregnancy and the risks of delivering a small-for-gestational-age or preterm infant. *Scan J Work Environ Health* 1995; 21:412-8.

**30.** Ahlborg G, Bodin L, Hogstedt C. Heavy lifting during pregnancy—a hazard to the fetus? A prospective study. *Int Epidemiol Assoc* 1990; 19:90-7.

**31.** Hayne C R. Manual transport of loads by women. *Physiotherapy* 1981;67:226-31.

**32.** Schneider KT, Huch A, Huch R. Premature contractions: are they caused by maternal standing? *Acta Genet Med Gemmol*. 1985;34: 175-8.

**33.** Bodin L, Axelsson G, Ahlborg G Jr. The association of shift work and nitrous oxide exposure in pregnancy with birth weight and gestational age. *Epidemiology* 1999;10:429-36.

**34.** Xu X, Ding M, Li B, Christiani DC. Association of rotating shiftwork with preterm births and low birth weight among never smoking women textile workers in China. *Occup Environ Med* 1994;51:470-4.

**35.** Zhu JL, Hjollund NH, Olsen J. Shift work, duration of pregnancy, and birth weight: the National Birth Cohort in Denmark. *Am J Ob Gynecol* 2004;191:285-91.

**36.** Johnson JV, Lipscomb J. Long working hours, occupational health and the changing nature of work organization. *Am J Ind Med* 2006;49:921-9.

**37.** Caruso CC. Possible broad impacts of long work hours. *Ind Health* 2006;44:531-6.

**38.** Rowland AS, Baird DD, Shore DL, Darden B, Wilcox AJ. Ethylene oxide exposure may increase the risk of spontaneous abortion, preterm birth, and postterm birth. *Epidemiology* 1996;7:363-8.

**39.** McDiarmid MA, Condon M. Organizational safety culture/climate and worker compliance with hazardous drug guidelines: lessons from the blood-borne pathogen experience. *J Occup Environ Med* 2005;47:740-9.