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### Risks of Preterm Delivery and Small for Gestational Age Infants: Effects of Nondaily and Low-Intensity Daily Smoking During Pregnancy

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### Abstract

**Background:** Few studies have examined the effects of nondaily smoking or low-intensity daily smoking and infant outcomes. We examined the associations between preterm delivery and small for gestational age (SGA) infants in relation to both nondaily and daily smoking.

**Methods:** We used population-based data on women who delivered live singleton infants using the 2009–11 Pregnancy Risk Assessment Monitoring System. Women's smoking status in the last 3 months of pregnancy was categorised as nonsmokers, quitters, nondaily smokers (<1 cigarette/ day), and daily smokers. Controlling for maternal age, maternal race/ethnicity, education, marital status, prepregnancy body mass index (BMI), trimester of prenatal care entry, parity, and alcohol use, we estimated adjusted prevalence ratios (PR) for the outcomes of preterm delivery (<37 weeks' gestation) and SGA.

**Results:** Of the 88 933 women, 13.1%, 1.7%, and 9.6% of the sample were quitters, nondaily smokers, and daily smokers, respectively, in the last 3 months of pregnancy. While nondaily smoking was not associated with preterm delivery, daily smoking was. However, we found no dose–response relationship with the number of cigarettes smoked per day. Risk of delivering a SGA infant was increased for both nondaily and daily smokers (PR 1.4, 95% CI 1.1, 1.8 and PR 2.0, 95% CI 1.9, 2.2 respectively).

**Conclusions:** Nondaily smoking in the last 3 months of pregnancy was associated with an increased risk of delivering a SGA infant. Pregnant women should be counselled that smoking, including nondaily and daily smoking, can adversely affect birth outcomes.

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Disclosure

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#### Keywords

Smoking; nondaily smoking; dose-response; pregnancy; infant outcomes; preterm delivery; small for gestational age

In 2014, an estimated 8% of women smoked in the last 3 months of pregnancy in the United States.<sup>1</sup> Approximately half of women who smoke prior to pregnancy quit during pregnancy, and a substantial percentage reduce or 'cut down' the number of cigarettes smoked.<sup>2</sup> Women who reduce smoking without quitting may do so to minimise harm to the fetus.<sup>3</sup> Furthermore, nondaily smokers are becoming an increasingly larger fraction of the smoking population, which may result in more nondaily smokers in pregnancy.<sup>4</sup>

Maternal smoking is causally associated with adverse pregnancy outcomes, including foetal growth restriction, placenta abruption, and preterm delivery.<sup>5</sup> The epidemiologic literature on the effects of maternal smoking and infant outcomes has included mostly studies of daily smokers. A meta-analysis of 20 prospective studies reported a modest 27% increase in risk of preterm delivery among daily smokers.<sup>6</sup> None of these studies examined the association between nondaily smoking and preterm delivery. Relative risk estimates for small for gestational age (SGA) have ranged from 1.5 to 2.5 in daily smokers.<sup>5</sup> A dose–response relationship between the number of cigarettes smoked per day and reductions in birthweight have been shown; however, few studies have examined the effects of low-intensity daily smoking on fetal growth.<sup>7,8</sup> We examined the associations between preterm delivery and SGA infants in relation to both nondaily and daily smoking.

#### Methods

We used population-based surveillance data from women delivering singleton livebirths using the 2009–11 Pregnancy Risk Assessment Monitoring System (PRAMS). The methodology has been described elsewhere.<sup>9</sup> Briefly, at each site a monthly stratified sample of 100–300 new mothers is selected systematically from birth certificate records. We included New York City and 31 states that achieved an overall weighted response rate of 65% for a given site and year in the study period. The PRAMS protocol was approved by institutional review boards at the Centers for Disease Control and Prevention and participating states.

Women who reported smoking in the past 2 years were asked in the PRAMS survey how many cigarettes they smoked per day on average during the 3 months before pregnancy and in the last 3 months of pregnancy. Categorical responses were none (0 cigarettes), <1, 1–5, 6–10, 11–20, 21–40, or 41 cigarettes smoked per day. Nonsmokers were women who reported no smoking before or during pregnancy. Quitters were women who reported any smoking before pregnancy and 'none' during pregnancy. Nondaily smokers were women who reported any smoking before pregnancy and <1 cigarette smoked per day during pregnancy. Daily smokers were women who reported any smoking before pregnancy.

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Preterm delivery was defined as <37 completed weeks of gestation based on the clinical estimate of gestation from the birth certificate. SGA was defined as the lowest 10th percentile of birthweight (also obtained from the birth certificate) for gestational age by infant sex and race.<sup>10</sup> Covariates were selected based on established associations with smoking and birth outcomes:<sup>11</sup> maternal age, parity, race/ethnicity, education, marital status, prepregnancy body mass index (BMI), trimester of prenatal care entry, and alcohol use during pregnancy.

The analysis was restricted to women delivering singleton livebirths and whose smoking status, gestational age and birthweight were not missing. Demographic characteristics were compared by smoking status (nonsmokers, quitters, nondaily smokers, and daily smokers). Prevalence and adjusted PR for preterm delivery and SGA by smoking status were estimated, controlling for maternal age, parity, race/ethnicity (excluded from the SGA model), education, marital status, prepregnancy BMI, trimester of prenatal care entry, and alcohol use. Because chronic and gestational hypertension are associated with smoking and poor pregnancy outcomes, we repeated the analyses of preterm delivery and of SGA after excluding women with hypertension complications. Analyses were conducted using sAs version 9.3 (SAS Institute, Inc., Cary, NC, USA) and suDAAN version 11 (RTI International, Raleigh, NC, US) to account for the complex survey design of PRAMS.

#### Results

Of the 105 778 women, 88 933 (84%) had non-missing smoking status, infant outcomes, and covariates. Overall, 13.1%, 1.7%, and 9.6% of the sample were quitters, nondaily smokers, and daily smokers during pregnancy respectively (Table 1).

The prevalence of preterm delivery was not different between quitters or nondaily smokers compared with nonsmokers (Table 2). Preterm delivery prevalence was higher in daily smokers compared with nonsmokers overall, in low-intensity daily smokers (1–5 cigarettes/day) and 6–10 cigarettes/day daily smokers. The point estimates for preterm delivery prevalence were higher for higher intensity (11–20 and 21 cigarettes/day) daily smokers compared with nonsmokers (Table 2), but there was no evidence of a dose–response relationship between cigarettes smoked per day and risk of preterm delivery. When we excluded women with hypertension, preterm delivery was associated with daily smoking (PR 1.3, 95% CI 1.2, 1.5), but not with nondaily smoking (PR 1.0, 95% CI 0.8, 1.3).

The prevalence of SGA was not different for quitters compared with nonsmokers; however, the prevalence of SGA was higher for nondaily and daily smokers compared with nonsmokers (Table 3). A dose–response relationship was observed between SGA and smoking intensity among daily smokers.

#### Comment

We found that nondaily smoking in the last 3 months of pregnancy was associated with a 1.4-fold increased risk of delivering an SGA infant compared with nonsmokers. As expected, we found modest associations between daily smoking and both SGA and preterm delivery. The prevalence of SGA increased in a dose–response fashion from nondaily to

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daily smoking as the number of cigarettes smoked per day increased. This finding is also consistent with previous studies in which low levels of tobacco smoking had significant effects on fetal growth.<sup>5</sup> England and colleagues<sup>8</sup> found infant birthweight declined sharply at low levels of tobacco exposure.

We did not find an association between preterm delivery and nondaily smoking, nor did we find a dose–response relationship between preterm delivery and cigarettes smoked per day in daily smokers. A meta-analysis<sup>6</sup> reported a dose–response relationship between preterm delivery and the number of cigarettes smoked per day at low- to moderate-intensity smoking, but was not further increased at 20 cigarettes or more smoked per day. Despite the lack of dose–response relationship, evidence from animal models suggests that even low levels of smoking could have important effects on offspring neurological development.<sup>12</sup>

The findings in this study have implications for clinical care. First, pregnant women should be screened for all tobacco use, including nondaily smoking.<sup>13</sup> Second, the findings are consistent with other studies that have shown that low levels of daily smoking (e.g. 1–5 cigarettes/day) had adverse effects on preterm birth and fetal growth. Although some have advocated reducing the number of cigarettes smoked for pregnant women who do not quit smoking based on improvements in birthweights compared with other smokers,<sup>3,14</sup> there is limited evidence that reduction alone has other substantial health benefits. Quitting smoking completely is the most beneficial for a pregnant woman, her fetus, and her baby.<sup>13</sup> Therefore, pregnant women should be advised that smoking low levels of smoking, both nondaily and daily smoking, confers adverse effects on the fetus.

This study has several limitations. Smoking status was self-reported and not biochemically verified. PRAMS is a confidential survey, and may identify more smokers than other data sources based on self-report, such as the birth certificate.<sup>15</sup> Nevertheless, misclassification of smokers as nonsmokers and potential recall bias, as the PRAMS survey is answered about 4 months postpartum, could bias our results towards the null. Second, nondaily smoking was defined using the response <1 cigarette smoked/day; some daily smokers who smoked part of a cigarette could have selected this option, or daily smokers could have misreported their use as nondaily smoking. These types of misclassification could have resulted in an overestimation of the association between nondaily smoking and adverse outcomes. However, we did not see an increased risk of preterm delivery in nondaily smokers which supports that there was not extensive misclassification in this direction. Third, we were unable to account for second hand smoke exposure or illicit substance use, which may have confounded our results. Finally, our findings may not be generalisable to women whose pregnancies did not result in livebirths.

In conclusion, we found evidence that nondaily smoking during the last 3 months of pregnancy is associated with fetal growth restriction. The findings provide further evidence that even low level levels of smoking can put a pregnancy at risk for adverse birth outcomes.

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Table 1.

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	Non-smokers ( $n = 64\ 860$ ) % (95% CI)	Quitters $(n = 11 696)$ % (95% CI)	Nondaily smokers $(n = 1694)$ % (95% CI)	Daily smokers ( <i>n</i> = 10 683) % (95% CI)
Total	75.6 (75.1, 76.1)	13.1 (12.7,13.5)	1.7 (1.6,1.9)	9.6 (9.3, 9.9)
Maternal age (years)				
<20	7.9 (7.5, 8.3)	12.9 (11.8,14.0)	12.9 (10.1,16.3)	11.8 (10.7,13.0)
20-24	19.1 (18.5,19.6)	31.5 (30.1,33.0)	34.9(30.9,39.1)	35.3 (33.6, 36.9)
25-34	57.0 (56.3, 57.6)	47.6 (46.0, 49.1)	46.1 (41.9,50.3)	45.6 (43.9, 47.4)
35	16.1 (15.6,16.5)	8.1 (7.3, 8.9)	6.2 (4.4, 8.6)	7.3 (6.6, 8.2)
Maternal race/ethnicity				
White, non-Hispanic	57.5 (56.9,58.0)	69.9 (68.5,71.3)	62.4 (58.1,66.6)	80.1 (78.8,81.4)
Black, non-Hispanic	13.4 (13.1,13.8)	10.7 (9.8,11.5)	14.8 (12.4,17.7)	9.8 (8.9, 10.7)
Hispanic	20.4 (20.0, 20.9)	13.1 (11.9,14.4)	15.1 (11.6,19.3)	4.9 (4.1, 5.8)
American Indian/Alaska Native	0.5 (0.5, 0.6)	1.7 (1.5, 2.0)	2.6 (1.8, 3.7)	1.6 (1.4,1.9)
Asian/Pacific Islander	6.0 (5.8, 6.2)	2.1 (1.8, 2.5)	2.0(1.3, 3.1)	0.9 (0.8,1.2)
Other	2.1 (1.9, 2.3)	2.4 (2.0, 2.9)	3.1 (1.8, 5.3)	2.7 (2.2, 3.2)
Maternal education (years)				
<12	13.7 (13.2,14.2)	14.6 (13.5,15.7)	20.7 (17.5, 24.5)	27.2 (25.6, 28.8)
12	22.1 (21.5, 22.7)	33.4(31.9,34.9)	38.8 (34.6, 43.2)	42.6 (40.9, 44.4)
13	64.2 (63.6, 64.8)	52.1 (50.5,53.6)	40.4 (36.4, 44.5)	30.2 (28.6,31.8)
Marital status				
Unmarried	30.8 (30.2,31.5)	53.6(52.1,55.1)	63.5 (59.3,67.5)	67.9 (66.2, 69.4)
Married	69.2 (68.5, 69.8)	46.4 (44.9, 47.9)	36.5 (32.5,40.7)	32.1 (30.6, 33.8)
Prepregnancy body mass index (kg	/m <sup>2</sup> )			
Underweight (<18.5)	4.0 (3.8, 4.2)	4.5 (3.9,5.2)	4.9 (3.4, 7.0)	6.7 (5.9, 7.6)
Normal weight (18.5–24.9)	51.7 (51.0,52.3)	46.3 (44.8, 47.9)	46.9(42.6,51.2)	45.5 (43.8, 47.2)
Overweight (25.0-29.9)	24.1 (23.5, 24.7)	24.6 (23.3, 26.0)	25.4 (22.0, 29.2)	23.1 (21.7,24.6)
Obese ( 30)	20.2 (19.7, 20.8)	24.6 (23.2, 26.0)	22.8 (19.4, 26.7)	24.7 (23.3, 26.2)
Parity				
First birth	41.7 (41.1, 42.4)	53.2(51.7,54.8)	47.3 (43.0,51.6)	36.8 (35.1,38.4)
Second or later birth	58.3 (57.6,58.9)	46.8 (45.2, 48.3)	52.7 (48.4, 57.0)	63.2 (61.6,64.9)

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	Non-smokers ( <i>n</i> = 64 860) % (95% CI)	Quitters $(n = 11 696) \% (95\% CI)$	Nondaily smokers $(n = 1694)$ % (95% CI)	Daily smokers $(n = 10.683)$ % (95% CI)
Entry into prenatal care				
First trimester	83.1 (82.6, 83.6)	80.2 (78.9,81.5)	78.5 (74.5,82.1)	73.7 (72.1, 75.2)
Second trimester	12.9 (12.5, 13.4)	16.0(14.8,17.2)	15.7 (12.7,19.3)	20.2 (18.8, 21.6)
Third trimester or none	4.0 (3.7, 4.3)	3.8 (3.2, 4.5)	5.7 (3.8, 8.6)	6.1 (5.3, 7.1)
Alcohol use during pregnancy				
Yes	7.4 (7.1, 7.7)	6.7 (5.9, 7.5)	8.6 (6.8,10.8)	6.9 (6.1, 7.8)
No	92.6 (92.3, 92.9)	93.3 (92.5, 94.1)	91.4 (89.2,93.2)	93.1 (92.2, 93.9)

CI, confidence interval.

# Table 2.

Preterm delivery by smoking status during the last 3 months of pregnancy (unweighted  $n = 88\,933$ )

		Prevalence ra	tio (95% CI)
Smoking status	Prevalence % (95% CI)	Unadjusted	Adjusted
Nonsmokers ( $n = 64\ 860$ )	7.4 (7.1, 7.7)	1.0 (Reference)	1.0 (Reference)
Quitters ( $n = 11 696$ )	7.6 (6.9, 8.4)	$1.0\ (0.9, 1.1)$	1.0 (0.9,1.2)
Nondaily smokers ( $n = 1694$ )	7.5 (6.1, 9.2)	$1.0\ (0.8, 1.3)$	1.0 (0.8,1.2)
Daily smokers $(n = 10.683)$	9.5 (8.8,10.3)	1.3 (1.2,1.4)	1.3 (1.2,1.4)
$1-5 \operatorname{cigs/day}(n = 5432)$	9.9(8.8, 11.0)	1.3 (1.2,1.5)	1.3 (1.2,1.5)
6–10 cigs/day ( $n = 3239$ )	9.3 (8.0,11.0)	1.3 (1.1,1.5)	1.3 (1.1,1.5)
$11-20 \operatorname{cigs/day}(n = 1656)$	8.6 (6.9,10.6)	1.2 (0.9,1.4)	1.2 (1.0,1.5)
21 cigs/day $(n = 356)$	10.6 (6.8,16.0)	1.4 (0.9, 2.2)	1.4 (0.9, 2.2)
CI, confidence interval.			

Prevalence ratios are adjusted for maternal age, race/ethnicity, education, marital status, prepregnancy body mass index, trimester of entry into prenatal care, and alcohol use during pregnancy.

Daily smokers include all women who smoked 1 cigarettes smoked per day.

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## Table 3.

Risk of small for gestational age by smoking status during the last 3 months of pregnancy (unweighted  $n = 88\,933$ )

		Prevalence ra	ttio (95% CI)
Smoking status	Prevalence % (95% CI)	Unadjusted	Adjusted
Nonsmokers ( $n = 64\ 860$ )	8.6 (8.3, 9.0)	1.0 (Reference)	1.0 (Reference)
Quitters $(n = 11 696)$	8.9 (8.1,9.7)	$1.0\ (0.9, 1.1)$	$0.9\ (0.9, 1.0)$
Nondaily smokers ( $n = 1694$ )	$13.4\ (10.8, 16.4)$	$1.6\ (1.3, 1.9)$	$1.4\ (1.1,1.8)$
Daily smokers $(n = 10.683)$	18.9 (17.6, 20.2)	2.2 (2.0, 2.4)	2.0 (1.9,2.2)
$1-5 \operatorname{cigs/day} (n = 5432)$	17.6 (16.0,19.3)	2.1 (1.9, 2.3)	1.9 (1.7,2.1)
$6-10 \operatorname{cigs/day}(n=3239)$	18.7 (16.5, 21.1)	2.2 (1.9, 2.5)	2.0 (1.8, 2.3)
$11-20 \operatorname{cigs/day}(n=1656)$	21.5 (18.1, 25.3)	2.5 (2.1, 3.0)	2.4 (2.0, 2.9)
21 cigs/day $(n = 356)$	25.8 (19.0,34.0)	3.0 (2.3, 4.0)	2.9 (2.1,4.0)
CI, confidence interval.			

Prevalence ratios are adjusted for maternal age, education, marital status, prepregnancy body mass index, trimester entry into prenatal care, and alcohol use during pregnancy.

Daily smokers include all women who smoked 1 cigarettes smoked per day.