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## Exposure to Cigarette Smoke In Utero:

### Comparison of Reports from Mother and Daughter

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### Abstract

**Background**—Smoking during pregnancy has been associated with asthma, obesity, and decreased cognitive functioning in the offspring. To study the role of in utero smoking exposure in offsprings' adult health outcomes, it may be necessary to rely upon reports by the offspring themselves.

**Methods**—We studied 34,949 mother-daughter pairs participating in the Nurses' Health Study II for whom data on the daughter's early passive cigarette smoke exposure had been obtained from both mother and daughter. We calculated sensitivity and specificity of daughter's early exposure to smoke (using mother's report as the gold standard), as well as  $\kappa$  statistics. Mother and daughter reports were also analyzed as risk factors for asthma and birthweight to demonstrate face validity.

**Results**—Sensitivity of daughters' reported prenatal exposure ranged from 74% to 85%, while specificity was between 90% and 95% ( $\kappa = 0.72–0.81$ ). Daughter's reported childhood exposure as a proxy for mother's report of smoking during pregnancy had a sensitivity of 89% and specificity of 88%. Results were similar for daughter's report of father's smoking during her childhood. Maternal smoking during pregnancy is consistently associated with reductions in offspring birthweight, and with asthma risk in offspring. The daughter's risk of being very low (<1500 g) or low birthweight (<2500 g) or of having asthma were similar when exposure was defined according to mother's report, daughter's report of fetal smoke exposure, and daughter's report of mother's smoking during childhood.

**Conclusions**—Daughter's report of mother's smoking prenatally and in childhood are good proxy measures for mother's own report of smoking during pregnancy.

Despite the known risks of smoking, over 10% of pregnant women in the US smoke.<sup>1</sup> Recent epidemiologic studies have suggested numerous ill consequences for the offspring of maternal smoking during pregnancy, including asthma,<sup>2</sup> decreased cognitive functioning,<sup>3</sup> sudden infant death syndrome,<sup>4</sup> obesity,<sup>5,6</sup> and attention deficit disorder.<sup>7</sup>

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Investigating the role of in utero exposure to cigarette smoke and outcomes in offspring later in life requires reliance on various sources to classify exposure, often including recalled data. Because prospective observational studies from conception to adulthood are not available to elucidate the role of fetal passive cigarette smoke exposure on later health, self-reported surrogate measures often have to be substituted.

The validity of a mother's own report of smoking during pregnancy has been examined using exhaled carbon monoxide and cotinine concentrations in plasma and saliva as biomarkers, as well as test-retest methods and medical record reviews as gold standards; many, though not all, studies have demonstrated good agreement.<sup>8-15</sup> In studies considering the impact of maternal smoking on health outcomes for the offspring in adulthood, it may be necessary to use reports by the offspring themselves, and even less is known about the reliability of these reports.

Here, questionnaire data from mother-daughter pairs from the Nurses' Health Study II and the Nurses' Mothers Cohort were used to assess the use of daughter's report of passive exposure to smoke as a surrogate for mother's report of smoking during pregnancy.

## **METHODS**

### **Study Population**

Nurses' Health Study II is a prospective cohort study started in 1989 when 116,608 female US nurses returned baseline questionnaires by mail. Information on lifestyle factors, anthropometric variables, and onset of disease have been updated through biennial self-administered questionnaires. In 2001, the mothers of approximately 40,000 Nurses' Health Study and Nurses' Health Study II participants were invited to participate in the Nurses' Mothers Cohort, which aimed to collect information on the perinatal and early-life exposure of the nurse daughters. This new study recruited the mothers of nurse participants who were alive, still participating in either of the original cohort studies, and had no history of cancer in 2001.

### **Cigarette Smoke Exposure**

In 1999, Nurses' Health Study II participants were asked "When you were a child, did either of your parents smoke regularly inside your home?" They were also asked "Did your mother smoke when she was pregnant with you?" In 2001 participants in the Nurses' Mothers Cohort were asked "Did the nurse's father/your partner ever smoke cigarettes during the pregnancy or early childhood of your nurse daughter?" and "Did you ever smoke cigarettes during the pregnancy with this nurse daughter?" Mothers also reported the number of cigarettes they smoked daily during pregnancy, whether they stopped smoking during pregnancy, and if so, during which trimester.

### **Other Covariates**

The 2001 Nurses' Mothers Cohort questionnaire collected data on factors related to the mother's health during pregnancy, including her own diagnosed asthma, prenatal care, and the daughter's perinatal characteristics. Separately Nurses' Health Study II participants could report their own doctor-diagnosed asthma at each 2-year survey period, although a specific date of onset was not collected. Furthermore, reproductive history of the nurses was collected at baseline, the daughter's reports of her own perinatal characteristics were collected in 1991, and any new pregnancies were self-reported at each biennial survey.

## Statistical Analysis

Characteristics of mothers and daughters in the study population were summarized with univariate statistics. To compare the various sources of data on the exposure to cigarette smoke in utero we compared mother-daughter pair reports of smoking during pregnancy using contingency tables for the 39,494 pairs. Sensitivity and specificity were calculated as the conditional probabilities of true positives and true negatives, respectively, comparing daughter's report of mother's smoking during pregnancy to the gold standard mother's report. Kappa ( $\kappa$ ) statistics were calculated to measure the agreement between mother and daughter reports.

To further consider whether childhood exposure was a suitable proxy for mother's report of daughter's fetal exposure, we compared daughter's report of passive childhood exposure with the mother's report of smoking during pregnancy. This was done because data on childhood exposure may be all that is available in some studies and we wanted to evaluate how suitable these data would be as a proxy of reported in utero exposure. Additionally we considered any early-life passive smoke exposure during fetal development, childhood, or both, comparing the nurse daughter's report against her mother's report. We excluded mother-daughter pairs who were missing cigarette smoke exposure information from our primary analysis, but we conducted sensitivity analyses including 2568 mother-daughter pairs in which we classified nurse participant's missing responses as inconsistent with the mother's report. In sensitivity analysis we also compared the daughter's and mother's reports of father's smoking during pregnancy and childhood and at both times. Using  $\kappa$  statistics we examined whether mother-daughter agreement varied by the number of cigarettes the mother reported that the father smoked.

To assess whether agreement might differ across subgroups, we examined  $\kappa$  statistics for subgroups defined by daughter's year of birth, by daughter's preterm birth status, and by whether the daughter had ever been pregnant. The first classification was included to account for differences in the practice and perceptions of cigarette smoking during pregnancy. The second stratification considered whether the nurse daughter's knowledge of her preterm birth might lead to differential recall of her mother's smoking habits. The third stratification explored whether women might learn more about their mother's experience during pregnancy once they themselves have become pregnant. We then looked at how daughter's report was affected by the number of cigarettes per day the mother reported smoking during pregnancy, whether she quit smoking during pregnancy, and if so, during which trimester she reported quitting smoking cigarettes. In a sensitivity analysis we also considered whether the mother's own asthma might have influenced her recall or her daughter's recall by stratifying. Agreement between mothers and daughters was estimated by stratum-specific  $\kappa$  statistics.

Lastly, to further assess the use of daughter's report of mother's smoking during pregnancy as a proxy for mother's report, we computed crude risk ratios for outcomes associated with maternal cigarette smoking during pregnancy.<sup>2,16-20</sup> First we used the daughter's report of an asthma diagnosis, and then studied both very low birth weight (<1500 g) and low birth weight (<2500 g) compared with normal birth weight (3000-4000 g) as reported by the mother.

## RESULTS

Daughters were an average of 34 (SD = 4.6) years old in 1989 when they enrolled in Nurses' Health Study II with a mean BMI of 23.7 (4.7). In 2001, when mothers were recruited for the Nurses' Mothers Cohort, 86% had been pregnant at least once and 15% reported a physician diagnosis of asthma (Table 1).

In our primary analysis nearly 85% of mother's reports of smoking during pregnancy was confirmed by their daughter (sensitivity = 85%). Conversely, for mothers who said that they did not smoke during pregnancy, more than 95% of daughters reported that their mothers did not smoke during that time (specificity = 95%). The  $\kappa$  statistic for agreement of mother's and daughters' reports of maternal smoking during pregnancy was 0.80 (95% CI = 0.79–0.81). In secondary analyses, including missing responses, we found 74% sensitivity and 90% specificity (Table 2).

In primary analysis, self-reported childhood exposure to cigarette smoke as a proxy for fetal exposure as reported by the participant's mother, yielded 89% sensitivity and 88% specificity. The  $\kappa$  statistic was 0.71 (95% CI = 0.70–0.72). The more conservative estimates in secondary analyses indicated comparable validity (sensitivity = 88%, specificity = 88%) (Table 3). When the daughter's report of any passive smoke exposure (in utero and during childhood) was compared with the mother's report, we found a sensitivity of 87% and specificity of 84%. Including the missing responses did not change our results (sensitivity = 87%, specificity = 84%) (data not shown).

Agreement between mother and daughter reports of fetal exposure did not differ greatly across decade of daughter's birth year ( $\kappa_{1940s} = 0.75$ ,  $\kappa_{1950s} = 0.81$ ,  $\kappa_{1960s} = 0.81$ ), although the older daughters and their mothers tended to have poorer agreement. Agreement was similar among daughters who reported being born preterm compared with term ( $\kappa_{\text{preterm}} = 0.82$  vs.  $\kappa_{\text{term}} = 0.80$ ). Further, agreement was the same ( $\kappa_{\text{yes}} = 0.80$ ,  $\kappa_{\text{no}} = 0.79$ ) whether or not the daughter had ever been pregnant. Daughters were more likely to report that their mother smoked during pregnancy if the mother did not report stopping smoking during pregnancy (90% vs. 58%). Among mothers who reported quitting smoking during pregnancy, the proportion of daughters reporting that their mother smoked was increased with mother's reported duration of smoking during pregnancy. Further, the proportion of daughters reporting that their mother smoked during pregnancy increased as the number of cigarettes the mother reported smoking daily increased (80% for 1–14 cigarettes/d, 94% for 15–24/d, 97% for 25–34/d, 94% for 35+/d).

When we stratified by mother's asthma, as reported on the 2001 Nurses' Mothers Cohort questionnaire, we found comparable agreement. The  $\kappa$  statistic was approximately 0.8 comparing daughters' and mothers' reports of mother's smoking during pregnancy whether or not the mother reported having asthma. Agreement was similar across strata of asthma when daughter's report of mother's smoking during childhood was compared with mother's report of smoking during pregnancy ( $\kappa = 0.7$ ).

When examining how each measure of maternal smoking during pregnancy predicted known consequences of this exposure, we found that the mother and daughter reports yielded similar crude risk ratios (Table 4). For self-reported asthma in the daughter, mother's report of smoking during pregnancy yielded a crude risk ratio of 1.15 while the risk ratio for daughter's report of mother's smoking during pregnancy was 1.18. When exposure was defined using daughter's report of mother smoking during the nurse participant's childhood, the estimated crude risk ratio was 1.16. Similarly when we estimated the risk of very low birth weight or low birth weight, we found similar risk ratios for mother's report of smoking during pregnancy, daughter's report of mother's smoking during pregnancy, and daughter's report of mother's smoking during childhood.

We took data from the published literature to estimate mothers' misreporting of smoking during pregnancy, and then estimated the probability of the mother being a smoker during pregnancy conditional on the daughter's report. This provides an estimate of the sensitivity of the daughter's report as a measure of true exposure given the reliability and validity of

mother's reports of smoking during pregnancy (see Appendix, available with the online version of this article). The probability that the mother truly smoked during pregnancy given that the daughter said that she did was between 76% and 84%. The probability that the mother truly smoked during pregnancy conditional on the daughter's report that her mother did not ranged from 8% to 28%.

In our sensitivity analyses exploring mother and daughter reports of father's smoking, we found that, of the daughters reporting that their father smoked during childhood, about 86% of mothers confirmed that this included his smoking during her pregnancy. Sensitivity of daughters' report of father's smoking as a measure of fetal exposure reported by the mother was 84% and 83% without and with counting the missing values, respectively. Respective values for specificity were both 86%. Results were similar when father's smoking during the daughter's childhood was considered without including fetal smoke exposure (sensitivity = 85%, specificity = 85%) (Table 5). There was good agreement between the daughter's dichotomized report of father smoking during her childhood against mother's report of father smoking during the mother's pregnancy ( $\kappa = 0.67$ , 95% CI = 0.66–0.68). Agreement was the same when the mother reported the daughter's childhood exposure.

## DISCUSSION

Using data from mother-daughter pairs, the daughter's report is a good proxy for mother's report of cigarette smoking during pregnancy. Reported childhood exposure to passive cigarette smoke has high sensitivity and specificity as a proxy for fetal cigarette smoke exposure. Agreement, as represented by the  $\kappa$  statistic, was excellent. Daughters were more likely to report that their mother smoked during pregnancy if their mother did not report stopping their smoking during pregnancy, and also as the daily amount the mother reported smoking during pregnancy increased. Both mother and daughter reports of daughter's exposure to cigarette smoke in utero yielded similar crude risk ratios for very low birth weight (<1500 g), low birth weight (<2500 g) and asthma, demonstrating face validity of both reports.

The previous literature on the validity of self-report of smoking during pregnancy has focused on reports by women currently pregnant. Some, but not all, have demonstrated good agreement between mothers' self-report of smoking and biomarkers.<sup>8–15</sup> Those studies evaluated the reliability and validity of mother's own self-report of recent smoking during her pregnancy, rather than the self-report of fetal exposure by the offspring themselves, as was done in the present study. In a recent review on validity of self-reported smoking status, the authors conclude that self-report alone underestimates maternal smoking during pregnancy and that biomarker measures may provide more reliable estimates of the truth.<sup>15</sup> Despite this known limitation of self-reports, biochemical markers are often either unavailable or impractical, particularly in retrospective studies. Thus questionnaire-based methods may then be the primary source of exposure data, and work such as that done by Kharrazi and colleagues<sup>21</sup> plays an important role in reducing the misclassification of cigarette smoking during pregnancy by examining how format and phrasing of the question influences the response.

As researchers seek to understand the consequences of early life and in utero exposure to cigarette smoke, self-report by the offspring themselves may be the only source of data. To the best of our knowledge, this is the first study to evaluate the offspring's report. Although we lack a true gold standard in the mothers, we have assessed the validity of daughter's report as a proxy for mother's report. Furthermore, using data from the present study population and from the published literature on the validity of mother's report against biomarkers, we estimated that the probability of the mother smoking cigarettes during

pregnancy given the daughter's report of her mother smoking during pregnancy was between 76% and 84%.

The perceptions of cigarette smoking have changed since the Nurses' Health Study II participants' fetal and childhood exposures, and it is unclear how this might influence the mother's or the daughter's reporting. Although timing of pregnancy with regard to the Surgeon General's report<sup>22</sup> in 1964 may not affect smoke exposure, it may lead to underreporting. In our study, 26% of mothers reported smoking during pregnancy with their daughter, while the estimated prevalence of cigarette smoking among US women during this time was between 28% and 45%.<sup>23</sup> Despite these concerns, the agreement between mothers and daughters was good for all cigarette smoke exposures considered in the present study and may underestimate the true association.

There are several limitations to the present study. The study population is limited to women with the resources to have become nurses by 1989 and who survived cancer-free until 2001. Further they also had to have mothers healthy enough to enroll in 2001. If these factors are related to our exposure of interest, the results might be different from those obtained from other mother-daughter pairs. However, while this left-censoring may be related to early-life cigarette smoke exposure, we expect that, had such participants been included, recall might be either equivalent or better than those included in the present study. It is also important to acknowledge that the phrasing of the questions was different across the 2 cohorts and that how a question is asked may influence reporting.<sup>21</sup> One of the major strengths of this study is the high statistical power, as it includes 34,949 mother-daughter pairs. Further, as previously mentioned, the prevalence of smoking is compatible with other published reports, which reduces the likelihood of mothers' smoking habits having been misreported.

This study demonstrates the utility of self-reported fetal and childhood exposure to smoke as a surrogate for maternal report of in utero exposure. Both mother's or daughter's report provided consistent measures of associations between early life exposure to cigarette smoke and 2 outcomes associated with maternal smoking during pregnancy—asthma and low birth weight. In epidemiologic studies, the data needed to best answer a question are frequently simply unavailable. Our results suggest that a woman's self-report of fetal and childhood passive exposure to cigarette smoke is a good proxy for her mother's report.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1

## Study Population Characteristics (n = 34,949)

Daughter characteristics	
Age in 1989 (yrs); mean (SD)	34 (4.6)
Preterm; %	6.9
Birth weight; %	
Very low (<1500 g)	0.3
Low (<2500 g)	6.2
Reference (3000–4000 g)	25.1
Father smoked during childhood; %	54.0
Ever been pregnant as reported in 2001; %	86.5
Ever had physician diagnosis of asthma	14.8
Mother characteristics	
Age in 2001 (yrs); mean (SD)	72 (6.5)
Years education at daughter's birth; %	
<8th grade	0.9
8th grade	3.2
Some high school	9.4
High school graduate	49.8
Some college	25.8
College graduate	10.6
Race/ethnicity	
White (non-Hispanic/Latino)	97.3
African American (non-Hispanic/Latino)	0.6
Hispanic or Latino	0.8
Asian/Pacific Islander	0.6
American Indian/Alaska Native	0.5
Other	0.7
Weight gain during pregnancy (lbs); %	
<10	3.3
10–14	10.3
15–19	19.1
20–29	38.6
30–40	15.8
>40	5.0
Received prenatal care during pregnancy; %	98.4
Gestational diabetes; %	0.4



**Cross-Classification of Daughter's Self-Reported Fetal Exposure to Smoke Compared With Their Mother's Self-Report of Smoking During Pregnancy**

**TABLE 2**

Daughter's Report of Fetal Exposure	Mother's Report of Smoking During Pregnancy			Primary Analysis <sup>a</sup>	Secondary Analysis <sup>b</sup>
	Yes	No	Total		
Yes	6,685	1,126	7,811	Sensitivity 84.5%	Sensitivity 73.6%
No	1,222	23,227	24,449	Specificity 95.4%	Specificity 90.2%
Total	7,907	24,353	32,260 <sup>c</sup>	—	—

<sup>a</sup> Does not include the missing pairs.

<sup>b</sup> Includes the 2568 pairs where daughter's report was missing, counting daughter's report as opposite to mother's.

<sup>c</sup> One hundred twenty-one pairs excluded from the total 34,949 where mother's report, the gold standard, was missing, 2568 pairs excluded where daughter's report was missing (1177 of these the mothers reported smoking during pregnancy).

**TABLE 3**  
 Comparison of Daughter's Report of Childhood Exposure to Smoke Compared With Mother's Report of Smoking During Pregnancy

Daughter's Report of Childhood Exposure	Mother's Report of Smoking During Pregnancy			Primary Analysis <sup>a</sup>	Secondary Analysis <sup>b</sup>
	Yes	No	Total		
Yes	7,987	3,080	11,067	Sensitivity 88.5% Specificity 88.0%	Sensitivity 87.9% Specificity 87.6%
No	1,039	22,541	23,580		
Total	9,026	25,621	34,647 <sup>c</sup>		

<sup>a</sup> Does not include the missing pairs.

<sup>b</sup> Includes the 181 pairs where daughter's report was missing, counting daughter's report as opposite to mother's.

<sup>c</sup> One hundred twenty-one pairs excluded from the total 34,949 where mother's report, the gold standard, was missing. 181 pairs also excluded where daughter's report of childhood cigarette smoke exposure (58 of which the mothers reported smoking during pregnancy).

Association Between Reports of Daughter's Exposure During Mother's Pregnancy and Outcomes Associated With Passive Exposure to Cigarette Smoke In Utero

**TABLE 4**

Outcome	Smoking; No.									
	Mother's Report During Pregnancy				Daughter's Report During Childhood					
	Yes	No	RR	Yes	No	RR	Yes	No	RR	
Birth weight; g										
<1500	44	48	1.34	37	45	1.32	49	43	1.31	
<2500	871	1,297	1.13	801	1,220	1.16	976	1,182	1.11	
3000–4000 <sup>a</sup>	3,117	5,634	1.00	2,779	5,343	1.00	3,552	5,172	1.00	
Asthma										
Yes	1,478	3,665	1.15	1,306	3,457	1.18	1,819	3,317	1.16	
No	7,606	22,079	1.00	6,539	21,059	1.00	9,308	20,324	1.00	

<sup>a</sup>Reference category.

**TABLE 5**  
 Cross-Classification of Father's Smoking During Pregnancy and Childhood as Reported by Nurses and Their Mothers

	Mother's Report; No.				Total
	Yes		No		
	During Pregnancy	In Childhood	At Both Times	Missing	
Nurse's report; no.					
Yes	479	333	15,726	1,685	658
No	360	157	2,794	12,330	246
Missing	4	1	103	65	8
Total	843	491	18,623	14,080	912
					34,949