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A systematic review and meta-analysis of prospective studies on the association between maternal cigarette smoking and preterm delivery

Nirav R. Shah, MD, MPH and Michael B. Bracken, PhD, MPH

Department of Epidemiology and Public Health, Yale University School of Medicine

Abstract

We have attempted to quantify the most up-to-date estimate of the association between cigarette smoking by the mother and preterm delivery. Studies were selected for inclusion in this review if they were prospective, reported data stratified across at least two levels of maternal smoking, and defined preterm delivery on the basis of gestational age. In a meta-analysis we combined results from multiple studies that reported on preterm delivery and maternal smoking during pregnancy. Pooled odds ratios were computed for various strata of smoking intensity with the Mantel-Haenszel fixed-effects model. Twenty studies met all inclusion criteria and were included in meta-analysis. The pooled point estimate from 20 prospective studies on any maternal smoking versus no maternal smoking was 1.27 (95% confidence interval, 1.21-1.33). Subgroup analyses stratifying maternal smoking on number of cigarettes per day suggest a dose-response relationship at low to moderate levels of smoking, which was not further increased at high levels of smoking. A nonsignificant level of publication bias appears to exist in the smoking-preterm delivery literature. Cigarette smoking is a preventable risk factor that is associated with preterm delivery. Consistent results across many study populations and research designs and evidence of a dose-response relationship support its causal role in preterm delivery.

Keywords

Preterm delivery; cigarette smoking; meta-analysis

Preterm delivery is the single most important contributor to infant mortality rates in technically developed countries,¹ where rates of preterm delivery have increased over the last 20 years. In part, this observed trend may be attributed to increasing numbers of multiple births, more frequent use of ultrasonography to determine gestational age, and a growing tendency to register live births at very early gestational ages.² However, maternal smoking is a potentially preventable cause for preterm delivery. Furthermore, a dose-response effect has been observed in single studies, in which mothers who smoke greater amounts during pregnancy have progressively higher rates of preterm deliveries. This study summarizes the currently available data on the association between smoking and preterm delivery and on a dose response of the association, by reporting pooled estimates for odds ratios in association with preterm delivery and smoking.

Material and methods

Studies and review articles relating preterm deliveries and maternal smoking were identified with MEDLINE (1966-1997) and by searches of references cited in identified articles. MEDLINE was searched with the subject headings *premature labor* and *smoking*, as well as the text words *preterm delivery* and *preterm birth*, which resulted in the identification of 104 citations. Any articles containing original data were retrieved in their entirety, with study type ascertained when the full text of the article was reviewed. Studies were limited to the English language. Although a few articles were identified in Eastern European literature by MEDLINE, they were mostly case reports or case-control studies and did not fulfill our inclusion criteria. Eight retrospective, case-control studies were also identified through this search and were not selected for analysis but are discussed in the Results section.

Studies selected for analysis had to meet the following requirements: (1) The study was prospective (ie, smoking exposure was ascertained before perinatal outcome); (2) the study reported data on rates of preterm delivery stratified across at least two levels of maternal smoking, or the study included a summary estimate (odds ratio or relative risk) with reported confidence intervals; (3) the study defined preterm delivery according to gestational age. The existence of publication bias was assessed among the selected studies by means of a funnel plot³ of individual study odds ratios plotted against study size.

The methods of Mantel and Haenszel⁴ were used to estimate effect size and confidence intervals. Calculations were conducted with Microsoft Excel⁵ software by methods described by Fleiss.⁶ Individual estimates from studies were pooled as odds ratios; odds ratio estimates were derived from the data for those studies that reported relative risks. The odds ratio is comparable to the risk ratio when the baseline risk is low (ie, when the event rate in the control group is <10%, as was the case in almost all of the identified studies).⁷ Whenever possible, adjusted odds ratios were used to provide more accurate estimates of the true underlying relation between smoking and preterm delivery. Most studies adjusted for maternal age, race, gravidity, parity, income, and other social and demographic factors.

Results

A total of 64 published articles were identified that reported original data on the association between maternal smoking and preterm delivery. Twenty studies in 21 reports⁸⁻²⁸ met all the inclusion criteria and were included for analysis (see Table I). Four studies reported outcomes only in the form of mean gestational age changes for children born to smokers versus nonsmokers. Whereas these data support the association between maternal smoking and preterm delivery, in none of these reports were sufficient data presented to provide results that could be pooled with data from the other 20 studies. As a result, these 4 studies are not included in the analysis. A total of 43 studies were excluded from analysis, most because they were not prospective studies (references available from the authors on request).

The overall association between cigarette smoking and preterm delivery is reasonably well described by cohort studies. However, most did not identify the duration of exposure, with the authors choosing simply to dichotomize duration of cigarette use into any maternal smoking during pregnancy versus none. The level or intensity of smoking, however, was better characterized. Most cohorts were split into two or three levels of exposure (for example, groups in which mothers actively smoked 0-9, 10-19, or ≥ 20 cigarettes per day). Only 1 study⁸ looked at exposure to passive smoking, and so passive smoking exposure is not included in this review.

Only 2 of 20 studies showed a protective, but statistically nonsignificant, association between smoking and preterm delivery.^{18, 19} In the first,¹⁸ preterm delivery was defined as >32 weeks but <37 weeks of gestation; hence a large portion of the very early preterm deliveries are

missing, where the observed association is likely to be strongest. For <32 weeks' gestation, the same study found a relative risk of 1.95 (95% confidence interval, 1.30-2.93) for smoking and preterm delivery, pointing to the masking of smoking's effect by narrowly defining preterm delivery. The data from the group with delivery at <32 weeks' gestation were not reported in a manner that could be combined with the group with delivery at >32 weeks' gestation; hence for this review the most conservative data (which showed a protective association) were used. The other article¹⁹ did not have a purely nonsmoking cohort for comparison; instead they used as controls women who on average smoked <1 cigarette per day (including nonsmokers). This study is similar to 2 other studies,^{12, 14} which, nevertheless, reported an increased odds of preterm delivery for mothers who smoked. Exposure misclassification of this sort would bring estimates toward the null (ie, decrease the association between smoking and preterm delivery).

Table I presents data on any maternal smoking during pregnancy versus no maternal smoking. When multiple data were present in the original report, efforts were made to dichotomize results into any maternal smoking versus no maternal smoking before inclusion in this analysis. The pooled estimate with 95% confidence interval for any smoking versus no smoking and preterm delivery is 1.27 (1.21-1.33). A sensitivity analysis that excluded the 2 studies with the largest and the 2 studies with the smallest point estimates resulted in no significant changes to the pooled estimate (data not shown).

Tables IIA and IIB present maternal smoking data stratified into light to moderate smoking (<20 cigarettes per day) and heavy smoking. When data were not available for 0 to 20 cigarettes per day, alternate levels (eg, 0-9, 1-14 cigarettes per day) were used. Similarly, the heavy exposure pooled estimate used ≥ 11 , ≥ 15 , or ≥ 16 cigarettes per day when other data were not available. It was thought that 20 cigarettes per day, representing 1 pack per day, was a sensible cut point for exposure. The pooled estimate with 95% confidence interval is 1.22 (1.13-1.32) for light to moderate smoking and 1.31 (1.20-1.42) for heavy smoking.

Separating studies into two levels of smoking showed a trend toward a dose-response relationship between cigarette smoking during pregnancy and the incidence of preterm delivery. This trend was less apparent when studies were divided into 3 groups on the basis of predefined levels of smoking (see Tables IIIA, IIIB, and IIIC). For light smoking, defined as 0 to 10 cigarettes per day, the pooled estimate with 95% confidence interval was 1.25 (1.12-1.38). Moderate smoking, approximately 11 to 20 cigarettes per day, resulted in a pooled estimate of 1.38 (1.23-1.55). Heavy smoking, generally more than a pack per day, had a pooled estimate of 1.31 (1.19-1.45).

Eight case-control studies on the relationship between preterm delivery and maternal smoking were identified.²⁹⁻³⁶ Unlike the prospective studies, however; they varied widely in their quality and procedures. For example, one study³¹ selected controls from deliveries >39 weeks of gestation, to avoid misclassification bias that might occur with incorrect gestational dates for preterm infants, but this artificially inflates the association of smoking with preterm delivery. Another study³⁵ determined gestational age more carefully for cases than for controls, potentially introducing other biases.

Similarly, the definition of exposure to cigarette smoking varied widely from one case-control study to the next (see Table IV). Whereas some looked at smoking at a certain time point during pregnancy, others considered smoking status before pregnancy versus during pregnancy. One study³⁷ looked at exposure to passive cigarette smoking. Only 2 studies stratified women according to the level of smoking^{29, 30}; the others considered smoking a dichotomous variable. No case-control studies showed a protective effect from smoking on preterm delivery. Most studies reported odds ratios in the 2.0 to 3.0 range, with the overall range from 1.0 (no effect)

to 4.20. Because of the great heterogeneity between studies (eg, in choice of control group and in exposure definition and the like), the data were not considered suitable for statistical pooling.

A funnel plot to assess potential publication bias in the prospective studies is presented in Fig 1, which was created with the use of data presented in Table I. Publication bias occurs most often when small studies with “negative” results are less likely to be published. A biased plot would be asymmetric around the pooled estimate, spreading out unevenly to both sides. Among prospective studies of smoking and preterm delivery, there is a right-skewed distribution. This suggests that some studies with point estimates <1.27 (the pooled estimate) may have been conducted but were not published.

Comment

A truncated dose-response trend was observed when studies were separated into 3 groups of low, medium, and heavy smoking. It is possible that heterogeneity in design and execution of studies masked a dose-response relationship that, whereas it was apparent within individual studies, was less evident in the pooled groups. The heaviest smokers had an association between smoking and preterm delivery that was essentially the same as that for moderate smokers. An alternate explanation lies in the nature of the exposure; there are fewer people who smoke large amounts (≥ 40 cigarettes per day) relative to the low and medium smoking groups. As a result the heavy smoking group may be increasingly undifferentiated from the medium smoking group to create a clear dose-response contrast between medium and heavy smokers.

When a random-effects model was used to generate pooled odds ratios, results were essentially unchanged (data not shown). This type of model may better incorporate heterogeneity between studies than other models, and because its results were comparable to those found by the fixed-effects methods of Mantel and Haenszel, we may infer sufficient homogeneity between studies for this report.

There are several limitations to the data. Publication bias may affect the results of this study, but we believe its contribution is minimal. The overall pooled estimate of 1.27 closely approximates the point estimate of the largest study, with an odds ratio of 1.20. This suggests that, despite the possible existence of some publication bias, the pooled estimate is likely a valid estimate of the true underlying effect.

Another potentially limiting factor is that various methods were used to estimate gestational age, ranging from extrapolating the self-reported last menstrual period to estimates that were based on a combination of last menstrual period, ultrasonography, and clinical examination. Furthermore, there was some heterogeneity of exposure criteria, with cigarette smoking ascertained at different points in pregnancy and smoking categorization differing from one study to the next. Heterogeneity also existed in the rates of preterm delivery from one study to the next, ranging from 2% to 33%. This might be attributable to geographic differences between sites, different target populations and recruitment, and time when the study was conducted (earlier studies tended to have higher rates; studies published before 1983 had among them the four highest rates of preterm delivery). Finally, there are multiple known causes of preterm labor, which may have been differentially controlled among studies. Adjusted odds ratios were used whenever available to better control for possible sources of confounding, but the adjustments differed from one study to the next.

Despite these potential limitations, this analysis provides the most up-to-date and validated summary of the effect of maternal cigarette smoking on the incidence of preterm delivery. A prior meta-analysis conducted in 1984 found pooled odds ratios of 1.32 to 1.56 when preterm delivery was variously defined as before 34, 35, 36, 37, or 38 weeks of gestation.³⁹ The estimate for preterm delivery based on a gestational age <37 weeks, which was the cut point

used for this meta-analysis, found a pooled odds ratio of 1.40 (95% confidence interval, 1.30-1.51). This estimate was based on 42,000 subjects pooled from 5 studies, whereas the current meta-analysis pooled 20 studies and >100,000 subjects to get a pooled odds ratio of 1.27 (95% confidence interval, 1.21-1.33). The current meta-analysis used adjusted odds ratios whenever possible, whereas the 1984 meta-analysis used strictly unadjusted values. This report was limited to prospective studies to avoid any potential bias that might overestimate the effect of smoking in retrospective data collection.

A benefit of meta-analysis used to summarize data is that a broad range of study sites and populations are represented in the pooled estimate. This expands the generalizability of results, providing greater credibility and wider clinical and public health significance to the finding. Furthermore, there are a large number of observations in the overall analysis, which is oftentimes prohibitively difficult in any single study.

Maternal smoking has been shown to be associated with many other problems for the newborn in addition to preterm labor. There are strong associations with low birth weight,⁴⁰ spontaneous abortion,⁴¹ abruptio placentae,⁴² ectopic pregnancy,⁴³ impaired respiratory function in newborns,⁴⁴ and psychiatric adjustment of the child in later life,⁴⁵ to name just a few.

In his presidential address before the Royal Society of Medicine in 1965, Bradford Hill noted the following 9 conditions that help strengthen causal inference for an observed association: strength of the association, consistency, specificity, temporality, dose response, plausibility, coherence, experiment, and analogy. With all the data that are now available on the association between cigarette smoking and preterm delivery, these criteria have been met and any controversy regarding maternal smoking and preterm delivery appears to have been sufficiently addressed.

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Fig 1.
Funnel plot to evaluate publication bias—all prospective studies of any smoking versus none and preterm delivery. This figure was created with data presented in Table I.

Prospective studies on smoking and preterm delivery

Series	Year	Study	PTD definition (weeks ^a gestation)	Exposure criteria	Unexposed criteria	Exposed (PTD per total)	Unexposed (PTD per total)	Odds ratio	95% Confidence interval	Rate of preterm delivery (%)
Ahlborg and Bodin ⁸	1991	Sweden	<37	Smoked before first prenatal check	None	91/1291	86/2281	1.94	1.43-2.62	5
Arbuckle and Sherman ⁹	1989	Nutrition Canada	<37	Smoked during pregnancy	Never smoked	31/308	28/373	1.38	0.81-2.35	9
Donovan ¹⁰	1977	London, United Kingdom	<36	Smoked at time of questionnaire	No smoking in prior year	18/784	3/243	1.88	0.55-6.44	2
Doucette and Bracken ¹¹	1993	Yale University, New Haven, Conn	<37	> 0 cigarettes/d in month 2	0 cigarettes/d in month 2	75/1076	122/2630	1.54	1.14-2.07	5
Frazier et al ¹²	1961	Baltimore, Md	<38	Smoked every day	Occasional and nonsmokers	313/866	465/1491	1.25	1.05-1.49	33
Henriksen et al ¹³	1995	Aarhus, Denmark	<37	Smoked during pregnancy	Nonsmokers during pregnancy	54/1180	72/2426	1.57	1.09-2.25	3
Kramer et al ^{14*}	1992	Montreal, Quebec, Canada	<37	Any smoking during pregnancy	None on average during pregnancy	—	—	1.30	1.10-1.60	—
Naeye ¹⁵	1982	CPP of NINCDs	<37	Smokers	Nonsmokers	127/635	116/635	1.12	0.85-1.48	19
Nordentoft et al ^{16*}	1996	Copenhagen, Denmark	>25, <37	0-9 cigarettes/d at 20 wk	Nonsmoker at 20th wk	—	—	1.30	0.88-1.93	—
Obel ¹⁷	1979	Copenhagen, Denmark	<37	Smoking at 28 wk	Not smoking at 28 wk	87/853	84/1424	1.81	1.33-2.48	8
Peacock et al ¹⁸	1995	London, United Kingdom	>32, <37	Any cigarettes/d at booking, 28th wk	Nonsmoker	28/409	26/309	0.80	0.46-1.39	8
Rush and Kass ¹⁹	1972	Boston City Hospital	<37	≥ 1 cigarette/d	< 1 cigarette/d	113/531	104/441	0.88	0.65-1.19	22
Russell et al ²⁰	1968	Sheffield, United Kingdom	<38	≥ 5 cigarettes/d	None with <5 cigarettes/d	126/639	189/1426	1.61	1.25-2.06	15
Shiono et al ^{21*}	1986	California	>24, <37	≥ 1 pack/d during pregnancy	None during pregnancy	—	—	1.20	1.10-1.40	—
Siega-Riz et al ²²	1996	West Los Angeles	<37	Smoking	Not smoking	28/295	483/7244	1.47	0.98-2.19	7
Stein et al ²³	1987	Oxford, United Kingdom	<37	Smoking at 6 mo	Not smoking at 6 mo	7/122	7/348	2.97	1.02-8.63	3
van den Berg and Oechsle ²⁵	1984	CHDS, Kaiser	<37	Stopped because of pregnancy	Never smoked	338/4547	195/4249	1.67	1.39-2.00	6
Wen et al ²⁶	1990	Alabama	<37	Smoked at first prenatal visit	Not smoking	671/5042	1477/12107	1.10	1.00-1.22	13
Wisborg et al ²⁷	1996	Aarhus Denmark	<37	Smoked at 16 wk	Not smoking	75/1404	103/2707	1.43	1.05-1.94	4
Yerushalmy ²⁸	1964	California	<37	Any smoking during pregnancy	None	218/2584	223/3010	1.15	0.95-1.40	8
Combined [†]	—	—	—	—	—	—	—	1.27	1.21-1.33	—

PTD, Preterm delivery; CPP, Collaborative Perinatal Project; NINCDs, National Institute of Neurological and Communicative Disorders and Stroke; CHDS, Child Health and Development Studies.

* Individual cells not presented. Only odds ratios were given; hence preterm delivery rate was not calculable.

† Mantel-Haenszel fixed-effects model.

Table II A

Prospective studies on smoking and preterm delivery by level of smoking: Light to moderate smoking during pregnancy

Series	Year	Exposure criteria	Unexposed criteria	Exposed (PTD/total)	Unexposed (PTD/total)	Odds ratio	95% Confidence interval
Ahlborg and Bodin ⁸	1991	<20 cigarettes/d	No exposure	80/1159	86/2281	1.89	1.38-2.59
Doucette and Bracken ¹¹	1993	<20 cigarettes/d in month 2	0 cigarettes/d in month 2	68/984	122/2630	1.53	1.12-2.07
Kramer et al ¹⁴	1992	1-10 cigarettes/d	0 cigarettes/d on average during pregnancy	—	—	1.18	1.03-1.36
Nordentoft et al ¹⁶	1996	0-9 cigarettes/d at 20 wk	Nonsmoker at 20 wk	—	—	1.30	0.88-1.93
Peacock et al ¹⁸	1995	1-14 cigarettes/d at booking, 28th wk	Nonsmoker	21/289	26/309	0.85	0.47-1.55
Shiono et al ²¹	1986	<1 pack/d during pregnancy	None during pregnancy	—	—	1.10	0.90-1.20
van den Berg and Oedisi ²⁵	1977	Smokes <15 cigarettes/d	Never smoked	93/1600	195/4249	1.28	1.00-1.65
Wisborg et al ²⁶	1996	1-10 cigarettes/d at 16 wk	Nonsmoker	46/932	86/2339	1.36	0.94-1.96
Yerushalmy ²⁸	1964	1-10 cigarettes/d at interview	None during pregnancy	90/1059	223/3010	1.16	0.90-1.50
Combined*	—	—	—	—	—	1.22	1.13-1.32

PTD, Preterm delivery.

* Mantel-Haenszel fixed-effects model.

Table IIB
Prospective studies on smoking and preterm delivery by level of smoking: Heavy smoking during pregnancy

Series	Year	Exposure criteria	Unexposed criteria	Exposed (PTD/total)	Unexposed (PTD/total)	Odds ratio	95% Confidence interval
Ahlborg and Bodin ⁸	1991	Active; ≥20 cigarettes/d	No exposure	11/132	86/2281	2.32	1.21-4.46
Doucette and Bracken ¹¹	1993	≥21 cigarettes/d in month	0 cigarettes/d in month 2	7/92	122/2630	1.69	0.77-3.74
Kramer et al ¹⁴	1992	≥11 cigarettes/d	0 cigarettes/d on average during pregnancy	—	—	1.27	1.08-1.50
Nordentoft et al ¹⁶	1996	≥16 cigarettes/d at 20 wk	Nonsmoker at 20 wk	—	—	0.95	0.41-2.23
Peacock et al ¹⁸	1995	≥15 cigarettes/d at booking, 28th wk	Nonsmoker	7/120	26/309	0.67	0.28-1.60
Shiono et al ²¹	1986	≥1 pack/d during pregnancy	None during pregnancy	—	—	1.20	1.10-1.40
van den Berg and Oechsli ²⁵	1977	≥15 cigarettes/d	Never smoked	152/2077	195/4249	1.64	1.32-2.04
Wisborg et al ²⁷	1996	≥11 cigarettes/d at 16 wk	Nonsmoker	16/193	86/2339	2.37	1.36-4.13
Yerushalmy ²⁸	1964	≥21 cigarettes/d at interview	None during pregnancy	25/267	223/3010	1.29	0.84-1.99
Combined*	—	—	—	—	—	1.31	1.20-1.42

PTD, Preterm delivery.

* Mantel-Haenszel fixed-effects model.

Table IIIA
Prospective studies on smoking and preterm delivery by level of smoking: Light smoking during pregnancy

<i>Series</i>	<i>Year</i>	<i>Exposure criteria</i>	<i>Unexposed criteria</i>	<i>Exposed (PTD/total)</i>	<i>Unexposed (PTD/total)</i>	<i>Odds ratio</i>	<i>95% Confidence interval</i>
Ahlborg and Bodin ⁸	1991	1-9 cigarettes/d	No exposure	24/432	86/2281	1.50	0.94-2.39
Doucette and Bracken ¹¹	1993	1-10 cigarettes/d in month 2	0 cigarettes/d in month 2	46/635	122/2630	1.61	1.13-2.28
Kramer et al ¹⁴	1992	1-10 cigarettes/d	0 cigarettes/d on average during pregnancy	—	—	1.18	1.03-1.36
Nordentoft et al ¹⁶	1996	0-9 cigarettes/day at 20 wk	Nonsmoker at 20 wk	—	—	1.30	0.88-1.93
Wisborg et al ²⁷	1996	1-10 cigarettes/d at 16 wk	Nonsmoker	46/932	86/2339	1.36	0.94-1.96
Yerushalmi ²⁸	1964	1-10 cigarettes/d at interview	None during pregnancy	90/1059	223/3010	1.16	0.90-1.50
Combined*	—	—	—	—	—	1.25	1.12-1.38

PTD, Preterm delivery.

* Mantel-Haenszel fixed-effects model.

Table III B
Prospective studies on smoking and preterm delivery by level of smoking: Moderate smoking during pregnancy

Series	Year	Exposure criteria	Unexposed criteria	Exposed (PTD/total)	Unexposed (PTD/total)	Odds ratio	95% Confidence interval
Ahlborg and Bodin ⁹	1991	10-19 cigarettes/d	No exposure	56/727	86/2281	2.13	1.50-3.02
Doucette and Bracken ¹¹	1993	11-20 cigarettes/d in month 2	0 cigarettes/d in month 2	22/349	122/2630	1.38	0.87-2.21
Kramer et al ¹⁴	1992	≥11 cigarettes/d	0 cigarettes/d on average during pregnancy	—	—	1.27	1.08-1.50
Nordentoft et al ¹⁶	1996	10-15 cigarettes/d at 20 wk	Nonsmoker at 20 wk	—	—	1.79	1.12-2.85
Wisborg et al ²⁷	1996	≥11 cigarettes/d at 16 wk	Nonsmoker	16/193	86/2339	2.37	1.36-4.13
Yerushalmý ²⁸	1964	11-20 cigarettes/d	None during pregnancy	103/1258	223/3010	1.11	0.87-1.42
Combined [*]	—	—	—	—	—	1.38	1.23-1.55

PTD, Preterm delivery.

* Mantel-Haenszel fixed-effects model.

Table III C
Prospective studies on smoking and preterm delivery by level of smoking: Heavy smoking during pregnancy

Series	Year	Exposure criteria	Unexposed criteria	Exposed (PTD/total)	Unexposed (PTD/total)	Odds ratio	95% Confidence interval
Ahlborg and Bodin ⁸	1991	Active; ≥20 cigarettes/d	No exposure	11/132	86/2281	2.32	1.21-4.46
Doucette and Bracken ¹¹	1993	>20 cigarettes/d in month 2	0 cigarettes/d in month 2	7/92	122/2630	1.69	0.77-3.74
Shiono et al ²¹	1986	≥1 pack/d during pregnancy	None during pregnancy	—	—	1.20	1.10-1.40
van den Berg and Oechtsli ²⁵	1977	Smokes ≥15 cigarettes/d	Never smoked	152/2077	195/4249	1.64	1.32-2.04
Yerushalmy ²⁸	1964	≥21 cigarettes/d at interview	None during pregnancy	25/267	223/3010	1.29	0.84-1.99
Combined*	—	—	—	—	—	1.31	1.19-1.45

PTD, Preterm delivery.

* Mantel-Haenszel fixed-effects model.

Table IV

Case-control studies of smoking and preterm delivery

Series	Year	Study	PTD definition (wk)	Exposure criteria	Unexposed criteria	Odds ratio	95% Confidence interval
Berkowitz et al ^{29*}	1982	Yale	<37	≥10 cigarettes/d in 1st trimester	<10 cigarettes/d in 1st trimester	2.10	1.40-3.10
				≥10 cigarettes/d in 2nd trimester	<10 cigarettes/d in 2nd trimester	2.40	1.60-3.60
				≥10 cigarettes/d in 3rd trimester	<10 cigarettes/d in 3rd trimester	2.50	1.60-3.90
				1-9 cigarettes/d in 1st trimester	0 cigarettes/d in 1st trimester	1.20	0.70-2.20
				10-19 cigarettes/d in 1st trimester	0 cigarettes/d in 1st trimester	3.10	1.70-5.60
				≥20 cigarettes/d in 1st trimester	0 cigarettes/d in 1st trimester	1.60	0.90-2.70
				1-9 cigarettes/d in 2nd trimester	0 cigarettes/d in 2nd trimester	1.20	0.60-2.30
				10-19 cigarettes/d in 2nd trimester	0 cigarettes/d in 2nd trimester	2.80	1.50-5.10
				≥20 cigarettes/d in 2nd trimester	0 cigarettes/d in 2nd trimester	2.20	1.30-3.80
				1-9 cigarettes/d in 3rd trimester	0 cigarettes/d in 3rd trimester	1.00	0.50-1.90
de Haas et al ³⁰	1991	Brigham and Womens	20-37	10-19 cigarettes/d in 3rd trimester	0 cigarettes/d in 3rd trimester	2.90	1.60-5.40
				≥20 cigarettes/d in 3rd trimester	0 cigarettes/d in 3rd trimester	2.20	1.10-4.70
				Yes vs no at 1st prenatal visit	—	2.00	—
				<6 cigarettes/d at 1st prenatal visit vs none	—	1.30	—
				6-10 cigarettes/d at 1st prenatal visit vs none	—	2.20	—
Ekwo et al ³¹	1993	With preterm rupture of membranes	<37	≥11 cigarettes/d at 1st prenatal visit vs none	—	2.60	—
				Active; before and during pregnancy	—	4.20	1.80-10.00
				Active plus passive	Control, ≥39 wk	2.10	1.20-3.50
				Active	Control, ≥39 wk	1.70	0.70-4.30
				Active plus passive	Control, ≥39 wk	2.50	1.40-4.40

<i>Series</i>	<i>Year</i>	<i>Study</i>	<i>PTD definition (wk)</i>	<i>Exposure criteria</i>	<i>Unexposed criteria</i>	<i>Odds ratio</i>	<i>95% Confidence interval</i>
Ferraz et al ³²	1990	Brazil	<2.5 kg, <37	Smoking during pregnancy	—	1.90	1.60-2.40
Harger et al ³³	1990	United States; preterm rupture of membranes cases	20-36	Smoked but stopped during pregnancy	Not smoking during pregnancy	1.58	0.77-3.27
Hartikainen-Sorri and Sorri ³⁴	1989	All births	20-36	Presently smoking during pregnancy	Not smoking during pregnancy	2.08	1.37-3.13
			<37	Currently smoking	Nonsmoker	2.40	1.30-4.50
			<37	Currently smoking	Nonsmoker	3.40	1.60-7.20
Heffner et al ³⁵	1993	Brigham and Womens	20-36	≥1 cigarette/d during pregnancy	<500 cigarettes during lifetime and <1 cigarette/d	1.90	1.30-2.70
Williams et al ³⁶	1992	Preterm rupture of membranes	<37	Ever smoked during pregnancy	Never	2.00	1.50-2.70
		Non-preterm rupture of membranes	<37	Ever smoked during pregnancy	Never	1.70	1.30-2.10

PTD, Preterm delivery.

*Point estimates are for the same women followed from the first trimester through the third trimester; these are not independent observations.