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Effects of maternal smokeless tobacco use on selected pregnancy outcomes in Alaska Native women: a case–control study

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Abstract

Objective—To examine the potential effects of prenatal smokeless tobacco use on selected birth outcomes. Design. A population-based, case–control study using a retrospective medical record review.

Population—Singleton deliveries 1997–2005 to Alaska Native women residing in western Alaska.

Methods—Hospital discharge codes were used to identify potential case deliveries and a random control sample. Data on tobacco use and confirmation of pregnancy outcomes were abstracted from medical records for 1123 deliveries. Logistic regression was used to examine associations between tobacco use and pregnancy outcomes. Adjusted odds ratios (OR), 95% confidence intervals (95% CI), and *p*-values were calculated.

Main outcomes measures—Preterm delivery, pregnancy-associated hypertension, and placental abruption.

Results—In unadjusted analysis, smokeless tobacco use was not significantly associated with pre-term delivery (OR 1.44, 95% CI 0.97–2.15). After adjustment for parity, pre-pregnancy body mass index, and maternal age, the point estimate was attenuated and remained non-significant. No significant associations were observed between smokeless tobacco use and pregnancy-associated hypertension (adjusted OR 0.92, 95% CI 0.56–1.51) or placental abruption (adjusted OR 1.11, 95% CI 0.53–2.33).

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Conflicts of interest

All authors have explicitly stated that there are no conflicts of interest in connection with this article. The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Supporting information

Additional Supporting Information may be found in the online version of this article

Conclusions—Prenatal smokeless tobacco use does not appear to reduce risk of pregnancy-associated hypertension or to substantially increase risk of abruption. An association between smokeless tobacco and pre-term delivery could not be ruled out. Components in tobacco other than nicotine likely play a major role in decreased pre-eclampsia risk in smokers. Nicotine adversely affects fetal neurodevelopment and our results should not be construed to mean that smokeless tobacco use is safe during pregnancy.

Keywords

Abruption; cigarettes; pregnancy; pregnancy-associated hypertension; preterm delivery; smokeless tobacco

Introduction

Cigarette smoking during pregnancy increases the risk of many adverse pregnancy outcomes, including fetal growth restriction, preterm delivery, placenta previa and placental abruption; however, smoking reduces the risk of pre-eclampsia (1,2). The underlying mechanisms are not established, but because smokeless tobacco products do not expose users to products of combustion, it has been suggested that smokeless tobacco is safer than cigarettes (3,4). However, data suggest that maternal smokeless tobacco use may adversely affect pregnancy outcomes (5–7). Because smokeless tobacco is gaining popularity among women in many parts of the world (8), it is important to establish the health effects of prenatal use. In addition, comparing pregnancy outcomes in smokers and smokeless tobacco users may provide insight into the mechanisms underlying the adverse effects of smoking on maternal and infant health.

In parts of western Alaska, the prevalence of smokeless tobacco use in pregnant Alaska Native women exceeds 50% (9). Both commercial and homemade products are used; the homemade mixture (*iqmik*) includes leaf tobacco and ash from burned punk fungus, willow bush or driftwood. Because adding ash raises the pH and the amount of free (unprotonated) nicotine, nicotine exposure in users of *iqmik* is believed to be high (10). In response to concerns from local medical providers about the potential health effects of *iqmik* and commercial chew tobacco use during pregnancy, we conducted a population-based, retrospective case–control study to examine associations between maternal smokeless tobacco use in Alaska Native women and adverse birth outcomes. Based on input from local providers, a review of published literature, and a feasibility assessment, we selected for study preterm delivery, pregnancy-associated hypertension and placental abruption. To determine whether expected associations between cigarette smoking and adverse pregnancy outcomes were observed in this population, analyses of maternal cigarette smoking and these outcomes were also performed.

Material and methods

A large population of indigenous people resides in the study region in western Alaska and is relatively homogeneous with respect to socioeconomic status and culture. Nearly all (96%) pregnant Alaska Native women in the study region receive their prenatal care through a single health system, which includes village-based clinics staffed by health aides and a

regional hospital/medical center; women with high-risk pregnancies are referred to the Alaska Native Medical Center in Anchorage or to Providence Alaska Medical Center in Anchorage for specialty care during pregnancy and/or for delivery. Home and village deliveries are rare.

We used the electronic Resource and Patient Management Systems of the regional hospital/medical center and the Alaska Native Medical Center, to identify singleton deliveries to Alaska Native women who resided in the study region during pregnancy, used healthcare services at the regional hospital/medical center, and delivered at the regional hospital or a referral hospital (Alaska Native Medical Center or Providence Alaska Medical Center) between 1 January 1997 and 31 December 2005. The electronic data systems were searched for hospitalizations with International Classification of Diseases, 9th Revision, Clinical Modification (ICD9-CM) discharge codes indicating delivery of an infant (live born or stillborn). Procedure codes for manually assisted delivery or cesarean section were also identified (see Supplementary material, Appendix S1). Eligible deliveries at Providence Alaska Medical Center were identified from transfer records.

From the created data set of singleton deliveries, we identified potential case deliveries using ICD9-CM codes for the outcomes of interest (see Supplementary material, Appendix S1). Because we planned to examine multiple outcomes, we created one main control pool consisting of a random sample of approximately 10% of all singleton deliveries. Deliveries for the main control pool were selected without regard for case status. For each individual case–control analysis, the control deliveries consisted of those deliveries in the control pool that did not have the outcome of interest and that met the additional inclusion criteria for that particular analysis.

Two trained nurses completed the medical record abstractions. Inclusion criteria were: delivery ≥22 weeks of gestation; no maternal alcohol use after the first trimester and no cocaine, amphetamine, or opioid use at any time during pregnancy; and the infant was born without a major congenital anomaly. From records meeting inclusion criteria, abstractors collected: tobacco exposure; infant gender and birth size; maternal age at delivery, marital status, and highest level of education; gravidity and parity; maternal height and pre-pregnancy weight; maternal pre-existing medical conditions (including diabetes and chronic hypertension); provider's diagnosis of pregnancy complications; maternal blood pressure and urine protein measurements with corresponding gestational age estimates; maternal antihypertensive medication use before, during and after pregnancy; medications used during labor and delivery; gestational age at delivery (based on last menstrual period, ultrasound and provider's best estimate); and live birth or stillbirth. Maternal medical records before pregnancy and after delivery were also reviewed for evidence of pre-existing or persistent hypertension.

To ensure data quality and accuracy, three Centers for Disease Control investigators re-abstracted key variables from approximately 10% of the records to validate outcomes and tobacco exposure. Discrepancies were reviewed with the abstractors and retraining was provided to maintain consistency in abstraction practices.

All records meeting inclusion criteria were reviewed in detail to establish case status. Each delivery was eligible to become a case for any of the outcomes, regardless of ICD9-CM code, and regardless of whether the delivery was included in the main control pool. A delivery could serve as a case for more than one outcome and a delivery from the main control pool could be included in more than one control group.

Preterm case deliveries were <37 completed weeks gestation and control deliveries were ≥37 completed weeks gestation (based on the provider's best estimate of gestational age). We excluded stillborn deliveries, deliveries in which gestational age was unknown, case deliveries with a birthweight not plausible for a preterm birth (>95th centile for a 36-week delivery or 3980 g) and control deliveries with a birthweight not plausible for a term birth (<5th percentile for a 37-week delivery or 2390 g). Percentiles were determined using US vital statistics data for live births to American Indian and Alaska Native women.

Pregnancy-associated hypertension (PAH) case deliveries were deliveries with any clinician-diagnosed hypertensive disorder of pregnancy [pre-eclampsia, gestational hypertension, eclampsia, or HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count)] and documentation of hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg) on two or more occasions during pregnancy and separated by at least 4 h. We required that case deliveries with hypertension only during labor had a diastoloc blood pressure ≥90 mmHg, as well as proteinuria or treatment with magnesium sulfate. Deliveries with evidence of pre-existing hypertension or renal disease were excluded from both case and control groups. Case deliveries were subdivided into pre-eclampsia (hypertension with proteinuria, defined as a urine protein concentration of ≥300 mg/ 24 h, if a 24-h test was available, ≥1000 mg/L, if concentration was available, or ≥2+ on a urine dip) and gestational hypertension without proteinuria. Control deliveries had no hypertensive disorder diagnosis, no documented hypertension or proteinuria during pregnancy, no evidence of pre-existing hypertension or renal disease. We excluded from both case and control groups deliveries with missing antenatal or delivery hospitalization records or in which the mother received no prenatal care.

Abruption was defined as clinician-diagnosed placental abruption. In a sub-analysis, all deliveries with evidence of abruption from clinician diagnosis, placental pathology report, or report of abruption or blood in the amniotic fluid in the labor and delivery record, were included in the case group. The control group for both the main analysis and sub-analysis consisted of deliveries to women with no evidence of abruption from any source.

Tobacco exposure was abstracted from prenatal medical records, which included standard prenatal substance abuse forms. The type of product (cigarettes, *iqmik* or commercial chew tobacco) and the frequency of use were abstracted for two trimester groupings: the first/ second trimester and the third trimester. The highest frequency of tobacco use recorded for each trimester grouping was abstracted for each type of tobacco.

Statistical analysis

Before initiating the study, we conducted a feasibility assessment and performed power calculations to determine whether the available sample size (all singleton deliveries over a 9-

year period) was sufficient to detect associations between smokeless tobacco exposure and the outcomes of interest. We estimated that the sample would provide sufficient power (≥80%) to detect a two-fold increase in preterm delivery in smokeless tobacco users, a two-fold increase in PAH, and a three-fold increase in abruption compared with tobacco non-users. These estimates were determined to be acceptable based on our review of published studies available at the time. There were no previous studies on risk of abruption associated with smokeless tobacco use; however, local providers felt that the risk of abruption was greatly increased in smokeless tobacco users.

We categorized pregnancies into mutually exclusive exposure groups: no maternal tobacco use, continuous use of smokeless tobacco throughout pregnancy, use of smokeless tobacco but the mother quit during pregnancy, continuous maternal cigarette smoking, cigarette smoking but the mother quit during pregnancy, and use of both products (dual use). Because we had limited information on the use of cigarettes and smokeless products among dual users (concurrent dual use vs. switching from one product type to another), we excluded these pregnancies from all risk analyses. We also excluded from risk analyses pregnancies in which mothers quit tobacco because previous research suggests that cessation during pregnancy attenuates the effects of tobacco on some pregnancy outcomes, and because the number of quitters was too small to study separately.

Logistic regression was used to generate crude and adjusted odds ratios and 95% confidence intervals for deliveries to women with continuous chewing and with continuous smoking. Adjustment factors initially included in all analyses were maternal age, marital status, height, pre-pregnancy body mass index and parity. Education was not included in models because of the high proportion of missing values. Parameter estimates could not be computed for some models that included marital status because one of the categories of marital status contained only case or only control deliveries, so marital status was dropped from all models. Finally, maternal height contributed little to models and was also dropped. Final models for all outcomes therefore included maternal age, pre-pregnancy body mass index and parity. To determine whether missing information introduced bias in the full models, crude models were rerun using only data from deliveries included in the full models. Analyses were performed using generalized estimating equations to correct for correlation within women because mothers could be selected more than once during the study period if they had more than one singleton pregnancy.

Statistical analyses were performed using SAS software V.9 (SAS Institute Inc., Cary, NC, USA) for Windows. The study proposal and related materials were reviewed and approved by the institutional review boards (IRBs) of the Centers for Disease Control and Prevention and the Mayo Clinic, and by the Alaska Area IRB. The Alaska Area IRB approved the protocol by full committee, expedited review.

Results

A total of 1296 deliveries were selected for inclusion in this study, including 844 deliveries selected based on ICD9-CM codes for preterm delivery, PAH and/or placental abruption, and 557 randomly selected deliveries. Of the 557 deliveries, 105 (18.9%) also had been selected

as potential case deliveries based on ICD9-CM codes. We excluded from the full analysis 164 deliveries because of substance abuse or congenital anomalies and nine because tobacco exposure was unknown, leaving 1123 for final analysis. Of these, 707 were potential case deliveries and 502 made up the main control pool. Deliveries in the control pool were eligible to become case deliveries for any of the outcomes. Case and control designations are depicted in Figure 1.

For analysis of preterm delivery, 1104 deliveries were eligible for inclusion; 291 were preterm deliveries (3.4% of which were identified from medical record reviews in the control pool and not from ICD9-CM codes) and 449 were term control deliveries (Figure 1). Preterm case and control deliveries differed with respect to maternal age and cases were more likely than controls to be complicated by PAH or by abruption (Table 1). In unadjusted analysis, continuous maternal smokeless tobacco use was not significantly associated with preterm delivery (odds ratio = 1.44, 95% confidence interval 0.97–2.15) (Table 2). After adjustment for potential confounders, the point estimate was slightly attenuated and remained non-significant.

In unadjusted and adjusted analyses, there was no significant association observed between continuous maternal smoking and preterm delivery, although the point estimates were >1, as expected.

For analysis of PAH, 1090 deliveries were eligible for inclusion; 224 deliveries were PAH cases (3.1% of which were identified from medical record reviews in the main control pool and not from ICD9-CM codes) and 315 were control deliveries not complicated by hypertension (Figure 1). The PAH case and control deliveries differed with respect to maternal age, marital status and parity (data not shown). Of the case deliveries, 17% were also complicated by preterm delivery (compared with 5.1% of controls, $p < 0.001$), and 3.6% were also complicated by abruption (compared with 1.3% of controls, $p = 0.07$). In unadjusted analysis, there was no significant association observed between continuous maternal smokeless tobacco use and PAH (Table 3). Adjustment for potential confounders did not change this finding. When pre-eclampsia and gestational hypertension were examined separately, there was no significant association between these outcomes and maternal smokeless tobacco use.

In unadjusted and adjusted analyses, there were no sig-nificant associations observed between maternal cigarette smoking and PAH, although point estimates were <1, as expected. This finding did not change when pre-eclampsia and gestational hypertension were examined separately (Table 3).

There were 82 abruption case deliveries (all identified from ICD9-CM codes) and 485 control deliveries. Abruption case and control deliveries differed with respect to maternal age (data not shown). Thirty-nine percent of case deliveries were also preterm (compared with 7% of controls, $p < 0.001$), and 9.8% were also complicated by PAH (compared with 7% of controls $p = 0.38$). In unadjusted and adjusted analyses, there were no significant associations between maternal smokeless tobacco use and placental abruption (Table 4). An

expanded definition of abruption did not change this finding. There were no sig-nificant associations between maternal cigarette smoking and abruption (Table 4).

Discussion

The adverse effects of prenatal cigarette smoking are well documented, but the underlying mechanisms and components involved are not fully understood (11). In contrast, smokeless tobacco use is prevalent or gaining in popularity among women in many parts of the world, but little is known about the potential health effects of use during pregnancy. While cigarette smoking and smokeless tobacco use result in maternal and fetal exposure to nicotine, smokeless tobacco use does not result in exposure to products of combustion. Comparing pregnancy outcomes in smokers and smokeless tobacco users will increase our understanding of the components and mechanisms involved and provide important clinical information for populations in which smokeless tobacco use in women is high.

In our study, we found no statistically significant associations between smokeless tobacco use and increased risk of preterm delivery, PAH or placental abruption, although the point estimate for smokeless tobacco and preterm delivery was similar to those previously reported (11,12). Similar to previous studies (7), we did not find evidence that smokeless tobacco use protects against pre-eclampsia.

Cigarette smoking during pregnancy is associated with a modest increase in the risk of preterm delivery, with an estimated relative risk of 1.27 (12). Researchers also found an increased risk for preterm delivery in smokeless tobacco users. In a recent analysis using data from the Swedish Birth Register, the authors found a 1.3-fold increase in preterm delivery among smokeless tobacco (*snus*) users (13), and in a study in India, smokeless tobacco use was associated with a two-fold increase in preterm delivery (5). However, in a study in South Africa, the authors found no increase in deliveries <36 weeks of gestation among smokeless tobacco users (14). In our study, the adjusted odds ratio for preterm delivery overall was 1.23, similar to that in the Swedish study, although ours was not statistically significant. Because our sample size was insufficient to detect a modest association, it remains possible that smokeless tobacco increases the risk of preterm delivery and that nicotine contributes to the increased risk of preterm delivery in both smokeless tobacco users and smokers.

A reduced pre-eclampsia risk of approximately 30% among women who smoke during pregnancy has been well documented (11). It has been hypothesized that pre-eclampsia is the result of an imbalance of maternal pro-angiogenic and anti-angiogenic factors, with a shift toward an anti-angiogenic state. Further, carbon monoxide may play a key role in the protective effects of tobacco against pre-eclampsia through modulatory effects on the pro-angiogenic and anti-angiogenic balance, toward a pro-angiogenic state (15). Consistent with this latter hypothesis, the authors of a recent analysis using Swedish Birth Register data found no significant association between smokeless tobacco use and pre-eclampsia (adjusted odds ratio 1.11, 95% confidence interval 0.97–1.28) (16), which would be expected if products of combustion other than nicotine were responsible for the protective effects of smoking. In the current study, which has the advantage of a detailed medical record review,

our findings for both PAH and pre-eclampsia were similar to the Swedish study in that we did not find a protective effect. Together, these findings support that tobacco components other than nicotine play a major role in reducing the risk of PAH and pre-eclampsia in cigarette smokers.

Smoking during pregnancy is associated with an approximately two-fold increased risk for placental abruption (11). There are no previous publications to our knowledge in which abruption risk in smokeless tobacco users is assessed, and in the current study, we found no evidence that maternal smokeless tobacco use increases risk of abruption. Our findings should reassure local providers in Alaska that smokeless tobacco use does not appear to increase risk of abruption in their community.

Our study's strengths include that it addresses concerns among local providers about important maternal health issues, our sample was population-based, and we were able to conduct thorough medical records reviews. In particular, we used rigorous case definitions for PAH, which is often difficult in larger population-based studies. In addition, because our study population is relatively homogeneous and smokeless tobacco use is ubiquitous, confounding is less of a concern compared with many other populations. Although smokeless tobacco products in Alaska are varied, especially with respect to the addition of ash, they are more similar than products used in India, strengthening our ability to draw conclusions related to effects of nicotine vs. products of combustion. Finally, although our sample was small, we were able to analyze women who smoked cigarettes, and our point estimates are consistent with previous literature for pre-term delivery and for PAH. This suggests that our tobacco exposure data were reasonably accurate.

This study has several limitations. There is variation in the types and composition of smokeless tobacco products used in this population, and it is possible that the use of some products could result in adverse health effects that we missed because effects were masked when smokeless products were combined in our analysis. We did not have information on the proportions of ash and tobacco used to make *iqmik* or the portion size chewed, nor did we have biochemical measures of tobacco exposure. Our sample was too small to detect modest associations; however, we based our sample size calculations on the best-available published and anecdotal data available at the time. Finally, we relied on retrospective assessments of exposure and outcomes, which may have resulted in misclassification.

Nicotine has known adverse effects on neurodevelopment and has been classified as a developmental toxin by the California Environmental Protection Agency (17). In our study, we were unable to assess potential negative effects of nicotine from maternal smokeless tobacco use on fetal neurodevelopment; this area remains a concern for our study population. In addition, we examined a limited number of outcomes; prospective studies are needed to identify and quantify other potential adverse effects of smokeless tobacco on reproductive and child health outcomes. Providers should continue to advise pregnant women to avoid all forms of tobacco.

Conclusions

Maternal smokeless tobacco use during pregnancy does not appear to reduce risk of PAH or to substantially increase risk of abruption. An association between smokeless tobacco and preterm delivery could not be ruled out, leaving open the possibility that nicotine may play a central role in increasing risk of preterm delivery. Components in tobacco other than nicotine, such as products of combustion, may play a major role in decreased pre-eclampsia risk in smokers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

ICD9-CM	International Classification of Diseases, 9th Revision Clinical Modification
PAH	pregnancy-associated hypertension

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Key Message

Prenatal smokeless tobacco use does not appear to reduce risk of pregnancy associated hypertension or to substantially increase risk of abruption in this population of Alaska Native women.

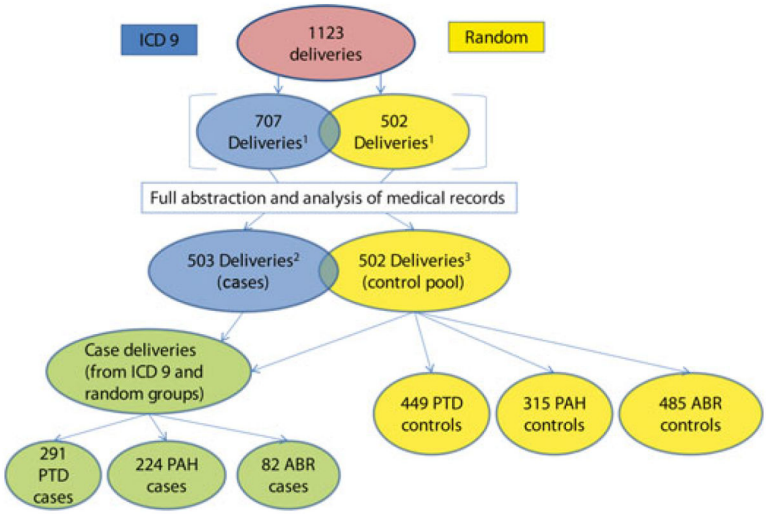

Figure 1.

Designation of case and control deliveries, Alaska Native women 1997–2005. [1]Numbers do not add up to 1123 because the random sample was selected without regard for ICD9-CM codes. [2]Case for at least one outcome (PTD, PAH, ABR). [3]72 served as both cases and control deliveries in different analyses. ABR, placental abruption; PAH, pregnancy-associated hypertension; PTD, preterm delivery.

Table 1

Preterm delivery: maternal characteristics of case and control deliveries, deliveries to quitters included, Alaska Native women 1997–2005.

	Case deliveries (*n* = 291)	Control deliveries (*n* = 449)	*p*-value
Mother's age, *n* (%)			0.03
<20 years	49 (16.8)	58 (12.9)	
20–29 years	151 (51.9)	277 (61.7)	
30+ years	91 (31.3)	114 (25.4)	
Missing (*n* = 0)			
Marital status, *n* (%)			0.37
Married	122 (44.5)	204 (48.0)	
Single, Divorced, Widowed	152 (55.5)	221 (52.0)	
Missing (*n* = 41)			
Education, *n* (%)			0.58
Less than High School	74 (31.0)	97 (27.0)	
High School or General	138 (57.7)	218 (60.7)	
Educational Development			
Some college or higher	27 (11.3)	44 (12.3)	
Missing (*n* = 142)			
Parity, *n* (%)			0.57
Nulliparous	69 (23.7)	98 (21.9)	
Parous	222 (76.3)	349 (78.1)	
Missing (*n* = 2)			
Trimester in prenatal care, *n* (%)			0.37
First	148 (52.7)	250 (56.1)	
Second or third	133 (47.3)	196 (43.9)	
Missing (*n* = 13)			
Body mass index, *n* (%)			0.13
Lean/normal	118 (47.8)	169 (44.6)	
Overweight	78 (31.6)	108 (28.5)	
Obese	36 (14.6)	58 (15.3)	
Extremely obese	15 (6.1)	44 (11.6)	
Missing (*n* = 114)			
Mother's height, cm: mean (SD)	164.8 (26.6)	166.9 (28.4)	0.32
(Missing: *n* = 1)			
Pregnancy-associated hypertension, *n* (%)	39 (13.4)	31 (6.9)	<0.001
Placental abruption, *n* (%)	32 (11.0)	5 (1.1)	<0.001
Tobacco use, *n* (%)			0.20
Non-users	57 (19.6)	116 (25.8)	
Smoke cigarettes only, continued	40 (13.7)	48 (10.7)	
Smoke cigarettes only, quit	11 (3.8)	25 (5.6)	
Chew smokeless only, continued	149 (51.2)	210 (46.8)	

	Case deliveries (*n* = 291)	Control deliveries (*n* = 449)	*p*-value
Chew smokeless only, quit	10 (3.4)	10 (2.2)	
Smoke cigarettes and chew smokeless	24 (8.2)	40 (8.9)	

Table 2

Preterm delivery: crude and multivariate analysis of tobacco exposure,[a] Alaska Native women 1997–2005.

		Continuous smokeless tobacco use			Continuous cigarette smoking		
	n **case/control deliveries**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Crude	246/374	1.44	0.97–2.15	0.07	1.70	0.95–3.01	0.07
Adjusted, full[b]	212/311	1.23	0.78–1.93	0.37	1.71	0.91–3.24	0.10
Crude, restricted data set[c]	212/311	1.39	0.89–2.15	0.14	1.69	0.91–3.14	0.10

95% CI, 95% confidence interval; OR, odds ratio.

[a]Deliveries to quitters and dual users excluded.

[b]Adjusted for parity, pre-pregnancy body mass index, age.

[c]Includes only those observations included in the full model.

Table 3

Pregnancy-associated hypertension: crude and multivariate analysis of tobacco exposure,[a] Alaska Native women 1997–2005.

		Continuous smokeless tobacco use			Continuous cigarette smoking		
	n **case/control deliveries**	**OR**	**95% CI**	***p*-Value**	**OR**	**95% CI**	***p*-value**
Pregnancy-associated hypertension							
Crude	180/266	0.88	0.56–1.38	0.57	0.68	0.34–1.35	0.27
Adjusted, full[a]	160/222	0.92	0.56–1.51	0.74	0.65	0.31–1.37	0.26
Crude, restricted data set[b]	160/222	0.78	0.48–1.27	0.33	0.63	0.31–1.31	0.22
Pre-eclampsia							
Crude	133/266	0.83	0.50–1.36	0.45	0.73	0.34–1.59	0.43
Adjusted, full[a]	119/222	0.90	0.52–1.56	0.70	0.69	0.30–1.58	0.38
Crude, restricted data set[b]	119/222	0.77	0.45–1.31	0.33	0.69	0.30–1.56	0.37
Gestational hypertension							
Crude	47/266	1.04	0.50–2.15	0.92	0.49	0.14–1.76	0.28
Adjusted, full[a]	41/222	0.93	0.42–2.03	0.85	0.52	0.14–1.90	0.32
Crude, restricted data set[b]	41/222	0.83	0.39–1.79	0.64	0.47	0.13–1.67	0.24

95% CI, 95% confidence interval; OR, odds ratio.

[a]Adjusted for parity, pre-pregnancy body mass index, age. Deliveries to quitters and dual users excluded.

[b]Includes only those observations included in the full model.

Table 4

Placental abruption: crude and multivariate analysis of tobacco exposure,[a] Alaska Native women, 1997–2005.

		Continuous smokeless tobacco use			Continuous cigarette smoking		
	n **case/control deliveries**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Primary study definition[b]							
Crude	63/407	1.25	0.66–2.37	0.49	1.22	0.50–2.93	0.66
Adjusted, full[c]	49/339	1.11	0.53–2.33	0.78	1.19	0.43–3.29	0.74
Crude, restricted dataset[d]	49/339	1.16	0.57–2.39	0.68	1.07	0.40–2.86	0.90
Expanded definition[e]							
Crude	88/407	1.07	0.63–1.83	0.80	1.04	0.48–2.23	0.93
Adjusted, full[c]	71/339	1.05	0.57–1.95	0.87	1.09	0.46–2.57	0.85

95% CI, 95% confidence interval; OR, odds ratio.

[a]Deliveries to quitters and dual users excluded.

[b]Clinician-diagnosed placental abruption.

[c]Adjusted for parity, pre-pregnancy body mass index, age.

[d]Includes only those observations included in the full model.

[e]Clinician-diagnosed placental abruption, note of hemorrhage on the placental pathology report, report of abruption or blood in the amniotic fluid in the labor and delivery record.