Maternal Smoking and Adverse Birth Outcomes Among Singletons and Twins

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ABSTRACT

Objectives. This study assessed the effects of maternal smoking on birth outcomes among singletons and twins.

Methods. An algorithm was developed to link twins with their siblings in the 1995 Perinatal Mortality Data Set. A random-effects logistic regression model was then used to estimate the association between maternal smoking and several adverse outcomes for a random sample of singletons and for all twins with available maternal smoking information.

Results. The algorithm successfully linked sibling pairs for 91% of the twin sample. Maternal smoking was associated with a significantly increased risk of low birthweight, very low birthweight, and gestation of less than 33 weeks for both singletons and twins and with an increased risk of gestation of less than 38 weeks, infant mortality, and placental abruption for singletons. Among smokers, negative impacts on the risk of low birthweight, very low birthweight, and extreme premature delivery were significantly higher for women carrying twins.

Conclusions. Some of the negative effects of smoking on low birthweight and preterm delivery are greater for twins than for singletons. Women carrying twins should be warned that smoking increases their already high risk of serious infant health problems. (*Am J Public Health*. 2000;90:395–400)

The relationship between prenatal maternal smoking and adverse outcomes in singleton births is well known.[1,2] Tobacco use during pregnancy has been associated with intrauterine growth retardation (and, thus, low birthweight), sudden infant death syndrome, premature delivery, placental abruption, and other negative maternal and infant outcomes.[3–6] The mechanisms by which the toxic chemicals in cigarettes produce adverse fetal effects are not precisely known. Carbon monoxide, however, is known to affect oxygen transfer to the placenta.[7] In addition, nicotine constricts the uterine arteries, also resulting in hypoxia.[7]

The consequences of maternal smoking for multiple-gestation pregnancies have been less extensively researched. Because twins place a higher demand for oxygen delivery on the placenta, they are significantly more likely than singletons to be born prematurely, to be of low birthweight, and to die during the first year of life.[8,9] As such, maternal smoking may pose especially serious risks for twins. In addition, women who smoke are actually at an increased risk for dizygotic twinning.[10,11]

Previous research has shown an association between maternal smoking and a number of adverse pregnancy outcomes among twins. In a study of Swedish births, Rydhstroem and Kallen found that maternal smoking was significantly associated with reduced gestational age, intrauterine growth retardation, stillbirth, and neonatal mortality among both singletons and twins.[12] Orlebeke and colleagues reported that smoking was associated with a 200-g reduction in mean birthweight among Dutch twins.[13] Similarly, Luke and Leurgans, using a novel sample of 924 mothers of twins participating in the 1989 to 1993 Twins Days Festivals in Twinsburg, Ohio, found that maternal smoking was associated with a 254-g reduction in mean birthweight.[14]

While some studies have explored maternal smoking and adverse birth outcomes among twins, the published literature includes few population-based studies. Also, most previous research has focused exclusively on twin births. Few studies have compared twin and singleton births in the same samples.

The present study used 1995 birth certificate data to investigate the impact of maternal smoking on a number of birth outcomes in a large, population-based sample of both singletons and twins. Such an analysis is timely, given the rising incidence of twins and births of higher plurality. In the United States, the rate of multiple births per 1000 live births increased by 14% between 1985 and 1991.[15]

We also describe a novel approach to matching twin pairs by means of population-level vital registration data without personal identifiers. Although the incidence of twinning is increasing, it is still a relatively rare event. Because fewer than 3% of births are of multiple gestation, the use of clinical data to explore the impact of tobacco use or other maternal risk factors on important (but rare) outcomes remains difficult. Vital records are an obvious population-based data source, yet twin pairs are not explicitly linked in birth certificate data available for public use. The algorithm described here can be used to identify and link most sibling pairs in these data in an effort to control for correlations between unobserved variables in twin pairs.

Methods

This study used individual-level 1995 data from the National Center for Health Sta-

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tistics Perinatal Mortality Data Set. These data comprise approximately 99% of live births to US citizens occurring in 1995 (n=3 899 589), including 96 785 infants identified as twins. It is not known why there was an odd number of twins in this data set.

The data were drawn from birth certificates, which provide a rich variety of data concerning birthweight, gestational age at delivery, pregnancy and labor/ delivery complications, and timing and frequency of prenatal care use. Birth certificates also include limited sociodemographic information such as maternal and paternal education level, race, ethnicity, and marital status.

Since 1989, self-reported smoking status and average daily consumption of cigarettes have been included in the birth certificate records of most states. Approximately 21% of 1995 twin births (n=20 149) did not include information on maternal smoking and thus were excluded from the sample. Of these exclusions, 91% were from 3 states (California, Indiana, and New York) that did not include maternal smoking information on birth certificates in 1995.

The statistical methodology used in this study required that sibling pairs be identified to control for unobserved maternal or pregnancy-specific factors. Although the data set indicates whether any specific infant was a singleton or twin (or higher gestation), twins are not explicitly linked in public use data. Other data useful in linking twins (such as complete date of delivery) are masked to preserve confidentiality. Therefore, a matching algorithm was developed to link infant twins to each other.

Infants were considered to be possible matches if the data indicated identical values for the following variables: state and county of birth, month of delivery, number of recorded prenatal care visits, maternal and paternal age in years, maternal race and years of education, and a 6-category marker for gestational age in weeks (17–20, 21–28, 29–32, 33–36, 37–40, more than 40). Many observations included missing values for variables such as paternal age. In such cases, infants were considered possible matches if they had identical values for the observed variables and had identical "skip" patterns of missing data. A twin was considered successfully matched if the algorithm yielded exactly 1 potential match with the identical observed pattern.

The algorithm identified unique siblings for 69 688 (91%) of the 76 636 birth records that included maternal smoking data. The 6948 excluded infants most commonly lacked a matching sibling (n=6717). In 231 cases, the matching algorithm identified 2 or more potential matches that could not be distinguished. (Including these multiple matches in the analyses described hereafter produced no appreciable change in estimated coefficients or standard errors.)

We verified the algorithm's accuracy by performing detailed consistency checks. We identified 3 variables not used in the algorithm that should be common between siblings and that are independently recorded on twin birth certificates: gestational age (in weeks rather than in the broad categories used in the match), maternal prenatal smoking, and placenta previa. We found complete agreement in 99.8% of cases. To compare outcomes for singleton and twin births, we also selected a random 5% singleton sample with information on smoking from the same data source (n=297 841).

Although low birthweight is a widely used measure, it captures only 1 limited dimension of infant health. This is especially true for twins, who are often born healthy in the range between 2000 and 2500 g. To provide a more complete picture of tobacco-related harms, we explored 6 outcomes: (1) low birthweight, defined as weight at birth under 2500 g; (2) very low birthweight, defined as weight at birth under 1500 g; (3) preterm delivery, defined as a gestation of less than 38 weeks; (4) severe preterm delivery, defined as a gestation of less than 33 weeks; (5) infant mortality, defined as death during the first 12 months after birth; and (6) placental abruption (premature separation of the placenta from the uterine wall).

In this study, smoking status was coded as a trichotomous variable. Women were classified as (1) nonsmokers, (2) those who reported smoking 1 to 10 cigarettes per day during pregnancy, and (3) those who reported smoking more than 10 cigarettes per day during pregnancy. Independent control variables included maternal age, race, Hispanic ethnicity, and education; trimester of prenatal care initiation; and infant sex.

Although multiple logistic regression can be used to predict discrete adverse outcomes, this framework ignores correlations in unobserved variables within twin pairs. Birth outcomes are influenced by such factors as overall maternal health, maternal nutrition, outcomes of previous pregnancies, and quality and content of prenatal care. Some of these factors can be controlled explicitly. However, many are unobservable or unavailable in existing population-based data. Thus, birth outcomes are likely to be correlated within twin pairs. Such residual correlations must be explicitly modeled for correct standard errors and consistent parameter estimates.

One solution is to include only 1 sibling per twin pair in the statistical analysis. This produces correct standard errors but results in a loss of half of the available sample. For some events (such as premature delivery or placental abruption), this restriction is appropriate, because the adverse event is common to both siblings. However, for rare outcomes that can differ between siblings (such as infant mortality), removing half of the sample sacrifices needed power, even within large data sets. To avoid such problems, we estimated a random-effects logit specification to capture sibling correlations due to pregnancy effects. We did so with the SAS GENMOD procedure, following the generalized estimating equations framework of Zeger and Liang.[16]

We used the resulting coefficients to conduct 2 other types of analyses. First, we calculated the population-attributable risk due to smoking for both singletons and twins. Ignoring confounders, population-attributable risk can be expressed as $p(r-1)/[p(r-1)+1]$, where p is the population prevalence of tobacco exposure and r is the relative risk of disease for the smoking-exposed group.[17] The estimated population-attributable risk captured the proportion of adverse outcomes in the general population that were due to maternal smoking. For each of the 6 outcomes, we estimated population-attributable risks separately for singletons and twins.

Second, we calculated the incremental risk of negative birth outcomes among singletons and twins exposed to tobacco in utero. We defined incremental risk as the number of adverse outcomes among pregnant smokers that were actually due to smoking. Incremental risk was the pertinent parameter with which to examine the efficacy and cost-effectiveness of interventions designed to improve outcomes within the tobacco-exposed group. Absent confounders, incremental risk is proportionate to the numerator in the population-attributable risk formula. In our analysis, both population-attributable risk and incremental risk were adjusted for the potential confounders listed earlier.[18]

Results

The prevalence of self-reported smoking during pregnancy was similar among mothers of singletons (13.4%) and twins (12.1%). Smoking prevalence varied across sociodemographic groups for mothers of both singletons and twins (Table 1). Rates were highest among non-Hispanic White women with lower levels of education. Smoking prevalence rates among women who initiated prenatal care after the first trimester were nearly twice those observed among women initiating care during the first 3 months of pregnancy (data not shown).

Twins experienced significantly higher incidence rates of all 6 negative outcomes,

TABLE 1—Prevalence of Maternal Smoking, by Demographic Characteristics; US Singleton and Twin Births, 1995

	Singletons	Twins
No. of mothers	297 841	69 688
Mothers who smoke, %	13.4	12.1***
Race/ethnicity, %		
White	16.6	1.1***
African American	9.9	1.2***
Hispanic	3.9	4.3
Other	8.8	8.1
Age, y, %		
<18	15.2	10.5***
19–29	14.5	13.7***
30–39	11.0	10.5*
40 and older	10.5	8.7*
Education, %		
Less than high school	21.4	1.1**
High school graduate	17.0	16.8
Some college or trade school	10.0	9.6
College graduate or more	2.6	2.4

*$P<.05$; **$P<.01$; ***$P<.001$ (differences between singletons and twins).

independent of smoking. Negative outcome incidence rates (per 1000 live births) for singletons and twins, respectively, were (1) low birthweight, 62.1 and 535; (2) very low birthweight, 11 and 100; (3) gestation of less than 38 weeks, 17/1000 and 702; (4) gestation of less than 33 weeks, 21 and 147; and (5) placental abruption, 6 and 12. Infant mortality was also significantly higher for twins, with a rate of 28 per 1000 vs 6 per 1000 among singleton births.

Additional analyses (results not shown) suggested that cases excluded from the sample because of missing maternal smoking data involved somewhat lower rates of infant mortality, low birthweight, and very low birthweight. Such discrepancies probably reflect regional differences in the prevalence of these outcomes.

For both singletons and twins, the rates of all 6 adverse birth outcomes were markedly higher among infants born to pregnant smokers (Table 2). Among singletons, the rate of low birthweight was 55 per 1000 live births for women who did not smoke but was approximately double that for smokers: 105 per 1000 among those smoking 1 to 10 cigarettes per day and 115 per 1000 among those smoking more than 10 cigarettes per day. Similarly, among twins, the low-birthweight rate was 518 per 1000 live births for women who did not smoke but rose to 672 among those smoking 1 to 10 cigarettes per day and 687 among those smoking more than 10 cigarettes per day.

A dose–response relationship between number of cigarettes smoked and risk of negative outcomes was not strongly suggested in these results, wherein all smokers consuming more than 10 cigarettes per day were combined. However, additional multivariate analyses for singletons and univariate analyses for twins suggested a dose–response relationship when heavy smokers (those consuming 20 or more cigarettes per day) were examined separately. In the twin group, the relatively small number of mothers who reported heavy smoking produced unstable multivariate results.

The risks of poor birth outcomes by smoking status, adjusted for potential confounders, are presented in Table 3. These results were also adjusted for unobserved correlations in shared risks within twin pairs, although this correction had a small impact on the resulting point estimates. Logistic regression results were used to compute adjusted odds ratios, which were then adjusted to indicate relative risks (according to the method of Zhang and Yu[19]). Maternal smoking was associated with significantly increased risks of low birthweight, very low birthweight, and gestation of less than 33 weeks for both singletons and twins and with increased risks of gestation of less than 38 weeks, infant mortality, and placental abruption for singletons. The effects of maternal smoking appeared to be greater among singletons than twins for the outcomes of low birthweight, gestation of less than 38 weeks, infant mortality, and placental abruption.

The same pattern of apparently elevated risks of maternal smoking for singletons as compared with twins arose in the calculations of population-attributable risk (Table 4). For each of the 6 outcomes, complete elimination of smoking during twin pregnancies produced small reductions in the population prevalence of these negative outcomes relative to those for singletons. For example, 11.1% of the incidence of low birthweight among all singleton births was due to smoking, as compared with only 3.5% among twins. However, singleton–twin comparisons of relative risks (Table 3) and population-attributable risks (Table 4) both masked the fact that the negative effects of maternal smoking were actually higher among twins for some important outcomes.

The "incremental risk" estimated the number of negative outcomes within the smoking-exposed group that could be avoided if all smoking were prevented during pregnancy. The incremental risk results (Table 4) suggest that the negative impact of maternal smoking on the risk of low birthweight, very low birthweight, and extreme prematurity was

TABLE 2—Rates of Birth Outcomes, by Smoking Status: US Singletons and Twins, 1995

	Rate per 1000 Singletons			Rate per 1000 Twins		
Outcome	Nonsmokers (n = 258 089)	1–10 Cigarettes per Day (n = 25 824)	>10 Cigarettes per Day (n = 13 928)	Nonsmokers (n = 67 360)	1–10 Cigarettes per Day (n = 6088)	>10 Cigarettes per Day (n = 3188)
Low birthweight	55	105	115	518	672	687
Very low birthweight	10	15	15	101	138	139
Gestation <38 weeks	167	199	197	698	699	702
Gestation <33 weeks	20	31	27	147	188	175
Infant mortality	4.9	9.0	9.3	30.3	36.8	37.3
Placental abruption	5.2	9.7	10.6	11.5	17.7	16.7

TABLE 3—Adjusted Relative Risks for Outcomes, by Smoking Status: US Singletons and Twins, 1995

	Relative Risk (95 % Confidence Interval)					
	Singletons			Twins		
Outcome	Nonsmokers	1–10 Cigarettes per Day	>10 Cigarettes per Day	Nonsmokers	1–10 Cigarettes per Day	>10 Cigarettes per Day
Low birthweight	1.0	1.84 (1.77, 1.92)	2.21 (2.10, 2.33)	1.0	1.28 (1.25, 1.30)	1.33 (1.30, 1.37)
Very low birthweight	1.0	1.39 (1.25, 1.55)	1.61 (1.39, 1.86)	1.0	1.36 (1.23, 1.50)	1.45 (1.29, 1.64)
Gestation < 38 weeks	1.0	1.15 (1.12, 1.19)	1.20 (1.15, 1.24)	1.0	1.00 (0.98, 1.02)	1.02 (0.99, 1.05)
Gestation < 33 weeks	1.0	1.38 (1.28, 1.49)	1.39 (1.25, 1.55)	1.0	1.26 (1.19, 1.33)	1.27 (1.15, 1.38)
Infant mortality	1.0	1.60 (1.38, 1.85)	1.76 (1.46, 2.13)	1.0	1.04 (0.85, 1.27)	1.25 (0.97, 1.60)
Placental abruption	1.0	1.65 (1.44, 1.91)	1.73 (1.45, 2.01)	1.0	1.45 (1.06, 1.97)	1.24 (0.88, 1.77)

significantly greater among women carrying twins. This further suggests that the benefits of smoking cessation and primary prevention are substantially greater for twins than for singletons for these outcomes.

For example, for every 1000 births to women who smoked, an estimated 55 cases of low birthweight were the result of maternal smoking among singleton births, as compared with 123 cases among twins. These results reflect the larger prevalence of negative outcomes among mothers who smoked while carrying twins, compared with mothers who smoked while carrying singletons (as suggested in Table 2). Within the twin group, population-attributable risk calculations appeared to minimize the role of smoking because of the high base rate of negative birth outcomes among smokers and nonsmokers alike.

Discussion

Maternal smoking is associated with statistically and clinically significant adverse outcomes among both singleton and twin births. The association between smoking and birthweight is well documented; however, maternal smoking is also an important factor in the severe outcomes of very low birthweight and extreme prematurity. The correlation between smoking and these adverse outcomes remained pronounced after we controlled for sociodemographic factors related to smoking behavior as well as for intersibling correlations in unobserved variables among twins.

In our data, smoking was associated with delivery before 38 weeks among singletons but not among twins. Approximately 70% of twins in this sample were delivered before 38 weeks of gestation, regardless of maternal smoking status. Thus, maternal smoking does not appear to further elevate the risk of this common outcome among twins. However, smoking does increase the risk of low birthweight and very low birthweight among twins and singletons, ostensibly through a mechanism involving intrauterine growth retardation.[5,7]

Because the base prevalence of adverse outcomes is so high among twins, the increased risks associated with maternal smoking are partially concealed by relative risk or population-attributable risk estimates within this group. However, the greater impact of smoking becomes apparent when one compares point estimates of smoking-attributable incremental risks for singletons and twins, illustrating the simple but important point that population-attributable risk comparisons can be misleading in examinations of outcomes across groups with different baseline risks.

Our results differ somewhat from those of Rydhstroem and Kallen, who found that maternal smoking had no effect on gestational duration among twins and that smoking had similar effects on growth retardation and perinatal death among both singletons and twins.[12] However, our finding that maternal smoking has a greater negative effect on twins than on singletons is biologically plausible. Multiple fetuses strain the uterine blood supply. Maternal smoking further disrupts this critical function, primarily through the process of fetal hypoxia.[7,20] Maternal smoking may also have different effects for monozygotic and dizygotic twins. Multiple placentas may create smoking-related risks different from those of a single fused placenta.

Our results underscore the importance of informing all women that tobacco use during pregnancy involves major and avoidable health risks.[21] The American College of Obstetricians and Gynecologists provides clinical guidelines for substance use during pregnancy and for caring for women with multiple gestations; however, tobacco use and other substance use are not specifically discussed in the care of multiple-gestation pregnancies.[22,23] Providers of reproductive health services, preconceptional counseling, and medical care to women should be aware of the risks of maternal tobacco use in regard to birth outcomes and should realize that some of these risks are elevated among women carrying twins.

Previous research among the general population of pregnant women indicates that interventions designed to reduce maternal smoking can be both efficacious and cost-effective.[2,24,25] A 1990 analysis estimated that between $20 million and $56 million could be saved annually in medical care and social service costs if 8% of pregnant smokers ceased their tobacco use.[24] Marks et al. argued that smoking cessation programs with low success

TABLE 4—Population-Attributable and Incremental Risks due to Maternal Smoking: US Singletons and Twins, 1995

	Population-Attributable Risk, %		Incremental Risk per 1000 Smokers	
Outcome	Singletons	Twins	Singletons	Twins
Low birthweight	11.1	3.5	55.3***	122.9***
Very low birthweight	5.7	4.5	4.3***	32.8***
Gestation <38 weeks	2.4	0.1	21.5***	1.4
Gestation <33 weeks	5.2	3.1	7.9***	32.6***
Infant mortality	6.3	1.3	2.3***	1.1
Placental abruption	9.4	3.3	3.9***	2.9*

*$P < .05$; **$P < .01$; ***$P < .001$ (significant difference from zero).

rates could still be cost-effective.[26] These authors estimated that interventions with quit rates of 15% have the potential to save between $3.31 and $6.58 per dollar spent by reducing the need for neonatal intensive care and other costly interventions.

A review by O'Campo and colleagues emphasized that smoking cessation interventions among pregnant women show significant aggregate benefits, although there is some variation in the array of strategies implemented and their resulting effectiveness.[24] Little appears to be known about the efficacy or cost-effectiveness of smoking cessation interventions for women carrying twins. The present findings suggest that some smoking-related risks are especially high in the case of twin births. Moreover, each pregnant smoker exposes 2 infants to tobacco risks. Thus, smoking cessation efforts for mothers of twins—including intensive interventions that involve ancillary services—may be especially cost-effective in this high-risk population.

This analysis involves some important limitations. First, we relied on self-reported smoking information from birth certificates. Studies suggest that women who are pregnant or have just given birth tend to underreport their smoking behavior.[2,27,28] An important related problem is that smoking is correlated with other behavioral risks such as poor nutrition, alcohol use, and illicit drug use. Such patterns may bias the resulting estimated impact of smoking on birth outcomes. However, there is no reason to believe that underreporting patterns would differ dramatically between women carrying twins and those carrying singletons.

A second limitation is that the analysis excluded observations with missing data regarding maternal smoking. The excluded cases were clustered in 3 states, 2 of which have large populations of great socioeconomic and ethnic diversity. Thus, while the study sample was large and population based, the exclusion of these 3 states limits our ability to make national generalizations from the results.

A third limitation is the lack of the statistical power necessary to reliably estimate the impact of maternal smoking behavior on rare outcomes among twins. It is striking that we obtained large standard errors in our estimates of the effects of smoking on infant mortality and rather large standard errors in our analysis of placental abruption within a sample that included most known 1995 twin births occurring in the United States. The strong link between smoking and important mediating factors (e.g., extreme prematurity) suggests the possibility of significant mortality effects that were not apparent in our multivariate analyses owing to the small sample size.

Despite these limitations, birth certificate data offer important advantages in examining adverse birth outcomes among twins. The current sample included 72% of all twin births occurring in the United States during an entire recent year. Although the linkage between smoking and common adverse outcomes is easily established in smaller clinical data sets, this large, population-based sample allows more precise and more readily generalizable analyses of important yet rare events such as placental abruption.

In addition, our research demonstrates the feasibility of identifying sibling pairs in twin studies from vital registration data. Because siblings share common characteristics of their mother and the specific pregnancy, unobserved sibling correlations play a large role in estimating factors related to birth outcomes. Failure to model these correlations produces downwardly biased standard error estimates for several outcomes. Ninety-one percent of twins in this large sample were successfully linked with a unique sibling via a matching algorithm. This high linkage rate made possible the use of appropriate statistical techniques with a large sample and may be useful in other studies focusing on multiple births.

The harmful effects of smoking on birth outcomes are well recognized. However, it is important for public health professionals and clinicians to understand that some smoking-related risks appear especially high for twin births. All women contemplating pregnancy and those who are pregnant should be advised of the dangers of prenatal smoking. In addition, women with multiple-gestation pregnancies should be further advised that they face specific increased tobacco-related risks. With the incidence of twins on the rise, the relationship between maternal tobacco use and adverse outcomes among twins deserves significant public health and clinical attention. □

Contributors

Dr. Pollack conceived the paper and performed the statistical analysis. Dr. Lantz organized the paper, wrote much of the final draft, and assisted in interpreting and describing the statistical results. Dr. Frohna assisted in interpreting and describing the statistical results, provided clinical expertise, and wrote sections of the paper.

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References

1. Hoyert DL. Medical and life-style risk factors affecting fetal mortality, 1989–1990. *Vital Health Stat 20*. 1996;No. 31:1–32.
2. Floyd RL, Rimer BK, Giovino GA, Mullen PD, Sullivan SE. A review of smoking in pregnancy: effects on pregnancy outcomes and cessation efforts. *Annu Rev Public Health*. 1993;14: 379–411.
3. Ananth CV, Savitz DA, Luther ER. Maternal cigarette smoking as a risk factor for placental abruption, placenta previa, and uterine bleeding in pregnancy. *Am J Epidemiol*. 1996;144: 881–889.
4. Floyd RL, Zahniser SC, Gunter EP, Kendrick JS. Smoking during pregnancy: prevalence, effects and intervention strategies. *Birth*. 1991;18:47–53.
5. Anderson H, Bland J, Peacock J. The effect of smoking on fetal growth. In: Poswillo D, Alberman E, eds. *Effects of Smoking on the Fetus, Neonate, and Child.* New York, NY: Oxford University Press Inc; 1992;8:89–105.
6. Ness RB, Grisso JA, Hirschinger N, et al. Cocaine and tobacco use and the risk of spontaneous abortion. *N Engl J Med*. 1999;340: 333–339.
7. Lambers DS, Clark KE. The maternal and fetal physiologic effects of nicotine. *Semin Perinatol.* 1996;20:115–126.
8. Guyer B, Martin JA, MacDorman MF, Anderson RN, Strobino DM. Annual summary of vital statistics—1996. *Pediatrics.* 1997;100: 905–918.
9. Luke B, Keith L. The contribution of singletons, twins, and triplets to low birth weight, infant mortality and handicap in the United States. *J Reprod Med*. 1992;37:661–666.
10. Olsen J, Bonnelykke B, Nielsen J. Tobacco smoking and twinning. *Acta Med Scand.* 1988; 224:491–494.
11. James WH. An hypothesis on the association between maternal smoking and dizygotic twinning. *Hum Reprod*. 1997;12:1391–1392.
12. Rydhstroem H, Kallen K. The effect of maternal smoking on birth weight in twin pregnancies. *Early Hum Dev.* 1996;46:43–53.
13. Orlebeke JF, Boomsma D, Van Baal GC, Blecker OP. Effect of maternal smoking on birth weight of twins: a study from the Dutch twin register. *Early Hum Dev.* 1994;37:161–166.
14. Luke B, Leurgans S. Maternal weight gains in ideal twin outcomes. *J Am Diet Assoc.* 1996;96: 178–181.
15. Mushinski M. Trends in multiple births. *Stat Bull Metrop Insur Co*. 1994;75(3):28–35.
16. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics.* 1986;42:121–130.
17. Mausner JS, Kramer S. *Epidemiology—An Introductory Text.* Philadelphia, Pa: WB Saunders Co; 1985.
18. Rockhill B, Newman B, Weinberg C. Use and misuse of population attributable fractions. *Am J Public Health.* 1998;88:15–19.
19. Zhang J, Yu KF. What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA*. 1998;280: 1690–1691.
20. Suzuki K, Minei LJ, Johnson EE. Effect of nicotine upon uterine blood flow in the pregnant rhe-

sus monkey. *Am J Obstet Gynecol.* 1980;136: 1009–1013.
21. Kogan MD, Alexander GR, Kotelchuck M, Nagey DA. Relation of content of prenatal care to the risk of low birthweight. *JAMA.* 1994; 271:1340–1345.
22. *Substance Abuse in Pregnancy*. Washington, DC: American College of Obstetricians and Gynecologists; 1994. ACOG technical bulletin 195.
23. *Special Problems of Multiple Gestation.* Washington, DC: American College of Obstetricians and Gynecologists; 1998. ACOG technical bulletin 253.
24. O'Campo P, Davis MV, Gielen AC. Smoking cessation interventions for pregnant women: review and future directions. *Semin Perinatol.* 1995;19:279–285.
25. *The Health Benefits of Smoking Cessation: A Report of the Surgeon General.* Washington, DC: US Dept of Health and Human Services; 1990. DHHS publication 90-8416.
26. Marks JS, Koplan JP, Hogue CJ, Dalmat ME. A cost-benefit/cost-effectiveness analysis of smoking cessation for pregnant women. *Am J Prev Med.* 1990;6:282–289.
27. Kendrick JS, Zahniser SC, Miller N, et al. Integrating smoking cessation into routine public prenatal care: the Smoking Cessation in Pregnancy Project. *Am J Public Health.* 1995;85: 217–222.
28. Weissfeld JL, Holloway JJ, Kirscht JP. Effects of deceptive self-reports of quitting on the results of treatment trials for smoking: a quantitative assessment. *J Clin Epidemiol.* 1989;42: 231–243.