International Journal of Epidemiology
© International Epidemiological Association 1992

Vol. 21, No. 6
Printed in Great Britain

Reinterpreting the Effects of Maternal Smoking on Infant Birthweight and Perinatal Mortality: A Multivariate Approach to Birthweight Standardization

PAUL B ENGLISH AND BRENDA ESKENAZI

English P B (Maternal and Child Health and Epidemiology Programs, School of Public Health, University of California, Berkeley, CA 94720, USA) and Eskenazi B. Reinterpreting the effects of maternal smoking on infant birthweight and perinatal mortality—a multivariate approach to birthweight standardization. *International Journal of Epidemiology* 1992; 21: 1097–1105.

Infants of women who smoke during pregnancy have lower birthweights and have been observed to have higher rates of perinatal mortality than infants of non-smokers. It is not clear whether this increased risk of mortality is due to an excess of small births among smokers or to an independent effect of smoking. Although infants of smokers have overall higher mortality rates than non-smokers, low birthweight (<2500 g) infants of smokers have lower mortality rates than low birthweight infants of non-smokers. However, comparison of birthweight-specific mortality between two groups is problematic when there are differences in the birthweight distributions. Methods that have been developed to standardize for these differences by comparing mortality rates relative to their own mean do not allow for simultaneous control of confounding variables. Using data from over 13 000 births of women who participated in a prepaid health care plan we present a method to standardize for birthweight while adjusting for variables that may confound the relationship between maternal smoking and perinatal mortality. After controlling for race, maternal age, education, parity, and number of cigarettes smoked, we found that 85% of the increased mortality due to smoking was attributable to an excess of small births in the birthweight distribution of offspring of smoking mothers, while 15% was due to higher birthweight-specific mortality at almost all standardized birthweights. Contrary to previous reports, we found that low birthweight infants of smoking mothers are at higher risk of perinatal mortality if a population-specific standard for birthweight is used.

Cigarette smoking during pregnancy has been shown to increase a woman's risk of delivering an infant of reduced birthweight.[1] Although some studies have found elevated risks of perinatal mortality among infants of smokers,[2–4] it is not clear whether this increased risk is due to the effect of smoking on birthweight or to an independent effect of smoking. Some authors have examined birthweight-specific mortality risks to answer this question.[5,6] They have found that although infants of smokers have higher overall mortality rates than non-smokers, low birthweight (<2500 g) infants of smokers actually have lower mortality rates than low birthweight (LBW) infants of non-smokers.[5–6] This paradoxical finding has also been noted among black infants who have better survival than white infants at low birthweights yet have higher overall mortality rates.[7] Comparison of birthweight-specific mortalities between two populations, however, could lead to biased results if the populations differ in their birthweight distributions.[8,9]

Wilcox and Russell have proposed a method of analysis which allows one to compare perinatal mortality in two populations which have different birthweight distributions.[10–12] They specifically used this method to examine differences between blacks and whites in fetal and perinatal mortality.[7,12] In this paper, we apply the Wilcox and Russell method to examine the relationship of maternal smoking and perinatal mortality. Their method helps elucidate whether differences in perinatal mortality between smokers and non-smokers are due to differences in the birthweight distribution or due to a change in birthweight-specific survival. The procedure proposed by Wilcox and Russell, however, has been criticized for its inability to

Maternal and Child Health and Epidemiology Programs, School of Public Health, University of California, Berkeley, CA 94720, USA.
Reprint requests: Dr Brenda Eskenazi, 312 Warren Hall, School of Public Health, University of California, Berkeley, CA 94720, USA.

simultaneously control for confounding variables which is vital in the analysis of smoking and perinatal mortality.[13,14] Thus, we propose here a method which adapts their procedure to a multivariate analysis.

METHODS

Participants

This study was based on the records of the Child Health and Development Studies (CHDS), a longitudinal study which followed over 20000 pregnancies from women enrolled at the Kaiser Permanente Hospital facilities primarily in Oakland, CA. Pregnant women were enrolled in the study from 1959 to 1966. Enrollees were socioeconomically diverse, with only the extremes, the very impoverished or the very affluent, not being represented.[15]

Women were included in this study if their pregancy terminated in either a perinatal death (defined as a fetal death of gestation of 28 weeks or more or a neonatal death within 28 days of birth) or a livebirth. Women were excluded if their infants were born with severe anomalies, if the birthweight was unknown, or if the pregnancy resulted in a multiple birth. After further excluding women who had no known smoking information or who quit smoking during pregnancy prior to the interview, the final sample available for analysis was 13208 births, with 8143 births of non-smokers, and 5065 births of smokers.

Women were questioned about their smoking status during the first CHDS interview, which usually took place in the first trimester at a prenatal care visit. For the purposes of this study, women were classified as smokers if they were current smokers at the time of this interview; women who had never smoked or who had quit prior to pregnancy were classified as non-smokers. For analysis, level of smoking consumption was categorized as 1–4, 5–9, 10–19, 20–29, and $\geqslant 30$ cigarettes per day. Educational achievement, parity (defined as the total number of previous livebirths and stillbirths), age, and race were also obtained from the interview. Information on birth outcome, i.e. stillbirths, neonatal deaths, and the birthweight (in ounces) of the liveborn infant was obtained from the mother's and infant's Kaiser medical chart.

Procedure

Birthweight distributions were calculated in 200 g intervals for smokers and non-smokers. Frequency distributions of birthweight are essentially normal, except for a long tail at the lowest birthweights.[10] Wilcox and Russell have proposed that the overall birthweight distribution should be separated into a 'predominant' normal distibution and a second skewed 'residual' distribution from the lower tail.[10] Each birthweight distribution can thus be defined by three parameters: the mean and standard deviation of the predominant distribution, and the proportion of births in the population that lie in the residual distribution. This residual distribution has been observed to be composed of small preterm births that are at high risk of perinatal mortality.[10]

In 1980, Rooth proposed that LBW be defined as less than two standard deviations from the mean of the birthweight distribution.[16] In the same year, Oeschli and van den Berg suggested a group distribution-adjusted LBW standard as the first percentile of the birthweight distribution for term births.[17] They applied this technique to maternal characteristics such as race and height as well as smoking.

Wilcox and Russell have built on Rooth's approach by proposing that the entire birthweight distribution for each population be standardized to z scores and scaled with the mean of the predominant distribution as the origin.[12] Birthweight-specific mortality rates are also plotted on this same scale. Higher overall mortality rates in one population can then be seen if: (a) the proportion of residual births is higher (higher mortality due to the residual distribution); or (b) the overall mortality curve is higher (higher birthweight-specific mortality or mortality due to the predominant distribution).

The residual distribution begins as the point ('truncation point') of the overall distribution which gives the lowest standard deviation and largest mean for the predominant distribution.[18] The best-fitting predominant and residual distributions for the study groups were estimated using a compiled program for the PC from a Fortran program developed by Wilcox and Russell.[7] Standardized birthweights (z scores with a standard deviation of 1 and a mean of 0) were also generated by this program.

Birthweight-specific perinatal mortality rates were calculated for smokers and non-smokers. Total perinatal mortality can be seen as the product of the number of infants at a given birthweight and the weight-specific mortality risk. We applied the raw birthweight-specific mortality curves to the estimates of the residual and predominant distributions instead of parameterizing the mortality curves (decreasing and increasing logistic risks) as suggested by Wilcox and Russell.[11] We chose to use the raw curves instead of estimating the parameters as we were unable to estimate the logistic mortality risk (ln[deaths/survivors]) at the lower birthweights when there were no survivors. In addition, we had few deaths at the upper birth-

weights, making it difficult to estimate the increasing logistic mortality risk.

To then estimate the mortality due to the residual and predominant distributions in each study group, the weight-specific mortality rate in each birthweight category was multiplied by the residual and predominant distributions that were estimated by the compiled Fortran program. The total mortality attributable to the residual and predominant distributions was calculated by summing the number of deaths predicted by the model in each birthweight group.

The birthweight-specific perinatal mortality curves and birthweight distributions were produced for both smokers and non-smokers using the z scores (mean = 0, SD = 1) instead of birthweight as their corresponding point on the x axis. These population standardized curves show the risk of mortality at each adjusted birthweight after the distributions for smokers and non-smokers have been realigned.

Multivariate Analysis

Several maternal characteristics including parity, age, education, and race were entered as covariates in a multivariate linear regression model[19] to simultaneously explain their effect on birthweight. These factors have been used as confounders in previous studies examining the relationship between smoking, and fetal and infant mortality.[2,13] Birthweight was used as the dependent variable instead of perinatal mortality because we wanted to adjust the birthweight distribution for input into the birthweight standardization procedure. Separate models were constructed for smokers and non-smokers. Categories were chosen as reference levels for the regression procedure which had the lowest perinatal mortality rates (Table 2). In the model including smokers, dose in cigarettes was entered as an additional covariate with 1–4 cigarettes/day chosen as the reference level. Indicator variables for missing values were created in both models to avoid losing observations during the regression.

Residual values (observed − predicted) for each individual from the multivariate regressions for smokers and non-smokers were generated using SAS software.[19] Each residual was then added to the mean birthweight for the smoking or non-smoking population to produce a new adjusted birthweight for each individual. The new birthweight frequencies that were produced from this procedure represented distributions that removed the effects of confounding variables. Birthweight-specific mortality rates were recalculated for this new distribution. Parameters of the predominant and residual distributions for smokers and non-smokers were then estimated again using the Wilcox and Russell method. The proportions of total mortality due to the predominant and residual distributions were also calculated.

RESULTS

The birthweight distributions and associated birthweight-specific mortality for infants of smokers and non-smokers can be seen in Figure 1. The average birthweight of infants of smokers was 198 g less than non-smokers ($t = 19.9$, $P = 0.0001$), and smokers had over twice the risk of delivering a LBW infant compared to non-smokers (RR = 2.11, 95% confidence interval (CI) : 1.83–2.42). There were 283 perinatal deaths, with 123 occurring among infants of smokers and 160 among infants of non-smokers. Infants of smokers had a 24% increase in perinatal mortality over infants of non-smokers (RR = 1.24, 95% CI : 0.98–1.56).

As has been found in previous studies, LBW infants of smokers had lower perinatal mortality than LBW infants of non-smokers (RR = 0.70, 95% CI : 0.54–0.90). This is seen in Figure 1, where the unstandardized birthweight and mortality curves show that infants of smokers have lower birthweight-specific mortality from approximately 1500 to 3250 g.

After standardizing the birthweight-specific mortality curves to their respective birthweights, a different picture emerges than was seen in Figure 1. In Figure 2 it is seen that smokers have *higher* birthweight-specific mortality than non-smokers at almost all standardized birthweights. Inspection of Table 1 reveals, however, that almost all (92.8%) of the excess mortality in infants of smokers is due to a higher proportion of excess small births (mortality attributable to the residual distribution) and not due to the higher birthweight-specific mortality (mortality due to the predominant distribution). Figure 2 shows this elevated frequency of births in the residual distribution of smokers. The proportion of births in the residual distribution was in fact found to be 56% higher (2.5% versus 1.6%) in smokers than in non-smokers (Table 1).

The relationship of the maternal characteristics with smoking frequency and perinatal mortality is shown in Table 2. Smoking frequency was lower in births of older and better educated women, yet was highest among births of white women compared to other races. The risk of perinatal mortality was highest among births of women younger than 18 years and older than 35 years and among births of women with the least education, the highest parity, and in births of black women.

The effect of adjusting for these maternal characteristics on the parameters of the Wilcox and Russell

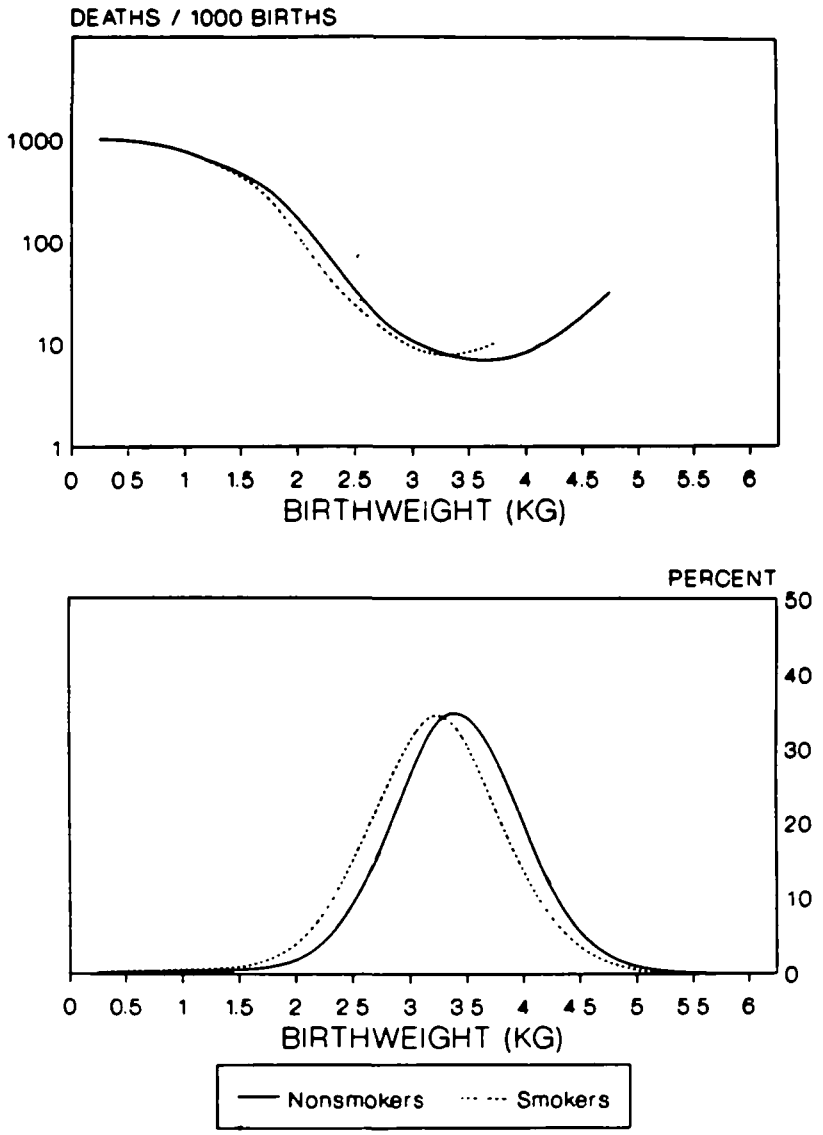

FIGURE 1 *Birthweight distributions and weight-specific perinatal mortality curves for infants of smokers and non-smokers. Data from Child Health and Development Studies, San Francisco East Bay Area, CA, 1959–1966. (Mortality rates have been smoothed by grouping weight into 500 g categories.)*

model using a multiple regression procedure is seen in Table 3. One pregnancy was eliminated from the non-smoking population because a negative adjusted birthweight was obtained from the multivariate regression procedure. Since this was a fetal death, perinatal mortality rates differed slightly for the unadjusted and multivariate adjusted models.

Comparing the multivariate adjusted results in Table 3 to the unadjusted results in Table 1, we find that as a result of controlling for confounding variables, there was a reduction of 6 g in the mean of the predominant distribution among smokers, while the mean decreased only 2 g among non-smokers. The proportion of births in the residual was only slightly reduced for smokers and non-smokers.

Partitioning the total mortality into its components in the multivariate model showed that the excess mortality due to smoking was reduced in the residual

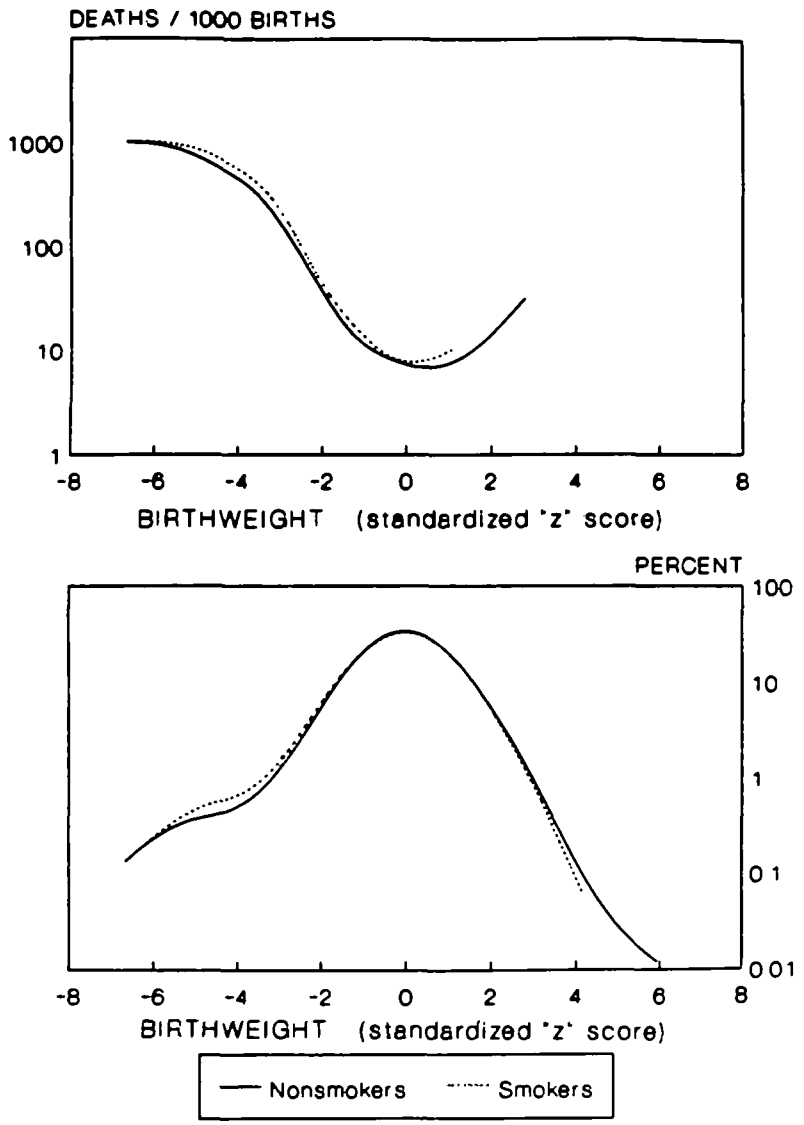

FIGURE 2 *Birthweight distributions and weight-specific perinatal mortality curves for infants of smokers and non-smokers, after conversion of birthweight to standardized z scores. Data from Child Health and Development Studies, San Francisco East Bay Area, CA, 1959–1966. (Mortality rates have been smoothed by grouping weight into 500 g categories.)*

distribution compared to the unadjusted analysis while the proportion of mortality due to the predominant distribution doubled (Table 3). Although a larger proportion of small births still explained most (84.6%) of excess perinatal mortality due to smoking, higher birthweight-specific mortality in the predominant distribution became a more important factor after multivariate adjustment, explaining 15.4% of the excess deaths, compared to only 7.2% in the unadjusted model. This is also reflected in Figure 3, which shows the birthweight-specific mortality curves after multivariate adjustment. The difference between the mortality risks for smokers and non-smokers is greater, especially between 3 and 4 standard deviations below the mean.

DISCUSSION

Previous studies investigating the relationship between smoking and perinatal mortality have found in LBW offspring of smokers an unexpected lower birthweight-

TABLE 1 *Unadjusted parameters of birthweight distributions and source of mortality*

A. Parameters of birthweight distribution

	Smokers (No. = 5065)	Non-smokers (No. = 8143)
Mean predominant (g)	3241.6	3424.1
Standard deviation (g)	476.5	474.6
Proportion in residual (%)	2.5	1.6
Truncation point (g)	2200.0	2400.0

B. Source of mortality

	Smokers (Deaths/1000 births)	Non-smokers (Deaths/1000 births)	Excess mortality (%)
Residual	13.68/1000	9.28/1000	4.40/1000 (92.8)
Predominant	10.73/1000	10.39/1000	0.34/1000 (7.2)
Total mortality[a]			
Calculated	24.41/1000	19.67/1000	4.74/1000 (100)
Observed	24.28/1000	19.65/1000	

[a] Error (difference between calculated and observed) is 0.5% for smokers and 0.1% for non-smokers.

TABLE 2 *Distribution of demographic characteristics among 13 208 births to study participants, Oakland, CA, 1959–1966*

	% of population (No. = 13 208)	% current smokers (No. = 5065)	Total perinatal mortality rate (Deaths/1000 births)	95% CI
All	100.0	38.4	21.4	(19.0– 23.9)
Maternal age (years)				
<18	0.8	49.5	36.7	(10.1– 91.2)
18–19	4.8	44.8	20.3	(10.9– 34.5)
20–24	31.1	41.8	17.1	(13.1– 21.0)
25–29	30.7	38.7	20.0	(15.7– 24.3)
30–34	18.3	33.7	20.3	(15.1– 26.8)
⩾35	14.2	33.3	35.2	(27.4– 44.6)
Age unknown	0.2	23.8	0	-
Education				
Less than high school	18.5	49.0	30.3	(23.9– 37.9)
High school graduate	31.7	42.2	20.0	(15.8– 24.3)
High school plus other training	30.6	34.1	21.3	(16.8– 25.7)
College graduate	18.9	28.5	15.3	(10.8– 20.9)
Education unknown	0.3	35.7	23.8	(0.5–126.0)
Parity				
Primipara	29.0	37.4	20.6	(16.3– 25.6)
Low multipara (1–2)	46.4	38.9	18.1	(14.8– 21.5)
High multipara (⩾3)	24.6	38.5	28.6	(23.1– 35.0)
Race				
Black	22.6	35.8	33.8	(27.6– 41.0)
White	67.0	41.4	17.2	(14.5– 19.9)
Other	10.3	24.0	21.4	(14.3– 30.6)
Race unknown	0.1	42.9	0	-

TABLE 3 *Multivariate adjusted parameters of birthweight distributions and source of mortality*

A. Parameters of birthweight distribution

	Smokers (No. = 5065)	Non-smokers (No. = 8142)
Mean predominant (g)	3235.3	3421.8
Standard deviation (g)	474.8	466.3
Proportion in residual (%)	2.4	1.5
Truncation point (g)	2200.0	2400.0

B. Source of mortality

	Smokers (Deaths/1000 births)	Non-smokers (Deaths/1000 births)	Excess mortality (%)
Residual	13.28/1000	9.22/1000	4.06/1000 (84.6)
Predominant	11.15/1000	10.41/1000	0.74/1000 (15.4)
Total mortality[a]			
Calculated	24.43/1000	19.63/1000	4.80/1000 (100)
Observed	24.30/1000	19.50/1000	

[a] Error (difference between calculated and observed) is 0.5% for smokers and 0.6% for non-smokers.

specific mortality rate than non-smokers.[5,6] In this study we have found that offspring of smokers have higher rates of perinatal mortality at these lower birthweights when one compares the mortality rates relative to the population-specific mean. We also found that the majority of the increased mortality was attributable to an excess of small births among smokers. After adjusting for potential confounders, higher birthweight-specific mortality (mortality due to the predominant distribution) for offspring of smokers accounted for only 15.4% of the excess mortality due to smoking.

Our study results are supported by previous findings showing associations of smoking with preterm births and placental complications.[3,20,21] Higher risks of placenta previa and abruptio placenta have been found among smokers at all gestations leading to a higher risk of perinatal death.[21] These complications have been estimated to account for as much as half of all the excess perinatal mortality due to smoking.[3] Specifically, the higher risk of perinatal mortality among offspring of smokers was found especially among the early gestations.[21] This concurs with our finding that the majority of perinatal deaths attributable to maternal smoking were due to an excess of births in the residual distribution. These births have been observed to be small by both size and gestation.[10]

The higher risk of perinatal mortality has been thought to act through the well-recognized effect of reduced birthweight in infants of smokers.[1,14] What we have shown in this analysis, however, is that even after controlling for the differences in the birthweight distribution of smokers and non-smokers, infants of smokers still have a higher, although minimal, risk of mortality that is independent of the effect of smoking on birthweight.

Our multivariate analysis was limited by the size of the dataset. Depending on the location of an individual birthweight within a 200 g category, small multivariate adjustments may have had no impact on moving an individual to another birthweight category. A larger population would allow for analysing the data in smaller birthweight intervals. However, even the adjustment performed in this study had an effect on partitioning the total mortality into its residual and predominant components. This demonstrates that some adjustment procedure is needed in applying the method of birthweight standardization proposed by Wilcox and Russell.

Also because of the size of the dataset, we applied the raw birthweight-specific mortality curves to the estimates of the residual and predominant distributions instead of using the parameters of the decreasing and increasing mortality risks sugggested by Wilcox and Russell.[11] These parameters were difficult to estimate with few numbers at the extreme lower and upper birthweights. Applying the raw rates instead of using the Wilcox-Russell parameters therefore

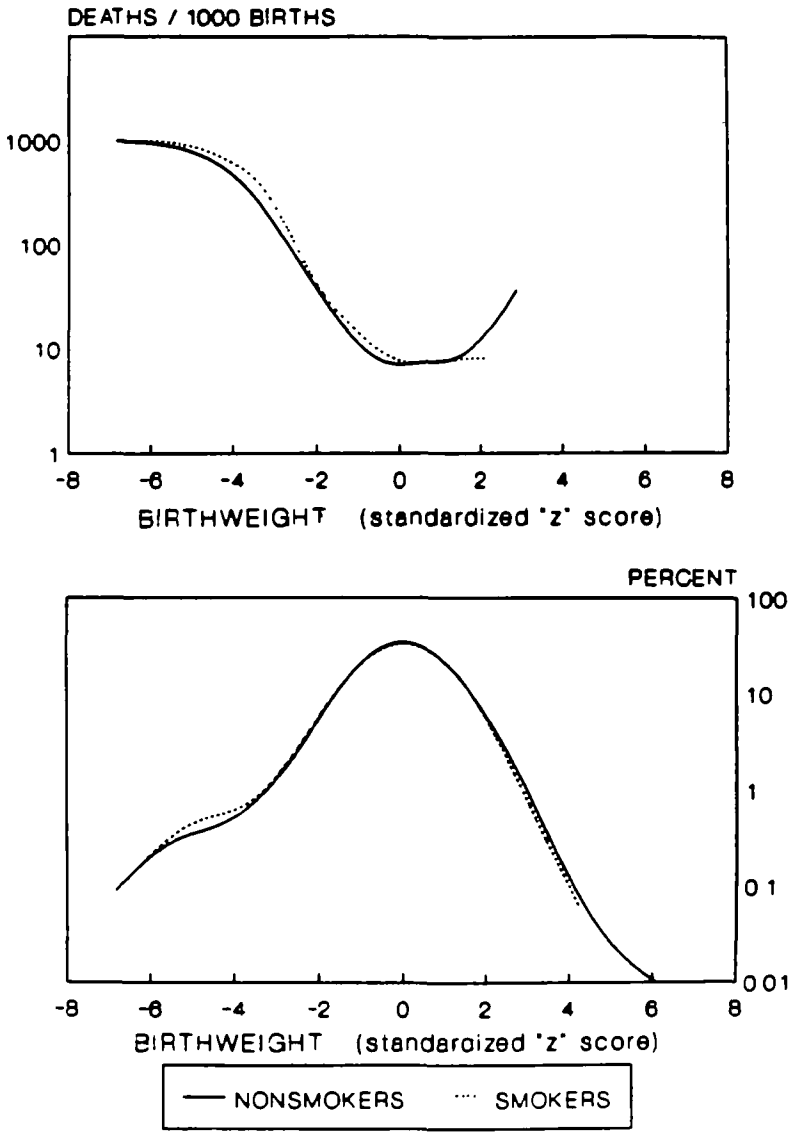

FIGURE 3 *Birthweight distributions and weight-specific perinatal mortality curves for infants of smokers and non-smokers, after multivariate adjustment and conversion of birthweight to standardized z scores. Data from Child Health and Development Studies, San Francisco East Bay Area, CA, 1959–1966. (Mortality rates have been smoothed by grouping weight into 500 g categories.)*

eliminated several estimation problems in this analysis, and may be a useful method in applying the Wilcox and Russell model to small datasets.

Despite the size limitation, there were several advantages in using this dataset. The data were from a prospective study, which recorded detailed information on smoking prenatally. The women were from a wide range of socioeconomic backgrounds, not just the deprived or affluent.[17] Additionally, information on birth outcomes were based on medical records, not from vital statistics data.

Since race is such a powerful predictor of both mortality and birthweight, separate models should be developed for black and white populations. Blacks may be more susceptible than whites to the effects of smoking possibly due to socioeconomic factors[22] or to differences in the metabolism of nicotine.[23] Preliminary analyses in this dataset showed that the

effects of smoking on perinatal mortality may differ in blacks and whites.

In summary, the data presented here suggest that after taking into account differences in the birthweight distributions of offspring of smoking and non-smoking women, smoking has a small independent effect on perinatal mortality. Most important, however, is that smokers have an excess of very low birthweight infants that are at high risk of perinatal death. Because these infants are likely to be premature, the results of this study suggest that women who smoke during pregnancy are at higher risk of delivering such infants, and should be monitored by their clinician for signs of placental complications and other risk factors for premature delivery.

ACKNOWLEDGEMENTS

We thank Dr Robert Sholtz and Dr Frank Oechsli for their suggestions regarding the methods used in this paper. Drs Allen Wilcox, Jeffrey Gould, and Nicholas Jewell provided helpful comments on an earlier draft. Special thanks to Dr Frank Oechsli for the use of his compiled version of the Wilcox-Russell Fortran program, and to the Child Health and Development Studies for the use of their data. This research was supported by funds provided by the Cigarette and Tobacco Surtax Fund of the State of California through the Tobacco-Related Disease Research Program of the University of California, Grant Number 1RT465.

REFERENCES

[1] Sexton M, Hebel J R. A clinical trial of change in maternal smoking and its effect on birthweight. *JAMA* 1984; **251**: 911–15.

[2] Kleinman J C, Pierre M B, Madans J H, Land G H, Schramm W F. The effects of maternal smoking on fetal and infant mortality. *Am J Epidemiol* 1988; **127**: 274–82.

[3] Meyer M B, Jonas B S, Tonascia J A. Perinatal events associated with maternal smoking during pregnancy. *Am J Epidemiol* 1976; **103**: 464–76.

[4] Rush D, Kass E H. Maternal smoking: A reassessment of the association with perinatal mortality. *Am J Epidemiol* 1972; **96**: 183–96.

[5] Butler N R, Alberman E D, (eds). *Perinatal Problems. The Second Report of the 1958 British Perinatal Survey*. Edinburgh and London: Livingstone, 1969; pp 36–84.

[6] Yerushalmy J. The relationship of parents' cigarette smoking to outcome of pregnancy—implications as to the problems of inferring causation from observed associations. *Am J Epidemiol* 1971; **93**: 443–56.

[7] Wilcox A J, Russell I T. Why small black infants have a lower mortality rate than small white infants: The case for population-specific standards for birth weight. *J Pediatr* 1990; **116**: 7–10.

[8] Wilcox A J, Russell I T. Perinatal mortality: Standardizing for birthweight is biased. *Am J Epidemiol* 1983; **118**: 857–64.

[9] Terrin M, Meyer M B. Birth weight-specific rates as a bias in the effects of smoking and other perinatal hazards. *Obstet Gynecol* 1981; **58**: 636–38.

[10] Wilcox A J, Russell I T. Birthweight and perinatal mortality I. On the frequency distribution of birthweight. *Int J Epidemiol* 1983; **12**: 314–18.

[11] Wilcox A J, Russell I T. Birthweight and perinatal mortality II. On weight-specific mortality. *Int J Epidemiol* 1983; **12**: 319–25.

[12] Wilcox A J, Russell I T. Birthweight and Perinatal Mortality III. Towards a new method of analysis. *Int J Epidemiol* 1986; **15**: 188–96.

[13] Malloy M H, Kleinman J C, Land G H, Schramm W F. The association of maternal smoking with age and cause of infant death. *Am J Epidemiol* 1988; **128**: 46–55.

[14] Kiely J L. Some conceptual problems in multivariable analyses of perinatal mortality. *Paediatr Perinat Epidemiol* 1991; **5**: 243–57.

[15] van den Berg B J. The California Child Health and Development Studies In: Medwick S A *et al.* (eds) *Handbook of Longitudinal Reasearch*. New York: Praeger Publishers, 1984; pp 166–79.

[16] Rooth G. Low birthweight revised. *Lancet* 1980; **i**: 639–41.

[17] Oechsli F W, and van den Berg B J. *Characteristics of the Mother and Child; Birthweight Distribution and Neonatal Mortality*. Proceedings of the Pacific Division, AAAS; Annual meeting, June 22–27, 1980. Abstracts, p 54.

[18] Wilcox A J. *Birthweight and Perinatal Mortality*. PhD dissertation, University of North Carolina, 1979.

[19] *SAS Institute, Inc. Version 5.18*, Cary, NC: SAS Institute, Inc., 1985.

[20] Shiono P H, Klebanoff M A, Rhoads G G. Smoking and drinking during pregnancy. Their effects on preterm birth. *JAMA* 1986; **255**: 82–84.

[21] Meyer M B, Tonascia J A. Maternal smoking, pregnancy complications, and perinatal mortality. *Am J Obstet Gynecol* 1977; **128**: 494–502.

[22] Sterling T D, Weinkam J J. Comparison of smoking-related risk factors among black and white males. *Am J Industr Med* 1989; **15**: 319–33.

[23] Wagenknecht L E, Cutter G R, Haley N J *et al.* Racial differences in serum cotinine levels among smokers in the coronary artery risk development in adults study. *Am J Public Health* 1990; **80**: 1053–56.

(Revised version received June 1992)