

## DETERMINANTS OF PRETERM BIRTH RATES IN CANADA FROM 1981 THROUGH 1983 AND FROM 1992 THROUGH 1994

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### ABSTRACT

**Background** The rates of preterm birth have increased in many countries, including Canada, over the past 20 years. However, the factors underlying the increase are poorly understood.

**Methods** We used data from the Statistics Canada live-birth and stillbirth data bases to determine the effects of changes in the frequency of multiple births, registration of births occurring very early in gestation, patterns of obstetrical intervention, and use of ultrasonographic dating of gestational age on the rates of preterm birth in Canada from 1981 through 1983 and from 1992 through 1994. All births in 9 of the 12 provinces and territories of Canada were included. Logistic-regression analysis and Poisson regression analysis were used to estimate changes between the two three-year periods, after adjustment for the above-mentioned determinants of the likelihood of preterm births.

**Results** Preterm births increased from 6.3 percent of live births in 1981 through 1983 to 6.8 percent in 1992 through 1994, a relative increase of 9 percent (95 percent confidence interval, 7 to 10 percent). Among singleton births, preterm births increased by 5 percent (95 percent confidence interval, 3 to 6 percent). Multiple births increased from 1.9 percent to 2.1 percent of all live births; the rates of preterm birth among live births resulting from multiple gestation increased by 25 percent (95 percent confidence interval, 21 to 28 percent). Adjustment for the determinants of the likelihood of preterm birth reduced the increase in the rate of preterm birth to 3 percent among all live births and 1 percent among singleton births.

**Conclusions** The recent increase in preterm births in Canada is largely attributable to changes in the frequency of multiple births, obstetrical intervention, and the use of ultrasound-based estimates of gestational age. (N Engl J Med 1998;339:1434-9.)

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IN many industrialized countries, the proportion of infants born before term (at less than 37 weeks of gestation) has increased in the past 20 years. In Canada, for instance, the proportion of infants born at less than 37 weeks of gestation increased from 6.3 percent to 6.8 percent of all live births between 1981 and 1992.<sup>1,2</sup> With the possible exceptions of France<sup>3,4</sup> and Finland,<sup>5</sup> other industrialized countries have also seen an increase in

the frequency of preterm births.<sup>6-9</sup> The increase in preterm births in Canada is particularly enigmatic, because the proportion of live-born infants weighing less than 2500 g decreased during the same period.<sup>1,2</sup>

Preterm birth is usually considered the most important cause of perinatal mortality in industrialized countries,<sup>9</sup> and therefore the above-mentioned temporal trends have led various experts to conclude that reducing the occurrence of preterm births is the most important perinatal challenge in such countries.<sup>10,11</sup> Factors potentially responsible for the increase in the rates of preterm births include increases in multiple-gestation pregnancies<sup>12-14</sup> and increases in the use of ultrasound-based estimates of gestational age.<sup>15,16</sup> Also, as a result of recent changes in birth-registration procedures, births of infants very early during gestation (at less than 22 weeks [early-gestation births]) and with extremely low birth weights (under 500 g)<sup>17-20</sup> have been registered as live births rather than being registered as stillbirths or left unregistered as miscarriages. In this study, we estimated the contribution of these and related factors to the rate of preterm birth in Canada.

### METHODS

We used data from the Canadian live-birth and stillbirth data bases of Statistics Canada, which contain information on all births in Canada. The information in these data bases has been collated from birth certificates and registrations of stillbirths.<sup>21</sup> The information about gestational age on these certificates is obtained from the physician involved with the birth or from the mother. The analyses were carried out on all births that occurred in 9 of the 12 provinces and territories of Canada; the exceptions were Newfoundland (for which data from before 1990 were unavailable), Ontario (owing to concerns about the quality of the data<sup>22</sup>), and British Columbia (because we were denied access to the data).

We first characterized trends in the distribution of gestational ages for all live births in the study population during the years from 1981 through 1983 and from 1992 through 1994. Means and standard deviations were calculated after the data were stratified according to whether the births were singleton or multiple.

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Differences between the two periods in means and variances were assessed by the *t*-test and the *F* test,<sup>23</sup> respectively. Second, we calculated the rates of preterm birth within various subcategories (at less than 23 weeks of gestation, 23 to 27 weeks, 28 to 33 weeks, 34 to 36 weeks, and less than 37 weeks). We anticipated that subcategories at the lower end of the gestational-age distribution would grow because of a recent tendency to register extremely immature infants.<sup>17-20</sup> Changes over time (rates in 1992 through 1994 as compared with 1981 through 1983) were estimated by using relative risks. In order to assess whether changes in the classification of births (as stillbirths or live births) were responsible for changes in the rates of preterm birth, all the above-mentioned calculations were repeated for total births rather than live births alone.

We used logistic-regression analysis to study the effects of changes in the frequency of multiple births and in maternal age and parity on rates of preterm birth. An indicator variable was used to represent multiple births in the model (with values of 0 and 1 for singleton and multiple births, respectively). Similarly, adjustment for maternal age and parity was carried out by using indicator variables to represent categories of maternal age (less than 20 years, 20 to 24 years, 25 to 29 years, 30 to 34 years, and 35 or more years) and parity (0, 1, 2 or 3, and 4 or more). Since 40 to 50 percent of multiple births are preterm, the odds ratio obtained directly from logistic-regression analysis could not be used as an estimate of the relative risk. Instead, we used the logistic-regression equation (with the intercept and appropriate coefficients) to estimate the absolute risk of preterm birth in 1981 through 1983 and in 1992 through 1994; relative risks were then calculated from these estimates.

The analysis was first carried out on all live births and repeated on live births at 28 or more weeks of gestation. The latter analysis was designed to account for the effect of increases in the registration of births very early in gestation. Analyses were also carried out on total births, with status at birth (stillbirth vs. live birth) included as an additional independent variable.

The contribution of these and other factors to the increase in preterm births was also analyzed by Poisson regression modeling. The dependent variable in the Poisson model was the number of preterm live births. Data were stratified according to province or territory (9 strata), year (14 strata), and sex (2 strata), which resulted in 252 strata. The independent variables included in the analysis (besides province or territory, year, and sex) were the proportion of births in each maternal age and parity category (as previously defined for the logistic-regression analysis); the proportion of births at gestational ages of less than 20 weeks, 20 to 22 weeks, and 23 to 27 weeks; the proportion of multiple births; the rate of stillbirth; and the proportion of births with missing information on gestational age. We estimated the effect of early use of ultrasonography by using the proportion of live births at 41 or more weeks of gestation (and, alternatively, the proportion at 42 or more weeks) as a proxy. Increasing use of early ultrasonography in determining gestational age is known to result in marked reductions in the number of births classified as post-term<sup>15</sup> and some increase in the number of births classified as preterm<sup>16</sup> (since gestational age based on the last menstrual period can be falsely high because of late ovulation). Although the use of such a proxy variable has limitations (discussed below), the changes in the method of assessment of gestational age have probably affected the rates of preterm birth.<sup>15,16</sup>

Numerical problems with model fitting (collinearity) were considered to be present if aberrantly large standard errors were encountered.<sup>24,25</sup> In that case, correlations between regression coefficients were examined to confirm that the results of the model were compromised, and the model was then excluded. All statistical tests were two-sided.

## RESULTS

The mean week of gestation for all live births decreased from 39.3 to 39.1 weeks between 1981

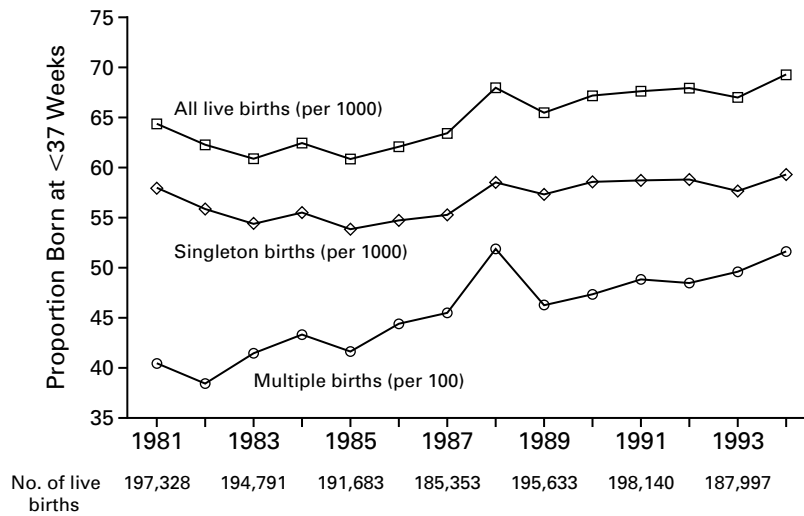
**TABLE 1.** MEAN ( $\pm$ SD) WEEK OF GESTATION FOR ALL LIVE BIRTHS, SINGLETON BIRTHS, AND MULTIPLE BIRTHS IN 1981 THROUGH 1983 AND 1992 THROUGH 1994 IN NINE PROVINCES AND TERRITORIES OF CANADA.

CATEGORY OF LIVE BIRTHS	1981-1983	1992-1994
All		
No.	587,978	567,486
Gestational age (wk)	39.3 $\pm$ 2.0	39.1 $\pm$ 2.0
Singletons		
No.	577,013	555,351
Gestational age (wk)	39.4 $\pm$ 1.9	39.2 $\pm$ 1.9
Multiple births		
No.	10,965	12,135
Gestational age (wk)	36.4 $\pm$ 3.5	35.7 $\pm$ 3.3
Twins		
No.	10,725	11,769
Gestational age (wk)	36.5 $\pm$ 3.5	35.8 $\pm$ 3.2
Higher-order multiple births		
No.	240	366
Gestational age (wk)	32.9 $\pm$ 3.9	32.2 $\pm$ 3.3

through 1983 and 1992 through 1994 ( $P<0.001$ ) (Table 1). Among singleton live births, the mean week of gestation also declined slightly during the study period, from 39.4 to 39.2 weeks ( $P<0.001$ ). Among multiple births, the mean week of gestation decreased from 36.4 to 35.7 weeks ( $P<0.001$ ). The frequency of multiple births increased from 1.9 percent (95 percent confidence interval, 1.8 to 1.9 percent) of all live births in 1981 through 1983 to 2.1 percent (95 percent confidence interval, 2.1 to 2.2 percent) in 1992 through 1994.

Trends among twin and higher-order multiple births are also shown in Table 1. The mean gestational age of twins decreased from 36.5 to 35.8 weeks ( $P<0.001$ ), and among triplet and higher-order births it decreased from 32.9 to 32.2 weeks ( $P=0.01$ ). The standard deviation for gestational age for twin births decreased from 3.5 to 3.2 weeks ( $P<0.001$ ), and that for higher-order births from 3.9 to 3.3 weeks ( $P=0.01$ ). Analyses of total births (stillbirths plus live births) showed similar patterns.

Figure 1 shows the trends in preterm births from 1981 through 1994, and Table 2 shows changes in specific gestational-age categories between 1981 through 1983 and 1992 through 1994. The proportion of all live births that were preterm (those occurring at less than 37 weeks of gestation) increased from 6.3 percent to 6.8 percent, a 9 percent increase (95 percent confidence interval, 7 to 10 percent). Although the proportion of live births occurring at less than 23 weeks of gestation increased by 14 percent, the proportion of live births between 28 and 36 weeks of gestation also increased by 9 percent. The rate of preterm births increased by 5 percent among singletons (95 percent confidence interval,



**Figure 1.** Rates of Preterm Birth (at <37 Weeks) among All Live Births, Singleton Births, and Multiple Births in Nine Provinces and Territories of Canada from 1981 through 1994.

The rates of preterm birth among all live births and singleton births are expressed per 1000 live births with known gestational age, whereas those for multiple births are expressed per 100 live births.

3 to 6 percent) and by 25 percent among births resulting from multiple gestation (95 percent confidence interval, 21 to 28 percent). Analyses of total births showed similar trends.

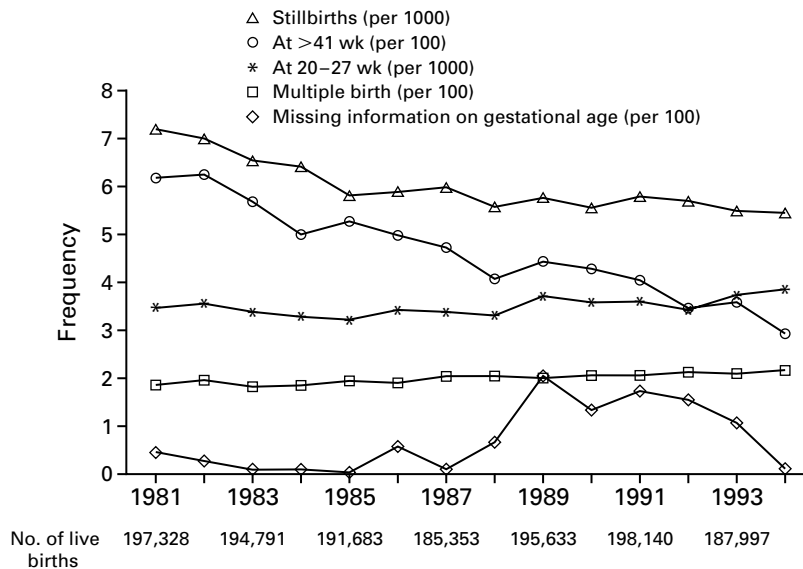
The proportion of live births that occurred at 41 weeks or more of gestation decreased from 19.3 percent to 18.0 percent between 1981 through 1983 and 1992 through 1994, and live births at 42 or more weeks decreased from 6.0 percent of all live births to 3.3 percent. The mean birth weight of infants born alive for whom information on gestational age was missing increased from 3264 to 3358 g between 1981 through 1983 and 1992 through 1994. The proportion of live-born infants with low birth weight (under 2500 g) in this group decreased from 10.1 percent to 5.9 percent over the same period. Sensitivity analyses to determine the effect of missing information on gestational age (in which low birth weight was used as a rough proxy for preterm birth among those for whom gestational age was missing) revealed that the change in the proportion for whom gestational age was missing had a small effect on the overall rates of preterm birth and on the increase in rates of preterm birth between 1981 through 1983 and 1992 through 1994.

The results of unadjusted logistic-regression analyses revealed that the rate of preterm live birth increased by 9 percent overall between 1981 through 1983 and 1992 through 1994. Adjustment for multiple births reduced the increase to 7 percent, whereas adjustment for maternal age and parity had a small influence in the opposite direction. Adjustment for maternal age, parity, and multiple births si-

**TABLE 2.** PRETERM BIRTHS ACCORDING TO GESTATIONAL-AGE CATEGORY FOR ALL LIVE BIRTHS, SINGLETON BIRTHS, AND MULTIPLE BIRTHS IN 1981 THROUGH 1983 AND 1992 THROUGH 1994 IN NINE PROVINCES AND TERRITORIES OF CANADA.

GESTATIONAL AGE (WK)	PRETERM BIRTH RATE (PER 100 LIVE BIRTHS)		RELATIVE RISK IN 1992-1994 vs. 1981-1983 (95% CI)*
	1981-1983	1992-1994	
All live births			
<23	0.05	0.06	1.14 (0.97-1.33)
23-27	0.30	0.31	1.05 (0.98-1.12)
28-33	1.31	1.38	1.06 (1.02-1.09)
34-36	4.59	5.06	1.10 (1.08-1.12)
Data not available	0.26	0.93	3.57 (3.37-3.78)
<37	6.25	6.81	1.09 (1.07-1.10)
Singleton live births			
<23	0.04	0.05	1.08 (0.92-1.29)
23-27	0.25	0.25	1.02 (0.94-1.10)
28-33	1.12	1.11	0.99 (0.96-1.03)
34-36	4.20	4.46	1.06 (1.04-1.08)
Data not available	0.26	0.94	3.60 (3.39-3.81)
<37	5.61	5.86	1.05 (1.03-1.06)
Multiple live births			
<23	0.47	0.57	1.23 (0.85-1.76)
23-27	3.04	3.18	1.04 (0.90-1.21)
28-33	11.26	13.68	1.21 (1.13-1.30)
34-36	25.31	32.49	1.28 (1.23-1.34)
Data not available	0.25	0.48	1.94 (1.23-3.06)
<37	40.08	49.92	1.25 (1.21-1.28)

\*CI denotes confidence interval.



**Figure 2.** Trends in Several Potential Determinants of Preterm Birth in Nine Provinces and Territories of Canada from 1981 through 1994.

The rates for live births at 20 to 27 weeks and for stillbirths are expressed per 1000 live births, and those for multiple births, live births at more than 41 weeks, and births for which data on gestational age were missing are expressed per 100 live births.

multaneously did not substantially alter the increase in rates of preterm birth.

Among singletons, the rate of preterm birth increased 5 percent between 1981 through 1983 and 1992 through 1994. Logistic-regression adjustment for maternal age and parity had little effect on this estimate. Similarly, the increase in rates of preterm birth among births resulting from multiple gestation changed little after adjustment for maternal age and parity.

Figure 2 shows the trends in several potential determinants of preterm birth rates over the study period. Poisson regression analysis revealed that among all live births, preterm births increased by 8 percent (95 percent confidence interval, 7 to 10 percent) between 1981 through 1983 and 1992 through 1994 (this 8 percent estimate differs from the 9 percent obtained in other analyses, because live births with missing gestational age were included in the rate denominators in this analysis). Sequential adjustment for live births with missing data on gestational age, early-gestation births, multiple births, and stillbirths reduced the 8 percent increase in preterm births across the study period to 4 percent (95 percent confidence interval, 2 to 6 percent). Further adjustment for the use of ultrasound-based assessment of gestational age (using the proportion of births at 41 or more weeks of gestation as a proxy) reduced the change in the rate of preterm birth to 3 percent (95 percent confidence interval, 1 to 5 percent).

Among singleton births, adjustment for missing

data on gestational age, registration of early-gestation births, and declining rates of stillbirth led to a decline in the observed increase in preterm births between 1981 through 1983 and 1992 through 1994, from a 4 percent increase (95 percent confidence interval, 2 to 5 percent) to a 1 percent increase (95 percent confidence interval, -1 to 3 percent). Regression adjustment did not substantially affect the observed increase in preterm births as a percentage of multiple births between 1981 through 1983 and 1992 through 1994.

Among all live births, each unit increase in the rate of multiple births (i.e., 1 per 100 live births) was associated with a 5 percent increase in the rate of preterm births. Each unit decrease in the rate of stillbirths (i.e., 1 per 1000 live births) was associated with a 1 percent increase in the preterm birth rate. Decreases in stillbirths were associated with increases in preterm births as a proportion of all live births ( $P < 0.001$ ) and of singleton births ( $P < 0.001$ ), but not of multiple births.

## DISCUSSION

We examined changes in the frequency of preterm birth in 9 of the 12 provinces and territories of Canada between 1981 through 1983 and 1992 through 1994. The changes in mean gestational age and in the proportion of preterm births suggest a small shift toward the lower (left) end of the distribution of gestational ages. One noteworthy finding is the difference between singleton and multiple births in the tempo-

ral trends in preterm births. There were small increases in the rate of preterm birth among singleton live births, but large increases among live births after multiple gestation. The standard deviation for gestational age did not change among singleton births, but it decreased among twin and triplet births. These findings suggest that increased obstetrical intervention has truncated the upper (right) tail of the distribution of gestational ages among multiple births. A small part of the increase in preterm births among births resulting from multiple gestation may also be due to more precise estimation of gestational age in pregnancies that resulted from assisted-reproduction techniques. Our results also confirm previous findings of an increasing tendency to register live births at very early gestational ages (20 to 22 weeks and 23 to 27 weeks).<sup>17-20</sup>

The increase in the rates of preterm birth during the study period can be explained largely by changes in the frequency and character of multiple births, increases in obstetrical intervention (as indicated by declining numbers of stillbirths), greater registration of early-gestation births, and increased use of ultrasound-based estimates of gestational age. Among singleton births, the increase in preterm births could be entirely explained by changes in obstetrical intervention, changes in birth registration, and missing data on gestational age. Declining rates of stillbirth were associated with an increase in preterm births, even after adjustment for increased registration of live births at early stages of gestation. Whether these shifts from stillbirths to preterm live births were attended by a corresponding increase in neonatal and infant mortality is not known.

Although adjustment for multiple births, obstetrical intervention, early-gestation births, and early use of ultrasonography appears to account for a substantial proportion of the increase in preterm births, this explanation does not alter the higher burden of illness implied by the increase in rates of preterm birth. For instance, even if a substantial fraction of the increase in preterm births is attributed to changes in the frequency of multiple births, this does not change the costs associated with that component of the increase in preterm births. The only components of the increase that appear artifactual are those due to changes in the frequency of missing data on gestational age and in the method of ascertainment of gestational age (i.e., the increased use of early ultrasonographic dating).

Controlling for other factors, such as preterm induction of labor, preterm cesarean section, and early use of ultrasonography, could unmask a true decline in the rate of spontaneous preterm birth. Even though our analyses controlled for declining rates of stillbirth and post-term birth, adjustment for preterm induction of labor, preterm cesarean section, and early use of ultrasonography would probably have an

additional effect on trends in preterm births. Moreover, the proxy variable for early ultrasonographic dating used in our analysis may also have captured other changes in obstetrical practice, such as increases in the rate of induction of labor. More clinical information (such as that available in hospital-based studies) is required for a comprehensive assessment of trends in preterm births.

In summary, substantial increases in the rates of preterm births have occurred among births resulting from multiple gestation, concurrently with increases in the frequency of multiple births. The small increases in preterm births among singletons can be explained by simultaneous changes in patterns of obstetrical intervention and registration of early-gestation births.

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