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Changes in Stillbirth and Infant Mortality Associated With Increases in Preterm Birth Among Twins

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ABSTRACT. *Objective.* **To examine whether the recent substantial increase in preterm birth among twins has been associated with changes in fetal and infant mortality.**

Design. **Cohort study based on information in the linked live birth, stillbirth, and mortality databases of Statistics Canada.**

Setting. **Ten of 12 provinces and territories in Canada.**

Participants. **All twin live births and stillbirths between 1985 and 1996, along with information on deaths during infancy (1985–1997).**

Main Outcome Measure. **Fetal and infant mortality rates.**

Results. **The rate of preterm birth among twin live births increased significantly by 17% (95% confidence interval: 14%–20%) from 42.5% between 1985 and 1987 to 49.6% between 1994 and 1996. Overall, stillbirth rates among twins declined from 22.4 per 1000 total births in 1985 to 1987 to 18.8 per 1000 total births in 1994 to 1996. Among twin fetuses ≥34 weeks' gestation, stillbirth rates decreased from 9.5 per 1000 in 1985 to 1987 to 5.4 per 1000 fetuses at risk in 1994 to 1996. Infant mortality rates among twin live births declined substantially in all categories of gestational age above 24 weeks except for live births at 32 to 33 and 34 to 36 weeks' gestation.**

Conclusions. **The recent increase in preterm birth among twins was associated with a substantial reduction in stillbirth rates at and near term gestation. Infant mortality rates declined concurrently, although the absence of a significant decrease in infant mortality among twin live births at 32 to 33 and 34 to 36 weeks' gestational age needs additional scrutiny.** *Pediatrics* **2001;108:1055–1061;** ***twins, stillbirth, infant mortality, preterm birth.***

ABBREVIATION. CI, confidence interval.

Recent increases in maternal age and in the use of ovarian stimulation and in vitro fertilization have led to increases in the frequency of twins and triplet and higher-order multiple births.[1–4] In Canada, multiple births increased in frequency from 18.2 per 1000 total births in 1974 to 19.3 in 1980, 21.2 in 1990, and 25.3 in 1997,[5–8] while twin births increased from 17.9 per 1000 total births in 1974 to 18.9 in 1980, 20.5 in 1990, and 24.2 in 1997.[5–8] Because twin births constitute over 95% of multiple births, most of the absolute increase in multiple births can be attributed to increases in twins, although on a relative scale, triplet and higher-order multiples have increased to a far greater extent.

Over the same time period, there has been a substantial increase in the rate of preterm birth (<37 weeks' gestation) among multiple births.[9,10] In Canada, the rate of preterm birth among multiple births increased from 33% in 1974 to 40% in 1981 to 1983, 50% in 1992 to 1994, and 53% in 1997.[5–8] The mean gestational age of twin live births has decreased from 36.5 weeks in 1981 to 1983 to 35.8 weeks in 1992 to 1994.[9] Similarly, in the United States preterm birth rates among twins have increased from 41% in 1981 to 55% in 1997.[10]

This large increase in preterm birth among multi-

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ple births contrasts with a modest increase in preterm birth among singletons (increases of 25% vs 5% among multiple births vs singletons, respectively, between 1981–1983 and 1992–1994).[9] Although the increase in preterm birth among both singletons[11] and multiple births[10,12] seems to be primarily attributable to increases in preterm induction/cesarean section, the increase in preterm birth was associated with a decline in fetal mortality among singletons but not among multiple births.[9] If increased obstetric intervention is saving compromised singleton fetuses through early delivery, it is unclear why this anticipated benefit is not evident among multiple births, given the rising rates of preterm birth. Furthermore, although infant mortality among both singletons and twins has decreased over the period when preterm birth rates have increased,[8,10] it is unclear whether the decline in infant mortality among twins has been related to obstetric intervention or to other factors, such as the temporal decline in sudden infant death syndrome. We therefore conducted a study to examine changes in gestational age-specific, birth weight-specific, and cause of death-specific fetal and infant mortality among twin births in Canada in relation to concurrent increases in preterm birth.

METHODS

We used data from the live-birth and stillbirth databases of Statistics Canada for the years 1985 to 1996 and data from the mortality database for the years 1985 to 1997. Information in these databases is obtained from live birth, stillbirth, and death registrations. Information on gestational age in the live birth and stillbirth registrations is obtained from the responsible physician or the mother. The live birth and mortality databases were linked using a previously validated probabilistic methodology[13,14] to obtain perinatal information on infant deaths. The linkage process involved a comparison of fields common to records within both databases, an assignment of weights based on the closeness of the ensuing matches, and a global assessment of the likelihood of a valid match. Relevant birth and death registration documents were examined to resolve tentative links. The completeness and validity of the linked data has been studied for deaths that occurred in 2 provinces (infant deaths in Nova Scotia and neonatal deaths in Alberta) using information from hospital sources; 99% of such deaths were located within the linked files.[15]

The linked file was subjected to data quality checks and procedures to eliminate duplicate records. Births to mothers residing in Ontario were excluded from the analysis because of previously documented problems with data quality[16] and significant numbers of unlinked deaths. Births from Newfoundland were also excluded because data from this province are not available before 1991. In common with other large databases, we observed that a few live births with a birth weight of <500 g and a gestational age of <22 weeks seemed to have survived infancy. Given the extremely low probability of survival at this birth weight and gestational age,[17] we assumed that survival was attributable to a missing death certificate. Correspondingly, we reclassified the survival status of such live births to death on the first day of life; such reclassification of survival status is identified in all analyses.

We examined stillbirth and infant mortality rates within specific categories of gestational age and birth weight; the categories were created with the intention of providing reasonable homogeneity with regard to prognosis, while increasing the statistical stability of the estimates. Causes of death, classified in the databases with *International Classification of Diseases, Ninth Revision* codes, were also examined to help elucidate those causes responsible for reductions in mortality. Given the focus on stillbirth and infant death rates, each twin birth was considered separately (rather than as a twin set). Thus, gestational age-specific stillbirth rates were estimated per 1000 fetuses at risk in any particular gestational age category (ie, all fetuses stillborn or live born at that or a later gestational age).

The time span of the study was divided into 4 equal periods and time trends were assessed first by contrasting event rates in the earliest versus most recent periods (1985–1987 vs 1994–1996) and also by estimating trends over the 4 time periods. Contrasts between periods were made by computing relative risks, relative risk reductions, and their 95% confidence intervals (CIs), while trends over time were assessed using χ^2 tests for trends in proportions. Logistic regression, with stillbirth or infant death as the outcome, was used to examine whether period changes in mortality could be attributed to simultaneous changes in the distribution or risk of determinants such as maternal age, parity, and birth order. In a supplementary analysis, we repeated the statistical assessment of the primary temporal contrasts (preterm birth, low birth weight, stillbirth, stillbirth ≥34 weeks, and infant mortality in 1985–1987 vs 1994–1996) using the procedure of generalized estimating equations[18] to adjust the variance estimates for the correlation in the outcomes of a single twin pregnancy. Because our data source did not identify twin sets, we created sets using identifiers such as birth date, maternal age, and province of residence (approximately 13 800 sets for 28 400 twin births).

RESULTS

The rate of preterm birth among twin live births increased significantly by 17% (95% CI: 14%–20%, $P < .001$), from 42.5% in 1985 to 1987 to 49.6% in 1994 to 1996. Most of this increase was attributable to increases in twin live births between 34 and 36 weeks' gestation; such live births increased by 23% (95% CI: 19%–28%) from 27.1% in 1985 to 1987 to 33.3% in 1994 to 1996. There was a smaller 8% (95% CI: 0%–18%) increase in live births at 32 to 33 weeks from 6.7% of twin live births in 1985 to 1987 to 7.3% in 1994 to 1996 ($P = .06$). Figure 1 shows the overall "shift to the left" in the gestational age distribution of twin live births. In contrast, low birth weight rates were essentially stable, registering a modest increase of 2% (95% CI: 0%–4%, $P = .07$), from 48.5% in 1985 to 1987 to 49.6% in 1994 to 1996. However, live births <500 g increased in frequency from 5.4 per 1000 twin live births in 1985 to 1987 to 7.6 in 1994 to 1996 (42% increase, 95% CI: 5%–91%, P value for trend = .004).

Stillbirth rates among twins declined from 22.4 per 1000 total births in 1985 to 1987 to 18.7 per 1000 in 1988 to 1990, 20.3 per 1000 in 1991 to 1993 and 18.8 per 1000 total births in 1994 to 1996. The 16% (95% CI: 1%–28%) overall decline in stillbirth rates between 1985 and 1987 and 1994 and 1996 was significant ($P = .03$), although the pattern of the decrease was not consistent (P for linear trend = .09, Table 1). Gestational age-specific stillbirth rates increased significantly at 22 to 23 weeks' gestation and declined significantly at 34 to 36 and 37 to 41 weeks' gestational age (Fig 2). Among fetuses reaching 34 or more completed weeks' gestation, stillbirth rates decreased from 9.5 per 1000 in 1985 to 1987, to 7.7 per 1000 in 1988 to 1990, 6.8 per 1000 in 1991 to 1993, and 5.4 per 1000 fetuses at risk in 1994 to 1996 (P for trend <.001, Fig 2). This represents a 43% (95% CI: 23%–58%, $P <$ .001) decrease in stillbirths between 1985 and 1987 and 1994 and 1996 among fetuses reaching ≥34 weeks' gestation.

The infant mortality rate decreased from 39.0 per 1000 twin live births in 1985 to 1987 to 35.6 per 1000 in 1988 to 1990, 29.1 per 1000 in 1991 to 1993, and 29.6 per 1000 twin live births in 1994 to 1996 (P for trend <.001). Infant mortality rates among twin live births

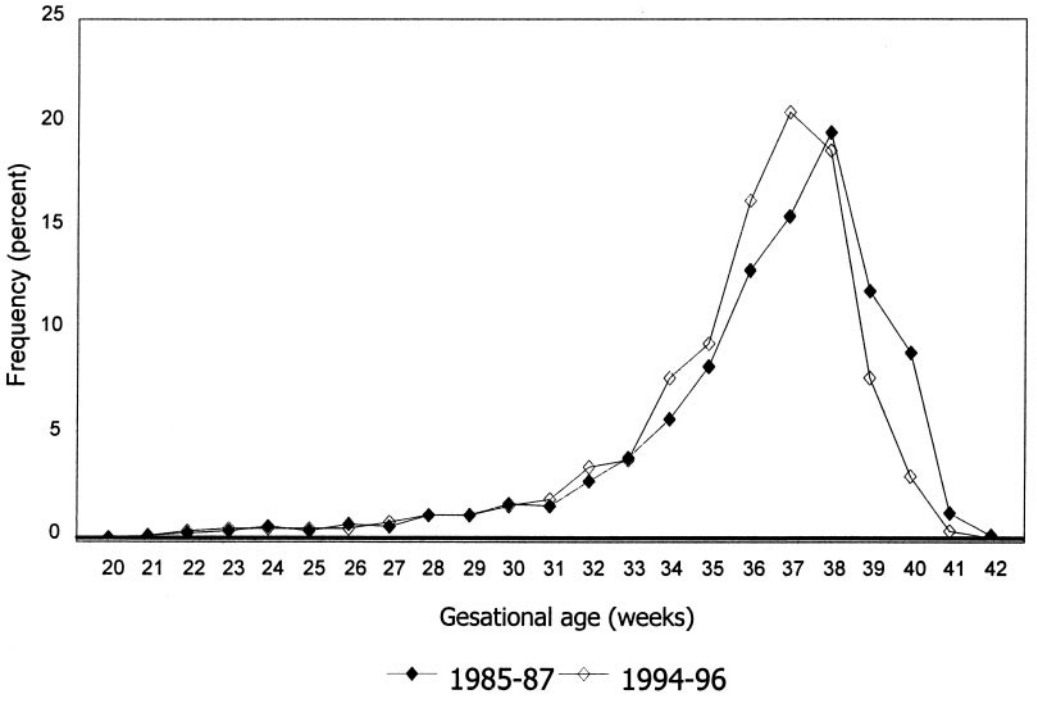

Fig 1. Gestational age distribution of twin live births in 1985 to 1987 and 1994 to 1996, Canada (excluding Ontario and Newfoundland).

TABLE 1. Gestational Age-Specific Risk of Stillbirth Among Twin Fetuses in Canada in 1985 to 1987, 1994 to 1996, and Trends in Stillbirth Rates Between 1985 to 1987 and 1994 to 1996*

Gestational Age (Weeks)	1985–1987			1994–1996			Relative Risk (95% CI) 1994–1996 Versus 1985–1987	*P* Value for Trend†
	Fetuses at Risk	Stillbirths		Fetuses at Risk	Stillbirths			
		Number	Rate		Number	Rate		
<22	13 513	30	2.2	14 850	29	2.0	0.88 (0.53–1.46)	.43
22–23	13 441	33	2.5	14 776	53	3.6	1.46 (0.95–2.25)	.02
24–25	13 324	26	2.0	14 605	34	2.3	1.19 (0.72–1.99)	.44
26–27	13 169	36	2.7	14 430	28	1.9	0.71 (0.43–1.16)	.21
28–31	12 965	43	3.3	14 220	34	2.4	0.72 (0.46–1.13)	.37
32–33	12 185	25	2.1	13 358	32	2.4	1.17 (0.69–1.97)	.58
34–36	11 274	48	4.3	12 266	33	2.7	0.63 (0.41–0.98)	.05
37–41	7 651	59	7.7	7 376	33	4.5	0.58 (0.38–0.89)	.005
≥42	31	0	0.0	10	0	0.0	—	—
NA	31	3	96.8	48	4	83.3	0.86 (0.21–3.59)	.39
Total	13 544	303	22.4	14 898	280	18.8	0.84 (0.72–0.99)	.09

* Stillbirth rates are expressed per 1000 fetuses at risk.
† Linear trend estimated over the periods 1985–1987, 1988–1990, 1991–1993, and 1994–1996.

≥500 g decreased from 34.5 per 1000 twin live births in 1985 to 1987, to 30.1 in 1988 to 1990, 23.3 in 1991 to 1993, and 22.4 per in 1994 to 1996 (*P* for trend <.001). Gestational age-specific infant mortality rates decreased significantly at 24 to 25 weeks, 26 to 27 weeks, 28 to 31 weeks, and at term gestation (Table 2). Infant mortality reductions at 32 to 33 and 34 to 36 weeks were of slightly lower magnitude than in adjacent gestational age categories and were not statistically significant, although in the combined category (32–36 weeks) infant mortality decreased from 16.9 in 1985 to 1987 to 11.8 per 1000 live births in 1994 to 1996 (relative risk: 0.71, 95% CI: 0.52–1.00, $P = .05$). The pattern of reductions in neonatal mortality rates was generally similar: overall neonatal mortality decreased from 31.3 in 1985 to 1987 to 29.8 in 1988 to 1990, 23.6 in 1991 to 1993, and 25.0 per 1000 live births in 1994 to 1996 (*P* for trend <.001).

The pattern of decline in birth weight-specific infant mortality was also generally consistent with the declines in gestational age-specific infant mortality; infant mortality decreased significantly among live births between 500 to 749 g, 750 to 999 g, 1000 to 1249 g, and 2500 to 3999 g (Table 3). Infant mortality among twin live births <500 g increased significantly from 859 per 1000 live births in 1985 to 1987 to 964 per 1000 live births in 1994 to 1996 (*P* for trend = .008).

Table 4 lists the principal causes of stillbirth among twin pregnancies reaching ≥34 weeks' gestation and causes of infant death among all infants. Significant reductions were observed in stillbirths because of complications of the placenta, cord, and membranes (54% decrease, 95% CI: 22%–73%); intrauterine hypoxia and birth asphyxia (60% decrease, 95% CI: 2%–83%); and unspecified conditions originating in the perinatal period (64% decrease, 95% CI: 28%–82%). Among causes of infant death (all gesta-

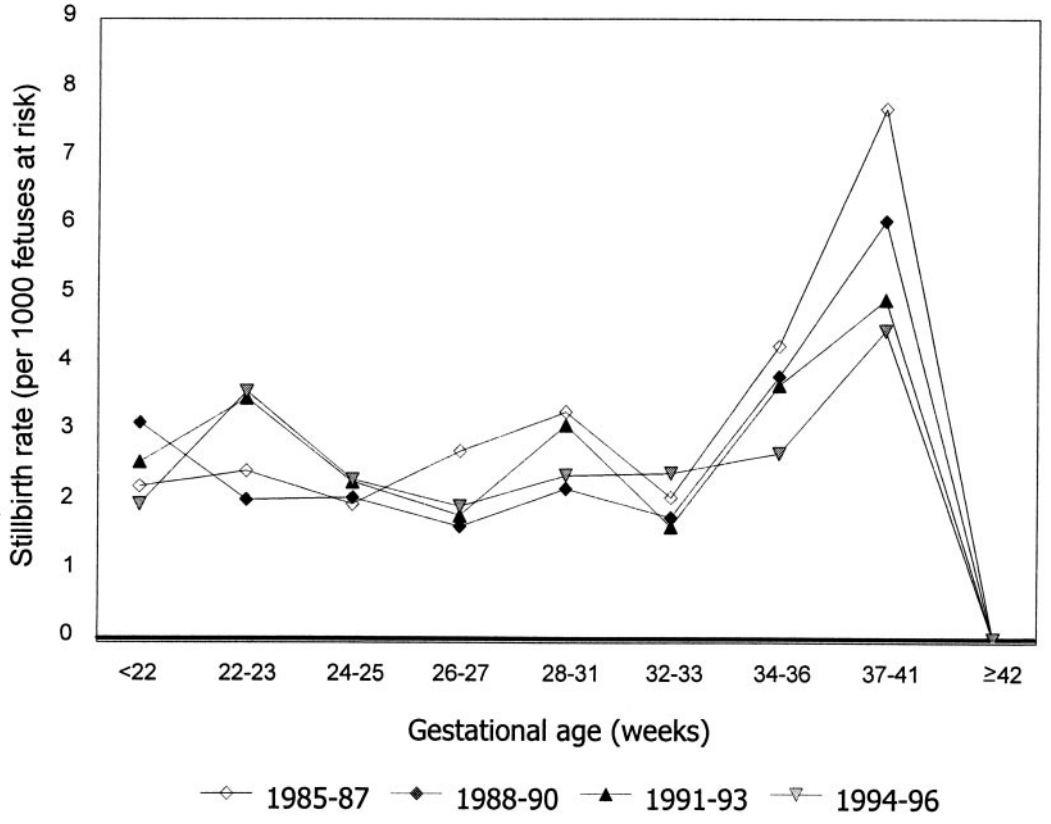

Fig 2. Gestational age-specific fetal mortality among twin births during 4 periods between 1985 and 1996, Canada (excluding Ontario and Newfoundland).

TABLE 2. Gestational Age-Specific Risk of Infant Death Among Twin Live Births in Canada in 1985 to 1987, 1994 to 1996, and Trends in Infant Mortality Between 1985 to 1987 and 1994 to 1996*

Gestational Age (Weeks)	1985–1987			1994–1996			Relative Risk (95% CI) 1994–1996 Versus 1985–1987	*P* Value for Trend†
	Live Births	Infant Deaths		Live Births	Infant Deaths			
		Number	Rate		Number	Rate		
<22‡	42	42	1000.0	45	44	977.8	0.98 (0.94–1.02)	.22
22–23	84	81	964.3	118	110	932.2	0.97 (0.91–1.03)	.07
24–25	129	100	775.2	141	87	617.0	0.80 (0.68–0.93)	<.001
26–27	168	75	446.4	182	34	186.8	0.42 (0.30–0.59)	<.001
28–31	737	84	114.0	828	52	62.8	0.55 (0.40–0.77)	<.001
32–33	886	27	30.5	1060	22	20.8	0.68 (0.39–1.19)	.33
34–36	3575	47	13.1	4857	48	9.9	0.75 (0.50–1.12)	.18
37–41	7561	57	7.5	7333	35	4.8	0.63 (0.42–0.96)	.004
≥42	31	0	0.0	10	0	0.0	—	—
NA	28	3	107.1	44	0	0.0	0.00 (0.00–1.49)	.01
Total	13 241	516	39.0	14 618	432	29.6	0.76 (0.67–0.86)	<.001

* Rates of infant death are expressed per 1000 live births.
† Linear trend estimated over the periods 1985–1987, 1988–1990, 1991–1993, and 1994–1996.
‡ Two infant survivors at <22 weeks' gestation and <500 g birth weight were reclassified as infant deaths in 1985–1987; 1 such infant survivor was reclassified in 1991–1993; there were so such infant survivors in 1988–1990 and 1994–1996.

tional ages), significant declines occurred among several cause of death categories, including respiratory distress syndrome (53% decrease, 95% CI: 35%–67%), short gestation, and unspecified low birth weight (69% decrease, 95% CI: 49%–81%) and miscellaneous causes of death (25% decrease, 95% CI: 5%–42%), while infant deaths attributable to complications of the placenta, cord, and membranes increased substantially (relative risk: 2.61, 95% CI: 1.50–4.53). Among live births 34 weeks' gestation and over, infant mortality rates attributable to complications of the placenta, cord, and membranes did not show any change between 1985 to 1987 and 1994 to 1996 (relative risk: 1.22, 95% CI: 0.27–5.45). The increase in stillbirths at 22 to 23 weeks' gestation was attributable to small, nonsignificant increases in several causes of death.

Logistic regression analysis showed that the temporal reductions in stillbirth and infant mortality rates between 1985 to 1987 and 1994 to 1996 were independent of changes in maternal age, parity, and birth order (Table 5). Adjusted stillbirth rates decreased by 20% (95% CI: 6%–33%), adjusted stillbirth rates among twins reaching 34 weeks' gestation de-

TABLE 3. Birth Weight-Specific Risk of Infant Death Among Twin Live Births in Canada in 1985 to 1987, 1994 to 1996, and Trends in Infant Mortality Between 1985 to 1987 and 1994 to 1996*

Birth Weight (g)	1985–1987			1994–1996			Relative Risk (95% CI) 1994–1996 Versus 1985–1987	*P* Value for Trend†
	Live Births	Infant Deaths		Live Births	Infant Deaths			
		Number	Rate		Number	Rate		
<500‡	71	61	859.2	111	107	964.0	1.12 (1.01–1.24)	.008
500–749	192	163	849.0	204	139	681.4	0.80 (0.72–0.90)	<.001
750–999	175	82	468.6	196	36	183.7	0.39 (0.28–0.55)	<.001
1000–1249	283	51	180.2	319	24	75.2	0.42 (0.26–0.66)	<.001
1250–1499	401	31	77.3	415	21	50.6	0.65 (0.38–1.12)	.07
1500–1999	1589	39	24.5	1766	38	21.5	0.88 (0.56–1.36)	.76
2000–2499	3678	38	10.3	4213	38	9.0	0.87 (0.56–1.37)	.21
2500–3999	6754	41	6.1	7325	26	3.5	0.58 (0.36–0.95)	.008
4000–6999	38	1	26.3	22	0	0.0	0.00 (0.00–67.4)	.62
NA	60	9	150.0	47	3	63.8	0.43 (0.12–1.48)	.07
Total	13 241	516	39.0	14 618	432	29.6	0.76 (0.67–0.86)	<.001

* Rates of infant death are expressed per 1000 live births.
† Linear trend estimated over the periods 1985–1987, 1988–1990, 1991–1993, and 1994–1996.
‡ Two infant survivors at <22 weeks' gestation and <500 g birth weight were reclassified as infant deaths in 1985–1987; 1 such infant survivor was reclassified in 1991–1993; there were no such infant survivors in 1988–1990 and 1994–1996.

TABLE 4. Causes of Death Among Stillbirths (≥34 Weeks' Gestation) and Infant Deaths, Twin Births in Canada (Excluding Ontario and Newfoundland), 1985 to 1987 and 1994 to 1996

	Cause of Death (*International Classification of Diseases, Ninth Revision* Code)	Deaths 1985–1987		Deaths 1994–1996		Relative Risk (95% CI)
		Number	Rate	Number	Rate	1994–1996 Versus 1985–1987
Stillbirths	Congenital anomalies (740–759)	3	2.7	8	6.5	2.45 (0.65–9.24)
	Maternal complications of pregnancy (761)	8	7.1	14	11.4	1.61 (0.68–3.83)
	Complications of placenta/cord/membranes (762)	42	37.3	21	17.1	0.46 (0.27–0.78)
	Slow fetal growth (764)	5	4.4	1	0.8	0.18 (0.02–1.57)
	Intrauterine hypoxia and birth asphyxia (768)	16	14.2	7	5.7	0.40 (0.17–0.98)
	Conditions in the perinatal period (779.9)	28	24.8	11	9.0	0.36 (0.18–0.72)
	All other causes	5	4.4	4	3.3	0.74 (0.20–2.74)
	Total	107	94.9	66	53.8	0.57 (0.42–0.77)
Infant deaths	Congenital anomalies (740–759)	77	5.8	72	4.9	0.85 (0.61–1.17)
	Maternal complications of pregnancy (761)	75	5.7	90	6.2	1.09 (0.80–1.48)
	Complications of placenta/cord/membranes (762)	17	1.3	49	3.4	2.61 (1.50–4.53)
	Short gestation, low birth weight (765)	61	4.6	21	1.4	0.31 (0.19–0.51)
	Intrauterine hypoxia and birth asphyxia (768)	16	1.2	13	0.9	0.74 (0.35–1.53)
	Respiratory distress syndrome (769)	101	7.6	52	3.6	0.47 (0.33–0.65)
	Infections specific to the perinatal period (771)	6	0.5	3	0.2	0.45 (0.11–1.81)
	Sudden infant death syndrome (798.0)	22	1.7	16	1.1	0.66 (0.35–1.25)
	All other causes	141	10.6	116	7.9	0.75 (0.58–0.95)
	Total	516	39.0	432	29.6	0.76 (0.67–0.86)

clined by 51% (95% CI: 33%–65%), and adjusted infant mortality rates decreased by 22% (95% CI: 11%–32%) between 1985 to 1987 and 1994 to 1996. Maternal age <20 years and nulliparity were associated with an increased risk of fetal and infant mortality (relative to mothers aged 20–24 years and parity 1–2, respectively), whereas older maternal age groups appeared to be at lower risk for infant death. Second-born twins were consistently at higher risk for both fetal and infant death.

Results of analyses adjusting for the nonindependence between the twin births from a single pregnancy were mostly similar. Between 1985 to 1987 and 1994 to 1996, there was a statistically significant increase in preterm birth rates ($P < .001$), statistically significant reductions in stillbirth rates among twin pregnancies reaching 34 weeks ($P = .001$), and in infant mortality rates ($P < .001$) but no statistically significant changes in low birth weight rates ($P = .15$) or overall stillbirth rates ($P = .14$).

DISCUSSION

Our study demonstrates a gestational age-dependent decline in stillbirth rates and an overall decrease in infant mortality during an era when preterm birth rates among twin births increased substantially. Stillbirth rates declined among twin pregnancies reaching 34 weeks' gestational age. On the other hand, infant mortality rates declined in several categories of preterm (24–25 weeks, 26–27 weeks, and 28–31 weeks) and term infants and in several categories of low (500–749 g, 1000–1249 g, and 1250–1499 g) and normal birth weight infants.

This dichotomy in the pattern of change in fetal and infant mortality suggests that different factors are primarily responsible for the reductions in stillbirth and infant death. The increase in preterm birth among twins, which seems primarily attributable to increased labor induction/cesarean section at 34–36 weeks' gestation,[10,12] has been accompanied by a

TABLE 5. Logistic Regression* Analysis for Stillbirth and Infant Death, Canada (Excluding Ontario and Newfoundland), 1985 to 1987 and 1994 to 1996

	Stillbirth		Stillbirth ≥34 Weeks		Infant Death	
	Relative Risk	95% CI	Relative Risk	95% CI	Relative Risk	95% CI
Crude model*						
1994–1996	0.82	0.72–0.93	0.55	0.40–0.75	0.76	0.66–0.86
1985–1987 (ref)	1.00	—	1.00	—	1.00	—
Adjusted model*						
1994–1996	0.80	0.67–0.94	0.49	0.35–0.67	0.78	0.68–0.89
1985–1987 (ref)	1.00	—	1.00	—	1.00	—
Age						
<20 y	1.60	1.11–2.31	1.46	0.69–3.07	1.52	1.16–2.00
20–24 (ref)	1.00	—	1.00	—	1.00	—
25–29	0.93	0.74–1.17	0.94	0.61–1.45	0.73	0.62–0.87
30–34	0.92	0.72–1.17	0.91	0.57–1.46	0.64	0.53–0.77
35–39	0.94	0.67–1.31	1.87	1.10–3.16	0.50	0.37–0.67
≥40	0.67	0.24–1.82	1.32	0.31–5.59	0.40	0.16–0.99
Parity nulliparous	1.85	1.44–2.37	2.50	1.44–4.34	1.50	1.24–1.81
1–2 (ref)	1.00	—	1.00	—	1.00	—
≥3	0.95	0.75–1.21	0.94	0.63–1.39	0.92	0.75–1.12
Birth order						
2	1.91	1.55–2.36	4.55	2.90–7.14	1.41	1.21–1.66
1 (ref)	1.00	—	1.00	—	1.00	—

* Subjects with missing values excluded from the crude and adjusted models leaving 28 123, 23 290, and 27 547 subjects in the stillbirth, stillbirth ≥34 weeks, and infant deaths models, respectively.

significant reduction in stillbirths at that and later gestational ages. The cause for the decrease in infant mortality at early and late gestation (and at low and normal birth weight) seems to be multifactorial. Several efficacious clinical interventions introduced in recent years (for example, antenatal glucocorticoid therapy,[19] exogenous surfactant[20]) are probably responsible for the observed reductions in infant mortality. Nevertheless, factors contributing to reductions in fetal and infant death overlap with earlier delivery of compromised fetuses helping to reduce both fetal and neonatal mortality and advances in neonatal care allowing safe birth at an earlier gestational age.

The risk of stillbirth increases with increasing gestational age (Fig 2). A "shift to the left" in the gestational age distribution, through increased obstetric intervention, should therefore theoretically lead to a decline in overall stillbirth rates. Our study demonstrates that the observed shift to the left in the gestational age distribution has been associated with a decline in stillbirth rates, with gestational age-specific reductions in stillbirth occurring at the same gestation where increases in obstetric intervention have occurred, namely ≥34 weeks. The causes of stillbirth that showed reductions (eg, complications of the placenta, cord, and membranes; intrauterine hypoxia and birth asphyxia; and unspecified conditions in the perinatal period) suggest a global change in obstetric management, rather than an increase in obstetric intervention for any particular indication. In fact, labor induction rates among twin pregnancies at 34 to 36 weeks' gestation have increased in recent years because of increases in the frequency of indications such as hypertension, prelabor rupture of membranes, oligohydramnios, abnormal biophysical profile, etc.[12] Similar temporal changes have probably occurred in the management of singleton high-risk pregnancies as well.[9,11]

Reductions in infant mortality among live births at 32 to 33 weeks and 34 to 36 weeks were not significant between 1985 to 1987 and 1994 to 1996 (although the reduction was of borderline significance among live births between 32–36 weeks). This is surprising given reductions in infant mortality among live births at both earlier and later gestational ages. One potential explanation is that increased obstetric intervention at preterm gestational ages (eg, at 34–36 weeks) is reducing stillbirth rates through the early delivery of compromised fetuses but diluting potential reductions in infant mortality because of additional infant deaths among these earlier-delivered fetuses. In other words, we may be observing some transfer of stillbirths to infant deaths, which is counteracting reductions in infant mortality because of recent improvements in clinical care (eg, antenatal glucocorticoid therapy, exogenous surfactant therapy). Although delivery at preterm gestation may prevent stillbirth, infant mortality rates among moderately (32–33 weeks) and mildly preterm (34–36 weeks) infants are high (compared with term infants).[21] It is noteworthy that infant mortality among singleton infants at 32 to 36 weeks has declined substantially since 1985 to 1987.[8,22] It is also noteworthy that infant mortality rates in the United States among twin live births between 32 to 36 weeks' gestation declined significantly between 1983 to 1984 and 1995 to 1996.[10] However, overall infant mortality among twin live births in the 2 countries is comparable (29.2 in the United States in 1995–1996 vs 29.6 per 1000 live births in Canada in 1994–1996). Additional studies are required to better explain the lack of a significant reduction in infant mortality among twin live births between 32 to 33 and 34 to 36 weeks' gestational age.

Our study provides some insights into the discordant temporal associations between increases in preterm birth and reductions in fetal death rates that have been observed among singleton and multiple births.[9] Temporal reductions in fetal mortality

among twin births at later gestations are being overshadowed by the high background rate of earlier stillbirths. It is well established that fetal wastage at early gestational ages is relatively high among twin pregnancies and especially among triplet and higher-order multiple pregnancies.[23–26] Although triplets and higher-order multiple births constitute a small fraction of all multiple births, this difference in stillbirth rates and recent increases in higher-order multiple births mean that temporal trends in stillbirth rates yield slightly different results when multiple births are studied as a whole (vs when twins are examined separately).

Twin births at 22 to 23 weeks' gestation and at birth weights <500 g increased between 1985 to 1987 and 1994 to 1996, as did rates of stillbirth and infant death at these gestational ages and birth weights. This finding is consistent with previous studies which have showed an increase in the registration of live births and stillbirths at the borderline of viability.[27–30] Improvements in obstetric and neonatal care, and in the consequent survival of infants at the borderline of viability, have led to changes in attitudes and to increases in the registration of such births.

As with other studies arising from large perinatal databases, ours is subject to potential errors. Recent changes in gestational age ascertainment, with ultrasound-based ascertainment replacing menstrual dating, are responsible for a small (artifactual) increase in preterm birth.[9,11] This cannot explain the large increases in preterm birth observed among twin births, however, because the same changes in the measurement of gestational age among singleton births have been accompanied by much smaller increases in preterm birth.[10] Other study limitations include the potential for transcription errors and incorrect coding of causes of death.

CONCLUSION

Our study shows gestational age-specific declines in stillbirth and infant mortality among twins during an era when preterm birth rates have increased drastically. The reduction in stillbirth rates has been evident at and beyond 34 weeks' gestation, while reductions in infant mortality rates have been observed at both early and term gestations. The absence of a reduction in infant mortality rates at 32 to 33 weeks' and 34 to 36 weeks' gestational age among twins is a cause for concern and suggests that some fraction of stillbirths averted by obstetric intervention may be subsequently dying in infancy.

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