The Effect of Plurality and Gestation on the Prevention or Postponement of Infant Mortality: 1989–1991 Versus 1999–2001

Barbara Luke¹ and Morton B. Brown²

¹ University of Miami School of Nursing and Health Studies, Coral Gables, Florida, and the Department of Obstetrics and Gynecology, and the

Department of Pediatrics, Miller School of Medicine, University of Miami, Miami, Florida, United States of America

² Department of Biostatistics, School of Public Health, University of Michigan, Ann Arbor, Michigan, United States of America

dvances in perinatal technology that improved Asurvival may have also resulted in prolonged death from the neonatal to the postneonatal period for some infants. The objectives of this study were to determine if the medical advances that occurred in the 1990s benefited infants of multiple births more than their singleton counterparts, and if these changes prevented or postponed mortality for the smallest and most immature infants. The study population included live births of 22 to 43 weeks' gestation from the 1989-1991 and 1999-2001 US Birth Cohort Linked Birth/Infant Death Data Sets. Odds ratios were calculated to evaluate the change in risk by plurality, gestation, and to compare the change to that for singletons. Neonatal and infant mortality rates declined for all pluralities; postneonatal mortality increased for births at less than 26 weeks, but declined at later gestations. In general, the risk of death for twins and triplets compared to singletons decreased, and the improvement in survival was greater for multiples during the early neonatal period and overall. Infant mortality rates improved by 28% for singletons, 32% for twins and triplets during the 1990s, although for the most premature infants, some deaths were postponed from the early to the late neonatal period.

In 2004 there were 139,494 infants in multiple pregnancies born in the United States, the highest number ever recorded (Martin et al., 2006). Multiple pregnancies have risen dramatically since 1980, with a 93% increase in twins and a 544% increase in triplet and higher order births (quadruplets and quintuplets). This contemporary trend of increasing multiple pregnancies has been reported in many industrialized nations, including Japan, Sweden, Finland, Denmark, Canada, Australia, Austria, Israel, the Netherlands, and the United Kingdom (Gissler & Tiitinen, 2001; Imaizumi, 1997). It is estimated that approximately one-fourth of the rise in multiple births is due to the long-term trend of childbearing at older maternal ages, while for three-fourths is attributable to the use of assisted reproductive technologies (ART; Centers for Disease Control, 2000; Jewell & Yip, 1995; Reynolds et al., 2003; Wilcox et al., 1996). Although infants of multiple births comprise only 3% of all live births, they are disproportionately represented among preterm (less than 37 weeks, 16%), very preterm (less than 32 weeks, 22%), low birthweight (32%), and very low birthweight (27%) infant populations (Martin et al., 2003). The average birthweight and gestational age is 3316 g at 38.7 weeks for singletons, compared to 2333 g at 35.2 weeks for twins, 1700 g at 32.1 weeks for triplets, 1276 g at 29.7 weeks for quadruplets, and 1103 g at 28.4 weeks for quintuplets (Martin et al., 2006). National vital statistics are increasingly being reported separately as singletons versus multiples because of the effect of the latter on estimates of low birthweight and prematurity (Blondel et al., 2002; Centers for Disease Control, 1999; Friede et al., 1987).

Advances in perinatal technology that have dramatically increased the survival of very low birthweight infants may have also resulted in prolonging the time to death with a postponement of mortality from the neonatal to the postneonatal period (Friede et al., 1987; Gould et al., 2000). In an assessment of infant mortality among very low birthweight infants in California, Gould et al. (2000) concluded that although the average time to death was significantly increased in very low birthweight infants weighing greater than 750 g between 1987 and 1993, advances in perinatal technology dramatically decreased overall very low birthweight mortality. Analyses of infant mortality rates in New York City between 1988 and 1989 and between 1992 and 1993 concluded that the declines between these two periods were attributable to improvements in birthweight-specific death rates and

Received 19 December, 2006; accepted 26 March, 2007.

Address for correspondence: Barbara Luke, School of Nursing and Health Studies, University of Miami, 5801 Red Road, Coral Gables, Florida 33143, USA. E-mail: bluke@med.miami.edu

not to a positive shift in the birthweight distribution of the population (Racine et al., 1998). The objectives of this study were to determine if the medical advances that occurred in the 1990s benefited infants of multiple births more than their singleton counterparts, and if these changes prevented or postponed mortality for the smallest and most immature infants.

Methods

The data sets for this study included the Birth Cohort Linked Birth/Infant Death Data Set for 1989–1991 and 1999–2001, the earliest and most recent years for which plurality-specific data are available. The methodology takes advantage of two existing data sources: state-linked files for the identification of linked birth and infant death certificates, and National Center for Health Statistics (NCHS) natality and mortality computerized statistical files, the source of computer records for the two linked certificates. All states link infant death certificates to their corresponding birth certificates for legal and statistical purposes. When the birth and death of an infant occur in different states, copies of the records are exchanged by the state of death and the state of birth in order to affect a link. In addition, if a third state is identified as the state of residence at the time of birth or death, that state is also sent a copy of the appropriate certificate by the state where the birth or death occurred. The NCHS natality and mortality files, produced annually, include statistical data from birth and death certificates that are provided to NCHS by States under the Vital Statistics Cooperative Program. The data have been coded according to uniform coding specifications, have passed rigid quality control standards, have been edited and reviewed, and are the basis for official US birth and death statistics. To initiate processing, NCHS obtains matching birth certificate numbers from states for all infant deaths that occurred in their jurisdiction. This information is used to extract final, edited mortality and natality data from the NCHS natality and mortality statistical files. Individual birth and death records are selected from their respective files and linked into a single statistical record, thereby establishing a national linked record file. After the initial linkage,

Table 1

Characteristics of the Study Population by Plurality, 1989-1991 and 1999-2001

Characteristic	Singl	etons	Tw	ins	Trip	lets	All Pluralities*	
	1989–1991	1999–2001	1989–1991	1999–2001	1989–1991	1999–2001	1989–1991	1999–2001
(<i>N</i> , mothers)**	11,039,476	10,814,840	131,550	169,222	2616	6327	11,173,642	10,990,389
Maternal age in years: mean (<i>SD</i>)	26.4 (5.7)	27.1 (6.2)	27.7 (5.6)	29.2 (6.2)	29.8 (4.8)	32.0 (5.2)	26.4 (5.7)	27.2 (6.2)
Maternal age groups (%)								
< 20	12.8	11.9	7.7	6.0	2.5	1.2	12.7	11.7
20–34	78.4	75.0	80.6	73.4	80.5	68.8	78.4	74.9
> 34	8.8	13.1	11.8	20.6	16.9	30.0	8.9	13.4
Maternal race (%)								
White	79.3	78.8	78.0	79.1	88.0	89.4	79.2	78.9
Black	16.3	15.2	18.8	16.6	9.9	7.3	16.3	15.3
Other	4.5	5.9	3.3	4.3	2.1	3.3	4.4	5.9
Maternal Education in yrs (%)								
≤ 12	63.9	54.1	59.6	44.6	44.1	26.6	63.8	53.9
13–15	19.2	21.5	20.5	22.5	20.6	22.8	19.3	21.5
≥16	16.9	24.3	19.9	32.8	35.3	50.5	17.0	24.6
Primipara (%)	41.6	41.0	20.5	22.0	18.6	21.6	41.1	40.4
Married (%)	72.3	66.7	73.9	73.4	88.6	91.8	72.3	67.0
Smoker (%)	12.4	9.3	11.7	7.6	6.1	2.4	12.4	9.3
N, infants, live-born	11,039,476	10,814,840	263,099	338,444	7848	18,981	11,310,423	11,172,265
N, infant deaths	75,321	52,995	7714	6751	492	812	83,527	60,558
Birthweight (grams)	3337 (545)	3314 (536)	2434 (635)	2378 (614)	1821 (573)	1729 (540)	3315 (565)	3283 (565)
Gestational categories (weeks; %)								
22–23	0.1	0.1	0.8	0.8	2.2	2.1	0.1	0.1
24–25	0.1	0.1	1.0	1.1	2.9	2.9	0.2	0.2
26–28	0.3	0.3	2.4	2.5	6.7	8.1	0.3	0.4
29–32	0.8	0.9	7.9	9.0	25.1	31.7	1.0	1.2
33–36	6.8	7.4	34.7	42.8	51.0	47.7	7.5	8.6
37–40	67.5	73.9	48.6	41.2	11.1	6.6	67.0	72.7
41–43	24.3	17.3	4.7	2.6	1.1	1.0	23.8	16.8

Note: *Singletons, twins, and triplets.

**The numbers of mothers were calculated based on the number of infants per pregnancy, but because some multiple pregnancies may have included fetal deaths, this is only an estimate.

Table 2

Neonatal, Postneonatal, and Infant Mortality Rates by Plurality and Gestation, 1989–1991 vs. 1999–2001

	Neonatal (NNMR)* 1989–1991 1999–2001		Postneonatal (PNMR)** 1989–1991 1999–2001		Infant (IMR)***		Per cent change, 1999–2001 vs. 1989–199			
Plurality					1989–1991	1999-2001	NNMR	PNMR	IMR	<i>p</i> value
All gestations										
Singletons	3.74	2.81	3.09	2.09	6.82	4.90	-24.9	-32.4	-28.2	< .0001
Twins	22.08	15.18	7.24	4.77	29.32	19.95	-31.3	-34.1	-32.0	< .0001
Triplets	51.35	36.67	11.34	6.11	62.69	42.78	-28.6	-46.1	-31.8	< .0001
22–23 weeks										
Singletons	804.77	721.81	31.37	34.63	836.14	756.44	-10.3	+10.4	-9.5	< .0001
Twins	884.24	773.60	10.35	31.34	894.59	804.94	-12.5	+202.8	-10.0	< .0001
Triplets	958.58	816.83	5.92	19.80	964.50	836.63	-14.8	_	-13.3	< .0001
24–25 weeks										
Singletons	434.28	299.04	60.18	63.76	494.46	362.81	-31.1	+5.9	-26.6	< .0001
Twins	553.81	336.68	60.56	66.67	614.37	403.35	-39.2	+10.1	-34.3	< .0001
Triplets	552.17	381.13	47.83	34.48	600.00	415.61	-31.0	_	-30.7	< .0001
26–28 weeks										
Singletons	153.48	89.97	45.79	33.15	199.27	123.11	-41.4	-27.6	-38.2	< .0001
Twins	181.12	88.03	45.12	25.52	226.24	113.54	-51.4	-43.4	-49.8	< .0001
Triplets	128.11	48.99	49.71	24.17	177.82	73.15	-61.8	-51.4	-58.9	< .0001
29–32 weeks										
Singletons	40.19	26.15	17.82	11.36	58.01	37.51	-34.9	-36.3	-35.3	<.0001
Twins	24.44	13.43	15.06	8.09	39.50	21.52	-45.0	-46.3	-45.5	<.0001
Triplets	13.72	8.15	11.18	4.49	24.90	12.64	-40.6	-59.8	-49.2	<.0001
33–36 weeks										
Singletons	6.92	5.00	6.42	4.03	13.34	9.04	-27.7	-37.2	-32.2	< .0001
Twins	4.99	2.85	6.07	3.25	11.06	6.10	-42.9	-44.8	-44.8	< .0001
Triplets§	4.03	3.05	5.85	2.38	9.88	5.44	-24.3	-44.9	-44.9	< .0001
37–40 weeks										
Singletons	1.34	0.97	2.53	1.63	3.87	2.60	-27.6	-35.6	-32.8	< .0001
Twins	2.15	1.88	3.98	2.27	6.13	4.15	-12.6	-43.0	-32.3	< .0001
41–43 weeks										
Singletons	1.29	0.87	2.28	1.52	3.57	2.39	-32.6	-33.3	-33.1	< .0001
Twins	3.68	2.03	5.07	2.93	8.75	4.96	-44.8	-42.2	-43.3	< .0001

Note: *Neonatal mortality rate, deaths during days 0–27 after birth, per 1000 live births. **Postneonatal mortality rate, deaths during days 28–364 after birth, per 1000 live births.

***Infant mortality rate, deaths during days 0–364 after birth, per 1000 live births. § Includes triplets born 33–36 weeks and later. Rates in italics are based on small numbers (less than 20 in the numerator) and should be interpreted with caution. — Indicates difference in rates not calculated because of small numbers.

NCHS returns to the states where the deaths occurred with computer lists of unlinked infant death certificates for follow-up linking. If the birth occurred in a state different from the state of death, the state of birth identified on the death certificate is contacted to obtain the linking birth certificate. State additions and corrections are incorporated, and a final, national linked file is produced.

Three-year periods were chosen to dampen yearto-year fluctuations. The data were limited to live-born infants of 20 to 43 weeks' gestation. To reduce implausible birthweight-gestational age combinations, the data was cleaned in the following manner: for each week of gestation the upper range for birthweight was defined using the gender-specific 97th percentile for singletons (Kramer et al., 2001) and the lower limit as the 5th percentile for triplets (Min et al., 2004). The data was grouped by weeks of gestation as 22–23, 24–25, 26–28, 29–32, 33–36, 37–40, and 41–43, and as less than 26 weeks versus 26 weeks or greater. Plurality of each infant was categorized as singletons, twins, and triplets. Infant mortality was defined as neonatal (0–27 days, including early, 0–6 days and late, 7–27 days), postneonatal (28–364 days, including early, 28–167 days and late, 168–364 days), and infant (0–364 days) according to NCHS definitions (Kochanek et al., 2004).

The analyses included three aspects. First, pluralityspecific neonatal, postneonatal, and infant mortality rates were calculated overall and by gestation periods for 1989–1991 and 1999–2001 and compared using χ^2 analyses. Second, the plurality-specific odds ratios and 95% confidence intervals of neonatal, postneonatal, and infant death compared to the risk for singletons within each time period (1989–1991 and 1999–2001) was calculated, overall and for births at less than 26 weeks and births at 26 weeks or greater. Third, within each plurality the change in the risk of early and late neonatal and postneonatal mortality, and in overall infant mortality from 1989-1991 to 1999-2001 for all gestations and for births at less than 26 weeks and 26 weeks or greater was calculated. The odds ratios for twins and triplets were then compared to the singleton odds ratios to evaluate if the change in risk (improvement in survival) had been greater or lesser for multiples than for singletons.

Results

The study population for 1989–1991 and 1999–2001 included 11,310,423 and 11,172,265 live births, and 83,527 and 60,558 infant deaths, respectively. Between the two time periods, there was a shift to older maternal ages, higher maternal education, and a decrease in smoking during pregnancy overall and for each plurality, as well as a decrease in postmaturity (Table 1). The plurality- and gestation-specific mortality rates are given in Table 2. Overall, the neonatal and infant mortality rates declined significantly overall and at each gestation period; postneonatal mortality increased for births at less than 26 weeks, but declined for births at later gestations. The greatest declines in mortality rates were among births at 26 to 36 weeks.

The odds ratios and 95% confidence intervals representing the change in the risk of death between 1989-1991 and 1999-2001 by plurality and gestation are given in Table 3. For all infant deaths (0-364 days after birth), survival significantly improved for every plurality overall and for births less than 26 weeks and 26 weeks or greater. During the neonatal period, the greatest improvements occurred during the early neonatal period (0-6 days), significant for every plurality and in all gestation categories, whereas in the late neonatal period (7-27 days) significant improvements only occurred for singletons overall and for singletons and twins born at 26 weeks or greater. Both early and late postneonatal survival improved overall for all pluralities, as well as for singletons at less than 26 weeks and 26 weeks or greater. For twins and triplets, late postneonatal survival improved among births at less than 26 weeks, early postneonatal survival improved for births at 26 weeks or greater. For twins born at 26 weeks or greater, late postneonatal survival also improved significantly. The plurality-specific change in risk of death between 1989–1991 and 1999–2001 compared to the change for singletons is also given in Table 3. For all infant deaths (0–364 days after birth) significantly greater improvements in survival occurred among twins overall, among both pluralities at both less than 26 weeks and 26 weeks or greater. During the early neonatal period (0–6 days), greater improvements occurred among twins and triplets overall and at both earlier and later gestations, but during the late neonatal period (7–27 days) only among twins for births 26 weeks or greater. During the postneonatal period, significantly greater improvements occurred in the early period (28–167 days) for both twins and triplets for births at 26 weeks or greater, and during the late period (168–364 days) only for twins born at 26 weeks or greater.

Discussion

This population-based study of all live births in the United States between 1989-1991 and 1999-2001 documents the substantial improvement in survival among all infants that has been achieved during the past decade. This improvement has been greater for twins and triplets than for singletons and greater during the early versus late neonatal period. Despite this encouraging progress, the continuing rise in multiple births has important public health implications. In 2002, nearly one out of every five neonatal deaths was an infant born from a multiple pregnancy (MacDorman et al., 2005), and an estimated 19% of all NICU days are associated with multiple pregnancies (Ross et al., 1999). The 2004 prematurity rate of 12.5% represents the highest level in 25 years, and the low birthweight rate of 8.1% has also risen to a new peak (Martin et al., 2006). These figures fall far short of the United States' 2010 Health People 2010 Objectives of 7.6% for prematurity and 5.0% for low birthweight. Although infants of multiple births contribute disproportionately to both of these adverse outcomes, this increase in prematurity and low birthweight is also occurring among singleton births.

Table 3

	Neonatal deaths (0–27 days)				Pos	tneonatal dea	ths (28–3	364 days)	Infant deaths (0–364 days)				
	19	1989–1991		1999–2001		1989–1991		1999–2001		1989–1991		1999–2001	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95%CI	OR	95% CI	
All gestations			4.00						4.00		4.00		
Singletons	1.00		1.00		1.00		1.00		1.00		1.00		
Twins	6.02	5.86-6.19	5.46	5.30-5.62	2.40	2.29–2.51	2.32	2.21–2.44	4.40	4.30–4.51	4.49	4.38–4.61	
Triplets	14.44	13.06–15.97	13.49	12.50-14.56	3.89	3.16–4.80	3.04	2.53–3.65	9.74	8.89–10.67	10.27	9.57-11.02	
< 26 weeks													
Singletons	1.00		1.00		1.00		1.00		1.00		1.00		
Twins	1.66	1.55-1.77	1.22	1.16-1.29	1.11	0.94-1.31	1.11	0.98-1.26	1.64	1.53-1.76	1.22	1.15-1.29	
Triplets	1.88	1.51-2.35	1.52	1.33-1.73	0.93	0.51-1.70	0.64	0.43-0.95	1.79	1.42-2.25	1.38	1.21-1.57	
•		1.01 2.00	110	1.00 1.70	0100	0.01 1.70		0.10 0.00		1.12 2.20	1100	1.21 1.07	
≥ 26 weeks													
Singletons	1.00		1.00		1.00		1.00		1.00		1.00		
Twins	3.82	3.66–3.98	3.25	3.10–3.41	2.25	2.14–2.36	1.97	1.86-2.08	2.97	2.88–3.07	2.57	2.48–2.67	
Triplets	6.29	5.23-7.57	5.05	4.31–5.92	3.53	2.82-4.42	2.54	2.06-3.13	4.80	4.16-5.54	3.72	3.28-4.22	

Twin Research and Human Genetics June 2007

Table 4

The Odds Ratios and 95% Confidence Intervals (CIs) Representing the Change in Risk of Neonatal, Postneonatal, and Infant Death Between 1989–1991 and 1999–2001 by Plurality and Gestation

		Neor	natal			Postne		All Infant Deaths			
	Early (0–6 days)		Late (7–27 days)		Early (2	Early (28–167 days)		Late (168–364 days)		(0—364 days)	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95%CI	
All gestations											
Singleton	0.71	0.70-0.72	0.90	0.88-0.92	0.67	0.66-0.68	0.70	0.68-0.72	0.72	0.71-0.72	
Twin	0.64	0.61-0.66	0.95	0.89-1.01	0.66	0.62-0.70	0.64	0.57-0.71	0.67	0.66-0.69	
Triplet	0.63	0.57–0.71	1.18	0.96-1.45	0.53	0.42-0.66	0.54	0.32-0.90	0.67	0.62-0.72	
< 26 weeks											
Singleton	0.56	0.55-0.57	1.12	1.07-1.18	0.84	0.79-0.90	0.75	0.66-0.86	0.62	0.60-0.63	
Twin	0.41	0.39-0.43	1.03	0.92-1.14	0.88	0.77-1.01	0.62	0.45-0.86	0.46	0.44-0.48	
Triplet	0.44	0.38–0.51	1.26	0.86-1.85	0.78	0.40–1.54	0.19	0.04-0.98	0.48	0.41-0.56	
< 26 weeks											
Singleton	0.65	0.64-0.66	0.81	0.79-0.83	0.65	0.64-0.66	0.69	0.67-0.71	0.68	0.67-0.68	
Twin	0.56	0.53-0.59	0.69	0.63-0.75	0.57	0.53-0.61	0.59	0.52-0.67	0.59	0.56-0.6	
Triplet	0.45	0.35–0.57	0.83	0.62-1.12	0.44	0.34–0.58	0.61	0.35-1.08	0.52	0.46-0.60	
Comparison to sing	gleton OR	s*									
All gestations											
Singleton	1.00		1.00		1.00		1.00		1.00		
Twin	0.90	0.87-0.93	1.05	0.99-1.12	0.99	0.93-1.04	0.91	0.81-1.01	0.94	0.92-0.96	
Triplet	0.90	0.82-0.98	1.31	1.11–1.55	0.79	0.64–0.97	0.77	0.52-1.15	0.93	0.87-1.00	
< 26 weeks											
Singleton	1.00		1.00		1.00		1.00		1.00		
Twin	0.73	0.69-0.77	0.91	0.82-1.01	1.04	0.91–1.20	0.83	0.61-1.12	0.74	0.70-0.79	
Triplet	0.78	0.64–0.83	1.12	0.71–1.17	0.93	0.69–1.58	0.25	0.26-2.59	0.77	0.65-0.8	
\geq 26 weeks											
Singleton	1.00		1.00		1.00		1.00		1.00		
Twin	0.86	0.81–0.91	0.85	0.78-0.93	0.88	0.82-0.94	0.86	0.76-0.97	0.87	0.83-0.9	
Triplet	0.68	0.55-0.85	1.03	0.81-1.31	0.68	0.54-0.86	0.89	0.58-1.36	0.77	0.68-0.8	

Note: Odds ratios < 1 denote improvement in survival

*The plurality-specific change in risk of death between 1989–1991 and 1999–2001 compared to the change for singletons.

During the 1990s, clinical studies reported that postponement of infant death for infants with birthweights of less than 1000 g had increased from two days in 1991 to 10 days in 2001 (Meadow et al., 1996, 2004). Our findings indicate that this postponement has occurred primarily from the early to the late neonatal period, and only among births at less than 26 weeks-the smallest and most premature infants. This has also been the infant population which demonstrated the greatest improvement in survival during this time period: a 38% improvement for singletons, 54% for twins, and 52% for triplets. Although survival rates have improved dramatically during the 1990s, studies have shown that this improvement has slowed or even ceased during the late 1990s, particularly among the smallest infants (Horbar et al., 2002; Meadow et al., 2004).

The survival prognosis of infants born at the threshold of viability remains problematic. Data from the National Institute of Child Health and Human Development Neonatal Centers in 1995–1996 indicated neonatal survival rates of 30% at 23 weeks, 52% at 24 weeks, and 76% at 25 weeks, which is comparable with the results reported in this study (Lemons et al., 2001). However, the incidence of moderate or severe neurodevelopmental disability in survivors is high, ranging from 30 to 50% by 18 to 30 months of age (Emsley et al., 1998; Tudehope et al., 1995; Wood et al., 2000). The potential spectrum of long-term health consequences of prematurity evident in early childhood through young adulthood includes visual impairment (Ley et al., 2004; Martin et al., 2004; O'Connor et al., 2004), alterations in renal structure and function (Amann et al., 2004; Rodriguez-Soriano et al., 2005), neurobehavioral deficits (Anderson et al., 2003; Breslau et al., 2004; O'Keefe et al., 2003), impaired motor development (Evensen et al., 2004; Hediger et al., 2002), and chronic health conditions (Hack et al., 2005), particularly if also born small for gestational age.

The use of vital statistics data has limitations. First, there is the potential for misclassification of gestational age. We have attempted to minimize this error by cleaning the data to eliminate implausible birthweightgestational age combinations, but it is still possible that some remain despite this effort. Second, because of the intracluster correlation of mortality risk for infants born in a multiple versus singleton pregnancy, the risk of death for these infants is acknowledged to be greater, beyond that due to lowered birthweight and younger gestational age (Huang et al., 2003; Johnson & Zhang, 2002). The annual linked birth and death files are reported as individual births, although NCHS has released a matched multiple birth file that links multiple births to the same mother; this matched file is only available for births between 1995 and 2000, which includes only a portion of the time period evaluated in the current study. Despite these limitations, the use of multi-year, population-based data provides the best available data for evaluating national trends in live births.

Conclusion

Medical advances in the 1990s resulted in reductions in infant mortality by 28% for singletons, 32% for twins and triplets. For births at less than 26 weeks, 94% of the improvement in survival occurred within the early neonatal period, compared to 34% of the improvement for births at 26 weeks or greater. Because of their greater risk for adverse growth and developmental sequelae, the improved survival of smaller and more immature infants has major public health implications

Acknowledgments

This study was supported by grants RO3 HD048498-01 and RO3 HD047627-01A1 from the National Institute of Child Health and Human Development of the National Institutes of Health.

Presented at the 19th Annual meeting, Society for Pediatric and Perinatal Epidemiologic Research, Seattle, Washington, June 20–21, 2006.

References

- Amann, K., Plank, C., & Dotsch, J. (2004). Low nephron number: A new cardiovascular risk factor in children? *Pediatric Nephrology*, 19, 1319–1323.
- Anderson, P., Doyle, L. W., and the Victorian Infant Collaborative Study Group (2003). Neurobehavioral outcomes of school-age children born extremely low birth weight or very preterm in the 1990s. *Journal of the American Medical Association*, 289, 3264–3272.
- Blondel, B., Kogan, M. D., Alexander, G. R., Dattani, N., Kramer, M. S., Macfarlane, A., & Wen, S.W. (2002).
 The impact of the increasing number of multiple births on the rates of preterm birth and low birthweight: An international study. *American Journal of Public Health*, 92, 1323–1330.
- Breslau, N., Paneth, N. S., & Lucia, V. C. (2004). The lingering academic deficits of low birth weight children. *Pediatrics*, 114, 1035–1040.
- Centers for Disease Control (1999). Impact of multiple births on low birthweight - Massachusetts, 1989–1996. Morbidity and Mortality Weekly Report, 48, 289–292.
- Centers for Disease Control (2000). Contribution of assisted reproductive technology and ovulation-inducing drugs to triplet and higher-order multiple births — United States, 1980–1997. Morbidity and Mortality Weekly Report, 49, 535–538.

- Emsley, H. C., Wardle, S. P., Sims, D. G., Chiswick, M. L., & D'Souza, S. W. (1998). Increased survival and deteriorating developmental outcome in 23 to 25 week old gestation infants, 1990–1994 compared with 1984–1989. Archives of Diseases of Childhood. Fetal and Neonatal Edition, 78, F99–F104.
- Evensen, K. A. I., Vik, T., Helbostad, J., Indredavik, M. S., Kulseng, S., & Brubakk, A. -M. (2004). Motor skills in adolescents with low birth weight. Archives of Disease in Childhood. Fetal and Neonatal Edition, 89, F451–F455.
- Friede, A., Rhodes, P. H., Guyer, B., Binkin, N. J., Hannan, M. T., & Hogue, C. J. R. (1987). The postponement of neonatal deaths into the postneonatal period: Evidence from Massachusetts. *American Journal of Epidemiology*, 127, 181–170.
- Gissler, M., & Tiitinen, A. (2001). IVF treatments and their outcomes in Finland in the 1990s. *Acta Obstetrics and Gynecology Scandinavia*, 80, 937–944.
- Gould, J. B., Benitz, W. E., & Liu, H. (2000). Mortality and time to death in very low birth weight infants: California, 1987 and 1993. *Pediatrics*, 105, e37.
- Hack, M., Taylor, H. G., Drotar, D., Schluchter, M., Cartar, L., Andreias, L., Wilson-Costello, D., & Klein, N. (2005). Chronic conditions, functional limitations, and special health care needs of school-aged children born with extremely low-birth-weight in the 1990s. *Journal* of the American Medical Association, 294, 318–325.
- Hediger, M. L., Overpeck, M. D., Ruan, W. J., & Troendle, J. F. (2002). Birthweight and gestational age effects on motor and social development. *Paediatric and Perinatal Epidemiology*, 16, 33–46.
- Horbar, J. D., Badger, G. J., Carpenter, J. H., Fanaroff, A. A., Kilpatrick, S., LaCorte, M., Phibbs, R., & Soll, R. F. for the Members of the Vermont Oxford Network (2002). Trends in mortality and morbidity for very low birthweight infants, 1991–1999. *Pediatrics*, 110, 143–151.
- Huang, J. S., Lu, S. –E., & Ananth, C. V. (2003). The clustering of neonatal deaths in triplet pregnancies: Application of response conditional multivariate logistic regression models. *Journal of Clinical Epidemiology*, 56, 1202–1209.
- Imaizumi, Y. (1997). Trends in twinning rates in ten countries, 1972–1996. Acta Geneticae Medicae et Gemellolgiae, 46, 209–218.
- Jewell, S. E., & Yip, R. (1995). Increasing trends in plural births in the United States. Obstetrics and Gynecology, 85, 229–232.
- Johnson, C. D., & Zhang, J. (2002). Survival of other fetuses after a fetal death in twin or triplet pregnancies. Obstetrics and Gynecology, 99, 698–703.
- Kochanek, K. D., Murphy, S. L., Anderson, R. N., & Scott,
 C. (2004). *Deaths: Final data for 2002*. (National Vital Statistics Reports vol. 53, no. 5). Hyattsville, MD: National Center for Health Statistics.

- Kramer, M. S., Platt, R. W., Wen, S. W., Joseph, K. S., Allen, A., Abrahamowicz, M., Blondel, B., Bréart, G., and the Fetal/Infant Health Study Group of the Canadian Perinatal Surveillance System (2001). A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics*, 108, e35.
- Lemons, J. A., Bauer, C. R., Oh, W., Korones, S. B., Papile, L. -A., Stoll, B. J., Verter, J., Temprosa, M., Wright, L. L., Ehrenkranz, R. A., Fanaroff, A. A., Stark, A., Carlo, W., Tyson, J. E., Donovan, E. F., Shankaran, S., & Stevenson DK (2001). Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. *Pediatrics*, 107, e1.
- Ley, D., Marsal, K., Dahlgren, J., & Hellstrom, A. (2004). Abnormal retinal optic nerve morphology in young adults after intrauterine growth restriction. *Pediatric Research*, 56, 139–143.
- MacDorman, M. F., Martin, J. A., Mathews, T. J., Hoyert, D. L., & Ventura, S. J. (2005). Explaining the 2001–02 infant mortality increase: Data from the Linked Birth/Infant Death Data Set (National Vital Statistics Reports vol. 53, no. 12). Hyattsville, MD: National Center for Health Statistics.
- Martin, J. A., Hamilton, B. E., Sutton, P. D., Ventura, S. J., Menacker, F., & Munson, M. L. (2006). *Births: Final data for 2004*. (National Vital Statistics Reports vol. 55, no. 1). Hyattsville, MD: National Center for Health Statistics.
- Martin, J. A., Hamilton, B. E., Sutton, P. D., Ventura, S. J., Menacker, F., & Munson, M. L. (2003). *Births: Final data for 2002.* (National Vital Statistics Reports vol. 52, no. 10). Hyattsville, MD: National Center for Health Statistics.
- Martin, L., Ley, D., Marsal, K., & Hellstrom, A. (2004). Visual function in young adults following intrauterine growth retardation. *Journal of Pediatric Ophthalmology and Strabismus*, 41, 212–218.
- Meadow, W., Lee, G., Lin, K., & Lantos, J. (2004). Changes in mortality for extremely low birth weight infants in the 1990s: Implications for treatment decisions and resource use. *Pediatrics*, 113, 1223–1229.
- Meadow, W., Reimshisel, T., & Lantos, J. (1996). Birth weight-specific mortality for extremely low birth weight infants vanishes by four days of life: Epidemiology and ethics in the neonatal intensive care unit. *Pediatrics*, 97, 636–643.

- Min, S. -J., Luke, B., Min, L., Misiunas, R., Nugent, C., Van de Ven, C., Martin, D., Gonzalez-Quintero, V. H., Eardley, S., Witter, F. R., Mauldin, J. G., & Newman, R. B. (2004). Birth weight references for triplets. *American Journal of Obstetrics and Gynecology*, 191, 809-814.
- O'Connor, A. R., Stephenson, T. J., Johnson, A., Tobin, M. J., Ratib, S., Moseley, M., & Fielder, A. R. (2004). Visual function in low birthweight children. *British Journal of Ophthalmology*, 88, 1149–1153.
- O'Keefe, M. J., O'Callaghan, M., Williams, G. M., Najman, J. M., & Bor, W. (2003). Learning, cognitive, and attention problems in adolescents born small for gestational age. *Pediatrics*, 112, 301–307.
- Racine, A. D., Joyce, T. J., Li, W., & Chiasson, M. A. (1998). Recent declines in New York City infant mortality rates. *Pediatrics*, 101, 682–688.
- Reynolds, M. A., Schieve, L. A., Martin, J. A., Jeng, G., & Macaluso, M. (2003). Trends in multiple births conceived using assisted reproductive technology, United States, 1997–2000. *Pediatrics*, 111, 1159–1162.
- Rodriguez-Soriano, J., Aguirre, M., Oliveros, R., & Vallo, A. (2005). Long-term renal follow-up of extremely low birth weight infants. *Pediatric Nephrology*, 20, 579–584.
- Ross, M. G., Downey, C. A., Bemis-Heys, R., Nguyen, M., Jacques, D. L., & Stanziano, G. (1999). Prediction by maternal risk factors of neonatal intensive care admissions: Evaluation of >59,000 women in national managed care programs. *American Journal of Obstetrics and Gynecology*, 181, 835–842.
- Tudehope, D., Burns, Y. R., Gray, P. H., Mohay, H. A., O'Callaghan, M. J., & Rogers, Y. M. (1995). Changing patterns of survival and outcome at 4 years of children who weighed 500–999 g at birth. *Journal of Paediatric Child Health*, 31, 451–456.
- Wilcox, L. S., Kiely, J. L., Melvin, C. L., & Martin, M. C. (1996). Assisted reproductive technologies: Estimates of their contribution to multiple births and newborn hospital days in the United States. *Fertility and Sterility*, 65, 361–366.
- Wood, N. S., Marlow, N., Costeloe, K., Gibson, A. T., & Wilkinson, A. R. (2000). Neurologic and developmental disability after extremely preterm birth. EPI-Cure Study Group. *New England Journal of Medicine*, 343, 378–384.