



Acta Genet Med Gemellol 43: 25-31 (1994)
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International Congress
40th Anniversary of The Mendel Institute

Mortality and Morbidity among Twins: Recent Observations from the United States

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Abstract. The increasing number of twin (and higher order) births is a matter of national concern for two reasons: First, the differential rates of preterm (<37 weeks) delivery and low birthweight (<2,500g) among twins compared to singletons; and second, the inordinate contribution of these infants to overall infant mortality, morbidity and long-term handicap. Data from all births in the U.S. during 1987 and 1988 was used to calculate distribution frequencies for gestational age at delivery, and birthweight, as well as mortality and handicap rates and the corresponding relative risks of these latter events for twins compared to singletons. A suggestion for improvement in the mortality and handicap rates and reduced costs among survivors is presented. This proposal is based upon data from the singleton and twin literature and the use of the prenatal intervention of adequate maternal nutrition during the pregnancy.

Key words: Twins, Multiples, Mortality, Morbidity, Preterm delivery, Low birthweight, Maternal weight gain, Handicap.

Although twin births number only approximately 2% of all births in the United States, they generally are held to account for 8-10% of all perinatal deaths as well as a disproportionate amount of infant, childhood, and long-term morbidity [2,6,7,15,16,24]. In one frequently cited study (published in 1982 and based on approximately 7 million births), Williams et al [24] calculated that compared to singletons, the likelihood of fetal mortality, perinatal mortality, and neonatal mortality among twins was 3.4, 5.4, and 7.3, respectively. The major reason for this increased risk of mortality derives from a combination of two factors: the higher proportion of pregnancies which deliver preterm (<than 37 weeks) and the higher proportion of newborn twins with birthweights <2,500g.

The distribution of singleton and twin births by length of gestation in the U.S.A. during 1987 is shown in Table 1. Overall, the percent of twins born at less than 37 weeks was 44.5 vs 9.4 for singletons. Data for the birthweight distribution in the same year is presented in Table 2. Overall, the percent of twins with birthweights less than 2,500g was 50.3 compared to 5.9 for singletons.

That these vast differences between twins and singletons is a matter of national concern is better understood by an examination of the comparative rates of low birthweight (LBW) (<2,500g) and very low birthweight (VLBW) (<1,500g) per 1,000 livebirths among twins and singletons. A recent study by Luke and Keith [12] based on U.S. vital statistics for the 1988 birth cohort determined that the rate of LBW for twins was 502/1,000 livebirths compared to 59.9 for singletons and that the rate of VLBW for twins was 98.7/1,000 livebirths compared to 10.3 for singletons.

Whereas the work of Williams et al [24] provided a broad understanding of the differential mortality of twins compared to singletons, this study is somewhat limited in its scope in that it is based on data from a cohort of births from only one state (California). As such, these data do not lend themselves to national extrapolations. In view of the fact that the publications of Luke and her associates [12, 14] are based on

Table 1 - Distribution (%) of singleton and twin livebirths by gestational age, United States, 1987

Gestation Period	Singletons	Twins
<28 weeks	0.7	4.7
28-31 weeks	1.0	6.3
32-35 weeks	4.5	22.3
36 weeks	3.2	11.3
37-39 weeks	40.0	41.4
40 weeks	22.1	7.1
>41 weeks	28.5	6.9

Adapted from unpublished data, National Center for Health Statistics, courtesy of Selma Taffel. Source: Luke B [11].

Table 2 - Distribution (%) of singleton and twin livebirths by birthweight, United States, 1987

Weight (grams)	Singletons	Twins
<1,000	0.5	4.8
1,000-1,499	0.5	5.1
1,500-1,999	1.0	12.5
2,000-2,499	3.8	27.9
2,500-2,999	15.7	31.4
3,000-3,499	37.1	15.2
>3,500	41.3	3.1

Adapted from United States Vital Statistics. Source: Luke B [11].

national samples, they will be cited in later sections of this paper. The use of national samples (based on 1 to 3 years of all births in the U.S.A.) avoids many of the biases that are present in much of the older literature on mortality and morbidity among twins. Among these are small sample size, incomparability of study populations, and the use of 10-20 year samples of hospital data without regard to the fact that medical practice and survivability changed drastically within that time.

The Changing Pattern of Twin Births in the United States

Prior to 1973, the relative number of twin births paralleled that of singletons. After 1973, however, when ovulation inducing agents, hormonal therapies, and IVF technology became available, twin births increased at twice the rate of singletons (65% versus 32%) [14]. As a result, the frequency of twin births increased from 1:55 in 1973 to 1:43 in 1990 [14]. These changes did not occur randomly, however. Whereas the proportion of twin births declined by 30-50% for all women aged 24 or less between 1973 and 1990, it increased by 65-75% for women aged 30-39 during these same years [14].

Two different but interrelated phenomena occurred in the pattern of twins births in the U.S. between 1973 and 1990. First, the absolute change in the number of twin births; and second, selective changes in the ages of the women having them. By 1990, the number of twin births was the highest number ever recorded in the U.S. (93,865), and these births comprised 96.9% of all multiple births [14]. The shift in the age of mothers having twins relates primarily to the older age of women having children [14]. This change was evident in both white and black women. For example, among white women, births of all pluralities decreased or changed only slightly for ages 29 and younger, whereas singleton and twin births increased 20-25% for ages 40-44. Among black women, births of all pluralities decreased or changed only slightly for ages 24 and younger, whereas singleton and twin births increased by 20-68% for ages 30-39 [14].

The overall trend of delayed childbearing was accompanied by a trend to limit family size [14]. Between 1973 and 1990, the proportion of all births to women aged 30 and older nearly doubled from 16.9% to 30.2%, and the proportion of first births in this cohort increased nearly fourfold from 4.6% to 18.1% [14]. At the same time, women aged 30 or older with families of two or less children more than doubled from 21.5% to 51.8%, and the proportion with three or more children declined by nearly half from 78.4% to 47.6% [14].

The causes of these changes are social as well as medical, and a detailed discussion of this topic is beyond the scope of this paper.

Mortality and Morbidity Among Survivors

The differences in the rates of LBW and VLBW among singletons and twins cited above are exceptionally important for survival, morbidity, and long-term handicap. Compared to singleton children, the relative risk of LBW and VLBW for twins is greatly magnified, and among post-natal survivors, the risk for severe handicap is almost doubled for twins [14]. Based on the cohort of U.S. births in 1988, Luke and Keith [12] assessed the

differential contribution of twins compared to singletons on infant mortality rates using race-plurality and birthweight specific rates from National Infant Mortality Surveillance Project [22]. They also calculated the incidence of birthweight specific handicap using published rates from the U.S. Congress study, "Healthy Children: Investing in the Future" [23]. Infant mortality was 56.6/1,000 livebirths among twins compared to only 8.6/1,000 livebirths among singletons [12]. Thus in 1988, the relative risk for mortality among twins was 6.6 times that of singletons. The accompanying handicap rates, along with the relative risks for twins compared to singletons, for the 1988 U.S. birth cohort are shown in Table 3. Data such as these underscore the differential contributions of twins, compared to singletons, to overall mortality and morbidity. They also provide the basis for proposals to reduce mortality and morbidity, and thus future costs.

Table 3 - Handicap per 1,000 postnatal survivors, by plurality and by relative risk associated with plurality, United States birth cohort, 1988

	Severe (RR)	Moderate (RR)	Overall (RR)
Singletons	19.7 (1.0)	70.6 (1.0)	90.4 (1.0)
Twins	34.0 (1.7)	92.3 (1.3)	126.3 (1.4)

Source: Luke and Keith [12].

Strategies for Reducing Twin Mortality and Morbidity

To date, no proven or effective therapy exists to uniformly reduce the risk of preterm delivery and low birthweight among twins. Bed rest is widely discussed in the medical literature, but this intervention remains controversial after decades of investigation, and controlled trials have not shown a beneficial value. Despite this, some of the literature from the late 1960s and mid-1970s, using historical controls, is able to document a beneficial effect from bed rest in terms of increased fetal weight (approximately 4-500g) when mothers are put to rest late in the second trimester. However, these latter studies have been criticized as representing inappropriate uses of limited medical and social resources. Regardless of any cost consideration, the concept of bed rest has never been subject to rigorous international definition or standardization, and it is conceivable that the existing favorable studies could not be duplicated under more rigorous clinical protocols.

By way of contrast, little opposition exists to the concept of reducing paid work and household labors for pregnant women. This idea was first pioneered by Papiernik and his colleagues in a series of papers beginning in the late 1970s and culminating in the late 1980s [5]. The physiological basis for the beneficial effect of changing from the standing to the reclining position has recently been clarified by Schneider and colleagues [18]. Simply stated, these investigations showed that the gravid uterus exerts pressure on the maternal vena cava after prolonged standing. This pressure is of sufficient nature such that contractions, albeit premature, represent an adaptive response to normalize impending cardiac deficiencies. This adaptive response becomes, in effect, an 'erect' form of the supine hypotensive syndrome.

A recent proposal for reducing twin mortality and morbidity relates to the positive effect of adequate maternal weight gain on birthweight [13]. This proposal recognizes the following: first, efforts to increase gestation length in twins have met with limited success to date; and second, in the final analysis, birthweight depends both on the rate of intrauterine growth as well as on the length of gestation. The former may be amenable to intervention, both in singleton [1,3,9,19,20] and twin [4,10,11,17] gestations.

Recommendations for weight gain in singleton gestations, at least in the United States, have varied widely in recent decades. Older recommendations (i.e. 20 lbs.) were not based on rigorous scientific data, but rather on the late 19th century admonitions of German obstetricians, which bordered on semi-starvation [11]. This advice was set forth in times when rickets was prevalent and low birthweight was viewed as a means of helping a fetus pass through a deformed maternal pelvis. The 1990 recommendation of the U.S. Institute of Medicine/National Academy of Sciences [8] for a 25-35 pound gain in singleton pregnancy is somewhat more generous than many of those of the past, but is still considered barely adequate by many authorities.

The 'ideal' maternal weight gain for twins has only been considered recently. Total weight gain of 35-45 pounds has been proposed by two groups [4,17] based on optimal outcome analyses which were retrospectively correlated to maternal weight gain. A further analysis, that of Luke [11], was specific in advocating a 24 pound gain by the 24th week. Luke et al [13] subsequently emphasized that the value of early and adequate maternal weight gain in twin pregnancies was strengthened by the natural tendency of the twin placenta (compared to the singleton placenta) to age and that such early maternal weight gains may positively influence placental growth and development.

In the theoretical model proposed by Luke et al in 1992 [13], implementation of prenatal nutritional programs capable of shifting the distribution of twin birthweights by an increment of 500g was shown to have startling effects on neonatal mortality, newborn length of stay (a valid proxy for morbidity) and long-term handicaps. Specifically, a theoretical redistribution of twin birthweights to make them more comparable to those of singletons would result in 60% fewer twins with birthweights less than 1,500g and 85% fewer deaths among twins in this weight category [13]. In addition, there would be a reduction in twin LOS. For birthweights below 2,500g, LOS would be reduced by 491,000 days (a 60% reduction) and for birthweights below 1,500g, 233,000 days (a 64% reduction). A conservative estimate of the averted NICU costs of such a change is \$419 million (U.S.) (\$1,000/day saved) per year [13].

Perhaps of greater long-term importance, the proposed shift in birthweight distribution in the Luke model would result in a dramatic reduction in the incidence of moderate and severe handicap [13]. Dr. Luke and her co-workers stated: "Among infants with birthweights below 1,000g, an estimated 17% will sustain severe handicap and 31% moderate handicap; for infants with birthweights between 1,000 and 1,500g, 11% will have severe handicap and 16% moderate handicap [21]. The lifetime costs of special services (in 1986 dollars) for a child with severe handicap is estimated to be \$413,000, and \$106,000 for a child with a moderate handicap [23]. The positive shift in twin birthweight distributions would result in a 41% reduction in the number of twin children with handicaps and a 59% reduction in the proportion of all twin children with handicaps. Lifetime costs of special services for moderately and severely handicapped twin children would be reduced by 58.2%, or \$219 million" [23].*

The beneficial effect of a theoretical increase in all twin birthweights was summarized as follows: "Twins represent an extreme model of the two most common obstetrical problems in the United States today: low birthweight and preterm delivery. Higher maternal weight gain to achieve a positive shift in twin birthweight distributions will result in significant reductions in morbidity, mortality, handicap, and their associated costs. With the rising number of twin births, it is time to implement into practice what research has demonstrated – that higher weight gains can improve twin birthweights" [13].*

(*) Dr. Luke's original references are numbered with the appropriate citations in this paper's bibliography.

Acknowledgement: Financial support provided by the Center for The Study of Multiple Birth, Chicago.

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