# Perinatal and Early Childhood Outcomes of Twins Versus Triplets


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The purpose of this prospective cohort study of twins and triplets was to evaluate perinatal and early childhood outcomes through 18 months of age. The study population included 141 twin pregnancies (282 twin children) and 8 triplet pregnancies (24 triplet children) recruited between May, 1996 and June, 2001. Mothers of triplets versus twins were significantly more likely to have infertility treatments, to be overweight or obese before conception, to be admitted antenatally, and to deliver by cesarean section. Length of gestation for triplets was significantly shorter (–2.31 weeks, $p < .0001$), and more likely to be less than 35 weeks (Adjusted Odds Ratio [AOR] 9.38, 95% confidence interval [CI] 3.22–27.29). Average birthweight for triplets was significantly lighter (–495 grams, $p < .0001$), and more likely to be low birthweight (AOR 11.38, 95% CI 3.11–41.61). Triplets were also more likely to be admitted to neonatal intensive care (AOR 7.97, 95% CI 2.13–29.77), to require mechanical ventilation (AOR 5.67, 95% CI 2.05–15.65), to develop respiratory distress syndrome (AOR 12.50, 95% CI 3.89–40.20), or a major morbidity (retinopathy of prematurity, necrotizing enterocolitis, ventilator support, or grade III or IV intraventricular hemorrhage, AOR 5.67, 95% CI 2.05–15.65). Weight, length, and head circumference was significantly smaller at birth for triplets compared to twins, and these differences remained through 18 months of age, along with lower mental developmental scores at the oldest age. Compared to twins, triplets have greater neonatal morbidity, and through 18 months of age lower mental and motor scores, slower postnatal growth and more residual stunting, particularly of length and head circumference.


In 2003, there were 136,328 infants of multifetal pregnancies born in the United States, the highest number ever recorded, including 128,665 twins and 7110 triplets (Martin et al., 2005). Multiple births have risen dramatically in the past two decades, including an 88% increase in twins and a 573% increase in triplets and higher order multiples since 1980. Although one fourth of this rise is due to childbearing among women of older ages, three fourths is due to infertility treatments and assisted reproductive technologies, where the risk of multiple births can be as high as 25 to 50% (Chandra & Stephen, 1998; Martin et al., 2003; Mosher & Pratt, 1990; Stephen & Chandra, 1998; Wilcox & Mosher, 1993). Although they comprise only 3% of all live births, infants of multiple births are disproportionately represented among the low birthweight and premature infant populations. The average birthweight and gestational age for singletons is 3332 g at 38.8 weeks, compared to 2347 g at 35.3 weeks for twins and 1687 g at 32.2 weeks for triplets (Martin et al., 2003). Multiples account for 13% of all preterm births (less than 37 weeks), 15% of all early preterm births (less than 32 weeks), 19% of all NICU days, 21% of all low birthweight infants (LBW, less than 2500 g), and 25% of all very low birthweight infants (VLBW, less than 1500 g; Martin et al., 2005; Martin et al., 1997; Taffel, 1992; Ventura et al., 1997). Because of these factors, children of multiple births have a higher risk of dying before their first birthday, and the survivors have a greater risk of mental and physical disabilities. It is estimated that twin pregnancies produce a child with cerebral palsy 12 times more often than do singleton pregnancies (Grether et al., 1993) and that one fifth of all triplet pregnancies and one half of all quadruplet pregnancies result in at least one child with a major handicap (Yokoyama et al., 1995). First trimester multifetal pregnancy reduction, the process of eliminating some of the embryos, has emerged as a method to improve the survival rates for the remaining fetuses and to decrease maternal morbidity. Reducing from triplets to twins, though, remains controversial (Bollen et al., 1993; Boulot et al., 1993; Haning et al., 1996; Lipitz et al., 1994; Sebire et al., 1997). With contemporary perinatal care, maternal and neonatal outcomes may


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be comparable for twins and triplets (Garite et al., 2004), but there is little longitudinal evidence beyond delivery. For this reason, we undertook this analysis, to evaluate perinatal and early childhood outcomes in twins versus triplets.

## Material and Methods

### Study Population

Study participants were recruited through the outpatient obstetrical department of the University of Michigan Health System from births occurring between May, 1996 and June, 2001. All women who gave birth to live-born twins or triplets, as identified from the delivery room log, received a letter from the Principal Investigator (BL) and Project Director (RM) inviting them to join the study. A follow-up telephone call to each woman from the Project Director provided an opportunity to answer any questions about the study. Each woman who agreed to join the study was then sent a consent form to sign. Several weeks before each of the evaluations (at 8 and 18 months, corrected for prematurity) the family was contacted to set up appointments. This study was approved by the Institutional Review Board of the University of Michigan.

### Medical Record Review

The abstracted or calculated data obtained from the medical records of mothers and infants participating in the study included: (1) Mother's record: age, race, Hispanic ethnicity, parity, smoking habits, infertility treatments, fetal reduction, medical insurance, height, pregravid weight, chorionicity, preterm premature rupture of membranes, preeclampsia. Pregravid body mass index (BMI) was calculated from height and pregravid weight as (weight/ht$^2$) and categorized as underweight (BMI less than 19.8), normal weight (BMI 19.8–26.0), overweight (BMI 26.1–29.0), or obese (BMI greater than 29.0); (2) Infants' records: plurality, birth order, gender, birthweight, birth length, head circumference, gestational age estimate, and medical interventions and diagnoses. Major morbidity was defined as retinopathy of prematurity, necrotising enterocolitis, ventilator support, or grade III or IV intraventricular hemorrhage. This summary measure has been used in other studies, and it has correlated well with length of newborn stay and costs (Luke et al., 2005). Each of these diagnoses have been associated with long-term morbidity (Hintz et al., 2005; Oshiki et al., 2005; Quinn et al., 2004; Salhab et al., 2004; Sherlock et al., 2005).

### Growth Assessment

Each study visit growth included assessments of weight, recumbent length, and head circumference. Weight of children was measured on an electronic, leveled pan scale (Seca Delta Model 707, Hamburg, Germany) calibrated to zero. If a diaper was worn, the diaper's weight was subtracted from the observed weight of the infant. Recumbent length was measured using an infantometer. Length was recorded in centimeters as the distance between the headboard and the footboard, with the child's head against the headboard, legs straightened, and toes pointing upward. For gestational-corrected age and gender growth parameters (weight, head circumference, and length) *z* scores were based on the revised (2000) NCHS/CDC growth charts.

### Developmental and Neurological Assessments

The developmental progress of each infant was assessed at each visit via the administration of the Bayley Scales of Infant Development–II (Bayley, 1993). This is a widely used and highly regarded measure of development in the age groups of interest, with well-developed norms and documented validity and reliability (Davoli, 1996). A comprehensive neuromotor examination was performed at each evaluation by a physical therapist (EA) who has extensive experience with premature and low birthweight infant assessments. The 8 and 18 month examinations follow the format suggested by Ellison (1998), which includes complete physical inspection and assessment of tone and posture using the Infant Neurological International Battery (INFANIB) scoring system (Ellison et al., 1985). The INFANIB has been used in the follow-up of preterm infants (Bozynski et al., 1993) and has been found to have predictive validity with regard to diagnosis of cerebral palsy (Stavrakas et al., 1991).

### Power Analysis

We hypothesized that with a sample size of 282 twins and 24 triplets at birth, 196 twins and 15 triplets at 8 months, and 160 twins and 12 triplets at 18 months, assuming a significance level of .05, two-sided tests, we would have 84% power to detect a significant difference in major morbidity during the neonatal period (25% for twins vs. 54% for triplets), and more than 70% power to detect a significant difference in growth (% of *z* scores less than –1) at 8 months (10% for twins vs. 33% for triplets), and 18 months (6% for twins vs. 33% for triplets).

### Statistical Analysis

Descriptive statistics, which were generated to characterize the study population, are given in Table 1 for mothers and Table 2 for infants. Differences between continuous variables were compared with Student *t* tests, and differences in categorical variables were compared by $\chi^2$ tests or the Fischer exact test when the cell size was less than 5. All tests were two-sided, with a significance level of $p \leq .05$. Multiple regression models were used to estimate the effect of plurality (triplet status) on birthweight, length of gestation, *z* score of weight, length, and head circumference at 8 and 18 months of age, and mental and motor development at 8 and 18 months of age, adjusting for potentially confounding factors. Multiple logistic regression models were used to estimate odds ratios of neonatal interventions and diagnoses by triplet status, adjusting for potentially confounding factors.



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**Table 1**

Description of the Study Population: Mothers*

| | Twins | Triplets | *p* value |
|---|---|---|---|
| (*N*, mothers) | (141) | (8) | |
| Maternal age (years) | 31.3 (5.5) | 31.6 (4.8) | .81 |
| > 35 years (%) | 20% | 12.5% | .59 |
| Race and ethnicity (%) | | | |
| White, non-Hispanic | 90% | 100% | |
| Black, non-Hispanic | 5% | 0% | .62 |
| Other | 5% | 0% | |
| Parity | 0.64 (0.9) | 0.63 (0.5) | .91 |
| Primiparas (%) | 55% | 37.5% | .11 |
| Smokers (%) | 7% | 0% | .26 |
| Infertility treatments (%) | 48% | 100% | < .0001 |
| Fetal reduction (%) | 4% | 0% | .30 |
| Insurance (%) | | | |
| Private or HMO | 94% | 88% | .50 |
| Medicaid | 6% | 12% | |
| Body mass index (BMI) | 24.9 (5.9) | 25.3 (7.2) | .76 |
| Underweight | 12% | 12% | |
| Normal weight | 62% | 0% | < .0001 |
| Overweight | 7% | 50% | |
| Obese | 19% | 38% | |
| Placental membranes | | | |
| Di- or trichorionic | 80% | 75% | |
| Monochorionic | 11% | 13% | .82 |
| Unknown | 9% | 12% | |
| Males per sibship (%) | | | |
| None | 26% | 25% | |
| One | 40% | 38% | < .0001 |
| Two | 34% | 25% | |
| Three | — | 12% | |
| Preterm PROM (%) | 13% | 25% | .10 |
| Preeclampsia (%) | 13% | 25% | .10 |

Note: *Data presented as means (standard deviations) or percentages.

## Results

The study population included 141 twin pregnancies and 8 triplet pregnancies. Mothers of triplets were more likely to have infertility treatments and to be overweight or obese prior to conception. They were also more likely to require antenatal admissions, and to be delivered by cesarean section. Triplet newborns were more likely to be admitted to the neonatal intensive care unit, receive supplemental oxygen, antibiotics, and intravenous fluids, and to require ventilator support. Triplets were also more likely to develop respiratory distress syndrome, to be low birthweight and born before 35 weeks gestation, and to have a major morbidity. The triplets were born 2.31 weeks earlier and 495 grams lighter than the twins. There were no neonatal or infant deaths among twins or triplets.

The growth of twins and triplets through 18 months of age are shown in Table 3. The effect of plurality (triplet status) on *z* score of weight, length, and head circumference at 8 and 18 months is shown in Table 4. Triplets had significantly shorter lengths, smaller head circumferences, and lighter weights at birth. Generally, they remained smaller in each of these growth parameters through 18 months of age, with nearly twice as many *z* scores less than –1 compared to twins, and significantly lower *z* scores of length and head circumference at the oldest ages. The mental and motor development of twins and triplets through 18 months of age is shown in Table 5. The effect of plurality (triplet status) on mental and motor development is shown in Table 6. Generally, triplets scored lower on these developmental tests, with significant differences particularly in mental development at 18 months of age, although none of the twins or triplets was diagnosed with cerebral palsy.

**Table 2**
Description of the Study Population: Infants*

| | Twins | Triplets | *p* value | AOR‡ | 95% CI | *p* value |
|---|---|---|---|---|---|---|
| (*N*, infants) | (282) | (24) | | | | |
| Neonatal interventions (%) | | | | | | |
| NICU admit | 52% | 100% | < .0001 | 7.97 | 2.13–29.77 | .002 |
| Supplemental oxygen | 35% | 79% | < .0001 | 9.47 | 2.99–29.95 | < .0001 |
| Mechanical ventilation | 23% | 54% | .001 | 5.67 | 2.05–15.65 | .001 |
| Intravenous fluids | 42% | 67% | .02 | 3.52 | 1.27–9.80 | .016 |
| Phototherapy | 29% | 8% | .03 | 0.36 | 0.08–1.69 | .196 |
| Neonatal diagnoses (%) | | | | | | |
| Very low birthweight (< 1500 g) | 9% | 13% | .598 | 3.03 | 0.66–13.88 | .154 |
| Low birthweight (< 2500 g) | 47% | 88% | < .0001 | 11.38 | 3.11–41.61 | < .0001 |
| Gestation < 32 weeks | 12% | 13% | .970 | 1.53 | 0.31–7.62 | .603 |
| Gestation < 35 weeks | 33% | 75% | < .0001 | 9.38 | 3.22–27.29 | < .0001 |
| RDS | 28% | 71% | < .0001 | 12.50 | 3.89–40.20 | < .0001 |
| Anemia | 6% | 8% | .711 | 2.48 | 0.43–14.35 | .312 |
| Hyperbilirubinemia | 27% | 33% | .501 | 2.22 | 0.82–6.03 | .116 |
| ABCs** | 13% | 4% | .189 | 0.54 | 0.06–4.94 | .592 |
| Retinopathy of prematurity | 2% | 0% | .435 | — | — — | — |
| IVH (grade III or IV) | 4% | 0% | .303 | — | — — | — |
| Necrotising enterocolitis | 1% | 0% | .612 | — | — — | — |
| Major morbidity*** | 25% | 54% | .002 | 5.67 | 2.05–15.65 | .001 |
| | **Twins** | **Triplets** | ***p* value** | **Regression coefficient‡** | **Standard error** | ***p* value** |
| Gestation (weeks) | 35.4 (2.6) | 33.4 (1.4) | < .0001 | –2.31 weeks | 0.511 | < .0001 |
| Birthweight (grams) | 2377 (559) | 1958 (363) | .0001 | –495 grams | 113 | < .0001 |

Note: *Data presented as means (standard deviation) or percentages.
**ABCs are apnea, bradycardia, or cyanosis.
‡Models adjusted for infertility treatment, pregravid body mass index, total prenatal visits, and males per pair.
***Major morbidity defined as retinopathy of prematurity, necrotising enterocolitis, ventilator support, or intraventricular hemorrhage (grade III or IV).

## Comment

This study confirms the overall higher perinatal and neonatal morbidity, and reduced early childhood growth and development experienced by triplets compared to twins. The triplets in this study cohort averaged higher birthweights and longer gestations compared to national averages (1958 g at 33.4 weeks vs. 1678 g at 32.0 weeks, Martin et al., 2003), most likely because all of the mothers of triplets participated in a specialized prenatal program which included individualized diet therapy (Luke et al., 2003). Despite this earlier advantage, the triplet children still evidenced substantial residual stunting in length and head circumferences and lower mental development by 18 months of age. Limitations of this study include the small sample size, substantial attrition rate during the follow-up (predominately of healthy multiples), and lack of ethnic and racial diversity in the study population.

Studies have shown that infants with lower birthweights are more likely to remain shorter and lighter throughout childhood, especially those children who experienced intrauterine growth restriction rather than just shortened gestation (Binkin et al., 1988). Extremely low birthweight children (500–999 g) demonstrate the most severe continued growth retardation after birth, with slower growth in height and weight by eight years of age (Kitchen et al., 1992). Other studies have demonstrated that children who experienced intrauterine growth restriction before birth not only remain shorter and lighter than normal birthweight children, but they are also weaker in physical performance by adolescence (Martorell et al., 1998). This may represent a long-term deficit in muscle development. Because of their higher rates of low birthweight and prematurity, children of multiple gestations are at greater risk for lower physical and mental indices during childhood compared to singletons (Brandes et al., 1992; Luke et al., 1995). In a cross-sectional study of twin children ages 2 to 12, boys with severe intrauterine growth retardation at birth (birthweight *z* scores less than –2.0) had a significant increased risk of moderate stunting (*z* score between –2.0 and –1.2) in their current weight (odds ratio [OR] 2.67, 95% confidence interval [CI] 1.55–4.58), while girls with severe intrauterine growth retardation at birth were at significant increased risk of moderate stunting in their current height (OR



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**Table 3**

Growth of Twins and Triplets Through 18 Months of Age*

| | Twins | Triplets | *p* value |
|---|---|---|---|
| At birth (*N*) | (282) | (24) | |
| Birthweight (g) | 2377 (559) | 1958 (363) | .0001 |
| Length (cm) | 45.6 (3.9) | 43.2 (3.1) | .0002 |
| Head circumference (cm) | 32.3 (2.3) | 30.6 (1.5) | .0001 |
| *z* score weight (SDU) | –0.64 (0.85) | –0.49 (0.63) | .39 |
| *z* scores weight < –1 (%) | 31.6% | 25.0% | .51 |
| At 8 months** (*N*) | (196) | (15) | |
| Weight (kg) | 8.8 (1.3) | 8.1 (1.0) | .06 |
| Length (cm) | 71.3 (3.7) | 69.5 (5.3) | .11 |
| Head circumference (cm) | 45.4 (1.6) | 45.3 (2.0) | .91 |
| *z* scores (SDU) | | | |
| Weight | –0.11 (1.19) | –0.34 (0.92) | .46 |
| Length | 0.34 (1.16) | –0.41 (1.30) | .03 |
| Head circumference | 45.4 (1.6) | 45.3 (2.0) | .91 |
| Change in *z* score of weight between birth and 8 months | 0.54 (1.23) | 0.25 (0.67) | .14 |
| *z* scores < –1 (%) | | | |
| Weight | 21.7% | 33.3% | .30 |
| Length | 9.8% | 33.3% | .01 |
| Head circumference | 4.1% | 6.7% | .64 |
| At 18 months** (*N*) | (160) | (12) | |
| Weight (kg) | 11.5 (3.2) | 11.7 (1.3) | .63 |
| Length (cm) | 82.3 (3.8) | 80.4 (5.2) | .03 |
| Head circumference (cm) | 48.4 (1.7) | 41.8 (1.8) | .0001 |
| *z* scores (SDU) | | | |
| Weight | –0.27 (1.49) | –0.10 (0.99) | .73 |
| Length | 0.45 (1.07) | –0.74 (1.74) | .08 |
| Head circumference | 0.86 (1.12) | –4.36 (0.80) | .0001 |
| Change in *z* score of weight between birth and 18 months | 0.40 (1.323) | 0.38 (0.78) | .96 |
| *z* scores < –1 (%) | | | |
| Weight | 30.5% | 33.3% | .86 |
| Length | 6.3% | 33.3% | .004 |
| Head circumference | 4.8% | 100.0% | .001 |
| Birth to 18 months | | | |
| Total children, *z* scores < –1 | 27.3% | 45.8% | .05 |

Note: *Data presented as means (standard deviation) or percentages.

**Corrected for prematurity.

4.09, 95% CI 1.49–10.99; Luke et al., 1995). The fetal development of well-grown twins and triplets, though, is similar to that of singletons, and as this study has shown, may have long-lasting effects (Monset-Couchard et al., 2004). We have previously shown that twins (Min et al., 2000) and triplets (Min et al., 2004) growing at the plurality-specific 90th percentile are comparable to singletons at the 50th percentile at birth.

After two decades of steep increases, the rates of triplet and higher-order births in the United States have begun to abate, with the 2003 rate being 3% lower than the 1998 peak (Martin et al., 2005). In 1999, the American College of Obstetricians and Gynecologists and the American Society of Reproductive Medicine issued recommendations intended to prevent triplet and higher-order pregnancies (American College of Obstetricians and Gynecologists, 1999; American Society for Reproductive Medicine, 1999). Recent refinements in assisted reproductive technologies, in addition to these national recommendations, may be

**Table 4**

Effect of Plurality (Triplet Status) on Subsequent Early Childhood Growth*

| | Regression coefficient | Standard error | Significance |
|---|---|---|---|
| At 8 months | | | |
| *z* score of weight | –0.18 | 0.32 | .58 |
| *z* score of length | –0.62 | 0.35 | .08 |
| *z* score of head circumference | 0.20 | 0.29 | .49 |
| At 18 months | | | |
| *z* score of weight | 0.20 | 0.50 | .69 |
| *z* score of length | –1.24 | 0.38 | .002 |
| *z* score of head circumference | –5.22 | 0.66 | .001 |

Note: *Models adjusted for maternal age, black ethnicity, monochorionicity, and Medicaid status.

**Table 6**

Effect of Plurality (Triplet Status) on Mental and Motor Development*

| | Regression coefficient | Standard error | *p* value |
|---|---|---|---|
| Bayley Mental Score | | | |
| 8 months | –1.31 | 2.23 | .56 |
| 18 months | –11.86 | 3.31 | < .0001 |
| Bayley Motor Score | | | |
| 8 months | 0.82 | 3.72 | .83 |
| 18 months | –3.13 | 2.54 | .22 |
| INFANIB Score | | | |
| 8 months | 0.81 | 2.30 | .73 |
| 18 months | 2.33 | 1.48 | .12 |

Note: *Models adjusted for maternal age, black ethnicity, monochorionicity, and Medicaid status.

underlying the current changes in the incidence of higher-order multiples (Gardner et al., 1998; Templeton & Morris, 1998; Toner, 2002). Triplet pregnancies should be considered high-risk, not only during the perinatal period, but during early childhood as well, with both short- and longer-term outcomes substantially worse than for twins.

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**Table 5**

Mental and Motor Development of Twins Versus Triplets*

| | Twins | Triplets | *p* value |
|---|---|---|---|
| At 8 months (*N*) | (196) | (15) | |
| Bayley Mental Score** | 102.8 (8.5) | 100.3 (3.3) | .26 |
| % delayed | 1% | 0% | .70 |
| Bayley Motor Score** | 96.3 (13.6) | 96.5 (15.5) | .96 |
| % delayed | 20% | 27% | .57 |
| INFANIB Score** | 83.6 (8.7) | 83.4 (8.4) | .93 |
| % delayed | 29% | 7% | .07 |
| At 18 months (*N*) | (160) | (12) | |
| Bayley Mental Score | 102.0 (11.1) | 89.0 (8.2) | .0001 |
| % delayed | 6% | 17% | .15 |
| Bayley Motor Score | 102.8 (8.7) | 98.3 (6.3) | .08 |
| % delayed | 1% | 0% | .79 |
| INFANIB Score | 95.1 (5.1) | 97.7 (3.3) | .08 |
| % delayed | 1% | 0% | .77 |

Note: *Data presented as means (standard deviation) or percentages.
**Bayley mental or motor scores of mild or significant delay, and INFANIB score transient or abnormal.

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