Mortality and Morbidity of VLBW Infants With Trisomy 13 or Trisomy 18

WHAT’S KNOWN ON THIS SUBJECT: Infants with trisomy 13 (T13) or trisomy 18 (T18) are known to have poor survival. Little is known about how very low birth weight (VLBW) impacts survival and morbidities among infants with T13 or T18.

WHAT THIS STUDY ADDS: We examined the risks of mortality and neonatal morbidities for VLBW infants with T13 or T18 compared with VLBW infants with trisomy 21 and VLBW infants without birth defects in a 16-year cohort from the Neonatal Research Network.

abstract

OBJECTIVE: Little is known about how very low birth weight (VLBW) affects survival and morbidities among infants with trisomy 13 (T13) or trisomy 18 (T18). We examined the care plans for VLBW infants with T13 or T18 and compared their risks of mortality and neonatal morbidities with VLBW infants with trisomy 21 and VLBW infants without birth defects.

METHODS: Infants with birth weight 401 to 1500 g born or cared for at a participating center of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network during the period 1994–2009 were studied. Poisson regression models were used to examine risk of death and neonatal morbidities among infants with T13 or T18.

RESULTS: Of 52,262 VLBW infants, 38 (0.07%) had T13 and 128 (0.24%) had T18. Intensity of care in the delivery room varied depending on whether the trisomy was diagnosed before or after birth. The plan for subsequent care for the majority of the infants was to withdraw care or to provide comfort care. Eleven percent of infants with T13 and 9% of infants with T18 survived to hospital discharge. Survivors with T13 or T18 had significantly increased risk of patent ductus arteriosus and respiratory distress syndrome compared with infants without birth defects. No infant with T13 or T18 developed necrotizing enterocolitis.

CONCLUSIONS: In this cohort of liveborn VLBW infants with T13 or T18, the timing of trisomy diagnosis affected the plan for care, survival was poor, and death usually occurred early. Pediatrics 2014;133:226–235.
Trisomy 18 (T18) and trisomy 13 (T13) are the second and third most commonly diagnosed autosomal trisomies among liveborn infants after trisomy 21 (T21). The previous literature on infants with T13 or T18 has addressed mainly the operative interventions, management, and survival of these infants. Few studies have examined the dual risks of very low birth weight (VLBW) and T13 or T18. Boghossian et al published a descriptive report from the Vermont Oxford Network examining neonatal interventions, neonatal morbidities, and in-hospital mortality among VLBW infants with major chromosomal anomalies including T13 and T18. We undertook the current study to expand on these findings.

Data from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network (NRN) were used to (1) examine timing of trisomy diagnosis and plan for care among VLBW infants with T13 or T18 and (2) compare neonatal characteristics, delivery room interventions, and risk of in-hospital morbidities and mortality among VLBW infants with T13 or T18 to VLBW infants with T21 and VLBW infants with no major birth defects.

METHODS

Infants born January 1, 1994 through December 31, 2009 and cared for at NRN hospitals were studied. The NRN is a network of NICUs at academic centers in the United States and a data coordinating center, which was formed to conduct research to improve care for high-risk infants. From 1994 through 2007, all VLBW infants (401–1500 g) born at or admitted to an NRN center within 14 days of birth were included in a registry maintained by the NRN. Eligibility criteria changed in January 2008 to include inborn infants with birth weight (BW) 401 to 1000 g or gestational age (GA) 22 to 28 weeks or infants enrolled in another NRN study. Infants enrolled based on GA or other criteria with BW outside 401 to 1500 g were excluded from this report to maintain consistency over the study period. Trained research nurses entered maternal demographic, pregnancy, and delivery information, and infant data collected from birth to hospital discharge, death, or 120 days. The institutional review board at each center approved the registry and the additional medical record review undertaken in this study. Neonatal information included BW, GA, gender, race, mode of delivery, delivery room interventions, final status, and cause of death. Small for GA (SGA) was defined as BW <10th percentile. Neonatal morbidities diagnosed during the hospital stay were recorded for infants surviving >12 hours including respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), Bell’s Stage ≥IIA necrotizing enterocolitis, severe intraventricular hemorrhage (grade 3 or 4), periventricular leukomalacia, retinopathy of prematurity defined for infants still hospitalized at 28 days, bronchopulmonary dysplasia (BPD) defined as need for supplemental oxygen at 36 weeks’ postmenstrual age (PMA), and late-onset sepsis defined by positive blood culture after 72 hours of age and intent to treat with antibiotics for ≥5 days. Weight, length, and head circumference were measured at 36 ± 1 weeks PMA.

Collection of major birth defects changed during the study period. From 1994 through 1997, information was recorded in text fields in response to questions about pulmonary, cardiac, neurologic, and gastrointestinal (GI) malformations and a general question about syndromes and major malformations. Beginning in 1998, major birth defects were entered using codes from a predefined list in the study manual of operations. T13, T18, and T21 had predefined codes. Major defects not listed were described in text fields. Text fields and birth defect codes were reviewed to identify infants with T13, T18, or T21. Infants with T13, T18, or T21 who had co-occurring anomalies were included only in the appropriate trisomy group.

Medical records of infants with T13 or T18 were retrospectively reviewed, if available, to look for documentation of when the diagnosis of trisomy was first suspected and when it was confirmed by genetic testing. Plans for initial care in the delivery room and for subsequent care were recorded if noted in the record. For infants who survived to discharge, plans based on poor prognosis, such as hospice care, were also recorded.

Infants were classified into the following groups: T13, T18, T21, other major birth defect, and no major birth defect. All infants were included in the denominator for prevalence estimates and in models described subsequently. Analyses focused on comparisons between infants with T13 and T18, and between each of these groups and infants with T21 or with no major birth defect. Patients with suspected but not proven T13 (2 patients) or T18 (11 patients), multiple chromosomal abnormalities (1 patient with both T13 and 4p deletion), chromosome 18 translocation (2 patients), and a defect recorded as “triploidy trisomy 18” (1 patient) were excluded from the T13 and T18 groups and instead included with other major birth defects. Patients with known mosaic or partial T13 or T18 (described in Supplemental Table 6) were included in prevalence estimates but excluded from the trisomy groups for the primary analysis. Statistical significance for unadjusted comparisons was determined using the Fisher’s exact or χ² test for categorical variables or the t test for continuous variables. Kaplan-Meier survival curves were used to estimate time to death distributions with statistical significance.
significance between groups determined by the log-rank test. Poisson regression models with robust variance estimators\textsuperscript{11} were first used to assess factors associated with an increased risk for the outcome T13 or the outcome T18. A second set of models was used to assess risk of death and morbidity outcomes for infants with T13 or T18 compared with infants with T21 and infants with no major birth defect. Models comparing death and morbidity outcomes included a birth defect group indicator (T13, T18, T21, other major birth defect, no major birth defect) to allow for pairwise contrasts. Covariates included are noted in table footnotes. Adjusted relative risks (RR), 95% confidence intervals (CI), and Score or Wald $\chi^2$ tests are reported on the basis of parameter and variance estimates from these models. In this exploratory study, $P$ values were not adjusted for multiple comparisons and are presented largely for descriptive purposes.

**RESULTS**

**Prevalence of T13 and T18**

From 1994 through 2009, 52,262 VLBW infants were cared for at 22 NRN centers. A major birth defect was reported for 5%. Overall, 38 (0.07%) VLBW infants were identified with T13, of whom 12 had full T13 and 2 had mosaic T13; the other 24 were presumed to have full T13. T18 was reported for 128 infants (0.24%), of whom 58 had full T18, 2 had mosaic T18, and 1 had partial T18; the other 67 were presumed to have full T18 (Supplemental Table 7). The final analysis included 36 infants with T13 and 125 infants with T18 (Table 1).

**Risks of T13 and T18**

Risk of T13 was reduced for infants from multiple births compared with singletons. Risk of T18 increased significantly with maternal age and decreased for infants born to African American compared with white mothers. Males and infants from multiple births were at reduced risk for T18 compared with females and singletons (Supplemental Table 8).

**Timing of Diagnosis and Plan for Care**

Medical records were reviewed for 24 infants (67%) with T13 and 90 infants (72%) with T18. Where timing was known, the diagnosis was suspected prenatally for 14/21 (67%) infants with T13 and for 36/82 (44%) infants with T18 (Table 2). When the diagnosis was confirmed before birth, the plan was to withhold intensive care in the delivery room for a greater percent of infants with T13 than with T18 (89% vs 39%, $P = .005$) (Table 2). Provision of care in the delivery room varied according to whether the trisomy was confirmed prenatally or postnaturally. Full intensive care was received in the delivery room for 1 infant with T13 (11%) when the diagnosis was confirmed prenatally, whereas 9 (90%) of the 10 infants with T13 confirmed after birth received full intensive care, $P = .001$. Similarly, full intensive care was planned for only 4% of infants with T18 confirmed prenatally, but 95% of those confirmed after birth received full intensive care in the delivery room, $P < .001$. For infants with T13 or T18, the plan for subsequent care in the hospital also varied by timing of trisomy confirmation. Full intensive care (20%) or limited care (30%) was planned...

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**Table 1: Characteristics of VLBW Infants With T13 or T18 Compared With Other VLBW Infants in the NRN Born 1994–2009**

<table>
<thead>
<tr>
<th>Characteristic, N (%)</th>
<th>T13, n = 36</th>
<th>T18, n = 125</th>
<th>T21, n = 139</th>
<th>No Birth Defect, n = 49,600</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (y), mean (SD)</td>
<td>28 (7.7)</td>
<td>30 (12.3)</td>
<td>31 (7.9)</td>
<td>27 (6.7)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>15 (42)</td>
<td>30 (24)</td>
<td>34 (24)</td>
<td>19 (97)</td>
</tr>
<tr>
<td>25–29</td>
<td>1 (3)</td>
<td>3 (24)</td>
<td>4 (24)</td>
<td>24 (13)</td>
</tr>
<tr>
<td>30–34</td>
<td>3 (8)</td>
<td>21 (18)</td>
<td>32 (23)</td>
<td>10 (7)</td>
</tr>
<tr>
<td>35–39</td>
<td>10 (28)</td>
<td>25 (20)</td>
<td>29 (21)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>40+</td>
<td>2 (6)</td>
<td>28 (22)</td>
<td>20 (14)</td>
<td>16 (3)</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>1 (3)</td>
<td>15 (12)</td>
<td>22 (16)</td>
<td>12 (5)</td>
</tr>
<tr>
<td>BW (g), mean (SD)</td>
<td>1105 (269)</td>
<td>1101 (291)</td>
<td>1032 (296)</td>
<td>984 (53)</td>
</tr>
<tr>
<td>401–750</td>
<td>26 (72)</td>
<td>99 (79)</td>
<td>83 (60)</td>
<td>21 (6)</td>
</tr>
<tr>
<td>751–1000</td>
<td>12 (33)</td>
<td>48 (38)</td>
<td>38 (27)</td>
<td>12 (6)</td>
</tr>
<tr>
<td>1001–1250</td>
<td>10 (28)</td>
<td>34 (27)</td>
<td>44 (32)</td>
<td>12 (6)</td>
</tr>
<tr>
<td>1251–1500</td>
<td>12 (33)</td>
<td>48 (38)</td>
<td>38 (27)</td>
<td>12 (6)</td>
</tr>
<tr>
<td>GA (wk), mean (SD)</td>
<td>30 (5.0)</td>
<td>32 (5.8)</td>
<td>39 (5.6)</td>
<td>28 (5.0)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>2 (6)</td>
<td>4 (3)</td>
<td>22 (16)</td>
<td>8593 (18)</td>
</tr>
<tr>
<td>25–28</td>
<td>8 (22)</td>
<td>22 (18)</td>
<td>34 (24)</td>
<td>21 (8)</td>
</tr>
<tr>
<td>29+</td>
<td>26 (72)</td>
<td>99 (79)</td>
<td>83 (60)</td>
<td>18 (6)</td>
</tr>
<tr>
<td>SGA</td>
<td>19 (53)</td>
<td>98 (79)</td>
<td>55 (40)</td>
<td>9558 (19)</td>
</tr>
<tr>
<td>Male gender</td>
<td>17 (47)</td>
<td>47 (38)</td>
<td>61 (44)</td>
<td>2512 (51)</td>
</tr>
<tr>
<td>Maternal race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>13 (37)</td>
<td>27 (22)</td>
<td>38 (28)</td>
<td>20 (7)</td>
</tr>
<tr>
<td>White</td>
<td>21 (60)</td>
<td>86 (70)</td>
<td>96 (70)</td>
<td>26 (8)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3)</td>
<td>9 (7)</td>
<td>4 (3)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Maternal Hispanic ethnicity</td>
<td>5 (15)</td>
<td>40 (33)</td>
<td>27 (20)</td>
<td>7942 (17)</td>
</tr>
<tr>
<td>Appgar at 1 min $\leq 3$</td>
<td>17 (50)</td>
<td>83 (66)</td>
<td>41 (30)</td>
<td>15588 (53)</td>
</tr>
<tr>
<td>Appgar at 5 min $\leq 3$</td>
<td>14 (41)</td>
<td>44 (35)</td>
<td>18 (12)</td>
<td>5705 (12)</td>
</tr>
</tbody>
</table>

Information was missing in the groups shown for maternal age: 31 infants; multiple birth: 2; GA: 19; SGA: 33; male gender: 3; race: 449; Hispanic ethnicity: 1665; Appgar at 1 min: 886; Appgar at 5 min: 679. The numbers in the table do not include 2582 infants with other birth defects but no trisomy.* $P < .05$, **$P < .01$, ***$P < .001$ by $t$ test (means for maternal age, BW, GA), Mantel-Haenszel $x^2$ test (categorical maternal age, BW, GA), or the general association $x^2$ test. Pairwise comparisons were performed between infants with T13 versus T18, T21, and no birth defects, and between infants with T18 versus T21 and no birth defects. For each significant result, a “v13” or “v18” indicates the comparison group.
for infants whose diagnosis was confirmed after birth, but neither was planned for infants whose trisomy was confirmed before birth, \( P = .03 \). Full intensive care was planned for 11% of infants with T18 confirmed after birth but for no infants whose T18 was confirmed before birth, \( P = .26 \).

**Delivery, Interventions, and Ventilator Support**

The percent of infants delivered by cesarean delivery did not vary significantly between groups (Table 3). Generally, the birth resuscitation methods examined were used less frequently for infants with T13 compared with infants with T18. Chest compression was used more frequently for infants with T18 than for infants with T21 and infants with no birth defects. A smaller proportion of infants with T13 received ventilator support and surfactant therapy than did infants with T21 and infants with no birth defect. Among survivors past 12 hours, the percentage of infants with T13 and with T18 who underwent surgery was smaller than among those with T21.

**Co-occurring Birth Defects and Surgeries**

A co-occurring major birth defect was reported for 24 (67%) of the 36 infants with T13 and 93 (74%) of the 125 infants with T18. Congenital heart defects were most frequent, reported for 13 (36%) with T13 and 78 (62%) with T18 (Supplemental Tables 9 and 10).

Surgical procedures were reported for 3 infants with T13 and 5 infants with T18. All survived \( \geq 3 \) days. One infant with T13, atrial septal defect, and intestinal malrotation underwent Ladd’s procedure before dying on day 5 of life. Two infants with T13 and GI anomalies had GI procedures: small and large bowel diversion and subsequent stoma takedown and reanastomosis for 1 who survived to discharge on day 83; tracheoesophageal fistula repair for the other infant who also had a tracheostomy, release of tongue–lip adhesion, and central line placement and survived to discharge on day 110. All 5 infants with T18 who underwent surgery died before hospital discharge. PDA surgery was reported for 2 of the 5 infants, of whom 1 had interrupted aortic arch and a ventricular septal defect (VSD) and died on day 49, and the other had a VSD and died on day 27. Another infant with T18, tetralogy of Fallot, pulmonary atresia, and cleft palate had a tracheostomy before dying on day 10. The fourth infant had proximal esophageal atresia, underwent esophageal atresia repair and gastrostomy, and died on day 49. The fifth infant had meningomyelocele, microcephaly, and VSD and underwent myelomeningocele repair but died on day 4.

**Infant Characteristics**

Infants with T18 were more likely to be SGA than were infants in the other groups (Table 1). A greater percentage of infants with T18 were female and had white mothers compared with infants without birth defects. The proportion of infants with T18 with Hispanic mothers was greater than among infants with T13, T21, or no birth defect.
Mortality
Approximately 90% of VLBW infants with T13 (89%) or T18 (91%) died during the initial hospitalization (Table 4). Differences in timing of death are reflected in the survival curves for each group (Fig 1). Median age at death was 1 day (interquartile range 1–5) for infants with T13 and 4 days (interquartile range 1–9) for infants with T18.

Infants with T18 had >4 times the risk of death before discharge than infants with T21 (RR: 4.06; 95% CI: 2.87–5.75) and >9 times the risk compared with infants with no birth defect (RR: 9.24; 95% CI: 7.10–12.02; Table 5). Risk of death was similarly elevated for infants with T13 compared with each of these groups.

No information about status after the birth hospitalization was available for the 4 infants with T13 who survived to discharge. One with BW of 990 g was discharged on day 110. Two of the 4 infants with T13 were discharged from the hospital on oxygen, with 1 also on a cardiorespiratory monitor. Of the 11 infants with T18 who survived to discharge, status after discharge was known for 2. One infant with T18 and BW of 946 g was discharged on day 22 to hospice care at home with tube feedings but died after discharge (date unknown). The other infant stayed in the hospital for 15 days; was discharged during the month after discharge. Seven of the remaining 9 infants with T18 who survived to discharge were discharged to hospice care at home with tube feedings, oxygen, and a monitor; and died during the month after discharge. Seven of the remaining 9 infants with T18 who survived the hospital stay were discharged to hospice care (6 in the home, 1 in a facility) with 5 on nasogastric or nasojejunal tube feedings, 1 with gastrostomy feedings, and 3 on oxygen and with 2 of these also on a monitor. Final status of these patients is unknown. Special discharge instructions and final status are unknown for the remaining 2 infants with T18 who survived to discharge.

Morbidity Among Infants Who Survived >12 Hours
PDA was more frequent with T18 than with T13 (Tables 4 and 5). Risk of PDA was increased both for infants with T13 and those with T18 compared with infants without birth defects. Infants with T13 or T18 were also at increased risk for RDS compared with infants with T21 and infants with no birth defect. Among infants with T13 or T18 evaluated at 36 weeks, risk of BPD was increased compared with infants with T21 and infants with no birth defect (Table 5). Only 5 infants with T13 had measurements taken at 35 to 37 weeks PMA. These infants weighed less and had smaller head circumference on average than infants with no birth defect (Table 4). Similarly, infants with T18 weighed less, were shorter, and had smaller head circumference than infants with T21 and infants with no birth defect.

**DISCUSSION**
Among VLBW infants with T13 or T18 born and/or cared for at NNH centers over a 16-year period, timing of trisomy diagnosis influenced the level of care received at birth and subsequently in the hospital. When the trisomy was detected prenatally, provision of full intensive care at delivery was planned for only 1 (11%) infant with T13 and 1 (4%) infant with T18; the plan for subsequent care included either withholding all intensive care (100% of infants with T13; 60% of infants with T18) or providing limited care only (40% of infants with T18). In contrast, at least 90% of infants with T13 or T18 diagnosed postnatally were actively resuscitated at birth, and 2 (20%) infants with T13 and 6 (11%) infants with T18 had full intensive care planned subsequently. In the most recent American Academy of Pediatrics neonatal resuscitation guidelines, T13 but not T18 was included in the examples of conditions for which resuscitation is typically withheld. McGraw and Perlman reported that 44% of US neonatal providers would consider resuscitating a 36-week infant prenatally...
Infants who survived

Died by time of death

Infants who had a cranial sonogram within 28 d^c

Infants with sufficient information to include in analysis^a

Infants with growth measurements at 36 wk PMA, Mean (SD)\hspace{1cm}^d

Infants with growth measurements at 36 wk PMA, Median (25th–75th percentile)

### TABLE 4

<table>
<thead>
<tr>
<th>Outcome, n (%) or Mean (SD)/median</th>
<th>T13</th>
<th>T18</th>
<th>T21</th>
<th>No Birth Defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 36</td>
<td>n = 125</td>
<td>n = 139</td>
<td>n = 49,600</td>
<td></td>
</tr>
<tr>
<td>Survived to discharge</td>
<td>4 (11)</td>
<td>11 (9)</td>
<td>86 (62)</td>
<td>40,238 (81)</td>
</tr>
<tr>
<td>Died^f</td>
<td>32 (69)</td>
<td>114 (81)</td>
<td>53 (38)</td>
<td>9,582 (19)</td>
</tr>
<tr>
<td>Died by time of death^b</td>
<td>n = 17</td>
<td>n = 87</td>
<td>n = 126</td>
<td>n = 45,988</td>
</tr>
<tr>
<td>≤12 h</td>
<td>19 (53)</td>
<td>38 (30)</td>
<td>13 (9)</td>
<td>3,602 (7)</td>
</tr>
<tr>
<td>&gt;12–24 h</td>
<td>2 (6)</td>
<td>3 (2)</td>
<td>0 (0)</td>
<td>366 (&lt;1)</td>
</tr>
<tr>
<td>&gt;1–3 d</td>
<td>3 (8)</td>
<td>23 (18)</td>
<td>2 (1)</td>
<td>1,058 (2)</td>
</tr>
<tr>
<td>4–7 d</td>
<td>6 (17)</td>
<td>28 (22)</td>
<td>4 (3)</td>
<td>748 (2)</td>
</tr>
<tr>
<td>8–14 d</td>
<td>1 (3)</td>
<td>12 (10)</td>
<td>10 (7)</td>
<td>950 (2)</td>
</tr>
<tr>
<td>15–28 d</td>
<td>1 (3)</td>
<td>5 (4)</td>
<td>6 (4)</td>
<td>1,094 (2)</td>
</tr>
<tr>
<td>29+ days</td>
<td>0 (0)</td>
<td>5 (4)</td>
<td>18 (13)</td>
<td>1,513 (3)</td>
</tr>
<tr>
<td>Infants who survived &gt;12 h</td>
<td>n = 11</td>
<td>n = 45</td>
<td>n = 104</td>
<td>n = 40,115</td>
</tr>
<tr>
<td>PDA</td>
<td>7 (41)</td>
<td>62 (71)**^15</td>
<td>75 (60)</td>
<td>14,887 (52)**^16</td>
</tr>
<tr>
<td>NEC</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>20 (16)**^18</td>
<td>5,557 (8)**^18</td>
</tr>
<tr>
<td>RDS</td>
<td>14 (82)</td>
<td>71 (82)</td>
<td>84 (67)**^18</td>
<td>35,215 (77)</td>
</tr>
<tr>
<td>Infants who survived &gt;3 d</td>
<td>n = 12</td>
<td>n = 61</td>
<td>n = 124</td>
<td>n = 44,541</td>
</tr>
<tr>
<td>Late-onset sepsis</td>
<td>1 (8)</td>
<td>4 (7)</td>
<td>34 (27)**^18</td>
<td>10,621 (24)**^18</td>
</tr>
<tr>
<td>Infants who had a cranial sonogram within 28 d^c</td>
<td>n = 13</td>
<td>n = 60</td>
<td>n = 112</td>
<td>n = 42,099</td>
</tr>
<tr>
<td>Severe IVH</td>
<td>0 (0)</td>
<td>3 (5)</td>
<td>15 (13)</td>
<td>5,142 (12)</td>
</tr>
<tr>
<td>Infants who had a late cranial sonogram^d</td>
<td>n = 11</td>
<td>n = 45</td>
<td>n = 104</td>
<td>n = 40,115</td>
</tr>
<tr>
<td>PVL</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>4 (4)</td>
<td>1,699 (4)</td>
</tr>
<tr>
<td>Infants with sufficient information to include in analysis^a</td>
<td>n = 11</td>
<td>n = 47</td>
<td>n = 101</td>
<td>n = 40,090</td>
</tr>
<tr>
<td>Severe IVH or PVL</td>
<td>0 (0)</td>
<td>4 (9)</td>
<td>15 (15)</td>
<td>5,925 (15)</td>
</tr>
<tr>
<td>Infants still in the hospital at 28 d who had a ROP examination</td>
<td>n = 2</td>
<td>n = 4</td>
<td>n = 77</td>
<td>n = 31,419</td>
</tr>
<tr>
<td>ROP</td>
<td>0 (0)</td>
<td>1 (25)</td>
<td>22 (29)</td>
<td>15,154 (48)</td>
</tr>
<tr>
<td>ROP stage ≥3</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>5,565 (11)</td>
</tr>
<tr>
<td>Infants alive at 36 wk PMA</td>
<td>n = 5</td>
<td>n = 13</td>
<td>n = 98</td>
<td>n = 39,241</td>
</tr>
<tr>
<td>BPD^f</td>
<td>3 (60)</td>
<td>8 (62)</td>
<td>38 (39)</td>
<td>11,066 (28)**^18</td>
</tr>
<tr>
<td>Infants with growth measurements at 36 wk PMA, Mean (SD)\hspace{1cm}^d</td>
<td>n = 5</td>
<td>n = 29</td>
<td>n = 87</td>
<td>n = 31,920</td>
</tr>
<tr>
<td>Wt, g</td>
<td>1,568 (447)</td>
<td>1,264 (211)</td>
<td>1,765 (488)**^18</td>
<td>1,943 (533)<strong>^15,</strong>^18</td>
</tr>
<tr>
<td>Length, cm</td>
<td>40 (3.7)</td>
<td>38 (2.7)</td>
<td>41 (2.9)**^18</td>
<td>42 (2.9)**^18</td>
</tr>
<tr>
<td>Head circumference, cm</td>
<td>29 (1.9)</td>
<td>28 (1.8)</td>
<td>29 (1.8)**^18</td>
<td>31 (1.7)<strong>^15,</strong>^18</td>
</tr>
<tr>
<td>Length of hospital stay, d,^\P</td>
<td>1 (1–5)</td>
<td>4 (1–8)</td>
<td>60 (20–100)</td>
<td>54 (30–84)</td>
</tr>
</tbody>
</table>

IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.

Information was missing for infants in the groups shown for PDA: 26 infants; NEC: 19; RDS: 75; late-onset sepsis: 38; IVH: 33; PVL: 23; ROP: 5; ROP stage 5+: 22; BPD: 1,489. Most infants with missing information were among those with no major birth defect.

\(^a\) Cause of death was coded as congenital malformation for all infants with T15 and T18 and for 49% of infants with T21. Among the 9,582 infants with no birth defects who died, death was most frequently attributed to immaturity (34%), RDS alone or with other complications (23%), and sepsis and/or NEC (19%).

\(^b\) Percents are among all infants including survivors. Timing of death was missing for 3 infants with no major birth defect.

\(^c\) Severe IVH was defined as grade 3 or 4. For infants born 1994 through 1997, IVH was diagnosed based on the cranial sonogram with the most severe results; for infants born 1998 through 2009, the most severe sonogram taken within 28 d of birth was used.

\(^d\) For infants born 1994 through 1997, PVL was diagnosed based on a cranial sonogram taken at ≥2 wk of life; for infants born 1998 through 2009, PVL was determined based on a sonogram taken within 28 d of birth and/or a sonogram taken closest to 36 wk PMA (specified as after 28 d beginning in 2008).

\(^e\) Percentages were based on infants with nonmissing IVH and PVL outcomes, except that a diagnosis of either condition was sufficient to set the outcome to yes. Most infants who could not be evaluated were born 1994 through 1997 and had a sonogram showing no IVH but who did not have a sonogram at ≥2 wk so that PVL information was missing.

\(^f\) No shown are infants still in the hospital or discharged/transferred at 36 wk PMA with sufficient information to determine BPD status. BPD was defined as receiving supplemental oxygen at 36 wk PMA, or discharged/transferred on oxygen before 36 wk. All 5 infants with T15 and 11 of 15 infants with T18 were still in the hospital at 36 wk; 81% of infants with T21 and 68% of infants with no birth defect were still in the hospital: one infant with T18 was discharged from the hospital at 35 wk PMA, not on oxygen; the other infant was transferred at 34 wk PMA on oxygen and discharged from the hospital at 38 wk. Results were similar in the subset of infants still in the hospital at 36 wk.

\(^g\) No shown are infants who have at least one 36 wk measurement. In this group of infants, information was missing for weight for 37, length for 3482, head circumference for 1500.

\(^h\) The significantly shorter lengths of stay for infants with T15 and T18 reflect the higher mortality rates in these groups. The 4 infants with T15 who survived to discharge stayed in the hospital 36, 58, 85, and 110 d. Length of hospital stay ranged from 7 to 49 d (median: 28 d) for the 11 infants with T18 who were discharged from the hospital.

\(^i\) P ≤ .05, **P ≤ .01, ***P ≤ .001 by the χ^2 or the t test (means for weight, length, head circumference). Pairwise comparisons were performed between infants with T15 versus T18, T21, and no birth defects, and between infants with T18 versus T21, and no birth defects. For each significant result, a ‘v15’ or ‘v18’ indicates the comparison group.

Diagnosed with T18 and a congenital heart defect, with maternal preference being the main reason (70%) to initiate resuscitation.13 Intensive management was planned for fewer of our VLBW infants with prenatal diagnosis of T13 or T18; however, we had no information on the counseling parents might have received and the degree of accord in the decision-making between the care providers and parents. With the dual risks of VLBW and trisomy, more parents
may have been comfortable limiting medical care.

Parents and care providers face complex and challenging decisions regarding the management of infants with T13 and T18. Although provision of intensive care for infants with T21 has been standard for decades, this has not been the case for infants with T13 and T18. Despite the higher prevalence of serious birth defects with T13 and T18 compared with T21, only 20% of infants with T13 and 6% of infants with T18 underwent surgery, compared with 49% of infants with T21. Many care providers label the diagnoses of T13 and T18 as “lethal” and advocate providing palliative care only. More recently however, a more active approach has been called for by some. Several recent studies have contributed to altering the conventional picture of infants with these diagnoses. Two studies showed that, contrary to the expectations of care providers, parents of children with T13 or T18 who belong to support groups report having an enriching family experience, regardless of their children’s length of survival. Several recent studies have contributed to altering the conventional picture of infants with these diagnoses.
T18 and a congenital heart defect, the role of cardiac surgery for these infants remains controversial.3,5,18,23–28
The risks of PDA, RDS, and BPD were increased among infants with T13 or T18 compared with infants without birth defects. Our study and the majority of other studies cited here provide little information on the quality of life experienced by the surviving infants with T13 or T18. We have no data on overall resource utilization or on the difference in resource consumption between infants with prenatal versus postnatal diagnosis.

CONCLUSIONS
The intensity of delivery room care for VLBW infants with T13 or T18 varied depending on the timing of trisomy diagnosis. For the majority of infants, the plan for subsequent care was to withdraw care or to provide comfort care only. This practice influenced the timing of death and rates of survival to discharge. Median age at death was 1 day for VLBW infants with T13 and 4 days for those with T18. Despite the limited medical management received by most T13 and T18 infants, 11% of VLBW infants with T13 and 9% with T18 survived to hospital discharge. These data can be used to inform care providers and policy makers and to counsel affected families.

ACKNOWLEDGMENTS
The National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) provided grant support for the NRN's Generic Database Study.

Data collected at participating sites of the NICHD NRN were transmitted to RTI International, the data-coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Dr Abhik Das (DCC Principal Investigator) and Ms Nellie Hansen (DCC Statistician) had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

We are indebted to our medical and nursing colleagues and the infants and their parents who agreed to take part in this study. The following investigators, in addition to those listed as authors, participated in this study.

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Case Western Reserve University: Rainbow Babies & Children’s Hospital (grants U10 HD21364 and M01 RR80)—Avroy A. Fanaroff, MD; Bonnie S. Siner, RN

Cincinnati Children’s Hospital Medical Center: University Hospital and Good Samaritan Hospital (grants U10 HD27853 and M01 RR8084)—Kurt Schibler, MD; Edward F. Donovan, MD; Kate Bridges, MD; Barbara Alexander, RN; Holly L. Mincey, RN, BSN, Jody Hessling, RN; Marcia Worley Mersmann, RN, CCRC; Lenora Denise Jackson, CRC; Kristin Kirker, CRC; Estelle E. Fischer, MHSA MBA

Duke University School of Medicine, University Hospital, Alamance Regional Medical Center, and Durham Regional Hospital (grants U10 HD40492 and M01 RR30)—Ronald N. Goldberg, MD; C. Michael Cotten, MD, MHS; Kimberley A. Fisher, PhD, FNP-BC, IBLC

Emory University: Children’s Healthcare of Atlanta, Grady Memorial Hospital, and Emory University Hospital Midtown (General Clinical Research Center grants M01 RR39 and U10 HD27851)—David P. Carlton, MD; Lucky Jain, MD

Eunice Kennedy Shriver National Institute of Child Health and Human Development: Linda L. Wright, MD; Stephanie Wilson Archer, MA; Elizabeth M. McClure, MEd

Indiana University: Indiana University Hospital, Methodist Hospital, Riley Hospital for Children, and Wishard Health Services (grants U10 HD27856 and M01 RR750)—Brenda B. Poindexter, MD, MS; James A. Lemons, MD; Diana D. Appel, RN, BSN; Dianne E. Herron, RN; Lucy C. Miller, RN, BSN, CCRC

RTI International (grant U10HD36790)—W. Kenneth Poole, PhD; Dennis Wallace, PhD; Jeanette O’Dellonn Aumann, BS; Margaret M. Crawford, CCRP; Betty K. Hastings; James W. Pickett II, BS, Kristin M. Zaterka-Baxter, RN, BSN

Stanford University: California Pacific Medical Center, Dominican Hospital, El Camino Hospital, and Lucile Packard Children’s Hospital (grants U10 HD27880 and M01 RR70)—Krisa P. Van Meurs, MD; David K. Stevenson, MD; Charles E. Ahlfors, MD; Marian M. Adams, MD; Robert D. Stebbins, MD; Melinda S. Proud, RCP

University of Alabama at Birmingham: Health System and Children’s Hospital of Alabama (grants U10 HD34216 and M01 RR32)—Waldemar A. Carlo, MD; Namavigam Ambalavanan, MD; Shirley S. Cosby, RN, BSN

University of New Mexico: Health Sciences Center (grants U10 HD53089 and M01 RR997)—Kristi L. Watterberg, MD; Lu-Ann Papile, MD; Robin K. Ohls, MD

University of Rochester Medical Center: Golisano Children’s Hospital (grants U10 HD40521, M01 RR44, and UL1 RR024160)—Ronnie Guillet, MD, PhD; Carl T. D’Angio, MD; Dale L. Phelps, MD; Linda J. Reubens, RN, CCRC; Erica Burnell, RN; Rosemary L. Jensen; Mary Rowan, RN; Holly I. M. Wadkins, MA
REFERENCES


(Continued from first page)

**ABBREVIATIONS**

BPD—bronchopulmonary dysplasia  
BW—birth weight  
CI—confidence interval  
GA—gestational age  
GI—gastrointestinal  
NRN—Neonatal Research Network  
PDA—patent ductus arteriosus  
PMA—postmenstrual age  
RDS—respiratory distress syndrome  
RR—relative risk  
SGA—small for gestational age  
T13—trisomy 13  
T18—trisomy 18  
T21—trisomy 21  
VLBW—very low birth weight  
VSD—ventricular septal defect

Dr Boghossian participated in the conception and design of the study including the analysis plan, participated in the interpretation of the data, wrote the first and subsequent drafts of the manuscript, and helped to revise it critically for important intellectual content. Ms Hansen helped to design the analysis plan, was responsible for the data management and analysis, performed the analysis with guidance from Drs Boghossian, Bell, and Das, and helped to revise the manuscript critically for important intellectual content. Dr Bell participated in the conception and design of the study including the analysis plan, participated in the interpretation of the data, and revised the manuscript critically for important intellectual content. Dr Stoll participated in the design of the study, chaired the committee responsible for designing and managing the study from which the data were drawn, participated in the interpretation of the data, and helped to revise the manuscript critically for important intellectual content. Drs Murray, Carey, Adams-Chapman, Shankaran, Walsh, Laptook, and Faix participated in the conception and design of the study, participated in the interpretation of the data, and reviewed the manuscript critically for important intellectual content. Ms Newman and Ms Hale participated in the conception of the study, participated in the acquisition and interpretation of the data, and reviewed the manuscript critically for important intellectual content. Dr Das participated in the design of the study and the plan for data analysis, was responsible for the data management and participated in the analysis, and helped to revise the manuscript critically for important intellectual content. Ms Wilson, Ms Hensman, Ms Grisby, Ms Collins, Ms Vasil, Ms Finkle, Ms Maffett, Ms Ball, Ms Lacy, and Ms Bara participated in the acquisition of data and reviewed the manuscript critically for important intellectual content. Dr Higgins participated in the design of the study, participated in the interpretation of the data, and helped to revise the manuscript critically for important intellectual content.

doi:10.1542/peds.2013-1702

Accepted for publication Oct 30, 2013

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**FINANCIAL DISCLOSURE:** The authors have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** The National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) provided grant support for the Neonatal Research Network’s Generic Database Study. Drs Boghossian and Higgins are employed by the NICHD. The institutions of the other authors received grant funding from NICHD in support of this study (grants U10 HD27904, U10 HD21584, M01 RR80, U10 HD27853, M01 RR8084, U10 HD04492, M01 RR30, M01 RR39, U10 HD27851, U10 HD27856, M01 RR750, U10 HD36790, U10 HD27880, M01 RR70, U10 HD34216, M01 RR32, U10 HD53089, M01 RR997, U10 HD40521, M01 RR44, U11 RR024160, M01 RR653, U10 HD40689, U10 HD21573, U10 HD21385). Funded by the National Institutes of Health (NIH).

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.
Mortality and Morbidity of VLBW Infants With Trisomy 13 or Trisomy 18

Pediatrics 2014;133;226; originally published online January 20, 2014;
DOI: 10.1542/peds.2013-1702

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*Pediatrics* 2014;133;226; originally published online January 20, 2014; DOI: 10.1542/peds.2013-1702

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