

SPECIAL ARTICLE

# Level and Volume of Neonatal Intensive Care and Mortality in Very-Low-Birth-Weight Infants

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## ABSTRACT

### BACKGROUND

There has been a large increase in both the number of neonatal intensive care units (NICUs) in community hospitals and the complexity of the cases treated in these units. We examined differences in neonatal mortality among infants with very low birth weight (below 1500 g) among NICUs with various levels of care and different volumes of very-low-birth-weight infants.

### METHODS

We linked birth certificates, hospital discharge abstracts (including interhospital transfers), and fetal and infant death certificates to assess neonatal mortality rates among 48,237 very-low-birth-weight infants who were born in California hospitals between 1991 and 2000.

### RESULTS

Mortality rates among very-low-birth-weight infants varied according to both the volume of patients and the level of care at the delivery hospital. The effect of volume also varied according to the level of care. As compared with a high level of care and a high volume of very-low-birth-weight infants (more than 100 per year), lower levels of care and lower volumes (except for those of two small groups of hospitals) were associated with significantly higher odds ratios for death, ranging from 1.19 (95% confidence interval [CI], 1.04 to 1.37) to 2.72 (95% CI, 2.37 to 3.12). Less than one quarter of very-low-birth-weight deliveries occurred in facilities with NICUs that offered a high level of care and had a high volume, but 92% of very-low-birth-weight deliveries occurred in urban areas with more than 100 such deliveries.

### CONCLUSIONS

Mortality among very-low-birth-weight infants was lowest for deliveries that occurred in hospitals with NICUs that had both a high level of care and a high volume of such patients. Our results suggest that increased use of such facilities might reduce mortality among very-low-birth-weight infants.

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**P**ARALLELING THE LITERATURE ON ADULT care,<sup>1-3</sup> many studies of neonatal care have shown a lower mortality rate in hospitals with higher volumes of patients than in those with lower volumes.<sup>4-7</sup> Other studies have examined the association between the level of neonatal care and outcomes. Neonatal care is formally regionalized, with assigned levels of care and specific guidelines that define the characteristics of infants who should be delivered, and cared for, at each level of care. Each neonatal intensive care unit (NICU) that offers a lower level of care must have a formal contractual relationship with a NICU that provides tertiary care.<sup>8</sup> Higher levels of care are associated with lower neonatal mortality, particularly among infants with very low birth weight (below 1500 g).<sup>4-6,9-17</sup>

Growth in the number of NICUs in community hospitals throughout the United States over the past two decades (i.e., deregionalization) has resulted in increasing numbers of high-risk newborns receiving care in low-volume units offering midlevel care.<sup>6,11,18-21</sup> It is uncertain whether lower-volume, lower-level NICUs are associated with worse outcomes. One of the complexities in addressing this question is that the units with the highest level of care are also typically those with the highest volume, making it difficult to ascertain whether both volume and level are independent predictors of neonatal outcome.

We,<sup>4,6</sup> as well as other investigators,<sup>5,9-17,22-25</sup> have previously demonstrated a relationship between the level of NICU care and neonatal outcome. However, most previous studies, including our own, involved relatively small samples or narrowly defined networks and thus could not adequately assess interaction between volume and level of care. In addition, most studies were based on data collected before the routine use of surfactant-replacement therapy, which has substantially improved mortality rates among very-low-birth-weight infants.

These infants are a vulnerable group and thus particularly likely to be affected by hospital services; in 2000, they accounted for only 1.4% of births but 51% of infant deaths.<sup>26</sup> In the current study, we used data collected from all hospitals in California from 1991 to 2000 to examine the effects of NICU level of care and patient volume on mortality among very-low-birth-weight infants. These data reflect outcomes reported after the reduction in mortality associated with the introduction of surfactant-replacement therapy in 1990

and, for the most part, after the increased use of antenatal corticosteroid therapy that occurred after the publication of the results of the National Institute of Child Health and Human Development consensus conference in 1994.<sup>27-30</sup>

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## METHODS

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### STUDY DESIGN

We obtained data on very-low-birth-weight infants born in California hospitals and on in-hospital infant and fetal deaths for the period from January 1, 1991, to December 31, 2000 (66,838 infants). California birth and death certificates were linked to hospital-discharge abstracts for both mothers and infants. The death certificates included both infant and fetal death certificates. More than 99% of the maternal and infant discharge abstracts were successfully linked with infant birth certificates.<sup>31,32</sup> The birth-certificate data were also successfully linked to infant discharge abstracts from the receiving hospital for 99% of the infants who were transferred to another hospital. The study was approved by the human subjects committees at Stanford University and the California Office of Statewide Health Planning and Development, and the requirement for obtaining informed consent was waived.

### LEVELS OF CARE

We defined levels of care as follows: level 1, no NICU; level 2, a NICU that provides care for mildly ill infants but does not provide mechanical ventilation; level 3A, a NICU that provides mechanical ventilation with restrictions (e.g., only for infants with a birth weight above 1000 g); level 3B, a NICU that provides mechanical ventilation without restrictions but does not provide major surgery; level 3C, a NICU that provides major neonatal surgery but neither open-heart surgery nor extracorporeal membrane oxygenation (ECMO); and level 3D, a NICU that provides cardiac surgery requiring cardiopulmonary bypass or ECMO. These definitions are based on the draft version of the American Academy of Pediatrics report on NICU levels of care<sup>8,33</sup> to differentiate NICUs in community hospitals from true tertiary or regional perinatal centers (level 3C or 3D). We used the draft rather than the final version because the draft was a more accurate reflection of how hospitals in California were actually operating. The final version does not allow for NICUs that provide mechanical ventilation without re-

strictions but that do not provide major surgery (level 3B in the draft version); many California NICUs were actually providing this level of care during the study period.

We assigned levels of NICU care to each hospital, for each year, empirically from our data (see Section A-1 of the Supplementary Appendix, available with the full text of this article at [www.nejm.org](http://www.nejm.org)). For each year, we also counted the number of very-low-birth-weight infants who received care at each hospital (both those born in the hospital and those born elsewhere).

#### NEONATAL AND FETAL DEATHS

Because of improvements in neonatal care, the standard definition of a “neonatal death” — death within 28 days after birth — may be biased by the exclusion of continuously hospitalized infants who die after 28 days. Thus, we use the term “neonatal-related deaths” to refer to all neonatal deaths plus any deaths that occurred between 29 days and 1 year after delivery if the infant was continuously hospitalized. In 2000, deaths after 28 days accounted for 7.5% of all neonatal deaths.

Differences among hospitals in the level of obstetrical care, especially the ability to perform very rapid cesarean deliveries, can result in the live birth of infants who would otherwise die in utero. Thus, the exclusion of in-hospital fetal deaths would introduce a systematic bias against hospitals with large or high-risk obstetrical services. To arrive at a conservative estimate of the number of fetal deaths that occurred after the mother was admitted to the hospital, we identified in-hospital fetal deaths using the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) codes (see Table A-2 of the Supplementary Appendix) from the mother’s discharge abstract for procedures that are performed only if the fetus is still alive. When added to the neonatal deaths, in-hospital fetal deaths accounted for 22.8% of total deaths.

Data on infants with a birth weight below 500 g (5157 infants) were excluded to be consistent with previous studies and because of the variability in decisions about whether to treat such infants. Because some congenital anomalies can increase the risk of death among infants with very low birth weight, we used ICD-9-CM codes to identify and exclude infants with such anomalies (7667 infants) (see Table A-3 of the Supplementary Appendix). We also excluded fetal deaths that we could not confirm had occurred after

hospital admission (5777 fetal deaths), resulting in a final sample of 48,237 infants. A total of 6892 infants were transferred between hospitals; these infants remained in the sample, and deaths among them were attributed to the birth hospital.

#### STATISTICAL ANALYSIS

We used logistic regression to estimate odds ratios for mortality associated with the NICU level of care and annual volume of very-low-birth-weight infants. The dependent variable was in-hospital neonatal-related or fetal death. The standard errors for the hospital-level independent variables were corrected for within-hospital clustering with the use of the “cluster” option in Stata software, version 9.<sup>34</sup> We controlled for the year to offset the decline in neonatal mortality over the course of the study period.<sup>27,28</sup>

Regressions run separately for each level of care showed that the effects of the volume of very-low-birth-weight infants varied according to the NICU level. For ease of presentation, we created categorical variables for the volume for each level of care.

We tested several different nonlinear functional forms using birth weight and gestational age but used categorical variables for the final model because they produced a better fit. We used separate birth-weight functions for male singletons, female singletons, and multiple births with 100-g intervals up to 1000 g and 250-g intervals from 1000 to 1500 g. For gestational age, we used 2-week intervals through 33 weeks.

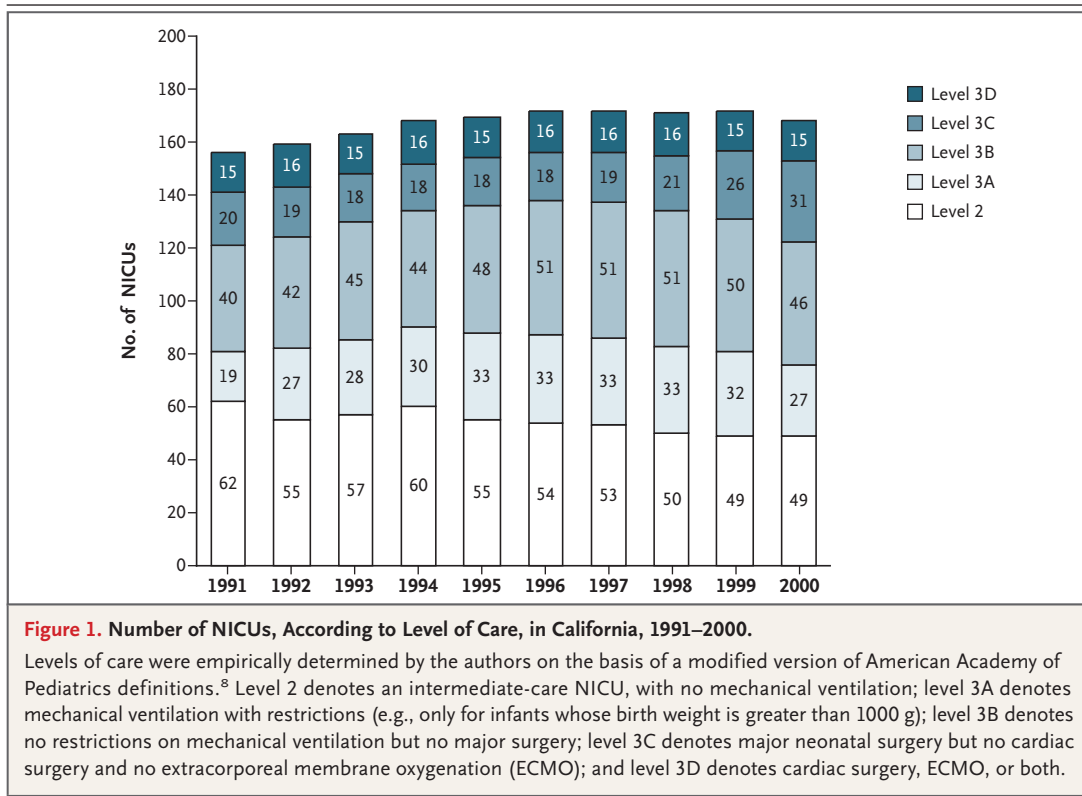
We tested a wide range of clinical and demographic variables from the birth certificate and discharge data to control for risk factors, and we considered only those variables that were present at birth (see Table A-4 of the Supplementary Appendix). We developed the model using a random 50% sample and then validated it by applying the estimated coefficients to the remaining data. A Hosmer–Lemeshow test revealed an acceptable fit ( $P=0.13$ ).<sup>35</sup> When applied to the entire data set, the model again fit well ( $P=0.34$  by the Hosmer–Lemeshow test; area under the receiver-operating-characteristic curve=0.86).

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## RESULTS

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The number of NICUs increased slightly between 1991 and 2000, and there was a noticeable shift upward in the levels of care provided (Fig. 1). Most



of the new NICUs in California in the 1990s were low- or moderate-volume units, as were most of the NICUs that upgraded their level of service (Table A-1 of the Supplementary Appendix).

The percentage of very-low-birth-weight deliveries in hospitals with level 3B, 3C, and 3D NICUs that treated more than 100 such infants decreased from 35.6% in 1991 to 21.5% in 2000 (Table 1), with most of this decline offset by the increase in deliveries at hospitals with level 3B or 3C NICUs that treated 26 to 50 very-low-birth-weight infants annually. The percentage of very-low-birth-weight deliveries in NICUs that treated 51 to 100 of these infants was constant over this time, and there were only minor changes at NICUs with other levels of care.

There was a wide range in the unadjusted mortality rates among NICU level-of-care and volume groups (Table 2). Mortality decreased as patient volume increased within each level of care and with higher levels of care within each volume group. Table 2 also shows the distribution of several risk factors for death according to the level of care.

As compared with deliveries at hospitals with a level 3B, 3C, or 3D NICU that treated at least

100 very-low-birth-weight infants per year, deliveries at hospitals with lower-level and lower-volume NICUs were associated with an increased risk of death (Table 3), adjusted for the risk factors shown in Table 2. (Table A-5 of the Supplementary Appendix, which shows odds ratios for death associated with the other covariates in the model.) The odds ratios decreased as volume increased within each level of care and as the NICU level of care increased within each volume group. The risk of death was significantly higher in level 3B and 3C NICUs that treated 50 or fewer very-low-birth-weight infants per year than in units with larger volumes. The risk of death for NICUs with various combinations of lower levels of care and patient volumes were significantly increased, with the exception of two very small groups of hospitals: those with level 2 NICUs that treated more than 25 very-low-birth-weight infants (four hospitals in 2000) and level 3A NICUs that treated more than 50 such infants (three hospitals in 2000). Although the number of NICUs in these two groups was smaller than normal for categorical variables, model specification tests showed that they should not be combined with smaller NICUs with the same level of care. A NICU that treats 50 very-

low-birth-weight infants per year corresponds to an average NICU census of about 15 patients. Thus, most of the increase in the risk of death was accounted for by hospitals with small to moderate-size NICUs.

Results were materially unchanged when we included infants with congenital anomalies and when we excluded in-hospital fetal deaths. We also performed an analysis stratified according to birth weight. Although the associations between mortality and NICU level and volume were greater for the smallest infants (below 1000 g), they were still significant for the larger infants (see Table A-6 of the Supplementary Appendix). The results of a model limited to infants born after 1995 were consistent with the overall results (data not shown). The very strong correlation between NICU volume and number of deliveries, as well as the lack of other data about obstetrical services, limited our ability to investigate the role of obstetrical factors. However, to address the possibility that obstetrical volume accounted for our results, we created a model based on estimates that included obstetrical volume; the effects on our results were minimal (see Table A-6 of the Supplementary Appendix).

We estimated the number of potentially preventable deaths on the basis of the odds ratios from Table 3 and the distribution of very-low-birth-weight deliveries across NICUs in 2000 from Table 1. Because the distance from the mother's home to a hospital determines the feasibility of delivery at that hospital, this analysis was restricted to geographic areas with at least 100 very-low-birth-weight deliveries in 2000. Since most births occurred in the large urban areas of California, this restriction excluded only 8% of such deliveries. Assuming that only 90% of the deliveries of very-low-birth-weight infants in the large urban areas could be shifted to hospitals with tertiary-level NICUs that care for at least 100 such infants annually, we estimated that 21% of the deaths of very-low-birth-weight infants in the year 2000 were potentially preventable (see Table A-7 of the Supplementary Appendix).

## DISCUSSION

Our study shows strong associations between both NICU level and volume at the delivery hospital and mortality. Our analysis of data from a 10-year period strengthens the evidence from pre-

**Table 1. Distribution of Very-Low-Birth-Weight Deliveries According to Annual Patient Volume and Level of NICU Care Available at the Delivery Hospital in California, 1991 and 2000.\***

| Level of Care and No. of Infants | 1991           | 2000 |
|----------------------------------|----------------|------|
|                                  | <i>percent</i> |      |
| Level 1                          |                |      |
| ≤10                              | 6.1            | 4.9  |
| >10                              | 2.6            | 4.0  |
| Level 2                          |                |      |
| ≤10                              | 1.4            | 1.3  |
| 11–25                            | 3.8            | 4.6  |
| >25                              | 8.0            | 6.4  |
| Level 3A                         |                |      |
| ≤25                              | 1.2            | 0.9  |
| 26–50                            | 2.3            | 4.5  |
| >50                              | 3.0            | 3.5  |
| Level 3B or 3C                   |                |      |
| ≤25                              | 2.4            | 3.5  |
| 26–50                            | 7.8            | 19.1 |
| Level 3B, 3C, or 3D              |                |      |
| 51–100                           | 25.9           | 25.8 |
| >100                             | 35.6           | 21.5 |

\* The numbers of very-low-birth-weight infants are the total numbers treated at each hospital, including infants transferred to or received from other facilities. Levels of care were empirically determined on the basis of a modified version of American Academy of Pediatrics definitions.<sup>8</sup> Level 2 denotes an intermediate-care NICU, with no mechanical ventilation; level 3A mechanical ventilation with restrictions (e.g., only for infants whose birth weight is greater than 1000 g); level 3B no restrictions on mechanical ventilation but no major surgery; level 3C major neonatal surgery but no cardiac surgery and no extracorporeal membrane oxygenation (ECMO); and level 3D cardiac surgery, ECMO, or both.

vious studies that used data from a period of 1 or 2 years. Mortality was lowest when very-low-birth-weight deliveries occurred in hospitals with tertiary-level NICUs that treat more than 100 of these infants annually.

High-volume, high-level NICUs represent the minority of NICUs in California. Fewer than 25% of very-low-birth-weight infants were delivered in such hospitals in 2000, and the proportion of such deliveries occurring in these hospitals has declined over time.

Some limitations of our study should be noted. Because of the observational design, it was not possible to assess whether there was a causal relationship between NICU features and neonatal mortality. Factors other than NICU level and volume may explain the observed associations. For example, hospitals with large, high-level NICUs may also have better obstetrical care. The ability to provide rapid emergency cesarean sections not only prevents some fetal deaths but also results in the delivery of many infants in healthier condition, with associated improvement in survival. Our results were robust when obstetrical volume

**Table 2. Characteristics of Very-Low-Birth-Weight Infants According to NICU Annual Volume and Level of Care, 1991–2000.\***

| Characteristic                       | Level 1      |             | Level 2      |               | Level 3A    |               | Levels 3B and 3C |               | Levels 3B, 3C, and 3D† |                |              |
|--------------------------------------|--------------|-------------|--------------|---------------|-------------|---------------|------------------|---------------|------------------------|----------------|--------------|
|                                      | 1–10 Infants | >10 Infants | 1–10 Infants | 11–25 Infants | ≤25 Infants | 26–50 Infants | ≤25 Infants      | 26–50 Infants | ≤25 Infants            | 51–100 Infants | >100 Infants |
| No. of infants                       | 2636         | 1379        | 872          | 2270          | 4071        | 1450          | 1470             | 6567          | 12,744                 | 12,704         |              |
| No. of deaths (%)                    | 909 (34.5)   | 405 (29.4)  | 275 (31.5)   | 597 (26.3)    | 863 (21.2)  | 342 (23.6)    | 300 (20.4)       | 1359 (20.7)   | 2536 (19.9)            | 2299 (18.1)    |              |
| Birth weight, sex, and plurality (%) |              |             |              |               |             |               |                  |               |                        |                |              |
| Singleton female                     |              |             |              |               |             |               |                  |               |                        |                |              |
| 500–599 g                            | 4.3          | 4.3         | 3.9          | 4.2           | 3.6         | 3.3           | 3.7              | 4.0           | 3.7                    | 3.5            | 3.2          |
| 600–699 g                            | 3.8          | 3.2         | 4.1          | 3.1           | 3.1         | 2.6           | 2.5              | 2.9           | 3.3                    | 3.2            | 3.2          |
| 700–799 g                            | 2.8          | 2.5         | 2.3          | 3.0           | 3.1         | 2.1           | 3.3              | 2.1           | 3.2                    | 3.8            | 3.5          |
| 800–899 g                            | 3.0          | 2.9         | 2.3          | 2.4           | 3.2         | 2.1           | 4.2              | 2.3           | 3.3                    | 2.9            | 3.4          |
| 900–999 g                            | 3.3          | 3.1         | 3.0          | 3.4           | 3.7         | 2.5           | 3.7              | 2.9           | 2.9                    | 3.7            | 3.3          |
| 1000–1249 g                          | 7.7          | 8.4         | 7.2          | 9.5           | 8.7         | 10.3          | 9.5              | 9.1           | 9.3                    | 9.1            | 9.3          |
| 1250–1499 g                          | 12.2         | 13.5        | 14.1         | 11.7          | 11.4        | 14.9          | 11.1             | 13.2          | 11.6                   | 11.0           | 10.6         |
| Singleton male                       |              |             |              |               |             |               |                  |               |                        |                |              |
| 500–599 g                            | 5.8          | 4.0         | 5.4          | 4.1           | 3.5         | 4.7           | 4.5              | 4.0           | 3.7                    | 3.5            | 2.9          |
| 600–699 g                            | 4.6          | 4.1         | 4.4          | 3.5           | 3.9         | 2.5           | 4.0              | 4.3           | 3.5                    | 3.6            | 3.0          |
| 700–799 g                            | 4.0          | 3.4         | 4.1          | 3.3           | 3.4         | 2.8           | 3.9              | 3.0           | 3.4                    | 3.6            | 3.3          |
| 800–899 g                            | 3.1          | 3.6         | 3.6          | 2.2           | 3.3         | 3.6           | 3.1              | 3.0           | 2.9                    | 3.2            | 3.2          |
| 900–999 g                            | 4.8          | 4.1         | 2.6          | 4.0           | 4.0         | 2.8           | 4.3              | 3.8           | 3.2                    | 3.9            | 3.8          |
| 1000–1249 g                          | 10.5         | 9.5         | 11.0         | 10.8          | 11.0        | 11.4          | 10.2             | 9.3           | 10.6                   | 10.2           | 9.9          |
| 1250–1499 g                          | 14.7         | 13.5        | 16.5         | 14.4          | 12.3        | 14.4          | 13.5             | 13.7          | 12.7                   | 12.4           | 11.2         |
| Multiple                             |              |             |              |               |             |               |                  |               |                        |                |              |
| 500–599 g                            | 1.4          | 1.0         | 0.9          | 1.9           | 1.7         | 1.8           | 1.3              | 1.5           | 1.7                    | 1.7            | 2.0          |
| 600–699 g                            | 1.0          | 1.7         | 1.8          | 1.6           | 2.0         | 1.7           | 1.7              | 1.8           | 1.5                    | 1.6            | 1.7          |
| 700–799 g                            | 1.1          | 1.7         | 0.9          | 1.2           | 1.5         | 0.7           | 1.2              | 1.3           | 1.5                    | 1.5            | 2.0          |
| 800–899 g                            | 1.0          | 1.4         | 1.1          | 0.7           | 1.9         | 0.6           | 2.0              | 1.5           | 1.8                    | 1.5            | 2.2          |
| 900–999 g                            | 1.0          | 1.5         | 1.5          | 1.7           | 2.0         | 1.8           | 2.0              | 1.3           | 1.9                    | 2.1            | 2.4          |
| 1000–1249 g                          | 3.3          | 5.3         | 3.7          | 5.2           | 5.5         | 5.9           | 4.9              | 6.5           | 5.9                    | 6.0            | 6.9          |
| 1250–1499 g                          | 6.6          | 7.2         | 5.5          | 8.1           | 7.1         | 7.4           | 5.5              | 8.5           | 8.4                    | 7.8            | 9.1          |



**Table 2. (Continued.)**

| Characteristic                          | Level 1      |             | Level 2      |               | Level 3A    |               | Levels 3B and 3C |               | Levels 3B, 3C, and 3D† |              |
|---|--------------|-------------|--------------|---------------|-------------|---------------|------------------|---------------|------------------------|--------------|
|   | 1-10 Infants | >10 Infants | 1-10 Infants | 11-25 Infants | ≤25 Infants | 26-50 Infants | ≤25 Infants      | 26-50 Infants | 51-100 Infants         | >100 Infants |
| High-risk maternal condition (%)        |              |             |              |               |             |               |                  |               |                        |              |
| Infant affected by maternal condition** | 6.6          | 6.8         | 9.6          | 8.4           | 8.1         | 5.2           | 8.8              | 7.7           | 9.3                    | 9.6          |
| Oligohydramnios                         | 0.8          | 0.6         | 1.4          | 1.2           | 1.3         | 0.8           | 1.2              | 1.3           | 1.5                    | 1.9          |
| Placental hemorrhage                    | 6.6          | 4.4         | 7.3          | 6.4           | 5.0         | 3.4           | 3.9              | 4.1           | 3.1                    | 3.0          |
| Premature rupture of membranes          | 3.8          | 6.0         | 5.5          | 5.6           | 3.8         | 3.0           | 6.7              | 6.0           | 8.3                    | 8.5          |
| Prolapsed cord                          | 2.3          | 1.4         | 1.9          | 1.7           | 1.1         | 0.9           | 1.5              | 1.0           | 1.5                    | 1.4          |
| Other††                                 | 0.72         | 0.22        | 0.57         | 0.88          | 0.56        | 0.48          | 0.66             | 0.65          | 0.74                   | 0.72         |

\* Data include all in-hospital, very-low-birth-weight deliveries and fetal deaths (a total of 48,237). Infants with a birth weight below 500 g and infants with major congenital anomalies were excluded.

† No NICU with a 3D level of care had fewer than 51 patients.

‡ The Asian, Native American, and Hispanic categories had no significant effect on mortality and were excluded from the final model. Data on race or ethnic group were obtained from information recorded on the birth certificate, as reported by the mother.

§ The other educational categories (12 years and <4 years of college) had no significant effect on mortality and were excluded from the final model. Data on maternal education were obtained from information recorded on the birth certificate, as reported by the mother.

¶ Information on these conditions was based on ICD-9-CM codes for small for gestational age and large for gestational age (764 and 766, respectively).

|| Nonimmune hydrops was classified as a congenital anomaly, and infants with this condition were excluded, along with infants who had other congenital anomalies. Hemolytic disease without a diagnosis of hydrops was included in the hemolytic-disorders variable.

\*\* Data on maternal hypertensive disorders and noxious substances were based on ICD-9-CM codes 760.0, 760.7, 760.72, and 760.73.

†† Data on chronic maternal circulatory and respiratory diseases and incompetent cervix were based on ICD-9-CM codes 760.3 and 761.0, respectively.

was added to the model, but the role of obstetrical volume merits further investigation.

Although our model controlled for many potential confounders, we could address only those variables available from birth certificates and discharge abstracts. These data are of high quality,<sup>36</sup> but they do not include information on all the potential differences in mortality. The risk factors we assessed did not differ significantly among the level-of-care and volume groups, but it is possible that unmeasured differences among the groups affected the results. Given that some high-risk cases are selectively referred to large tertiary-care centers, we would expect such factors to introduce a bias against the highest-level NICUs; consequently, they should not explain our findings. Our exclusion of infants with life-threatening congenital anomalies eliminated any bias due to referrals that were restricted to infants with treatable anomalies.

The only outcome we assessed was mortality; other outcomes, such as intraventricular hemorrhage and chronic lung disease, are also important. A recent study showed that a higher NICU volume was associated with a lower risk of intraventricular hemorrhage.<sup>37</sup> However, the relationship between volume and outcomes other than mortality requires additional study.

Studies using data from the Vermont Oxford Network showed weaker relationships between NICU volume and mortality<sup>38,39</sup> than we observed.<sup>4,6</sup> Further, in these analyses, volume explained less of the variance in mortality than it did in our study. One potential explanation for these differences is that our data included a broader sampling of hospitals, particularly community hospitals. Data from the Vermont Oxford Network also demonstrated considerable variation in outcomes across hospitals after taking the effects of NICU level and volume into account.<sup>38,39</sup>

On the basis of our model, we estimated that increased regionalization of NICU care may have the potential to prevent 21% of deaths among very-low-birth-weight infants. This estimate relies on several assumptions, including a causal relationship between large, high-level NICUs and reduced mortality, and a very high level of regionalization. Our observation that 92% of the very-low-birth-rate deliveries in our study occurred in urban areas with more than 100 such deliveries suggests that it would be geographically feasible to regionalize the vast majority of these deliveries

**Table 3. Odds Ratios for Mortality among Very-Low-Birth-Weight Infants, According to NICU Level of Care and Annual Patient Volume.\***

| Level of Care and No. of Infants | Odds Ratio (95% CI) | P Value |
|----------------------------------|---------------------|---------|
| Level 1                          |                     |         |
| ≤10                              | 2.72 (2.37–3.13)    | <0.001  |
| >10                              | 2.39 (1.91–3.00)    | <0.001  |
| Level 2                          |                     |         |
| ≤10                              | 2.53 (2.02–3.18)    | <0.001  |
| 11–25                            | 1.88 (1.56–2.26)    | <0.001  |
| >25                              | 1.22 (0.98–1.52)    | 0.08    |
| Level 3A                         |                     |         |
| ≤25                              | 1.69 (1.28–2.24)    | <0.001  |
| 26–50                            | 1.78 (1.35–2.34)    | <0.001  |
| >50                              | 1.08 (0.96–1.21)    | 0.22    |
| Level 3B or 3C                   |                     |         |
| ≤25                              | 1.51 (1.17–1.95)    | <0.002  |
| 26–50                            | 1.30 (1.12–1.50)    | <0.001  |
| Level 3B, 3C, or 3D              |                     |         |
| 51–100                           | 1.19 (1.04–1.37)    | 0.01    |
| >100                             | 1.00                |         |

\* The area under the receiver-operating-characteristic curve was 0.86. The reference group was hospitals with a level 3B, 3C, or 3D NICU that treat at least 100 very-low-birth-weight infants per year. Standard errors were corrected for clustering of patients within hospitals. The model included birth weight, gestational age, sex, multiple gestation, black race, maternal educational level, type of insurance, year (2000 was the reference variable), several obstetrical conditions (premature rupture of the membranes, fetal distress, placental complications, polyhydramnios, and oligohydramnios), and fetal and neonatal conditions (small for gestational age, exceptionally large for gestational age, hydrops, and hemolytic disorders). Infants with major congenital anomalies or a birth weight below 500 g were excluded.

in California. To do so would probably require the addition of some large perinatal centers, which, ideally, would be strategically located to maximize geographic access and could be created through the mergers of existing smaller NICUs. There could be some disadvantages to closing facilities that are not included in our estimates, and efforts to increase regionalization are likely to draw some opposition. Although it would be more difficult to regionalize very-low-birth-weight deliveries in more sparsely populated areas of the United States, our results suggest that reductions in mortality could be achieved by moving from low to moderate volumes, which may be a more feasible goal in these areas.

In conclusion, our study showed that the NICU volume and level in the hospitals where very-low-

birth-weight infants are born is strongly associated with mortality; the mortality was lowest for deliveries that occurred in hospitals with high-level and high-volume NICUs. Less than a quarter of very-low-birth-weight infants are born in hospitals with such NICUs, and this percentage has been declining over time. Our results suggest that increased regionalization of perinatal care might reduce mortality among very-low-birth-weight infants.

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