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# Very Low Birth Weight Preterm Infants With Surgical Short Bowel Syndrome: Incidence, Morbidity and Mortality, and Growth Outcomes at 18 to 22 Months

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## **Abstract**

**OBJECTIVES**—The objective of this study was to determine the (1) incidence of short bowel syndrome in very low birth weight (<1500 g) infants, (2) associated morbidity and mortality during initial hospitalization, and (3) impact on short-term growth and nutrition in extremely low birth weight (<1000 g) infants.

**METHODS**—Infants who were born from January 1, 2002, through June 30, 2005, and enrolled in the National Institute of Child Health and Human Development Neonatal Research Network were studied. Risk factors for developing short bowel syndrome as a result of partial bowel resection (surgical short bowel syndrome) and outcomes were evaluated for all neonates until hospital discharge, death, or 120 days. Extremely low birth weight survivors were further evaluated at 18 to 22 months' corrected age for feeding methods and growth.

**RESULTS**—The incidence of surgical short bowel syndrome in this cohort of 12 316 very low birth weight infants was 0.7%. Necrotizing enterocolitis was the most common diagnosis associated with surgical short bowel syndrome. More very low birth weight infants with short bowel syndrome (20%) died during initial hospitalization than those without necrotizing enterocolitis or short bowel syndrome (12%) but fewer than the infants with surgical necrotizing enterocolitis without short bowel syndrome (53%). Among 5657 extremely low birth weight infants, the incidence of surgical short bowel syndrome was 1.1%. At 18 to 22 months, extremely low birth weight infants with short bowel syndrome were more likely to still require tube feeding (33%) and to have been rehospitalized (79%). Moreover, these infants had growth delay with shorter lengths and smaller head circumferences than infants without necrotizing enterocolitis or short bowel syndrome.

**CONCLUSIONS**—Short bowel syndrome is rare in neonates but has a high mortality rate. At 18 to 22 months' corrected age, extremely low birth weight infants with short bowel syndrome were more likely to have growth failure than infants without short bowel syndrome.

## Keywords

short bowel syndrome; preterm; necrotizing enterocolitis; nutrition

SHORT BOWEL SYNDROME (SBS) is a devastating clinical problem that affects an estimated 20 000 Americans (children and adults). Although not consistently fatal, complications that are associated with this disorder include dehydration, malnutrition, sepsis, poor growth, and impaired neurodevelopment.1<sup>-5</sup> SBS is defined as insufficient bowel length to digest and absorb adequately nutrients that are needed to promote appropriate growth of the infant. SBS is often the result of massive small intestinal resection in infants as a result of necrotizing enterocolitis (NEC).6<sup>-7</sup> Overall, the number of children with this disorder seems to be increasing, likely as a result of reductions in neonatal mortality in both term and preterm neonates, putting more infants at risk for developing diseases that predispose to SBS.8<sup>-9</sup> The related health care costs that result from treating patients with SBS and its complications are very high. The quality-of-life burden on these children and their families is also very high.<sup>1,3</sup>

The most common cause of SBS in infants is NEC.10 The incidence of NEC in extremely low birth weight (ELBW) infants is ~10%, and the associated mortality is 30%.11·12 Infants who have NEC and are surgically treated have hospital lengths of stay that exceed those of gestational age (GA)-matched infants by 60 days. On the basis of this length of stay in 1 US hospital, the estimated hospital charges for infants with NEC exceeded those of matched control subjects by more than \$186 000, and the yearly additional charges related to NEC were \$6.5 million.13 Multiple factors have been identified as predictors of morbidity and mortality in patients with SBS14-16; however, SBS continues to constitute a major clinical challenge for neonatologists, gastroenterologists, and nutritionists, who often collectively treat these patients. It is associated with high morbidity and mortality because of chronic malabsorption that results from reduced bowel absorptive surface area and diminished mucosal function, including gut barrier dysfunction, frequent infections, and complications that are associated with specialized parenteral and enteral feeding.2, 17 In children, SBS may lead to poor growth, nutritional deficiencies, delayed neurodevelopment, and ultimately death. 18-20

Data illustrating the effect of SBS on subsequent growth and neurologic development in preterm infants are sparse.20<sup>-22</sup> We determined the incidence of surgical SBS and examined morbidity, mortality, and growth outcomes of children with and without surgical SBS in a large cohort of very low birth weight (VLBW) infants who were born between 2002 and 2005.

## **METHODS**

## **Study Population**

Infants studied were born January 1, 2002, and June 30, 2005, and enrolled in a registry of VLBW infants (401–1500 g birth weight) maintained by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Neonatal Research Network, a consortium of 16 tertiary neonatal centers within the United States. The registry includes nearly all VLBW infants who are delivered at participating centers or admitted to these centers within 14 days of birth. Trained personnel collect maternal and delivery data soon after birth and infant clinical data until discharge or death or within the first 120 days of life. <sup>23</sup> Infants who are still in the hospital at 120 days are followed for final status up to 1 year of life. Surviving ELBW infants (401–1000 g birth weight) complete a comprehensive visit at 18 to 22 months' corrected GA. The institutional review boards at each center approved participation in the registry and follow-up studies, and informed consent was obtained from parents or legal guardians for follow-up and, at 1 center, for participation in the registry.

#### **Clinical Outcomes**

Maternal and neonatal data that were collected during the initial hospitalization from birth until hospital discharge, 120 days, or death included mother's age, receipt of antenatal steroids, multiple birth, birth weight, GA, gender, race, major congenital anomalies, receipt of postnatal steroids, and diagnoses of NEC, patent ductus arteriosus (PDA), severe intraventricular hemorrhage (IVH) defined as grade 3 or 4, periventricular leukomalacia, bronchopulmonary dysplasia (BPD), and sepsis (culture-positive infection treated with antibiotics for ≥5 days). NEC was defined as modified Bells stage IIA or greater,24 and IVH was classified according to the method of Papile et al.25 BPD was defined by use of supplemental oxygen at 36 weeks' postmenstrual age. Standard reference fetal charts were used to classify infants as small for GA at birth (SGA), defined by a birth weight <10th percentile for gender and GA.26

Surgical SBS was recorded as a diagnosis when an infant had gastrointestinal surgery with significant re-section of bowel that resulted in total parenteral nutrition dependence as a result of malabsorption, severe diarrhea, gastric hypersecretion, secondary bacterial overgrowth, and failure to thrive.6<sup>10</sup> These infants were compared with (1) infants with surgical NEC and without SBS (NEC managed surgically and did not result in SBS), (2) medical NEC (NEC managed medically without surgery), and (3) infants with no NEC or SBS.

## Comprehensive Visit at 18 to 22 Months' Corrected Age

Information that was collected at the 18- to 22-month follow-up visit included primary caregiver's education; household income; infant's medical history including rehospitalizations since initial discharge; and measurements of weight, length (using horizontal stadiometer/length board), and head circumference. These growth parameters were classified as <10th percentile and converted to z scores on the basis of corrected age and gender using standard Centers for Disease Control and Prevention charts.<sup>27</sup> Hearing and vision screening, Bay-ley testing, and neurologic examinations are also performed during this visit by trained and certified examiners.

#### Statistical Analysis

The incidence of surgical SBS was first examined overall, by study center, and by diagnosis of NEC among all VLBW infants. Unadjusted relative risks (RRs) and 95% confidence intervals (CIs) were calculated by the Mantel-Haenszel method to describe the risk for SBS by birth weight, GA, and other baseline maternal and neonatal characteristics. Morbidities during the initial hospitalization and mortality were compared between the SBS, surgical NEC without SBS, medical NEC, and no NEC or SBS groups among VLBW infants and among ELBW infants overall and those who attended the follow-up visit. Distributions of time to death were estimated using the Kaplan-Meier method with comparisons among groups made using the log-rank test. Growth, feeding, and other outcomes that were ascertained at follow-up were compared among ELBW infants who completed the visit. Statistical significance for unadjusted comparisons between the SBS and other groups was determined by  $\chi^2$  tests for categorical variables and Wilcoxon tests for continuous variables. Poisson regression models with robust error variances<sup>28</sup> were used to examine differences between infants with surgical SBS and other groups on growth outcomes after adjustment for other variables. In addition to the SBS/NEC group indicator, covariates that were included in the models were study center, birth weight, GA, gender, race (nonwhite/white), major congenital anomaly (yes/no), multiple birth (yes/no), caregiver education (high school degree or not), severe IVH (yes/no), periventricular leukomalacia (yes/no), PDA (yes/no), postnatal steroid use (yes/no), antenatal steroid use (yes/no), BPD (yes/no), and shunt (yes/no). Adjusted relative risks and 95% confidence intervals from these models are shown. All analyses were completed using SAS software (SAS Institute, Cary, NC).<sup>29</sup>

## **RESULTS**

# VLBW Infants (401-1500 g)

Between January 1, 2002, and June 30, 2005, 12 316 infants with birth weight 401 to 1500 g were born at the 16 Neonatal Research Network study hospitals and survived >12 hours after birth or were admitted within 14 days of birth. Surgical SBS was reported for 89 (0.7% [7 per 1000]) of these neonates. The incidence of SBS among VLBW neonates ranged from 0.1% to 1.6% across the study centers. In this cohort of neonates, NEC was identified as the most common indicator for surgery that led to SBS (Table 1).

The overall incidence of SBS was higher in infants with proven NEC (8%) than in those without NEC (0.1%; P < .001). Thus, infants with NEC had an RR of 85.9 (95% CI: 45.8-160.9) for developing SBS compared with other infants without NEC. The risk for SBS increased with decreasing birth weight (Table 2). When compared with neonates with birth weight 1251 to 1500 g, those with birth weight 401 to 750 g had greater than twice the risk for developing SBS (RR: 2.74 [95% CI: 1.42–5.30]), as did infants with birth weight 751 to 1000 g (RR: 3.02 [95% CI: 1.60-5.71]). Similarly, infants of <25 and 25 to 28 weeks' GA had an RR of 2.02 and 2.15, respectively, for SBS compared with those of ≥29 weeks' GA; however, after controlling for NEC, there was no significant association between birth weight and the risk for SBS (P = .3) or between GA and risk for SBS (P = .3). This is attributed to the significant inverse relationship between birth weight and NEC (P < .001) and GA and NEC (P < .001) with the increased risk for NEC at lower birth weight and GA increasing the risk for SBS. In addition, the risk for SBS was increased for boys compared with girls (RR: 1.71 [95% CI: 1.11–2.63]) and appropriate for GA neonates compared with SGA neonates (RR: 1.88 [95% CI 1.00–3.54]). None of the other baseline neonatal or maternal characteristics examined was associated with an increased risk for SBS (Table 2).

Survival distributions over time varied between the groups (P < .001; Fig 1). The earliest death among infants with SBS occurred on day 51 of life, whereas deaths occurred at earlier ages in the other groups. By 60 days of life, 98% of infants with SBS, 89% of infants with no NEC or SBS, 86% of infants with medical NEC, and only 56% of those with surgical NEC without SBS were alive. By 180 days, survival was similar for infants with SBS (79%) and no NEC or SBS (78%), lower for infants with medical NEC (60%), and lowest for those with surgical NEC without SBS (43%). NEC complications and sepsis were the most common reported causes of death among infants with surgical NEC without SBS (82% of deaths), SBS (61%), and medical NEC (55%). In contrast, respiratory distress syndrome was the most common cause of death reported among infants with no NEC or SBS (39%).

#### **ELBW Infants (401 to 1000 g)**

Among the 5657 ELBW neonates, 61 (1.1% [11 per 1000]) had surgical SBS. Initial hospital morbidities and mortality were compared between ELBW infants with SBS and those with surgical NEC and without SBS, medical NEC, and no NEC or SBS (Table 3). The percentage of infants with PDA was higher among those with SBS compared with those with no NEC or SBS. Significantly more SBS infants had a diagnosis of sepsis and episodes of late-onset sepsis than infants in the other groups. By hospital discharge, death, or 120 days of life, full enteral feeds were achieved by a smaller percentage of infants with SBS (66%) compared with infants with medical NEC (83%) and infants with no NEC or SBS (78%). Among the subset of 4193 infants who survived until discharge, the percentage of infants who had achieved full enteral feeds by discharge was higher in each group but still lowest among infants with SBS (SBS: 74%; surgical NEC without SBS: 87%; medical NEC: 98%; no NEC or SBS: 98%).

No significant differences were found between the case fatality rate during the initial hospitalization in the group of infants with SBS (21%), medical NEC (29%), and no NEC or SBS (23%). A smaller percentage of infants with SBS died during this hospitalization than did those with surgical NEC (55%). Mortality was higher after the initial discharge for infants with SBS (10%) compared with infants with medical NEC (1%) or no NEC or SBS (2%).

# Infants 1001 to 1500 g

In this group of 6659 infants, the prevalence of surgical SBS was 0.4% (4 per 1000). Infants with SBS were more likely to have received postnatal steroids for respiratory disease than those with no NEC or SBS (Table 3). They were also more likely to receive a diagnosis of early-and/or late-onset sepsis (71%). The presence of PDA was higher in infants with SBS compared with infants with medical NEC and those with no NEC or SBS. Severe IVH was diagnosed in a higher proportion among the SBS group (19%) compared with the no NEC or SBS group (5%). The proportion of infants who had SBS and achieved full enteral feeds by discharge, death, or 120 days (79%) was similar to that among infants with surgical NEC and without SBS (69%) but significantly less than the proportion of infants with medical NEC (96%) or with no NEC or SBS (94%; P < .001). Among the subset of 6365 infants who survived to discharge, the proportions who achieved full enteral feeds were higher (SBS: 83%; surgical NEC without SBS: 89%; medical NEC: 98%; no NEC or SBS: 98%). Significantly more infants with SBS died during the initial hospitalization (18%), compared with those with medical NEC (4%) and no NEC or SBS (3%); however, the case fatality rate was less than for infants with surgical NEC and without SBS (50%).

# **Follow-up Outcomes of ELBW Neonates**

Overall, 1422 (25%) of the 5657 ELBW infants died during the initial hospitalization and 83 (1.5%) died after hospital discharge, leaving 4152 infants eligible for the 18- to 22-month follow-up. Of those who were eligible for follow-up, 3674 (88.5%) infants completed the follow-up visit. Among the children who completed follow-up, 42 (1.1%) had surgical SBS. The racial distribution of infants with SBS was different from that in each of the other 3 groups (Table 4), and a greater proportion of survivors with SBS had a major congenital malformation than did those in the other groups (10% vs 2%–3%).

Children who had SBS and attended follow-up were significantly more likely to have received a diagnosis of sepsis (81%) during the initial hospitalization compared with children with medical NEC and no NEC or SBS (Table 5). They were also more likely than children with medical NEC and no NEC or SBS to be receiving nutrition by enteral tube and using high-calorie supplements at the time of the follow-up visit (Table 5). When compared with infants with no NEC or SBS, a higher percentage of those with SBS had a usual diet of liquids only at the follow-up visit (Fig 2).

Nearly half (46%) of the surviving children who attended follow-up had been rehospitalized at least once since initial discharge with a total of 3640 rehospitalizations reported. Children with SBS were more likely than those in each of the other groups to have been rehospitalized, and their number of rehospitalizations was also significantly higher. Significant differences were found for the reasons for readmissions between infants with SBS and those in each of the other groups. Infants with SBS were more likely to have been rehospitalized as a result of infection or growth and nutrition (Table 5).

The proportion of children with weight below the 10th percentile for gender and adjusted age at the time of the follow-up visit was between 43% and 52%, depending on the group (Table 5). Among the 42 children with SBS, 31 (74%) were <10th percentile on at least 1 of weight, length, and head circumference at 18 to 22 months' corrected age (14 of these 31 children were

<10th percentile on all 3 measurements). Children with SBS were more likely than children with medical NEC and those with neither NEC nor SBS to have length and head circumference below the 10th percentile. Their age-adjusted *z* scores were also lower on these measures (length and head circumference) compared with the other 2 groups (Fig 3).

After adjustment for maternal and neonatal variables that are known to affect the risk for growth failure, the results were similar for weight and length <10th percentile with no statistically significant differences for weight (Table 6). The risk for length <10th percentile was higher for children with SBS compared with those with medical NEC (adjusted RR: 1.58 [95% CI: 1.12–2.22]) and those with no NEC or SBS (adjusted RR: 1.49 [95% CI: 1.15–1.93]). A statistically significant difference in the risk for head circumference <10th percentile was no longer found between children with SBS and those with medical NEC but remained compared with those with no NEC or SBS (adjusted RR: 1.51 [95% CI: 1.08–2.11]).

#### DISCUSSION

This study reviewed the epidemiology of surgical SBS among VLBW and ELBW neonates who were born between January 1, 2002, and June 30, 2005, and cared for at the 16 NICHD Neonatal Research Network centers. It also evaluated the outcome of these infants during their initial hospitalization. ELBW neonates were evaluated at 18 to 22 months' corrected age to assess nutrition and growth outcomes. On the basis of these prospectively collected data, the incidence rate of surgical SBS during the study period among VLBW infants was 0.7% (7 per 1000) and for ELBW neonates was 1.1% (11 per 1000). To our knowledge, our data are derived from the largest cohort of neonates assessed for the incidence of SBS across centers in the United States. Although this incidence does not include term infants, it represents the population of neonates who are most at risk to develop this condition.

This relatively large cohort of infants was recruited over 42 months at these centers compared with the longer period of recruitment or smaller numbers reported by other studies.14,30,31 The benefit of reporting epidemiology and outcome of this disease process over a relatively short period is that it can be assumed that variables that affect the epidemiology (eg, preterm births, NEC) and outcome (eg, parenteral nutrition, infection, antibiotics, ventilation, surgical techniques) are relatively unchanged during the duration of the study. 10,32 This study identifies NEC as the most common cause of SBS in preterm infants, which confirms the similar findings in smaller, single-center studies. 10.32 It also supports the hypothesis that birth weight and GA are inversely related to the incidence of SBS. It is interesting that after controlling for NEC, there was no longer a significant association between birth weight and risk for SBS or between GA and risk for SBS. This suggests that NEC is a confounder; therefore, less mature and smaller neonates are more likely to develop NEC and hence SBS. There is also an apparent protective effect of SGA for developing SBS. This is the result of confounding by GA in our cohort. Because all of the infants had VLBW, those who were SGA tended to be infants who were born at the later GAs. These infants were at lower risk for NEC and therefore lower risk for SBS.

In a previous population-based study, low birth weight singleton infants who were black, male, or born to mothers who were younger than 17 had increased risk for NEC. In this cohort, male neonates were at increased risk to develop SBS, whereas race and age of the mother were not associated with an increased risk for SBS. Infants with SBS had more documented complications during their initial hospitalization compared with other groups, which is similar to morbidities reported in other studies. The higher use of postnatal steroids in patients who subsequently develop SBS is concerning; however, this result is confounded by GA because infants who develop NEC and subsequently SBS are likely to have a lower GA, are sicker and likely to have a longer period of mechanical ventilation, and thus will be treated with postnatal

steroids for respiratory disease. These infants were also likely to have more comorbidities as a result of their prematurity.

Sepsis rates were higher for all patients who had surgery, regardless of whether it led to SBS. It would be important to identify the specific organisms that are responsible for sepsis in these patients and to determine the potential roles of gut barrier dysfunction, immune dysfunction, and small bowel bacterial overgrowth in these infants. The rate of sepsis for these children is much higher than that in the other VLBW infants or than the rates of sepsis in previous studies of this population. This high rate of sepsis is concerning and needs additional evaluation. The loss of lymphoid tissue, which is necessary for maintaining mucosal stability and providing a barrier to bacterial translocation, may be a contributing factor for the increased rate of sepsis. Recurrent sepsis may be partly responsible for the increased cost of caring for VLBW infants with NEC, because it could account for increased length of hospitalization and recurrent need for central line replacement. <sup>13</sup>

The increased mortality in patients with surgical NEC and without SBS compared with the neonates with SBS (Fig 1) may be influenced by the inclusion of neonates with abdominal drains and NEC totalis in the surgical NEC without SBS group because these patients did not meet the clinical definition of SBS. However this increased mortality in the infants with surgical NEC and without SBS compared with those with SBS was present even after exclusion of children who died in the first 30 days of life.

Growth deficits (weight, length, and head circumference) that were identified in the patients with SBS are also concerning. Although this study does not identify the reasons for this poor growth, it can be assumed that patients are not receiving adequate nutrition from their current mode of feeding (eg, enteral feeds may be given at goal rates, but nutrients are lost via the stool). The type and amounts of minerals and micronutrients that are needed by these patients might not be adequately supplied by the enteral or parenteral nutrition received. Recurrent infection and respiratory disease also contribute to increased metabolic requirements and nutrient losses and could contribute to growth failure. Children with surgical SBS are more likely to be on tube feedings and receiving all of their nutrition as liquid formula at 18 to 22 months' corrected age. At this age, children are usually eating solid table foods. Although physicians and nutritionists might be recommending adequate calories on the basis of weight from the diet, it must be assumed that not all of the calories and nutrients are absorbed. Another possibility is that because of their increased metabolic needs, the calories provided are inadequate. Previous studies have shown adequate growth of children who had SBS and were receiving total parenteral nutrition.35,36 The NICHD Neonatal Research Network did not collect parenteral nutrition use data during the period under review. Our data do confirm the findings in smaller studies that showed poor growth of infants with surgical SBS.20 The urgency to decrease or discontinue parenteral nutrition in these infants in an effort to prevent liver disease might be a contributing factor to inadequate growth. The profoundly poor growth that was observed in the children who had NEC that was managed surgically (with or without SBS) might contribute to the poor neurodevelopment previously reported.5,37

The strengths of this study include the assessment of a multicenter cohort of VLBW infants, a relatively high follow-up rate of ELBW survivors, and standardized assessment methods to ensure reliable evaluations at all centers. Limitations of this study include that this is not a population-based cohort but one from 16 academic medical centers. This could limit the generalizability of the findings, because these infants might not be representative of similar birth weight infants who are treated by nonacademic centers in the United States; however, most patients with this level of acuity are transferred to academic medical centers for treatment. An additional weakness is that the specific nutritional strategies that were used to treat these patients, including the duration of parenteral nutrition and types of enteral formula, were not

standardized and were not assessed to identify how children with appropriate growth parameters at follow-up were treated. Such data are needed in the future to identify best practices that can be implemented by other centers in cohort studies.

#### CONCLUSIONS

This study provides new information regarding the incidence of SBS in VLBW and ELBW infants. Among the ELBW infants who had surgical SBS and were assessed at 18 to 22 months' corrected age, the nutritional parameters of length and head circumference were less than those obtained for infants with medical NEC and those with no NEC or SBS; however, growth parameters of infants with surgical NEC and without SBS were similar to those of infants with surgical SBS. Multiple factors, including recurrent sepsis, malabsorption, postnatal steroid use, and cardiac disease (PDA), may have contributed to this poor nutritional outcome. These results pose additional crucial questions regarding the treatment of these vulnerable children, including prevention of recurrent sepsis and improved intestinal health. To improve the nutrition and neurodevelopment of ELBW neonates with SBS, it will be necessary to design studies to identify optimal parenteral and enteral nutrition support regimens. Additional investigation is also necessary to determine how much catchup growth is possible and over what time frame in ELBW growth-restricted infants who receive optimized nutritional regimens.

What's Known on This Subject

SBS is a rare disease that has devastating outcomes in preterm infants.

What This Study Adds

This study revealed that children with postsurgical SBS had growth deficits at 18 to 22 months' corrected age. The incidence of the disease in a high-risk group is described along with short-term outcome and outcome at 18 to 22 months' corrected age.

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#### **Abbreviations**

SBS short bowel syndrome
NEC necrotizing enterocolitis
ELBW extremely low birth weight

GA gestational age

VLBW very low birth weight

NICHD Eunice Kennedy Shriver National Institute of Child Health and Human

Development

PDA patent ductus arteriosus

IVH intraventricular hemorrhage

BPD bronchopulmonary dysplasia

SGA small for gestational age

RR relative risk

CI confidence interval

## **REFERENCES**

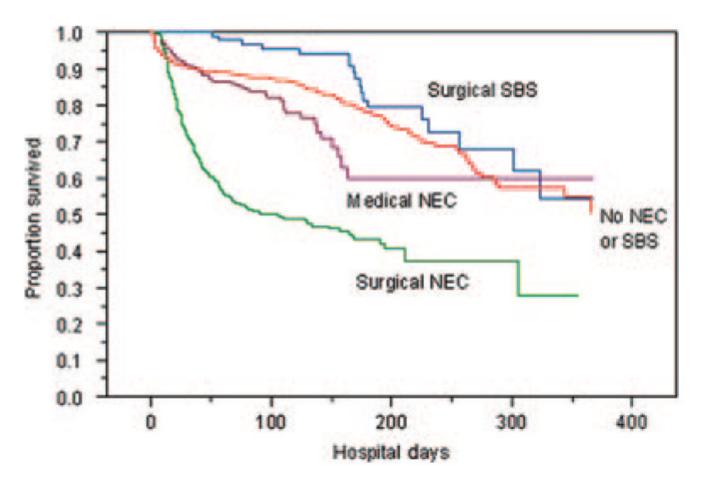
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**FIGURE 1.** Estimated time to in-hospital death for infants 401 to 1500 g birth weight. Differences in the survival distributions were significant (P < .001). Survival rates at 120 days were as follows: surgical SBS, 95% (n = 75); surgical NEC without SBS, 49% (n = 125); medical NEC, 78% (n = 68); no NEC or SBS, 86% (n = 903).

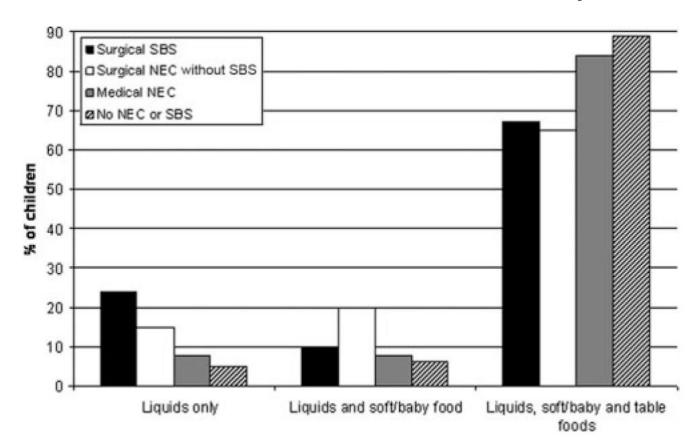


FIGURE 2. Types of food consumed by ELBW infants at 18 to 22 months' corrected age (n = 2159). There was a significant difference between the groups in the usual diet reported (P < .001).

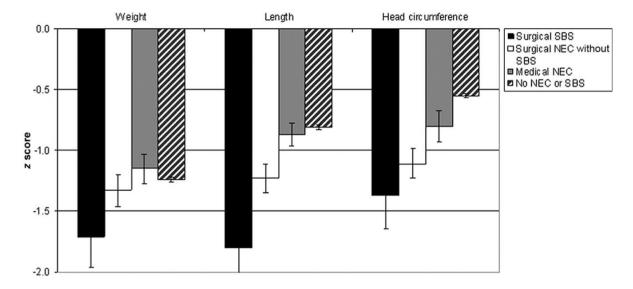


FIGURE 3.

z scores for anthropometric measurements obtained from ELBW infants at 18 to 22 months' corrected age (n weight = 3650, n length = 3636, n head circumference = 3645). Scores were significantly lower for infants with surgical SBS than for infants with medical NEC and no NEC or SBS on length (P < 0.01 for each) and head circumference (P < .05 and P < 0.01, respectively).

TABLE 1
Causes of Surgical SBS in VLBW Neonates: NICHD Neonatal Research Network 2002–2005

Disease	Frequency, %
NEC	96
Congenital defects (eg, intestinal atresia, gastroschisis)	2
Volvulus	2

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TABLE 2 Maternal and Neonatal Characteristics and the Risk for Surgical SBS Among Infants of 401 to 1500 g Birth Weight

Characteristic <sup>a</sup>	Total, N	Infants With Surgical SBS, n (%)	Unadjusted RR (95% CI) for Surgical SBS	P
Maternal				
Age, y				
≤19	1699	16 (0.9)	1.37 (0.80–2.35)	.278
≥20	10611	73 (0.7)	1.00	
Multiple gestation				
Yes	3199	19 (0.6)	0.77 (0.47–1.28)	.395
No	9117	70 (0.8)	1.00	
Antenatal steroids				
Yes	9437	69 (0.7)	1.09 (0.66–1.80)	.801
No	2825	19 (0.7)	1.00	
Neonatal				
$Inborn^b$				
No	1526	15 (1.0)	1.43 (0.82–2.49)	.197
Yes	10790	74 (0.7)	1.00	
Birth weight, g				
401–750	2639	27 (1.0)	2.74 (1.42–5.30)	<.001
751–1000	3018	34 (1.1)	3.02 (1.60-5.71)	
1001-1250	3175	15 (0.5)	1.27 (0.60–2.66)	
1251–1500	3484	13 (0.4)	1.00	
GA, wk				
<25	1577	14 (0.9)	2.02 (1.04–3.92)	.006
25–28	5502	52 (1.0)	2.15 (1.32–3.51)	
≥29	5234	23 (0.4)	1.00	
SGA at birth				
Yes	2584	11 (0.4)	0.53 (0.28-1.00)	.049
No	9729	78 (0.8)	1.00	
Gender				
Male	6289	57 (0.9)	1.71 (1.11–2.63)	.014
Female	6026	32 (0.5)	1.00	
Race				
Black	4579	33 (0.7)	1.12 (0.69–1.82)	.226
Hispanic	2156	22 (1.0)	1.59 (0.92–2.72)	
Other	598	2 (0.3)	0.52 (0.12–2.16)	
White	4975	32 (0.6)	1.00	
Major congenital anomaly				
Yes	497	6 (1.2)	1.72 (0.75–3.92)	.175
No	11819	83 (0.7)	1.00	

 $<sup>{\</sup>it a}^{\rm I} {\rm Information \ was \ missing \ for \ mother's \ age \ (6), \ antenatal \ steroids \ (54), \ GA \ (3), \ SGA \ (3), \ gender \ (1), \ and \ race \ (8).}$ 

 $<sup>^{\</sup>ensuremath{b}}\xspace$  Inborn is defined as an infant who is delivered at 1 of the NICHD neonatal research centers.

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TABLE 3

Neonatal Morbidities and Mortalities During Initial Hospitalization

Characteristic <sup>a</sup>	Surgical SBS $n/N$ (%)	Surgical NEC Without SBS $n/N$ (%)	Medical NEC $n/N$ (%)	No NEC or SBS $n/N$ (%)
Infants 401–1000 g birth weight	(n = 61)	(n = 328)	(n = 243)	(n = 5025)
Postnatal steroids	14/60 (23)	55/327 (17)	42/242 (17)	741/5011 (15)
PDA	38/61 (62)	193/328 (59)	129/243 (53)	2401/5019 (48) <sup>b</sup>
IVH grade 3 or 4	10/60 (17)	87/324 (27)	44/239 (18)	930/4819 (19)
PVL	2/60 (3)	$38/324 (12)^b$	16/240 (7)	245/4839 (5)
Shunt	1/61 (2)	15/326 (5)	8/243 (3)	114/5016 (2)
$Sepsis^{\mathcal{C}}$	53/61 (87)	208/327 (64) <sup>d</sup>	130/243 (54) <sup>d</sup>	1815/4999 (36) <sup>d</sup>
Episodes of late onset sepsis				
0	8/61 (13)	$126/327 (39)^d$	113/243 (47) <sup>d</sup>	3278/5007 (65) <sup>d</sup>
1	23/61 (38)	103/327 (31)	72/243 (30)	1208/5007 (24)
>2	30/61 (49)	98/327 (30)	58/243 (24)	521/5007 (10)
Full enteral feeds achieved by status $^{\it e}$	40/61 (66)	217/328 (66)	202/243 (83) <sup>f</sup>	3908/5023 (78) <sup>b</sup>
Full enteral feeds achieved among infants discharged to home?	32/43 (74)	$129/148~(87)^b$	166/169 (98) <sup>d</sup>	3748/3832 (98) <sup>d</sup>
Died before discharge	13/61 (21)	179/328 (55) <sup>d</sup>	70/243 (29)	1160/5025 (23)
Died after discharge <sup>h</sup>	5/48 (10)	6/149 (4)	2/173 (1)	$70/3865(2)^d$
Infants $1001-1500 \text{ g birth weight}^{i}$	(n = 28)	(n = 131)	(n = 159)	(n = 6341)
Postnatal steroids	3/28 (11)	8/129 (6)	7/159 (4)	$137/6332 (2)^f$
PDA	13/28 (46)	41/131 (31)	40/159 (25) <sup>b</sup>	1374/6336 (22)
IVH grade 3 or 4	5/27 (19)	11/117 (9)	15/146 (10)	292/5655 (5) <sup>f</sup>
PVL	2/27 (7)	5/119 (4)	$2/156(1)^b$	133/5752 (2)
Shunt	1/27 (4)	3/130 (2)	4/159 (3)	83/6333 (1)
$Sepsis^{\mathcal{C}}$	20/28 (71)	70/130 (54)	59/159 (37) <sup>d</sup>	$751/6330(12)^d$
Episodes of late-onset sepsis				
0	8/28 (29)	$60/130 (46)^b$	$101/159 (64)^d$	5649/6330 (89) <sup>d</sup>
1	11/28 (39)	52/130 (40)	48/159 (30)	578/6330 (9)

Characteristic <sup>a</sup>	Surgical SBS $n/N$ (%)	Surgical NEC Without Medical NEC No NEC or SBS SBS $n/N$ (%) $n/N$ (%) $n/N$ (%)	Medical NEC $n/N$ (%)	No NEC or SBS $n/N$ (%)
>2	9/28 (32)	18/130 (14)	10/159 (6)	103/6330 (2)
Full enteral feeds achieved by status $^{\it e}$	22/28 (79)	90/130 (69)	153/159 (96)	5981/6339 (94) <sup>d</sup>
Full enteral feeds achieved among infants discharged to home <sup>j</sup>	19/23 (83)	56/63 (89)	150/153 (98) <sup>d</sup>	5938/6125 (97) <sup>d</sup>
Died before discharge	5/28 (18)	66/131 (50) <sup>f</sup>	6/159 (4)	$192/6341 (3)^d$

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<sup>a</sup>Information was missing for postnatal steroids (17), PDA (6), IVH (215), periventricular leukomalacia (PVL; 194), shunt (11), sepsis (27), number of LOS episodes (19), and full enteral feeds (2).

 $^bP \leq .05$ 

 $^{\mathcal{C}}$  Culture-proven early- and/or late-onset sepsis treated with antibiotics for  $\geq \! 5.$ 

 $^d_{P\leq.001}$ 

 $^e$ Status is defined as hospital discharge, death, or 120 days of life.

 $f_{P\leq .01}$ , versus surgical SBS by the  $\chi^2$  test.

 $^{g}$ Among the subset of 4193 infants who were discharged to home, enteral feeds information was missing for 1.

 $^{h}$ Percentages are shown among the infants who survived to discharge (4235 infants overall).

information was missing for postnatal steroids (11), PDA (5), IVH (714), periventricular leukomalacia (PVL; 605), shunt (10), sepsis (12), number of LOS episodes (12), and full enteral feeds (3).

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 $^{J}$ Among the subset of 6365 infants who were discharged to home, enteral feeds information was missing for 1.

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**TABLE 4** 

Neonatal Characteristics Among Infants Who Weighed 401 to 1000 g at Birth and Attended Follow-up at 18 to 22 Months' Corrected Age

Characteristic	Surgical SBS $(n = 42)$ , $n/N$ (%)	Surgical NEC Without SBS $(n = 131)$ , $n/N$ (%)	Medical NEC $(n = 154)$ , $n/N$ (%)	No NEC or SBS $(n = 3347)$ , $n/N$ (%)
Inborn <sup>a</sup>	33/42 (79)	106/131 (81)	136/154 (88)	2990/3347 (89) <sup>b</sup>
Birth weight, g				
401–500	0/42 (0)	6/131 (5)	5/154 (3)	70/3347 (2)
501–750	15/42 (36)	59/131 (45)	62/154 (40)	1188/3347 (36)
751–1000	27/42 (64)	66/131 (50)	87/154 (57)	2089/3347 (62)
GA, wk				
<25	6/42 (14)	$51/131 (39)^{C}$	34/154 (22)	651/3346 (19)
25–28	30/42 (71)	74/131 (56)	103/154 (67)	2301/3346 (69)
>29	6/42 (14)	6/131 (5)	17/154 (11)	394/3346 (12)
SGA at birth	8/42 (19)	18/131 (14)	28/154 (18)	573/3346 (17)
Male	29/42 (69)	79/131 (60)	78/154 (51) <sup>b</sup>	1572/3347 (47) <sup>C</sup>
Race				
Black	13/42 (31)	54/131 (41) <sup>C</sup>	67/154 (44) <sup>d</sup>	1326/3344 (40) <sup>c</sup>
White	12/42 (29)	57/131 (44)	64/154 (42)	1236/3344 (37)
Hispanic	17/42 (40)	18/131 (14)	20/154 (13)	618/3344 (18)
Other	0/42 (0)	2/131 (2)	3/154 (2)	164/3344 (5)
Major congenital anomaly	4/42 (10)	$2/131(2)^b$	$3/154(2)^b$	89/3347 (3) <sup>C</sup>

 $<sup>^{\</sup>it a}$  Inbom is defined as an infant who is delivered at 1 of the NICHD neonatal research centers.

 $^b_{P \le .05}$ 

 $^{c}_{P\leq.01}$ 

 $^d$  P<:001 versus surgical SBS by the  $\chi^2$  test.

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Growth outcomes at follow-up

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**TABLE 5** 

Neonatal Morbidities and Growth Outcomes Among Infants Who Weighed 401 to 1000 g at Birth and Attended Follow-up at 18 to 22 Months' Corrected Age

Characteristic <sup>a</sup>	Surgical SBS $(n = 42)$ , $n/N$ (%)	Surgical NEC Without SBS $(n = 131)$ , $n/N$ (%)	Medical NEC $(n = 154)$ , $n/N$ (%)	No NEC or SBS $(n = 3347)$ , $n/N$ (%)
Before initial discharge				
Postnatal steroids	8/42 (19)	32/131 (24)	28/154 (18)	519/3346 (16)
PDA	23/42 (55)	70/131 (53)	75/154 (49)	1619/3347 (48)
IVH grade 3 or 4	7/41 (17)	34/131 (26)	20/154 (13)	421/3324 (13)
PVL	1/41 (2)	15/131 (11)	8/154 (5)	144/3337 (4)
Sepsis <sup>b</sup>	34/42 (81)	89/131 (68)	78/154 (51) <sup>C</sup>	$1229/3345 (37)^{C}$
Follow-up				
Shunt <sup>d</sup>	1/42 (2)	11/131 (8)	8/154 (5)	113/3347 (3)
Reanastomosis of large or small intestine $^{\theta}$	32/42 (76)	92/130 (71)	11/152 (7) <sup>c</sup>	84/3326 (3) <sup>C</sup>
Vitamin/mineral/nutrition supplements	18/42 (43)	42/130 (32)	43/152 (28)	872/3326 (26) <sup>f</sup>
High-calorie supplements	24/42 (57)	58/130 (45)	50/152 (33)8	774/3326 (23) <sup>c</sup>
Tube feeding	14/42 (33)	19/130 (15)8	$13/152 (9)^{C}$	184/3326 (6) <sup>c</sup>
No. of hospital readmissions				
0	9/42 (21)	54/130 (42) <i>f</i>	$71/152 (47)^f$	1826/3326 (55) <sup>c</sup>
<b>⊼</b> I	33/42 (79)	76/130 (58)	81/152 (53)	1500/3326 (45)
Reasons for readmissions				
Respiratory	16/78 (21)	$47/136 (35)^{C}$	$82/136 (60)^{C}$	$1326/2703 (49)^{C}$
CNS	1/78 (1)	12/136 (9)	2/136 (1)	123/2703 (5)
Surgery	(8) 8/9	36/136 (26)	23/136 (17)	520/2703 (19)
Infection	30/78 (38)	20/136 (15)	19/136 (14)	399/2703 (15)
Growth and nutrition	11/78 (14)	13/136 (10)	5/136 (4)	120/2703 (4)
Gastroesophageal reflux	0 (0)	4/136 (3)	0 (0)	15/2703 (<1)
Trauma	2/78 (3)	0 (0)	1/136 (1)	26/2703 (1)

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Characteristic <sup>a</sup>	Surgical SBS $(n = 42)$ , $n/N$ (%)	Surgical NEC Without Medical NEC No NEC or SBS SBS $(n=131)$ , $(n=154)$ , $(n=3347)$ , $n/N$ (%) $n/N$ (%)	Medical NEC $(n = 154)$ , $n/N$ (%)	No NEC or SBS $(n = 3347)$ , $n/N$ (%)
Weight <10th percentile	22/42 (52)	68/131 (52)	66/152 (43)	1605/3325 (48)
Length <10th percentile	24/42 (57)	65/131 (50)	48/152 (32)8	$1087/3311 (33)^{C}$
Head circumference <10th percentile	23/42 (55)	57/131 (44)	51/152 (34) <sup>f</sup>	875/3320 (26) <sup>c</sup>

PVL indicates periventricular leukomalacia; CNS, central nervous system.

anissing for postnatal steroids (1), IVH (24), PVL (11), sepsis (2), reanastomosis (24), nutrition supplements (24), caloric supplements (24), tube feeding (24), number of readmissions (24), reasons for readmissions (587; 16 in the SBS group, 45 in surgical NEC, 36 in medical NEC, 490 in no NEC or SBS), weight (24), length (38), and head circumference (29).

b Culture-proven early- and/or late-onset sepsis treated with antibiotics  $\geq \! 5$  days.

 $^{c}_{P\leq.001}$ 

 $^{\it d}$  Includes shunts placed before and after initial discharge.

 $^{\it e}$  Includes reanastomosis performed before and after initial discharge.

 $f_{P \le .05}$ 

 $^{g}P\leq .01$ , versus surgical SBS by the  $\chi^{2}$  test.

**TABLE 6** 

RR for Growth Outcomes for Infants With SBS Versus Infants Without SBS Among Infants Who Weighed 401 to 1000~g at Birth and Attended Follow-up at 18~to~22~Months Corrected Age

Outcome	Comparison	Adjusted RR (95% CI) <sup>a</sup>	P
Weight < 10th percentile	SBS vs surgical NEC	1.06 (0.78–1.44)	.724
	SBS vs medical NEC	1.21 (0.89–1.65)	.218
	SBS vs no NEC/SBS	1.06 (0.81-1.37)	.686
Length < 10th percentile	SBS vs surgical NEC	1.02 (0.75–1.39)	.902
	SBS vs medical NEC	1.58 (1.12–2.22)	.009
	SBS vs no NEC/SBS	1.49 (1.15–1.93)	.003
Head circumference <	SBS vs surgical NEC	1.11 (0.75–1.65)	.585
10th percentile	SBS vs medical NEC	1.26 (0.85–1.86)	.244
	SBS vs no NEC/SBS	1.51 (1.08–2.11)	.016

<sup>&</sup>lt;sup>a</sup>RRs from a modified Poisson regression model that included study center, SBS group, birth weight, GA, gender, race (nonwhite/white), major congenital anomaly, multiple birth, caregiver's education (HS degree or not), IVH grade 3 or 4, periventricular leukomalacia (PVL), PDA postnatal steroid use, antenatal steroid use, BPD, and shunt.