Clinical Predictors and Institutional Variation in Home Oxygen Use in Preterm Infants

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Objective To assess home oxygen use in preterm infants, identify risk factors predicting home oxygen use, and quantify the extent of institutional variation in home oxygen use across neonatal intensive care units.

Study design We conducted a retrospective cohort analysis of surviving infants of 23- to 31-week gestational age discharged home in 2009, with de-identified electronic medical record information from the Pediatrix Clinical Data Warehouse. Mixed-effects logistic regression quantified clinical risk factors and institutional variation affecting home oxygen use.

Results A total of 8167 infants were identified. Home oxygen use varied by gestational age, from 59% of infants 23 to 24 weeks gestational age to 7% of infants 29 to 31 weeks gestational age. Other risk factors included small for gestational age, congenital anomalies, mechanical ventilation in the first 72 hours, fraction of inhaled oxygen >0.4 in the first 72 hours, and patent ductus arteriosus. After adjusting for clinical risk factors, there was still a 4- to 5-fold difference in institutions' odds of home oxygen use.

Conclusions Home oxygen use was common in infants of earlier gestational ages and infants with more severe respiratory illness. Institutional variation accounted for 4- to 5-fold variation in home oxygen use. Families should be counseled about the likelihood of home oxygen use, and prospective research must identify optimal treatment strategies for high-risk infants. *(J Pediatr 2012;160:232-8)*.

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Premature infants have high rates of medical service use after neonatal intensive care unit (NICU) discharge.[1,2] One population of preterm infants with particularly high need for post-discharge services are patients with bronchopulmonary dysplasia (BPD), which affects 25% to 35% of infants with birth weights <1500 g.[1,3]

Home oxygen therapy is an option to facilitate discharge of infants with BPD as an alternative to prolonged hospitalization. Published guidelines for home oxygen use generally recommend consideration of home oxygen for infants with oxygen saturations <92% to 95% in room air.[4-6] Despite these consensus statements, however, decision-making about the use of this therapy is not straight-forward. Observational studies conducted before widespread surfactant use found that home oxygen therapy for infants with BPD improved growth, decreased work of breathing, and decreased incidence of sudden infant death syndrome.[7-9] The Benefits of Oxygen Saturation Targeting (BOOST) and Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (SUPPORT) trials, which compared randomized oxygen saturation targets for infants in the NICU, did not find improved growth at higher oxygen saturations; the Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity trial additionally found an increased risk of pneumonia and chronic lung disease-related events in infants with higher oxygen saturation targets.[10,11] The Supplemental Therapeutic Oxygen for Prethresold Retinopathy for Prematurity (SUPPORT) trial confirmed an increased risk of retinopathy of prematurity at higher oxygen saturation targets, but an increased mortality risk at lower oxygen saturation targets.[12] No clinical trial to date has specifically assessed the efficacy of home oxygen therapy on growth and neurodevelopment in infants with BPD.

Consistent with the inherent dilemmas in prescribing oxygen therapy, there is a lack of consensus in the United States about home oxygen use. Ellsbury et al surveyed 181 participants in the Vermont Oxford Network and found pulse oximetry criteria for initiating home oxygen therapy ranging from 84% to 96%; 51% of respondents additionally reported considering home oxygen for infants with normal saturations but tachypnea or poor growth.[13]

It is important to understand which patients are likely to receive home oxygen on discharge, to prepare families before discharge and structure appropriate follow-up.[14] Additionally, as quality improvement in neonatal intensive care strives to optimize outcomes, an assessment of practice variation in the United States may spur more comprehensive research on best practices for NICU graduates. Therefore, the goals of this study were: (1) to review the rates of home oxygen use in a large

BPD	Bronchopulmonary dysplasia
FiO_2	Fraction of inhaled oxygen
NICU	Neonatal intensive care unit
PDA	Patent ductus arteriosus

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cohort of preterm infants; (2) to identify clinical risk factors predicting home oxygen use in preterm infants; and (3) to determine the extent of institutional variation in home oxygen use in NICUs across the United States.

Methods

Data were obtained from the Pediatrix Clinical Data Warehouse, which maintains de-identified electronic medical record information including details of admission, clinical course, and discharge on all patients cared for in 280 NICUs in 33 states. The Pediatrix Medical Group cares for 15% to 20% of NICU admissions in the United States across a wide range of sizes and types of NICUs. Since 2005, the use of pull-down menus for automated data extraction has enabled more consistent evaluation of detailed information such as home oxygen use.[15]

This study was a retrospective cohort analysis of all surviving infants 23- to 31-weeks gestation who were discharged home from a Pediatrix center in 2009. Patients who were transferred before discharge were excluded. The primary outcome was home oxygen support; infants were only recorded as discharged home on oxygen when both the home oxygen variable and the respiratory support on the last day of hospitalization were consistent.

Gestational ages were combined in groups: 23 to 24 weeks, 25 to 26 weeks, 27 to 28 weeks, and 29 to 31 weeks. Birth weight was recorded as a continuous variable; small for gestational age was defined as birth weight <10th percentile for gestational age on the basis of published growth charts.[16] Initial respiratory illness severity was captured by recording the maximum ventilatory support required in the first 3 days of life (ranging from room air to mechanical ventilation) and the maximum fraction of inhaled oxygen (FiO_2) required in the first 3 days of life (recorded continuously from 0.21-1.00). Length of stay was reported as corrected age at discharge (gestational age at birth + days-hospitalized/7). BPD was defined as supplemental oxygen at 36 weeks' corrected age (very few infants were discharged on oxygen before 36 weeks' corrected age or were discharged home on oxygen despite no respiratory support at 36 weeks' corrected age; these infants were eventually excluded from analysis).[17] The physiologic test for BPD was not used for this analysis.[18] At 36 weeks' corrected age, infants without an oxygen requirement who still received some degree of non-invasive respiratory support, such as flow via nasal cannula without supplemental oxygen, were not defined as having BPD, but were categorized as requiring non-oxygen respiratory support. Additional variables included maternal demographics, perinatal information, and clinical morbidities. Treating hospitals were assigned a random identification number to maintain appropriate de-identification; hospitals' altitude was recorded as a continuous variable.

Data Analysis

Rates of missing demographic and morbidity data were assessed (infants missing data were retained in the dataset). Home oxygen use was calculated by gestational age group and respiratory status at 36 weeks corrected age (all infants, infants requiring non-oxygen respiratory support, and infants with BPD), comparing differences in proportions by using Mantel-Haenszel χ^2 tests for trend.

To quantify clinical risk factors and institutional variation in home oxygen use, two forward-stepwise mixed-effects logistic regression models were developed. In these models, clinical risk factors were treated as fixed effects and each hospital as a random intercept. This approach allowed us to interpret the predictors from the mixed-effects logistic regression comparing infants within a given facility and also allowed us to quantify the extent of institutional variation after adjusting for infants' clinical risk factors and center altitude. We developed two models. First, we identified early clinical risk factors predicting home oxygen use in all infants; second, we identified predictors of home oxygen use in the subset of infants with BPD.

To assess the relationship between institutional practice variation and home oxygen use, we calculated the proportion of home oxygen use for each institution discharging at least 20 patients. Similarly, we calculated each institution's proportion of home oxygen use in the subgroup of infants with BPD, including centers discharging at least 10 infants with BPD. To adjust institutional variation for differences in patient mix, we used the mixed-effects logistic regression models, converting the SD of the log-odds of random intercepts to the odds scale, to interpret this result as the degree to which facility effects increase or decrease the odds of home oxygen use with individual clinical risk factors such as gestational age and initial respiratory illness severity. Finally, we divided centers in groups on the basis of their rate of home oxygen in the BPD population and used a linear regression model with clustered SEs to assess the impact of high-, medium-, and low-oxygen-use centers on corrected age at discharge after adjusting for clinical risk factors.

This study was approved by the Medical College of Wisconsin institutional review board; the Clinical Data Warehouse was approved for research use by the Western institutional review board.

Results

Infants (n = 8167) were identified who were born between 23 and 31 weeks' gestation, survived to NICU discharge, and were discharged home from the admitting institution in 2009; they were cared for in 201 hospitals in 33 states. No infants were missing information on the primary outcome of home oxygen use.

A description of the 8167 infants is shown in **Table I**. Rates of BPD ranged from 71% of surviving 23- to 24-week gestational age infants to 11% of surviving 29- to 31-week gestational age infants. Data were missing in <3% of the study population, except as indicated in the **Table I**. Eighteen infants were discharged home on oxygen before 36 weeks corrected age; 41 infants were reported as having no respiratory support requirement at 36 weeks corrected age, but were discharged home on oxygen; 227 infants had missing or inconsistent information about corrected age at