Rates of Bronchopulmonary Dysplasia Following Implementation of a Novel Prevention Bundle

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Abstract

IMPORTANCE Bronchopulmonary dysplasia (BPD) rates in the United States remain high and have changed little in the last decade.

OBJECTIVE To develop a consistent BPD prevention bundle in a systematic approach to decrease BPD.

DESIGN, SETTING, AND PARTICIPANTS This quality improvement study included 484 infants with birth weights from 501 to 1500 g admitted to a level 3 neonatal intensive care unit in the Kaiser Permanente Southern California system from 2009 through 2019. The study period was divided into 3 periods: 1, baseline (2009); 2, initial changes based on ongoing cycles of Plan-Do-Study-Act (2010-2014); and 3, full implementation of successive Plan-Do-Study-Act results (2015-2019).

INTERVENTIONS A BPD prevention system of care bundle evolved with a shared mental model that BPD is avoidable.

MAIN OUTCOMES AND MEASURES The primary outcome was BPD in infants with less than 33 weeks' gestational age (hereafter referred to as BPD<33). Other measures included adjusted BPD<33, BPD severity grade, and adjusted median postmenstrual age (PMA) at hospital discharge. Balancing measures were adjusted mortality and adjusted mortality or specified morbidities.

RESULTS The study population included 484 infants with a mean (SD) birth weight of 1070 (277) g; a mean (SD) gestational age of 28.6 (2.9) weeks; 252 female infants (52.1%); and 61 Black infants (12.6%). During the 3 study periods, BPD<33 decreased from 9 of 29 patients (31.0%) to 3 of 184 patients (1.6%) (P < .001 for trend); special cause variation was observed. The standardized morbidity ratio for the adjusted BPD<33 decreased from 1.2 (95% CI, 0.7-1.9) in 2009 to 0.4 (95% CI, 0.2-0.8) in 2019. The rates of combined grades 1, 2, and 3 BPD decreased from 7 of 29 patients (24.1%) to 17 of 183 patients (9.3%) (P < .008 for trend). Grade 2 BPD rates decreased from 3 of 29 patients (10.3%) to 5 of 183 patients (2.7%) (P = .02 for trend). Adjusted median PMA at home discharge decreased by 2 weeks and adjusted mortality was unchanged, whereas adjusted mortality or specified morbidities decreased significantly.

CONCLUSIONS AND RELEVANCE A sustained low rate of BPD was observed in infants after the implementation of a detailed BPD system of care.

Key Points

Question Is it possible to develop a consistent prevention bundle to decrease rates of bronchopulmonary dysplasia (BPD)?

Findings In this quality improvement study evaluating 484 infants with birth weights 501 to 1500 g, BPD in infants with less than 33 weeks' gestational age decreased from 31% to 2%, and the adjusted standardized morbidity ratio among these infants decreased from 1.2 in 2009 to 0.4 in 2019. Adjusted median postmenstrual age at home discharge decreased by 2 weeks and adjusted mortality was unchanged, whereas adjusted mortality or specified morbidities decreased significantly.

Meaning A sustained low rate of BPD was observed after the implementation of a detailed BPD system of care.
Introduction

Bronchopulmonary dysplasia (BPD) or chronic lung disease is a common, serious complication of prematurity. The incidence of BPD remains high and has been mostly unchanged during the last decade, ranging from 20% in California to 28% across the US, and 42% among infants less than 28 weeks' gestation.

Various interventions for the prevention of BPD have been studied although their individual effects on BPD rates have either been modest or have influenced only short-term benefits. Significant variation in risk-adjusted rates of BPD holds out the hope that there are existing care practice interventions that, if identified and propagated, could significantly decrease BPD rates. Lee et al estimated that achievement of top quartile rates of BPD in California would decrease the rate of BPD by 25%.

Some centers have reported consistently low and sustained rates of BPD but efforts to identify key practice differences or to propagate their success through replicating some of their practices, such as bubble continuous positive airway pressure (CPAP), or efforts to avoid intubation have yielded little success, raising the concern that propagation of local successes or BPD prevention may not be possible.

The limited effect of individual interventions, wide variation in outcomes, and difficulty in propagating individual centers' success suggest that BPD prevention is a system problem involving many types of management decisions and many individuals. The system has a better chance to succeed if the mental model of the care team is shared (ie, a concept based on a finding by Wu that patient safety may be improved through a consistent shared vision and implementation of care), if the management decision points are identified, and if execution of these management decisions is more consistent. The present report describes a single-center quality improvement initiative to develop a BPD prevention system of care that is associated with a decrease in rates of BPD.

Methods

Our Context and Study Population

Kaiser Permanente Panorama City (KPPC) has a 24-bed neonatal intensive care unit (NICU) and is part of Kaiser Permanente Southern California (KPSC), an integrated health care system with 4.7 million members and approximately 41,000 yearly births during the study period. All KPSC medical records are in an electronic system. Our NICU at KPPC has been a nonsurgical level 3 NICU since mid-2008 and became certified as a California Children's Services community NICU in 2013. The annual local and referral birth population is approximately 4000 patients, including 300 NICU admissions of which approximately 45 neonates have birth weights (BWs) of 501 to 1500 g. Patients requiring surgical interventions are referred to KPSC surgical NICUs both prenatally and postnatally. Infants are transferred to lower acuity KPSC NICUs when they reach postmenstrual age (PMA) older than 32 weeks, require lower acuity respiratory support, such as high-flow nasal cannula at a fraction of inspired oxygen of 0.21, and are tolerating full feedings. Our team of 6 board-certified neonatologists (including all authors) provides in-house coverage 24 hours a day, 7 days a week. Daytime coverage is augmented by 3 board-certified pediatricians functioning as neonatal hospitalists. The same team of physicians provides in-house coverage 24 hours a day, 7 days a week at Kaiser Permanente Woodland Hills, the level 2 NICU where most of our patients with nonacute conditions are transported. This study followed the Standards for Quality Improvement Reporting Excellence (SQUIRE) reporting guideline for quality improvement studies. This study was approved by the KPSC Regional institutional review board with exemption of the requirement to obtain informed consent because the data were deidentified. No one received compensation or was offered any incentive for participating in this study.

This study was started as a response to an increase in rates of BPD in 2009, the first full year after moving our level 3 NICU to a different medical center with associated changes in physician,
nursing, and respiratory therapist staff. The quality improvement team included neonatologists (all authors), respiratory therapists, NICU registered nurses, and a multidisciplinary team. The aim of the study was to decrease BPD rates in our NICU through Plan-Do-Study-Act cycles between 2010 and 2019. All inborn and outborn NICU admissions with BWs of 501 to 1500 g from 2009 to 2019 were included in the study.

**Process**

In 2009, the quality improvement team at our NICU agreed that our increased BPD rate and inconsistencies in pulmonary management had to be improved. We agreed to work together to increase the consistency and quality of respiratory care–related practices. The rate of BPD was the major outcome measure. Our quality improvement team’s initial assessment was that a relative lack of a shared mental model for managing respiratory care and the related inconsistency of care were important factors associated with our worsening BPD rates.

**Key Drivers**

During the study period, we developed a list of key drivers for BPD prevention (Table 1). The key drivers included (1) a shared mental model that prevention of BPD is possible; (2) prevention vs rescue therapy to support postnatal lung growth and to minimize the inflammatory cascade and

**Table 1. Key Drivers**

| Driver | Initial changes period response (2010-2014) | Full implementation period response (2015-2019) |
|--------|---------------------------------------------|-----------------------------------------------|
| Shared mental model that BPD is avoidable but requires aggressive preventative care | Discussion on daily rounds of compliance with protocol for each infant | Written agreements on respiratory care specifics |
| Consistent management practices optimize the chance for success | Discussion at weekly neonatology meetings of challenges and opportunities regarding care agreements | |
| Postnatal age- and PMA-specific interventions | Written, more explicit “No BPD Roadmap” implemented especially for gestational age less than 28 wk and birth weight less than 1000 g, including high-frequency oscillatory ventilation as primary invasive ventilation, noninvasive ventilation as NAVA until 32 wk, human milk for both base and fortifiers | |
| | Expanded criteria for surfactant use | |
| | Observation rather than treatment of PDA | |
| | Avoid pharmacologic treatment of reflux | |

Abbreviations: BPD, bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; NAVA, neurally adjusted ventilatory assist; PDA, patent ductus arteriosus; PMA, postmenstrual age.

* Gestational age less than 28 weeks or birth weight less than 1000 g.
oxygen toxicity that lead to BPD; (3) consistent management across the team to minimize variations in care; and (4) management decision points based on developmental stages of the lung.

**Implementation**

The evolution of our care practices in response to the key drivers is given in Table 1. After a 1-year baseline period (2009), we entered a period of initial changes involving a range of respiratory and nonrespiratory interventions. The implementation included discussion of our system of care for each infant at daily sign-out rounds and debriefs on the process at weekly neonatology meetings. Changes in care practices were made if a new consensus was reached. Compliance with the consensus guideline was discussed at daily sign-out rounds and debriefs. Initial consensus practices included volume-targeted or high-frequency ventilation modalities for intubated patients, group decisions regarding rescue care with the administration of dexamethasone, postextubation pathway, prophylactic caffeine, vitamin A, and surfactant therapy.

By the full implementation period, the group’s belief in the value of the shared mental model decision point–specific consensus had grown such that more detailed respiratory and nonrespiratory management protocols were adopted and circulated as written protocols addressing postnatal and postconceptional age-specific respiratory management. Preventing BPD was envisioned as protecting against lung injury and supporting lung growth. Emphasis was placed on proactive intervention to prevent deterioration rather delaying intervention until deterioration occurred and rescue care was required. High expectations were embraced for acceptable respiratory status with an emphasis on full alveolar recruitment. The system of care in the full implementation period is described in eFigures 1, 2, and 3 and eAppendix 2 in the Supplement. We appreciate that studies of these interventions have shown variable benefit individually. Our intent was to assess the net association of their adoption in successive Plan-Do-Study-Act cycles with the outcome.

**Source of Data for Analysis**

Data sources included KPPC data that were submitted to the Vermont Oxford Network (VON), California Perinatal Quality Care Collaborative (CPQCC), and KPSC electronic medical records. Unless otherwise indicated, the data were obtained from VON.

**Data Elements for Analysis**

Maternal and infant demographic characteristics and respiratory care practice measures available in the VON registry for the KPPC NICU were collected for each period. The primary outcome was “BPD <33” as defined by VON to be infants younger than 33 weeks’ gestational age (GA) at birth and at our center on supplemental oxygen at 36 weeks’ PMA or, if discharged home before 36 weeks’ PMA, on supplemental oxygen at discharge.

Secondary BPD outcomes included the following. To address potential case mix bias, we reported our center’s unadjusted BPD rates for 2 subgroups composed of infants with GA less than 28 weeks or less than 26 weeks and reported our center’s adjusted BPD <33 as calculated by VON. To address potential BPD case definition bias, we used the following grading system that uses level of respiratory support administered at 36 weeks’ PMA regardless of prior or current oxygen therapy to define disease severity in infants of GA less than 33 weeks: grade 1, nasal cannula airflow 2 liters per minute or lower; grade 2, nasal cannula airflow higher than 2 liters per minute or noninvasive positive airway pressure; and grade 3, invasive mechanical ventilation. These diagnostic criteria are reported to best predict death or respiratory morbidity through 18 to 26 months’ corrected age. We also evaluated the use of supplemental oxygen or tracheostomy at discharge to home.

The NICU length of stay as another measure of BPD severity was presented as risk-adjusted PMA at discharge for our center reported by CPQCC (data accessed November 2020) for patients with 22 to 29 weeks’ GA or BW 401 to 1500 g. This population is similar but not identical to the population with BW 501 to 1500 g. The metric adjusts for the following covariates: GA, small for GA, malformation, multiple gestation, 5-minute Apgar score, sex, outborn, and no prenatal care.
Balancing measures were VON measures of adjusted mortality and adjusted mortality or specified morbidities (eAppendix 1 in the Supplement).

**Statistical Analysis**

Statistical process control charts (QI Macros, KnowWare International Inc) were used to display and analyze data for unadjusted BPD <33 over time. Special cause variation—an unexpected variation that results from unusual occurrences—was based on Montgomery rules, and the results are presented as a p-chart (Figure 1).

Adjusted rates of BPD <33, mortality, and mortality or specified morbidities were obtained from VON reported as a shrunken standardized morbidity ratio (SMR), which is the term VON uses to describe the risk-adjusted outcomes calculated for each hospital in the registry. The SMR includes patient-level adjustments for selected risk factors: GA, birth weight, small for GA, severity of congenital anomaly, multiple gestation, 1-minute Apgar score, sex, vaginal delivery, birth location (inborn or outborn), and altitude of center.

Unadjusted demographic characteristics, care practice, and outcome measures between the 3 study periods were compared by the χ² test or the Fischer exact test for categorical variables and by the Kruskal-Wallis test for continuous variables. Trends across the study periods were evaluated by the Cochran-Armitage test if the overall test was significant. A 2-sided P < .05 was considered statistically significant. Statistical analyses were performed using SAS, version 9.4 software (SAS Institute Inc).

**Results**

**Demographic Characteristics**

There were 484 infants with BW of 501 to 1500 g admitted during the study period, of whom 435 (89.9%) were inborn, 232 were male (47.9%), 252 were female (52.1%), and 61 were Black (12.6%) infants (Table 2). The mean (SD) BW of the population was 1070 (277) g, and the mean (SD) GA was 28.6 (2.9) weeks, with 190 infants (39%) born at GA less than 28 weeks. During the study period, the rates of GA less than 28 weeks and GA less than 26 weeks increased, rates of Black patients decreased, and 476 of 484 mothers (98.3%) received prenatal care.

**Care Practice Measures**

During the study period, care practice measures (process measures) that increased significantly included high-frequency ventilation and noninvasive ventilation (Table 2). Process measures that decreased significantly included indomethacin administration and transfers. Acute transfers did not
| Measure | No./total No. (%) | All years (2009-2019) | Baseline (2009) | Initial changes (2010-2014) | Final implementation (2015-2019) | \( \chi^2 \) or Fisher exact test* | Cochran-Armitage test |
|---------|------------------|-----------------------|-----------------|-----------------------------|-------------------------------|--------------------------|---------------------|
| **Demographic characteristics** | | | | | | | |
| Births and admissions, No. | 484 | 45 | 216 | 223 | | | |
| Birth weight, mean (SD), g | 1069.93 (277.39) | 1069.93 (277.39) | 1095.99 (276.22) | 1045.89 (281.06) | .17b | NA |
| GA, mean (SD), wk | 28.61 (2.88) | 28.75 (2.33) | 28.88 (2.73) | 28.35 (3.04) | .18 b | NA |
| GA <33 wk | 449/484 (92.8) | 43/45 (95.6) | 201/216 (93.1) | 205/223 (91.9) | .76 a | NA |
| GA <28 wk | 190/484 (39.3) | 14/45 (31.1) | 75/216 (34.7) | 101/223 (45.3) | .04* | .01 |
| GA <26 wk | 100/484 (20.7) | 5/45 (11.1) | 37/216 (17.1) | 58/223 (26.0) | .02* | .005 |
| SGA | 83/484 (17.1) | 8/45 (17.8) | 33/216 (15.3) | 42/223 (18.8) | .61 NA |
| Male | 232/484 (47.9) | 24/45 (53.3) | 104/216 (48.1) | 104/223 (46.6) | .72 NA |
| Female | 252/484 (52.1) | 21/45 (46.7) | 112/216 (51.9) | 119/223 (53.4) | | |
| Multiple gestation | 157/484 (32.4) | 16/45 (35.6) | 36/216 (16.9) | 75/223 (33.6) | .71 NA |
| **Race/ethnicity** | | | | | | | |
| Asian | 51/484 (10.5) | 5/45 (11.1) | 20/216 (9.3) | 26/223 (11.7) | .71 NA |
| Black | 61/484 (12.6) | 10/45 (22.2) | 30/216 (13.9) | 21/223 (9.4) | .05 a | .02 |
| Hispanic | 216/484 (44.6) | 18/45 (40.0) | 98/216 (45.4) | 100/223 (44.8) | .80 NA |
| Native American | 0/484 (0) | 0/45 | 0/216 | 0/223 | NA |
| Other | 12/484 (2.5) | 0/45 | 8/216 (3.7) | 4/223 (1.8) | .33* NA |
| White | 144/484 (29.8) | 12/45 (26.7) | 60/216 (27.8) | 72/223 (32.3) | .52 NA |
| **Prenatal care** | | | | | | | |
| Inborn | 435/484 (89.9) | 42/45 (93.3) | 197/216 (91.2) | 196/223 (87.9) | .43* NA |
| Cesarean delivery | 339/484 (70.0) | 32/45 (71.1) | 155/216 (71.8) | 152/223 (68.2) | .70 NA |
| **1-min Apgar score, mean (SD)** | | | | | | | |
| 6.16 (2.24) | 6.27 (2.24) | 6.12 (2.25) | 6.18 (2.27) | .97b NA |
| **5-min Apgar score, mean (SD)** | | | | | | | |
| 7.73 (2.01) | 7.73 (2.19) | 7.61 (2.2) | 7.83 (1.78) | .66* NA |
| Major anomaly | 16/484 (3.3) | 1/45 (2.2) | 6/216 (2.8) | 9/223 (4.0) | .70* NA |
| **Care practices** | | | | | | | |
| Antenatal steroid | 444/484 (91.7) | 42/45 (93.3) | 199/216 (92.1) | 203/223 (91.0) | .88* NA |
| Initial resuscitation with ETT ventilation | 325/484 (67.1) | 35/45 (77.8) | 142/216 (65.7) | 148/223 (66.4) | .32 NA |
| Initial resuscitation with surfactant | 246/482 (51.0) | 25/45 (55.6) | 85/214 (39.7) | 136/223 (61.0) | <.001 NA |
| High-flow nasal cannula after initial resuscitation | 350/465 (75.3) | 31/45 (68.9) | 155/204 (76.0) | 164/216 (75.9) | .53* NA |
| Nasal CPAP after initial resuscitation | 369/465 (79.4) | 25/45 (55.6) | 158/204 (77.5) | 186/216 (86.1) | <.001 <.001 |
| Nasal ventilation after initial resuscitation | 296/465 (63.7) | 16/45 (35.6) | 106/204 (52.0) | 174/216 (80.6) | <.001 <.001 |
| Conventional ventilation after initial resuscitation | 360/465 (77.4) | 37/45 (82.2) | 163/204 (79.9) | 160/216 (74.1) | .27 NA |
| High-frequency ventilation after initial resuscitation | 155/465 (33.3) | 16/45 (35.6) | 29/204 (14.2) | 110/216 (50.9) | <.001 NA |
| Surfactant at any time | 364/484 (75.2) | 37/45 (82.2) | 158/216 (73.1) | 169/223 (75.8) | .46 NA |
| Steroids for BPD at any site | 58/464 (12.5) | 10/45 (22.2) | 21/203 (10.3) | 27/216 (12.5) | .08 NA |
| Nitric oxide | 6/484 (1.2) | 0/45 (0) | 2/216 (0.9) | 4/223 (1.8) | .82* NA |
| Indomethacin for any reason | 86/465 (18.5) | 16/45 (35.6) | 63/204 (30.9) | 7/216 (3.2) | <.001 <.001 |
| Transferred to another facility | 118/465 (25.4) | 25/45 (55.6) | 46/204 (22.5) | 47/216 (21.8) | <.001 <.001 |
| Acute transfer | 38/465 (8.2) | 5/45 (11.1) | 19/204 (9.3) | 14/216 (6.5) | .51 NA |
| Nonacute transfer to Woodland Hills | 51/465 (11.0) | 11/45 (24.4) | 15/204 (7.4) | 25/216 (11.6) | <.001 NA |
| Nonacute transfer to other site | 29/465 (6.2) | 9/45 (20.0) | 12/204 (5.9) | 8/216 (3.7) | <.003 NA |
| **GA <33 wk excluded from BPD <33 measure** | | | | | | | |
| Died before 36 0/7 wk PMA including DR deaths | 47/449 (10.5) | 5/43 (11.6) | 22/201 (10.9) | 20/205 (9.8) | .88 NA |
| Alive but transferred to centers with data not linked by VON to our center | 24/402 (6.0) | 9/38 (23.7) | 14/179 (7.8) | 1/185 (0.5) | <.001* <.001 |

(continued)
changes significantly, with 38 of 465 patients (8.2%) throughout the study. Nonacute transfers to the Woodland Hills level 2 NICU included a total of 51 of 465 patients (11.0%). Nonacute transfers to other centers decreased from 9 of 45 patients (20.0%) to 18 of 216 patients (3.7%); this decrease was associated with California Children’s Services certification of the KPPC NICU. Process measures that did not change significantly included patent ductus arteriosus (PDA) ligation (11 of 484 patients [2.3%]) and administration of antenatal steroid (444 of 484 patients [91.7%]), surfactant (364 of 484 patients [75.2%]), postnatal steroid for BPD (58 of 464 patients [12.5%]), or nitric oxide (6 of 484 patients [1.2%]).

Outcomes

Of the study population of 484 patients, 35 were GA 33 weeks or older and were excluded for the determination of BPD <33. There were 449 patients with GA less than 33 weeks, of whom 47 died before 36 weeks’ PMA (Table 2). Most of those deaths occurred in extremely preterm infants born at lower or lowest perivable GA range, with more than half of early deaths occurring in the delivery room or within the first hour of NICU admission. The BPD <33 status was missing or not included in the VON BPD <33 metric for 24 patients. Of the remaining 378 patients, the rate of BPD <33
decreased from 9 of 29 patients (31.0%) to 3 of 184 patients (1.6%) during the 3 study periods (P < .001), and special cause variation was shown by statistical process control methods (Figure 1). The rate of BPD for patients of GA less than 28 weeks decreased from 4 of 8 patients (50.0%) to 1 of 81 patients (1.2%) (P < .001). The rate of BPD for patients of GA less than 26 weeks was 1 of 39 patients (2.6%) in the final implementation period, but the decreasing trend was not significant as assessed by the Cochran-Armitage test. The SMR for the adjusted BPD <33 decreased from 1.2 (95% CI, 0.7-1.9) in the baseline period to 0.4 (95% CI, 0.2-0.8) in 2019 at the end of the full implementation period with a combined rate of 0.2 (95% CI, 0.1-0.4) from 2017 to 2019 (Figure 2).

Grades of BPD could be assigned only to 377 of 378 patients whose combined grades 1, 2, and 3—referred to as any grade BPD—decreased from 7 of 29 patients (24.1%) to 17 of 183 patients (9.3%) (P < .008 for trend). The rate of grade 1 BPD decreased from 4 of 29 patients (13.8%) to 11 of 183 patients (6.0%), but this decreasing trend was not significant as assessed by the Cochran-Armitage test, whereas the decrease in the rate of grade 2 BPD from 3 of 29 patients (10.3%) to 5 of 183 patients (2.7%) was significant (P = .02 for trend). Grade 3 BPD was low across the study period with only 2 patients, 1 patient each for the initial and final implementation period. Oxygen at home discharge decreased from 4 of 29 patients (13.8%) to 4 of 183 patients (2.2%) (P = .03). One infant required tracheostomy tube placement in the last period (Table 2).

Adjusted median PMA at hospital discharge (Figure 3) decreased from 38.2 weeks (95% CI, 37.3-39.1 weeks) in the baseline period (2009) to 37.0 weeks (95% CI, 36.5-37.5 weeks) in 2019 at the end of the full implementation period, and was 36.8 weeks (95% CI, 36.6-37.1 weeks) for combined
years 2017 through 2019. Both of these values were significantly lower than all centers combined in the CPQCC registry. The adjusted mortality was unchanged during the study periods (eFigure 4 in the Supplement), whereas adjusted mortality or specified morbidities decreased significantly (eFigure 5 in the Supplement).

**Discussion**

During a 10-year period, we observed a substantial, sustained decrease in the metric BPD <33, from 31.0% in 2009 to 1.6% in the most recent 5-year period. This decrease was unlikely due to case mix bias because the SMR for BPD less than 33 weeks decreased considerably, and BPD rates were also low in the unadjusted subgroups of GA less than 28 weeks and of GA less than 26 weeks. This decrease was also unlikely due to case ascertainment bias because we had a low rate of patients with missing BPD data: 5.0% overall and only 1 of 185 patients in the full implementation period. In addition, the decrease was unlikely due to case definition bias because BPD decreased significantly by all of the following definitions: BPD <33, any grade BPD, grade 2 BPD, and oxygen at discharge. Grade 1 BPD decreased but the trend was not significant, whereas grade 3 BPD remained low throughout the study. The adjusted median PMA at discharge to home associated with cost and long-term outcome also decreased significantly to 36.8 weeks for the combined years 2017 through 2019, which is 2 weeks less than the CPQCC median. The decrease in BPD <33 was not at the cost of an increase in balancing factors because adjusted mortality was stable and there was a significant decrease in adjusted mortality or specified morbidities, a measure associated with long-term outcomes.

Given all these considerations, our outcomes were likely associated with our current care practices rather than with analytical biases. The reasons underpinning our success may be found in the evidence base for each individual intervention we adopted in our “BPD Prevention Bundle of Interventions” and “No BPD Roadmap.” The postnatal interventions of varying degrees of evidence supporting efficacy in preventing BPD included high-frequency ventilation, volume-targeted ventilation, surfactant therapy, and CPAP use; administration of caffeine; vitamin A; azithromycin; human breast milk; and inhaled or systemic steroids; and lowered oxygen saturation targets of 85% to 95% up to 34 weeks’ gestation. The interventions that we adopted that improved various aspects of short-term respiratory function, although they have not yet been shown to decrease BPD, included the use of extended CPAP, neurally adjusted ventilatory assist, high-flow nasal cannula, and inhaled β-agonists. Permissive hypercapnia and the use of diuretics were not encouraged in our bundle. Epoetin efficacy has been reported in studies but not in large randomized clinical trials or meta-analyses. Fluid restriction is included in our care practices, but its value in preventing or treating BPD has not been well established. Interventions we minimized that may increase BPD were treatment of PDA and antibiotic use.

The decrease in BPD <33 associated with the changes we implemented highlights the importance of a more fully delimited and implemented system of care over individual interventions, that is, the whole was greater than the sum of its parts. Our favorable outcomes were associated with the expansion of our shared mental model of BPD prevention and the standardization of management for a range of postnatal age-specific and postconceptional age-specific clinical scenarios for which management was defined (eAppendix 2 and eFigures 1, 2, and 3 in the Supplement).

For the shared mental model, preventing BPD was envisioned as protecting against lung injury and supporting lung growth, with emphasis on proactive and optimized respiratory support to prevent deterioration rather than on rescue care. Focused respiratory care interventions aimed at avoiding alveolar de-recruitment and oxygen toxicity were central. Pneumonia, PDA, or reflux were rarely accepted as reasons for respiratory deterioration. This may have had the additional benefit of lowering PDA ligation rates and antibiotic use, which have been associated with increased BPD rates. The changes in our shared mental model and management were the product of a sustained quality improvement effort.
The detailed postnatal and PMA standardization of care may have been a factor in our improvement because standardized practice itself tends to improve outcomes in clinical settings, including ventilator care in NICUs.17,66,67 Our efforts to standardize practice, strong leadership, a consensus/commitment culture, daily bedside rounds, weekly meetings, and vignette case discussions were necessary to achieve these outcomes.

Regarding the system of care, the bundle of these interventions in its entirety was associated with our favorable outcomes although we do not know the relative contribution of each intervention. We recommend that the first focus of subsequent studies be on replicating our system of care and our outcomes rather than on dissecting each element of the bundle to find the minimally required components to achieve favorable outcomes.

Strengths and Limitations
This study has several strengths. First, the degree of the observed decrease in BPD rates was clinically important and statistically significant. Second, the chance of case mix bias, case ascertainment bias, or case definition bias was unlikely. Third, we provided descriptions of our “No BPD Roadmap,” with ventilatory and nonventilatory management as clinical tools to facilitate replication of the implementation details of our strategy.

There are a few limitations to this study. This is a single-center study with a small sample size. The efficacy of this BPD prevention bundle has not been studied in a surgical population.

Conclusions
We observed a substantial, sustained decrease in BPD rates in association with the development and implementation of a detailed BPD prevention bundle. Our success may be associated with a shared mental model of care that BPD is preventable, the details of the system of care, and the consistency of its execution. We believe the bundle of care described in this report is sufficiently detailed to enable researchers to assess whether these outcomes can be replicated at other centers.

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**SUPPLEMENT.**
eAppendix 1. Shrunken Standardized Morbidity Ratio
eFigure 1. No BPD Road Map: Ventilatory Management for High-Risk Infants of GA <28 Weeks or BW <1000 g
eFigure 2. No BPD Road Map: Ventilatory Management for High-Risk Infants of GA 28-31 Weeks and BW =1000 g
eFigure 3. No BPD Road Map: Nonventilatory Management/Pharmacologic Therapies and Other Strategies for Very Low-Birth-Weight Infants (BW <1500 g)
eFigure 4. Risk-Adjusted Mortality in Infants 501 to 1500 g
eFigure 5. Risk-Adjusted Mortality or Specified Morbidities in Infants 501 to 1500 g
eAppendix 2. BPD Prevention Bundle Implementation