Quality Improvement Initiative to Reduce the Necrotizing Enterocolitis Rate in Premature Infants

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abstract

OBJECTIVE: To reduce the incidence of necrotizing enterocolitis (NEC) among very low birth weight (VLBW) infants admitted to 8 intensive care nurseries from a 2010 baseline of 8.0% to <4.0% by 2012 and sustain for 6 months using quality improvement (QI) methodology.

METHODS: A multidisciplinary NEC QI team used the Vermont Oxford Network definition of NEC and the Institute for Healthcare Improvement model. The specific aims were evidenced based and included (1) standardized early human milk feedings, (2) conservative feeding guidelines during blood transfusions and indomethacin treatment, and (3) restriction of ranitidine use in VLBW infants. Inclusion criteria included VLBW infants admitted within the study period without NEC. Exclusion criteria included established NEC or spontaneous intestinal perforation unrelated to NEC. The incidence of NEC and NEC-related surgery were tracked using statistical process control methodology.

RESULTS: The baseline NEC rate in 2010 was 8% (27 NEC cases in 335 VLBW infants). After initiation of early human-milk feeding and conservative feeds during blood transfusions guidelines in November 2011, only 3.1% (19 of 606 VLBW infants) had developed NEC through December 2013 (P = .001). Special cause variation was noted in June 2012 establishing a new centerline at 3.1%. NEC-related mortality decreased from a 2010 baseline mean of 2.7% to a new baseline mean of 0.9% from January 2011 to December 2013.

CONCLUSIONS: Implementation of QI initiatives decreased the NEC rate from 8.0% to <4.0%. Early human milk feedings and conservative feeding during blood transfusion policies appear to have significant impact on NEC reduction.

Necrotizing enterocolitis (NEC) is the most common gastrointestinal emergency affecting the premature population and a leading causes of neonatal morbidity and mortality.[1] The incidence of NEC in very low birth weight (VLBW) infants has remained constant over the years at 5% to 7%[2,3] with a slight increase reported from 2000 to 2009 among NICUs participating in the Vermont Oxford Network (VON).[3] Mortality from NEC varies, depending on amount of bowel involvement and comorbidities, with reports of up to 50% in those requiring surgery.[4] Recently, overall mortality has declined among extremely premature infants, except for that due to NEC.[5] Surviving infants with NEC are at increased risk for poor neurodevelopmental outcomes.[6] This consequence contributes to significant economic burden and marked stress for families. Thus,

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Dr Talavera designed the study, analyzed the data, and drafted the initial manuscript; Drs Bixler and Cozzi implemented the study design and drafted the initial manuscript; Mr Dail designed the data collection instruments and coordinated and supervised data collection for all sites and critically reviewed the manuscript; Drs Miller, McClead, and Reber conceptualized and designed the study and drafted the initial manuscript; and all authors approved the final manuscript as submitted.

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preventative strategies that reduce the incidence of NEC in VLBW infants are both a clinical and an economical priority for society.

The pathophysiology of this disease remains poorly understood, but it is likely multifactorial. This makes development of targeted treatments and prevention strategies challenging. There are several proposed causal mechanisms for development of NEC. These include an impaired mucosal intestinal barrier, immature vascular regulation, and an abnormal microbiome.[6] Alteration of gastric acidity and, in turn, microbial colonization with the use of ranitidine in VLBW infants has been linked to a 6.6-fold higher risk of developing NEC.[7] Furthermore, packed red blood cell transfusions are an independent risk factor for the development of NEC.[8–10]

Prevention strategies include the use of human milk feedings, especially mother's own milk (MOM)[11,12] and, perhaps, pasteurized donor milk.[13] Human milk provides protection through a synergistic mix of nutritional, bioactive, and immunomodulatory effects in the VLBW infants.[14] A recent Cochrane Review of 24 randomized clinical trials indicated that probiotics reduced the incidence of severe NEC[15]; however, support for this approach is not universal.[16]

The incidence of NEC in VLBW infants admitted to the intensive care nurseries of Nationwide Children's Hospital (NCH) in 2010 exceeded 8%. This rate was near the 75th percentile of children's hospitals submitting data to the VON database and exceeded the 75th percentile for all other VON participating center benchmark categories. Furthermore, 50% of NCH NEC patients requiring surgery had an overall case mortality exceeding 35%. These cumulative observations led us to implement a quality improvement (QI) initiative to reduce the incidence of NEC among VLBW infants admitted to the intensive care nurseries of NCH (Neonatal Services) from a baseline of 8.0% (~75th percentile) to <4.0% (<25th percentile) using as series of standardized evidence-based interventions. Second, we sought to determine the impact of these prevention strategies on NEC-related mortality and NEC-related surgery.

METHODS

Ethical Issues

This QI project involved implementing evidence-based interventions or best practices designed to reduce the NEC rate in VLBW infants admitted to Neonatal Services. Interventions did not involve multiple device comparisons or therapies, and patients were not subjected to randomization. QI and epidemiology staff members accessed medical records as part of their normal responsibilities. No personal health information was shared outside NCH. The NCH Institutional Review Board has oversight responsibility for all human subject research activity in NCH facilities, including the network of NICUs. Therefore, this QI project was not considered human subjects research and, per policy, approval by the Institutional Review Board was not required.

Setting

Neonatal Services at NCH is a joint venture between NCH and 6 Central Ohio maternity hospitals. The program comprises 191 neonatal beds distributed among 5 level III NICUs and 3 level II special care units. The various intensive care nurseries represent unique microsystems with at least 5 distinct nursing and support staff. Four physician groups, including 2 private practice neonatology groups, 1 academic neonatology group, and 1 academic surgical group, provide medical care and agree to collaborate under specific guidelines. In 2014, the affiliated maternity centers delivered >16 000 infants. Neonatal Services admitted >2300 neonates, of whom 35% were outborn. Sixteen percent of neonates are ≤1500 g birth weight, and >30% had major surgical problems.

Inclusions and Exclusions

All VLBW infants admitted to a Neonatal Services unit during the intervention period before developing NEC were included. VLBW infants with established NEC referred to NCH facilities for treatment and infants with isolated intestinal perforation were excluded. Per VON manual definition, NEC was diagnosed either by direct observation of intestine at surgery or pathologic examination postmortem or by using a set of strict clinical criteria. A clinical diagnosis of NEC was made based on at least 1 physical finding (bilious gastric aspirate or emesis, abdominal distention, or occult/gross blood in the stool in the absence of anal fissure) and at least 1 radiographic finding (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum).[17]

Multidisciplinary NEC Quality Improvement Team

This multidisciplinary QI team included medical and nursing staff from all neonatal units, Pediatric Surgery and Infectious Disease Specialists as well as clinical pharmacists, dieticians, and QI experts. The group met monthly to review the literature regarding the pathophysiology, presumed etiology, and evidenced-based research that supported putative NEC prevention strategies. They established the baseline incidence of NEC among all VLBW infants admitted to Neonatal Services. In addition, they established the strategic aim, key driver interventions, and designed changes and interventions outlined in Fig 1. These guidelines were approved by all clinical groups and disseminated

to all participating units. They were published online and easily accessible on the NCH Neonatal Services Web site and frequently reviewed during unit-specific meetings. The multidisciplinary NEC QI team was responsible for quarterly chart reviews to audit compliance with each baseline as well as during increased spikes in the NEC rate.

Key Driver Interventions

We identified several key drivers: (1) standardize early human milk feedings, (2) standardize restrictive feedings during blood product transfusion and indomethacin treatment guidelines, (3) restrictive ranitidine use in VLBW (<1500 g) infants (Fig 1).

Early Human Milk Feedings

The NEC reduction team developed a feeding protocol that emphasized early feedings and promoted the use of MOM or donor breast milk when MOM was unavailable.[18] This feeding guideline was implemented in all neonatal services units in August 2011. Donor breast milk was obtained from the Mother's Milk Bank of Ohio (OhioHealth, Columbus, OH). For infants <28 weeks' gestation, bolus trophic feeds of 10 mL/kg/day were divided every 6 hours within the first 3 days of life. When tolerated, feeds were advanced to every 3 hours at the same daily volume until the seventh day of life when volume was increased to 20 mL/kg/day. Feeds were then increased to 20 mL/kg/day until full feeds were achieved at 150 mL/kg/day volume.[19] This feeding advancement guideline was based on previous evidence demonstrating that prolonged small feeding volumes in preterm infants decreases the incidence of NEC.[20,21]

Restrictive Feedings During Gastrointestinal Blood Flow Alterations

On the basis of evidence-based reports,[9,22,23] a conservative feeding policy during transfusions of all blood products was implemented in August 2011 for infants ≤42 weeks. Feeds were held during transfusions but were permitted before and after the transfusion. This feeding guideline did not allow for a change in fortification or volume advancement on the day of transfusion.

The feeding guidelines during indomethacin therapy for patent ductus arteriosus treatment was initiated in April 2012. Infants were stratified according to age of infant and volume of feeds previously tolerated. If <2 weeks of age and <60 mL/kg/day of feeds is tolerated then infants were kept nil per os (NPO) or maintained on trophic (10 mL/kg/day) feeds during course of treatment. Clyman et al demonstrated that maintaining trophic feeds or nothing-by-mouth status during drug treatment did not alter the incidence of NEC.[24] If >2 weeks of age and >60 mL/kg/day feeding volume was tolerated at the time of treatment, feeds were reduced to only 20 ml/kg/day during drug treatment.

Restrictive Use of Ranitidine in VLBW Infants

A policy restricting the use of use ranitidine in VLBW infants (≤1500 g birth weight and ≤28 weeks' corrected gestational age) was implemented in April 2012 after reports of an association with an increased risk of infections, NEC, and fatal outcomes.[7]

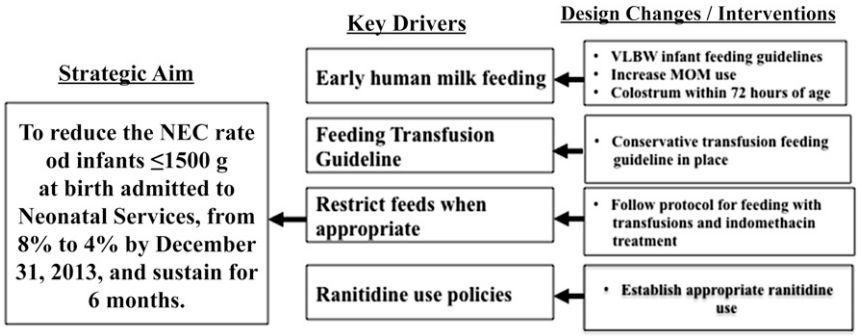

FIGURE 1
Key driver diagram summarizing specific interventions driving key baseline changes aimed at achieving the specific aim of NEC rate reduction by 50%. Key driver diagram based on Institute for Healthcare Improvement model of improvement.

Measures

VLBW infants were identified from the local VON database. Potential cases of NEC were obtained from the NCH enterprise data warehouse by searching for those patients discharged with the *International Classification of Diseases, Ninth Revision, Clinical Modification,* code for NEC (777.5). The enterprise data warehouse houses most clinical and administrative data from a variety of electronic interfaces at NCH. These potential NEC cases were then cross-referenced with the local VON database to ensure that no cases were missed. Medical records of candidate patients were reviewed to determine the patient's birth hospital and birth weight and to confirm the clinical and radiologic criteria for NEC. The baseline data of the proportion of VLBW infants who developed NEC and those requiring surgery were established via chart review of candidate subjects admitted to Neonatal Services in 2010. The NEC rate was defined as cases of NEC per VON definition (numerator) divided by the total number of infants ≤1500 g birth weight admitted to a Neonatal Services nursery for reasons other than NEC (denominator) during that occurrence. Recurrent NEC cases

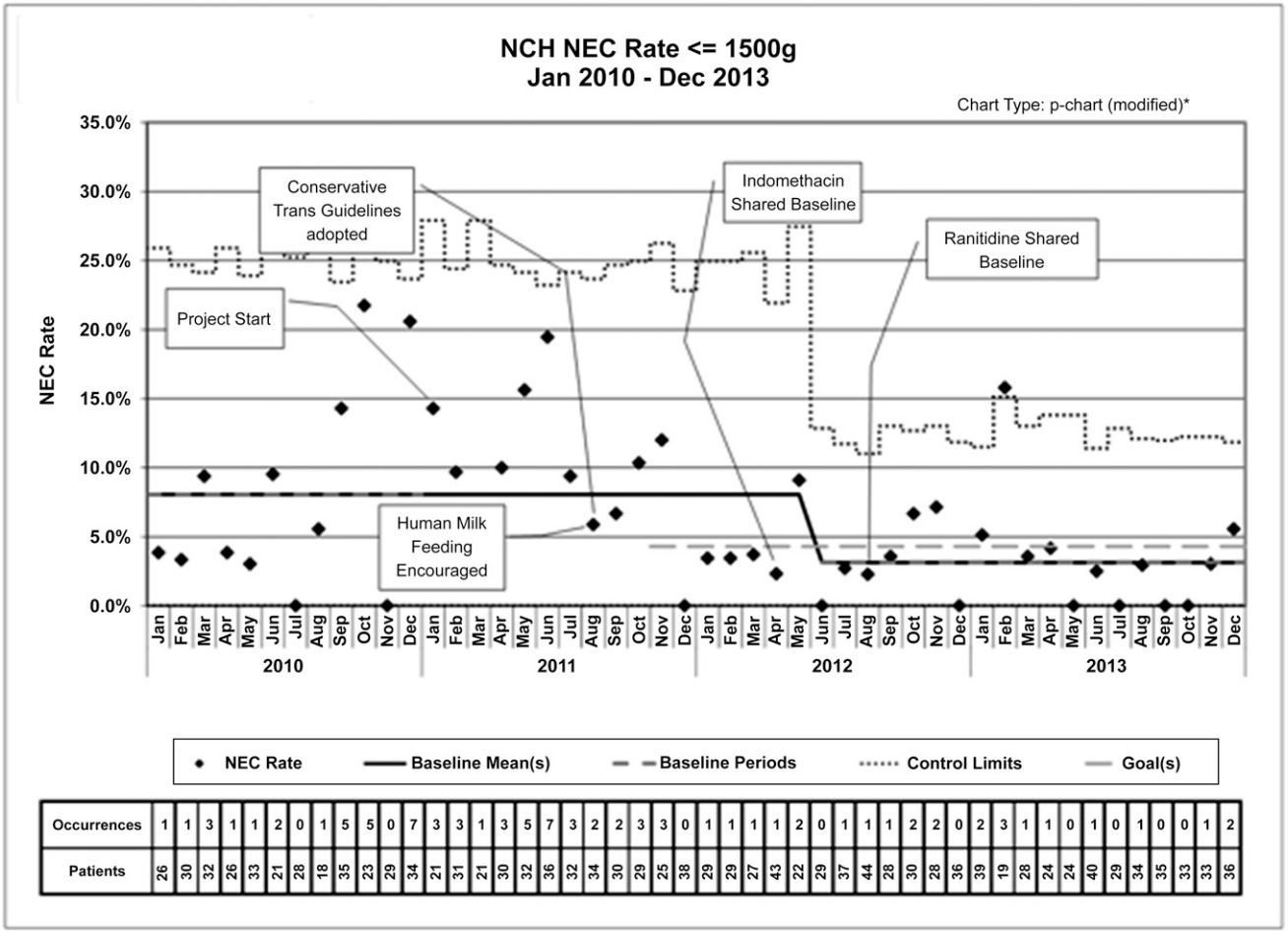

FIGURE 2

Overall NEC rate in VLBW infants from January 2010 to December 2013. Annotated p-chart showing change by month in proportion of patients ≤1500 g birth weight who developed NEC during admission to a Neonatal Services nursery. Callout indicates timing of improvement interventions. Control limits deviated from the standard because data dispersion (i.e., variation) is too large or too small to meet usual p-chart statistical assumptions.

were not "recounted" because of their relative rare occurrence.

Data Analysis

This study used a time-series, quasi-experimental design. Interventions were implemented at all Neonatal Services nurseries. Study subjects were identified by QI staff and monitored for the diagnosis of NEC, NEC-related surgery, mortality, and compliance with intervention protocols using statistical process control charting software developed locally and housed on the NCH intranet site. SPC uses statistical methods to analyze the inherent (common cause) variability in a process, to assess the process capability, and to identify of incidences of statistically significant ($P < .01$) variability due to special causes[25]. Additional statistical analysis of the incidence of NEC from 2011 to 2013 was performed by using χ^2 test and Fisher exact test to examine categorical variables. $P < .01$ was considered significant.

RESULTS

The baseline NEC rate in 2010 was 8% (27 NEC cases for 335 infants). After initiation of the early human-milk-based feeding guideline and the restriction of feeds during blood transfusions in November 2011, only 3.1% (19 of 606 VLBW infants) developed NEC through December 2013 ($P = .001$). A favorable special cause variation was noted in June 2012 (ie, Rule 2 refers to 8 points below the centerline)[25], establishing a new centerline at 3.1% (Fig 2). There was an outlier NEC rate spike in February 2013 that was near the upper control limit. The etiology of this special cause was not determined from medical record audits. However, the number of VLBW infants admitted that month was half to two-thirds of previous months. Regardless, the NEC rate returned to or below baseline mean for the remainder of the study period.

We have seen a stepwise increase in the percentage of discharged infants fed mother's own milk by day of life ≤3 from 0% before September 2010 to 30% from October 2010

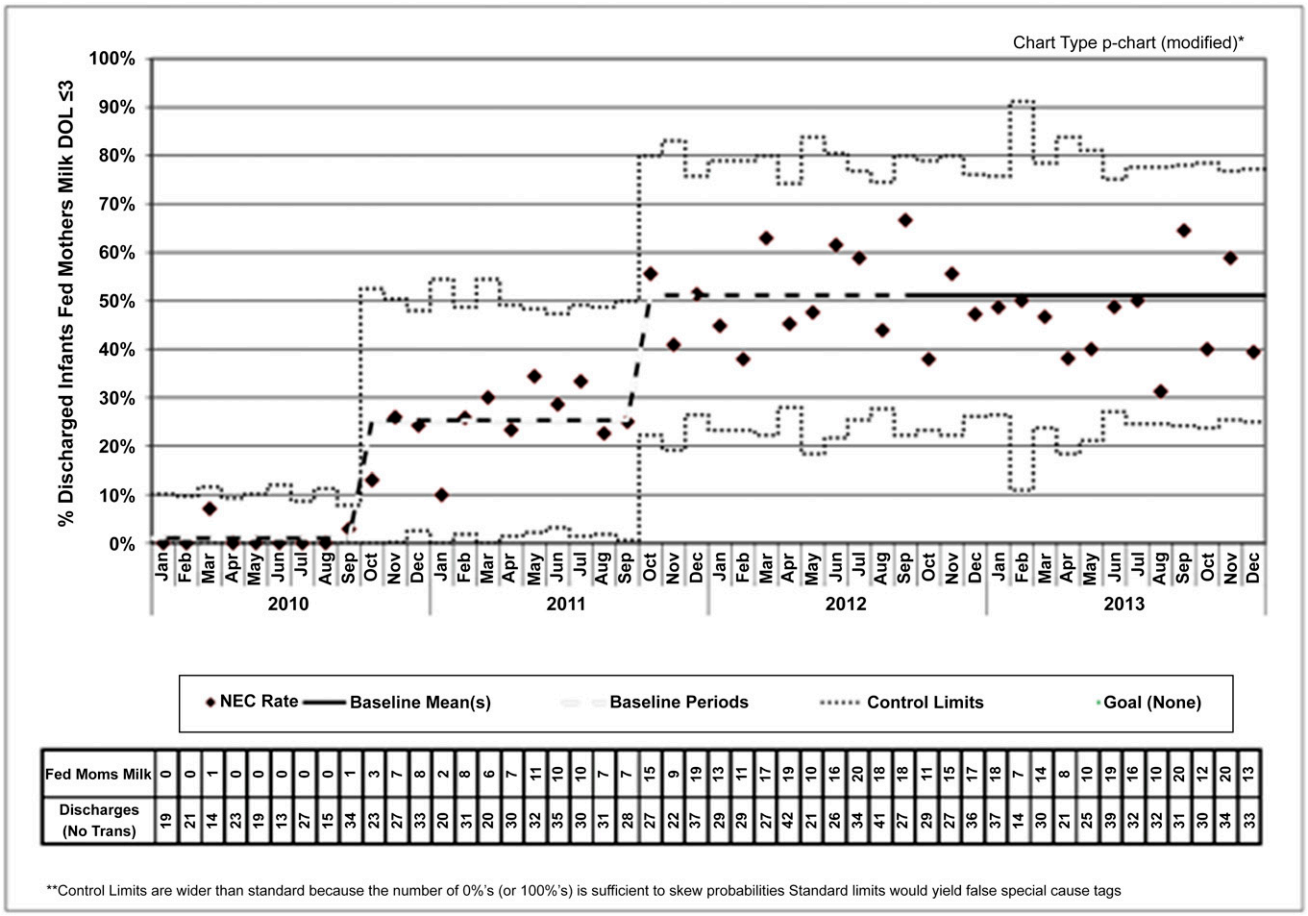

FIGURE 3

Annotated p-chart for percent of VLBW infants (≤1500 g) at birth who were fed MOM by day of life 3 and discharged. Control limits are wider than standard because the number of 0% (or 100%) is sufficient to skew probabilities. Standard limits would yield false special cause flags.

to September 2011, with a further increase to 50% by January 2012 (Fig 3). This increasing trend of early use of human milk started before this QI initiative, however, the progressive increase in mother's milk use can be attributed to the NEC reduction QI initiatives.

Implementation of these QI initiatives in August 2011 saw a sustained improvement in the number of patients between episodes of medical NEC from a baseline expected median of 8 to 22 sustained through January 2013 (data not shown). The number of patients between surgical NEC cases before implementation of the NEC QI initiatives began at a baseline expected median of 39. After implementation of the NEC QI initiatives during the same period, there were 490 patients between surgical NEC cases (data not shown).

Mortality among VLBW infants that develop NEC at NCH nurseries has decreased from a 2010 baseline mean of 2.7% before the NEC reduction QI interventions to 0.9% sustained from 2011 to 2013 (Fig 4).

DISCUSSION

In this QI initiative, we reduced the NEC rate among VLBW infants in our neonatal network from a baseline incidence of 8.0% to <4.0%. The largest decrease in incidence was noted after implementation of 3 key drivers: increased administration rates of maternal breast milk in the first 3 postnatal days, conservative feeding guideline during blood transfusions and during indomethacin therapy, and restriction of ranitidine use in infants ≤1500 g and ≤28 weeks of age. As a consequence, this QI initiative augmented efforts to increase the percentage of discharged infants fed MOM by day of life ≤3, an upward trend of 30% to 50%. Finally, the NEC-related mortality rate decreased during the study period from 2.7% to 0.9%.

Our first 2 interventions of increasing administration of early human milk feedings and conservative feeding policy during blood transfusion were both derived from previously published reports linking these to the increase risk of NEC.[26–28] The benefits of human milk are well known,[13,18] and the practice of using

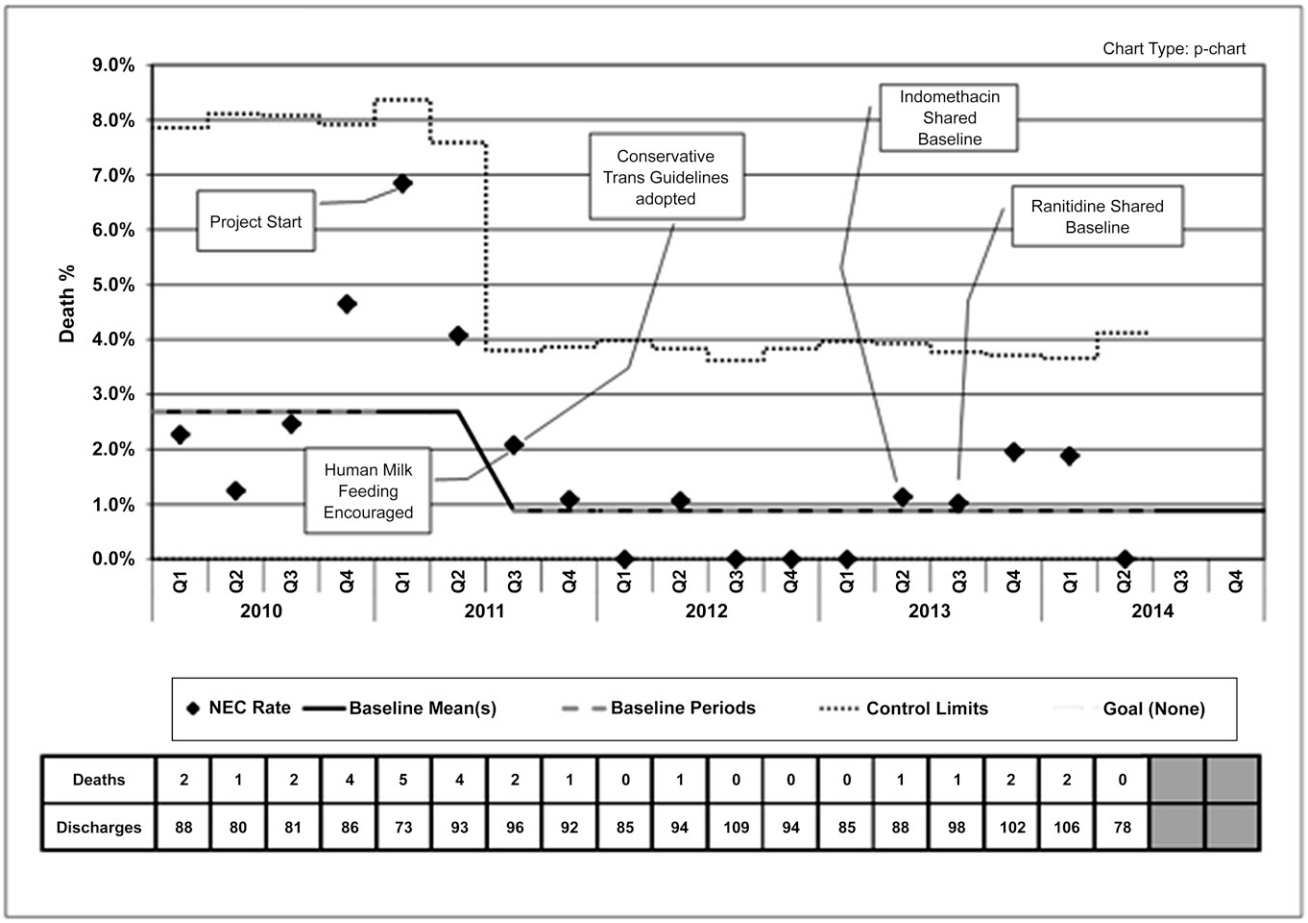

FIGURE 4

NEC mortality among Neonatal Services nurseries for VLBW (≤1500 g) infants. Annotated p-chart of death of patients ≤1500 g at birth who developed NEC while hospitalized in a Neonatal Services nursery. Denominator represents total admissions of patients weighing ≤1500 g at birth.

maternal breast milk and/or donor milk was already in full use within our Neonatal Service line at the start of this QI initiative. Nonetheless, this QI project provided a mechanism to reinforce our efforts toward NEC prevention as demonstrated by increased rates of early (<72 hours of age) mother's milk based feedings in infants' ≤28 weeks.

The association between blood transfusions and the onset of NEC is supported by a transfusion-related gut injury model that is directly related to decreased mesenteric oxygen delivery in the setting of severe anemia in the premature infant.[27–29] To this end, the conservative feeding transfusion policy of holding feeds and/or not changing volume or fortification on the same day as a transfusion was felt to be of low risk and potentially high benefit to the reduction of the incidence of NEC. Despite the overall decrease use of indomethacin therapy for hemodynamically significant patent ductus arteriosus, we instituted a conservative feeding guideline to ensure use of a standardized feeding regimen in our neonatal network.

The association among ranitidine use and the increased risk of infections, NEC, and worsened fatal outcomes for VLBW infants have been demonstrated in several retrospective analyses most recently by Terrin et al.[7,30] The practice within the Neonatal Services before this QI initiative was mostly to avoid the routine use of ranitidine in infants ≤1500 g and ≤28 weeks' corrected gestational age. However, compliance with this policy before the QI initiative was poor. During the QI initiative, compliance with restricted ranitidine use in VLBW infants improved with monitoring by clinical pharmacists assigned to the neonatal nurseries.

This QI initiative is easily generalizable to other NICUs. Maternal breastfeeding and breast milk administration is widely promoted in NICUs throughout the country. Improving support to new mothers by providing instruction, equipment, and space would be a simple way to improve maternal breast milk rates. Although donor breast milk provides a consistent approach to providing breast

milk when MOM is not available, its role in the prevention of NEC remains unclear. Reductions in the use of ranitidine and adoption of a conservative feeding policy during blood transfusions would be simple and low-cost actions that any unit could implement. We can also speculate that other unmeasured changes in practice or confounders during the study period might have contributed to the NEC rate reduction. However, the overall generalizability of this QI initiative would be high with low cost, low risk, and potential for high benefit.

As with all QI initiatives, the relationship between evidence-based interventions and outcomes are associational. A major limitation to this study includes a lack of a control nursery that did not implement our interventions. Thus, we do not know whether any 1 or combination of interventions are causal. We believe this is a function of randomized control trials. These QI initiatives do not attempt to control all variables. Rather, the effort is to improve compliance with evidence-based interventions, standardize care, and identify favorable special cause variation that is consistent with improvement in the outcome of interest.

CONCLUSIONS

Our initial NEC rate for Nationwide Children's Neonatal services was 8.0%, which was higher than the national average as reported by NICHD Neonatal Network Centers.[31] A key driver diagram was created to reflect key interventions supported by evidence-based medicine associated with NEC prevention. After instituting an early human milk feeding protocol, a conservative feeding policy during blood transfusions and indomethacin therapy, and restrictive ranitidine use in VLBW, we noted a decrease in the NEC rate to <4.0%. The interventions chosen were of low risk to the infants and, with such a significant drop in the NEC rate, potentially of an exceedingly high benefit. As discussed here, other units with little cost or need for additional services could easily adopt these initiatives. Continued analysis of our outcomes is needed to further refine our care processes and ensure sustainability over time.

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ABBREVIATIONS

MOM: mother's own milk
NCH: Nationwide Children's Hospital
NEC: necrotizing enterocolitis
QI: quality improvement
VLBW: very low birth weight infants ≤1500 g birth weight
VON: Vermont Oxford Network

REFERENCES

1. Hsueh W, Caplan MS, Qu XW, Tan XD, De Plaen IG, Gonzalez-Crussi F. Neonatal necrotizing enterocolitis: clinical considerations and pathogenetic concepts. *Pediatr Dev Pathol*. 2003;6(1):6–23
2. Johnson TJ, Patel AL, Bigger HR, Engstrom JL, Meier PP. Cost savings of human milk as a strategy to reduce the incidence of necrotizing enterocolitis in very low birth weight infants. *Neonatology*. 2015;107(4):271–276
3. Horbar JD, Carpenter JH, Badger GJ, et al. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. *Pediatrics*. 2012;129(6):1019–1026
4. Lin PW, Stoll BJ. Necrotising enterocolitis. *Lancet*. 2006;368(9543):1271–1283
5. Patel RM, Kandefer S, Walsh MC, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Causes and timing of death in extremely premature infants from 2000 through 2011. *N Engl J Med*. 2015;372(4):331–340
6. Sharma R, Hudak ML. A clinical perspective of necrotizing enterocolitis: past, present, and future. *Clin Perinatol*. 2013;40(1):27–51
7. Terrin G, Passariello A, De Curtis M, et al. Ranitidine is associated with infections, necrotizing enterocolitis, and fatal outcome in newborns. *Pediatrics*. 2012;129(1). Available at: www.pediatrics.org/cgi/content/full/129/1/e40
8. Wan-Huen P, Bateman D, Shapiro DM, Parravicini E. Packed red blood cell transfusion is an independent risk factor for necrotizing enterocolitis in premature infants. *J Perinatol*. 2013;33(10):786–790
9. Paul DA, Mackley A, Novitsky A, Zhao Y, Brooks A, Locke RG. Increased odds of necrotizing enterocolitis after transfusion of red blood cells in premature infants. *Pediatrics*. 2011;127(4):635–641
10. La Gamma EF, Blau J. Transfusion-related acute gut injury: feeding, flora, flow, and barrier defense. *Semin Perinatol*. 2012;36(4):294–305
11. Johnson TJ, Patel AL, Bigger HR, Engstrom JL, Meier PP. Economic benefits and costs of human milk feedings: a strategy to reduce the risk of prematurity-related morbidities in very-low-birth-weight infants. *Adv Nutr*. 2014;5(2):207–212

12. Reber KM, Nankervis CA. Necrotizing enterocolitis: preventative strategies. *Clin Perinatol*. 2004;31(1):157–167

13. Cristofalo EA, Schanler RJ, Blanco CL, et al Randomized trial of exclusive human milk versus preterm formula diets in extremely premature infants. J Pediatr. 2013;163(6):1592-5 e1

14. Meier PP, Engstrom JL, Patel AL, Jegier BJ, Bruns NE. Improving the use of human milk during and after the NICU stay. *Clin Perinatol*. 2010;37(1):217–245

15. AlFaleh K, Anabrees J. Probiotics for prevention of necrotizing enterocolitis in preterm infants. *Evid Based Child Health*. 2014;9(3):584–671

16. Abrahamsson TR, Rautava S, Moore AM, Neu J, Sherman PM. The time for a confirmative necrotizing enterocolitis probiotics prevention trial in the extremely low birth weight infant in North America is now! *J Pediatr*. 2014;165(2):389–394

17. Vermont Oxford Network. *Vermont Oxford Network Database Manual of Operations for Infants Born in Burlington, VT*. 2014. Available at: https://public.vtoxford.org/wp-content/uploads/2014/09/ELBW_FUP_Manual_2013_V16.pdf. Accessed February 15, 2016

18. Meinzen-Derr J, Poindexter B, Wrage L, Morrow AL, Stoll B, Donovan EF. Role of human milk in extremely low birth weight infants' risk of necrotizing enterocolitis or death. *J Perinatol*. 2009;29(1):57–62

19. Jadcherla SR, Dail J, Malkar MB, McClead R, Kelleher K, Nelin L. Impact of Process Optimization and Quality Improvement Measures on Neonatal Feeding Outcomes at an All-Referral Neonatal Intensive Care Unit. *JPEN J Parenter Enteral Nutr*. 2015;0148607115571667

20. Berseth CL, Bisquera JA, Paje VU. Prolonging small feeding volumes early in life decreases the incidence of necrotizing enterocolitis in very low birth weight infants. *Pediatrics*. 2003;111(3):529–534

21. Book LS, Herbst JJ, Jung AL. Comparison of fast- and slow-feeding rate schedules to the development of necrotizing enterocolitis. *J Pediatr*. 1976;89(3):463–466

22. El-Dib M, Narang S, Lee E, Massaro AN, Aly H. Red blood cell transfusion, feeding and necrotizing enterocolitis in preterm infants. *J Perinatol*. 2011;31(3):183–187

23. Blau J, Calo JM, Dozor D, Sutton M, Alpan G, La Gamma EF. Transfusion-related acute gut injury: necrotizing enterocolitis in very low birth weight neonates after packed red blood cell transfusion. *J Pediatr*. 2011;158(3):403–409

24. Clyman R, Wickremasinghe A, Jhaveri N, et al; Ductus Arteriosus Feed or Fast with Indomethacin or Ibuprofen (DAFFII) Investigators. Enteral feeding during indomethacin and ibuprofen treatment of a patent ductus arteriosus. *J Pediatr*. 2013;163(2):406–411

25. Provost LP, Murray S. *The Health Care Data Guide: Learning From Data For Improvement*. San Francisco, CA: Jossey-Bass; 2011

26. Sisk PM, Lovelady CA, Dillard RG, Gruber KJ, O'Shea TM. Early human milk feeding is associated with a lower risk of necrotizing enterocolitis in very low birth weight infants. *J Perinatol*. 2007;27(7):428–433

27. Marin T, Moore J, Kosmetatos N, et al. Red blood cell transfusion-related necrotizing enterocolitis in very-low-birthweight infants: a near-infrared spectroscopy investigation. *Transfusion*. 2013;53(11):2650–2658

28. Mally P, Golombek SG, Mishra R, et al. Association of necrotizing enterocolitis with elective packed red blood cell transfusions in stable, growing, premature neonates. *Am J Perinatol*. 2006;23(8):451–458

29. Marin T, Strickland OL. Transfusion-related necrotizing enterocolitis: a conceptual framework. *Adv Neonatal Care*. 2013;13(3):166–174

30. Patole S. Association of H2-blocker therapy and higher incidence of necrotizing enterocolitis: a case of excessive collateral damage? *Pediatrics*. 2006;117(2):531–532

31. Torrazza RM, Li N, Neu J. Decoding the enigma of necrotizing enterocolitis in premature infants. *Pathophysiology*. 2014;21(1):21–27

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