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QUALITY IMPROVEMENT ARTICLE

A quality improvement initiative to reduce necrotizing enterocolitis across hospital systems

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Abstract

Objective Necrotizing enterocolitis (NEC) is a devastating intestinal disease in premature infants. Local rates of NEC were unacceptably high. We hypothesized that utilizing quality improvement methodology to standardize care and apply evidence-based practices would reduce our rate of NEC.

Study design A multidisciplinary team used the model for improvement to prioritize interventions. Three neonatal intensive care units (NICUs) developed a standardized feeding protocol for very low birth weight (VLBW) infants, and employed strategies to increase the use of human milk, maximize intestinal perfusion, and promote a healthy microbiome.

Results The primary outcome measure, NEC in VLBW infants, decreased from 0.17 cases/100 VLBW patient days to 0.029, an 83% reduction, while the compliance with a standardized feeding protocol improved.

Conclusion Through reliable implementation of evidence-based practices, this project reduced the regional rate of NEC by 83%. A key outcome and primary driver of success was standardization across multiple NICUs, resulting in consistent application of best practices and reduction in variation.

Introduction

Necrotizing enterocolitis (NEC) is a devastating disease characterized by damage to intestinal mucosa, hypothesized to relate to ischemia and/or an exaggerated inflammatory response to pathogenic bacteria. NEC almost exclusively affects premature infants, and despite significant focus over the past decades, the pathophysiology remains incompletely understood. No effective treatment strategies exist, and in cases requiring surgery (35% of all cases), mortality exceeds 50% [1–5].

National benchmarking data illustrate the variability in rates of NEC across institutions, suggesting that differences in care practices may influence the risk of NEC. Reviewing local data over the past 10 years, regional rates of NEC among very low birth weight (VLBW) infants ranged from 9.5 to 15.8% across our three Level III/IV neonatal intensive care units (NICUs), at a time when the national average was 6%, and the top performing hospitals had rates <2.0% [6]. Because NEC occurs primarily in infants after the initiation of enteral feeding, interventions to prevent the disease have been centered on feeding practices and use of human milk as the primary source of nutrition [7–9].

The aim of this project, started in July 2010, was to decrease the number of VLBW infants (birth weight < 1500 g) diagnosed with necrotizing enterocolitis (Bell's stage II or higher) from 0.17 (cases per 100 VLBW patient days) to 0.07 by 30 June 2014. Having achieved that goal, a stretch goal was established to further decrease to 0.03 by 30 June 2015. This is roughly equivalent to an annual rate of 2%.

Methods

Context

Our neonatology group cares for the majority of infants born in the region. This includes 14 hospitals and close to 30,000 births/year. This operational framework for service

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delivery provides an opportunity to affect the outcomes of premature infants at a population level. Practice variation was noted across NICUs in the region, and a decision was made to focus on improving and standardizing practices with the goal of reducing the rate of NEC across hospital systems. Three NICUs (X, Y, and Z) participated in this improvement effort: [1] NICU X is a 60-bed Level III unit within an adult community hospital, which is consistently one of the busiest delivery services in the state (average of 229 VLBW infants/year); [2] NICU Y is a 50-bed Level III unit within the adult university hospital, with high rates of maternal co-morbidities (average of 136 VLBW infants/year); [3] NICU Z is a 59-bed Level IV unit within a free-standing children's hospital, and most patients are outborn infants (average of 59 VLBW infants/year) (Table 1). At the time this project began, these were the only three hospitals in the region that cared for VLBW infants, and therefore the only three that participated in this quality improvement (QI) project.

Interventions—quality improvement methods

This quality improvement (QI) effort began in July 2010 and the active improvement concluded in July 2015. A monitor and sustain phase continued through July 2016. A multidisciplinary team used the model for improvement to map current processes, conduct failure mode and effects analyses, and refine key drivers to prioritize interventions for improvement (Fig. 1). This collaborative group functioned as the overall steering team for the project, met monthly to review data, and plan interventions to test and share the learnings. Each failure (case of NEC) was also reviewed using a Root Cause Analysis process. In addition, each individual NICU had working teams that met more frequently to focus on site-specific interventions and tests of change. Key drivers focused on four main areas: (a) standardization of feeding practices; (b) use of human milk; (c) maintenance of a healthy microbiome; and (d) optimization of intestinal perfusion. Specific interventions (Table 2) were identified and simultaneously tested in a site-specific manner, and if adopted, were then spread to the other NICUs (Suppl. Figure 1). Data on outcomes and processes were shared at monthly meetings of the individual NICU teams and the regional neonatology group.

Interventions

Use of human milk

The strongest evidence for primary prevention of NEC lies with the use of human milk, and specifically, the mother's own breast milk [10, 11] . To encourage this, a number of interventions to support mothers in the provision of breast milk were undertaken, including initiating pumping within 6 h of delivery and increasing skin-to-skin (kangaroo) care. Local QI work on this topic was supported by a statewide effort led by the Ohio Perinatal Quality Collaborative that focused on increasing the use of human milk as a strategy for reducing nosocomial infection [12]. In addition, all units used pasteurized donor milk (DM) when maternal milk was not available. DM use was extended from 2 to 4 weeks of age to ensure infants were receiving human milk during the time of greatest NEC risk.

Feeding practices

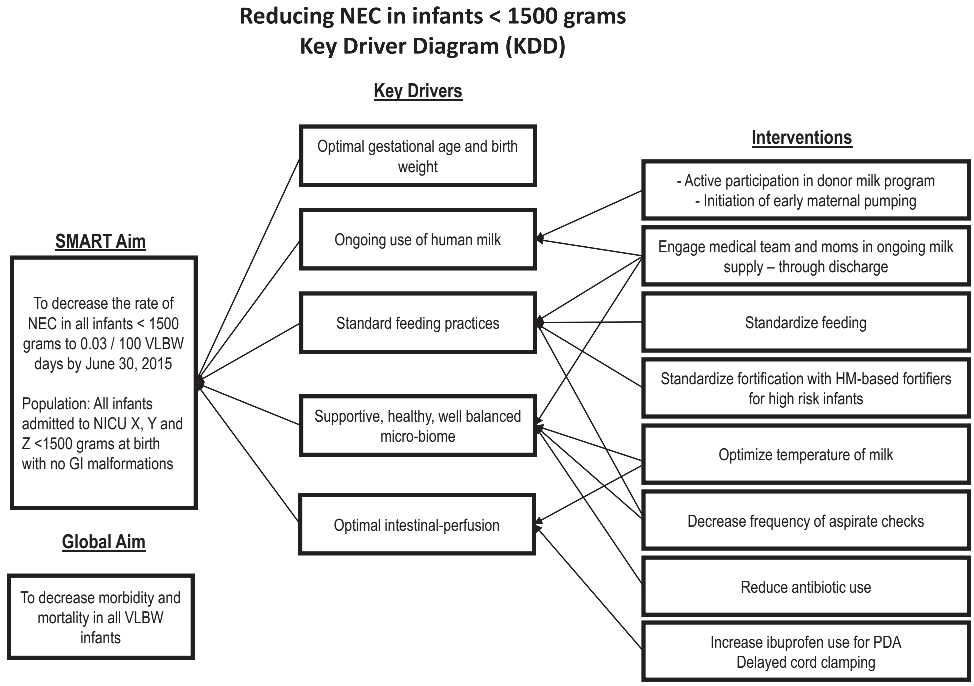
After a thorough literature review, presentation, and discussion with the NICU staff and the surgical colleagues, a standardized feeding protocol for VLBW infants was developed and implemented (Suppl. Figure 2). We also examined the practice of checking gastric aspirates, which has never been shown to improve outcomes or prevent harm for infants. Based on the lack of evidence for this practice and the concern that repeated aspiration of gastric contents into a tube coated with milk encourages the growth of pathogenic bacteria, the practice of checking gastric aspirates was discontinued. Process mapping revealed that the method for warming human milk prior to administration in our nurseries was inconsistent. Practices ranged from warm water baths, leaving the milk on the counter at room temperature, to warming in an individual's hands. Therefore, standardization of warming practices was also included as part of the QI effort.

Table 1 Comparison of participating NICUs

	Level of neonatal service	Population	#VLBW infants/year[a]	% change in NEC rate from 2009 to 2015[a]
NICU X	III	Inborn, maternity hospital	229	85% reduction
NICU Y	III	Inborn, maternity hospital	136	61% reduction
NICU Z	IV	Outborn, free-standing Children's Hospital	59	53% reduction

[a]Based on data from Vermont Oxford Network (using "All VLBW" population and location "All"), volume averaged over 7 years (2009–2015)

Fig. 1 Key driver diagram for necrotizing enterocolitis



Microbiome

Many premature infants were empirically started on antibiotics after birth, which has been demonstrated to increase risk of NEC and death [13–18]. A goal was established to decrease the total number of doses of antibiotics received by VLBW infants over the first 14 days of age. To decrease the empiric use of antibiotics in VLBW infants, a standardized decision tree (Suppl. Figure 3) was developed that utilized serial C-reactive protein concentrations in combination with other laboratory results and clinical status to reassure clinicians to stop initial courses of antibiotics after 48 h.

Intestinal perfusion

Patent ductus arteriosus (PDA) is common in preterm infants, and the current medical approaches to close PDA use nonsteroidal anti-inflammatory drugs, such as indomethacin and ibuprofen. Randomized, controlled trials have shown equal efficacy between these medications, with fewer intestinal complications associated with ibuprofen [19–23], therefore a change in the first-line pharmacotherapy was made from indomethacin to ibuprofen for PDA treatment. Because this change was supported (and somewhat hard-wired) by a change in formulary, and due to limitations in resources for data collection, we elected not to track this as a process measure. Delaying the umbilical cord clamping at birth by 30–60 s in preterm infants has been shown to decrease hypotension, need for blood transfusion, intraventricular hemorrhage, and NEC [24]. An optimal (delayed) cord clamping protocol was tested, modified, and then adopted and spread.

Measures

Eligible patients were defined as infants < 1500 g at birth without gastrointestinal malformation.

To best understand the results, evaluate interventions, and inform testing, the team made a conscious decision to operationally define the outcome measure in a novel way—NEC cases per 100 VLBW patient days. Most benchmarking databases and publications report an annual rate of NEC, calculated at the time of discharge or death of each infant. Defining the measure in this way makes the application of QI methodology, which requires rapid tests of change and correlation of changes in process with changes in outcome, difficult because the date of NEC is not known (and cases of NEC are not captured until the infant is discharged after a length of stay that may be several months long). Calculating the NEC rate per 100 VLBW patient days allows for real-time tracking without the lag imposed by waiting to record a case when the infant is discharged or dies.

Cases of NEC were defined as those with Bell's stage II or higher NEC during their NICU stay. Cases of NEC were identified by diagnosis codes from the electronic medical record, transport and admission logs, and local databases maintained by dieticians at each site. Cases were reviewed at monthly steering committee meetings to ensure the accuracy of diagnosis. In regards to distinguishing spontaneous intestinal perforations (SIP) from NEC, the

Table 2 Interventions, settings, and timing for each intervention

Category of intervention	Specific interventions	Hospital NICU Site of initial PDSA testing	Timing
Use of human milk	Early pumping	X, Y, Z	January 2012
	Extension of Donor Milk program	X, Y, Z	March 2012
	Skin-to-skin (kangaroo) care	Y, Z[a]	September 2013
	Pumping space	Z[b]	September 2013
Feeding practices	VLBW feeding protocol	X, Y, Z	March 2011
	Warming of milk	X, Z[a]	September 2012
	Gastric residuals (no checking)	X[b]	March 2013
Healthy microbiome	Antibiotic stewardship	X[a]	November 2014
Optimize intestinal perfusion	PDA treatment	X, Y[b]	November 2011
	Delayed cord clamping	X[b]	June 2014

[a]Intervention already in place in other NICU(s) prior to this project

[b]Intervention felt to be unnecessary or not applicable to particular unit context or patient population

diagnoses given by the neonatology and surgery teams, as documented in the electronic medical record, were upheld. Equivocal cases (especially those without direct visualization of the bowel) were classified as NEC. Birthweight-specific billing data from each hospital NICU was utilized to facilitate the most precise calculation of VLBW days as the denominator.

For process changes that required more small-scale testing and gradual implementation, process measures were tracked to follow the progress of implementation and assess compliance. The main process measure was adherence to the standardized feeding protocol, evaluated at five distinct time points (initiation of enteral feeding, volume of initial feed, duration of trophic-volume feeds, timing of fortification of human milk, and time to reach full enteral feeding) and aggregated across the three NICUs. Data from the Ohio Perinatal Quality Collaborative were used by each unit to track the improvements in maternal pumping within 6 h of delivery, provision of any human milk in the first 72 h of age, receipt of ≥100 mL/kg/day human milk by day 21, and receipt of ≥50% of feeds as mother's milk on the day-of-life 21. Additional process measures were collected at each site while they were implementing a given intervention, and included compliance with optimal cord clamping (NICU X) and number of empiric antibiotic doses received (NICU X). A balancing measure of growth was tracked. In addition, NICU X tracked the number of abdominal radiographs to be able to document improvements in the value associated with this QI effort.

Analysis

Analysis of both process and outcome measures took place using run charts and statistical process control (SPC) charts. For the primary outcome, measures were plotted as a u-chart (NEC cases per 100 VLBW patient days) and t-chart (days between NEC cases). Baseline mean and control limits were calculated and displayed for the period November 2011 to February 2013 and were carried forward. Data values were added monthly and monitored for evidence of significant change using standard SPC rules [25]. We determined a priori that if one of these criteria were met, we would conclude that a significant change occurred. Process of care measures were plotted monthly as run charts. As no baseline data were available for the process of care measures, the median line included all data points and was adjusted only when evidence of significant change occurred based on run chart rules.

Results

The primary outcome measure, NEC in VLBW infants, decreased from 0.17 cases per 100 VLBW patient days to 0.029 (Fig. 2), an 83% reduction, with shift in the median line twice over the time period of the project. An aggregate (NICUs X, Y, Z) days between the charts illustrate increasing periods of time between cases (Fig. 3).

The process measure of compliance with the standardized feeding protocol increased from 53 to 57%, with the highest reliability in the components of starting enteral feedings within 48 h of delivery and beginning with a small (trophic) volume for 3 days prior to advancing volume. The compliance measure was an all-or-none metric, and the later time points were affected in a cumulative manner by patient factors, such as feeding intolerance. A pareto of failures in compliance with the feeding protocol illustrates many of these patient factors (abdominal distension, emesis, high levels of respiratory support), and the distinction between

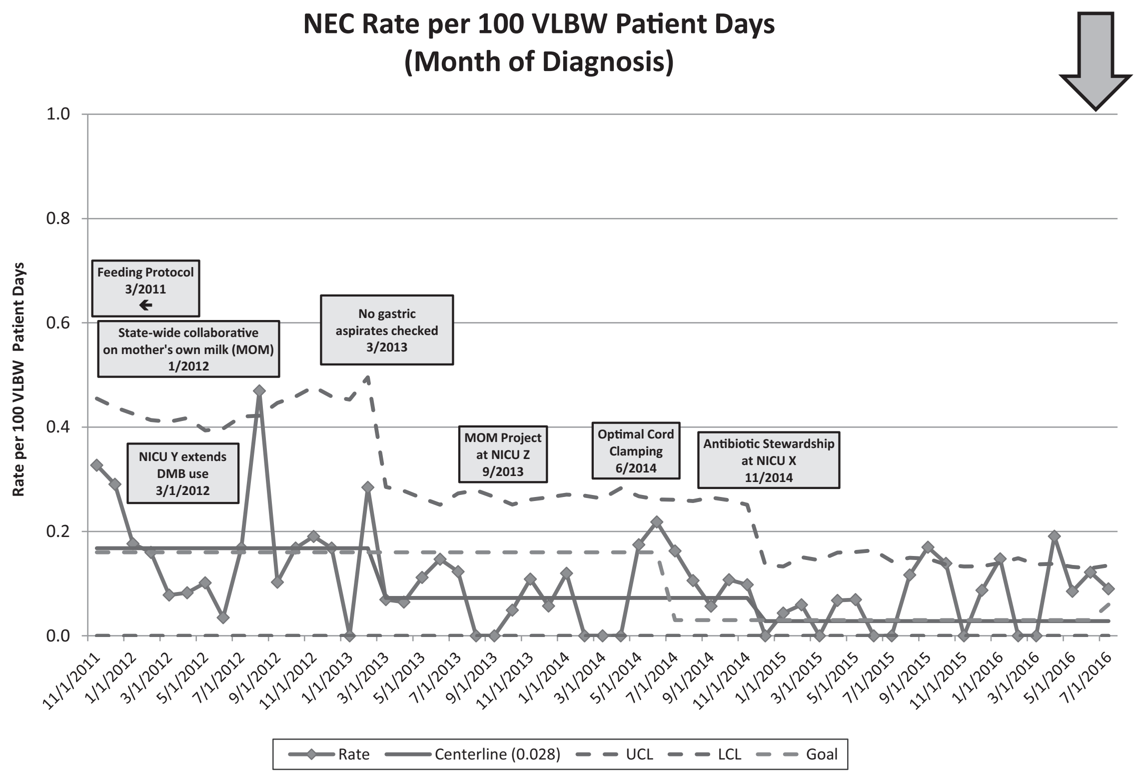


Fig. 2 Run chart of NEC cases in neonates < 1500 g at birth

"staff failures" (mistakes or intentional non-compliance by providers), and "patient failures" are also illustrated in Fig. 4a,b. Most failures of the feeding protocol were related to patient-specific factors, rather than staff failures that would be modifiable. Most of the "staff failures" were either unintentional mistakes in orders placed by the housestaff or a conscious decision to advance faster than the protocol would dictate (especially for older, SGA infants who were orally feeding), or slower than the protocol would dictate (often due to respiratory instability). The process measure of optimal cord clamping also has shown dramatic improvement over time, increasing to a mean of >95% (Suppl. Figure 4).

After testing a variety of physical spaces accessible to mothers for pumping while in the NICU, the team concluded that shared space between staff and mothers for milk expression was the most efficient use of space and reduced pumping wait times. Another intervention to increase the maternal milk supply was reporting of the proportion of enteral feedings that was mother's own milk during daily rounds. This raised the awareness of potential low milk supply issues, and engaged the team in the discussion and collective problem solving. Lastly, information about pumping was added to the sign-in log that parents use at the NICU entrance, as this was a consistent touchpoint for families.

Results of the testing of various feeding practices included the change to NOT checking gastric aspirates. A collateral benefit of this change was a decrease in the number of abdominal radiographs performed (Suppl. Figure 5), as the presence of gastric residuals historically prompted housestaff (especially those who are less experienced) to obtain an abdominal X-ray. This intervention was tested in one unit (NICU X) and then spread to NICU Y. NICU Z, which cares for a large population of surgical patients, chose not to adapt this change due to lack of buy-in from the surgical team. Audits also revealed that the temperature at which feedings were given varied widely, and milk was sometimes allowed to reach temperatures considered unsafe, or was left unrefrigerated for longer than the current guidelines recommended. After testing a number of processes for warming milk, mechanical warmers, designed specifically for human milk in the hospital setting, were purchased. The team decided not to pursue the routine changing of feeding tubes after the data showed that the average dwell time was only 7–10 days at baseline.

A change in practice to order a specific number of antibiotic doses was made, and pharmacists were empowered to discuss, during rounds, situations, in which antibiotics were continued in the face of negative cultures. Data on antibiotic use was shared (in a de-identified fashion) in monthly team meetings. This intervention was tested in one unit (NICU X)

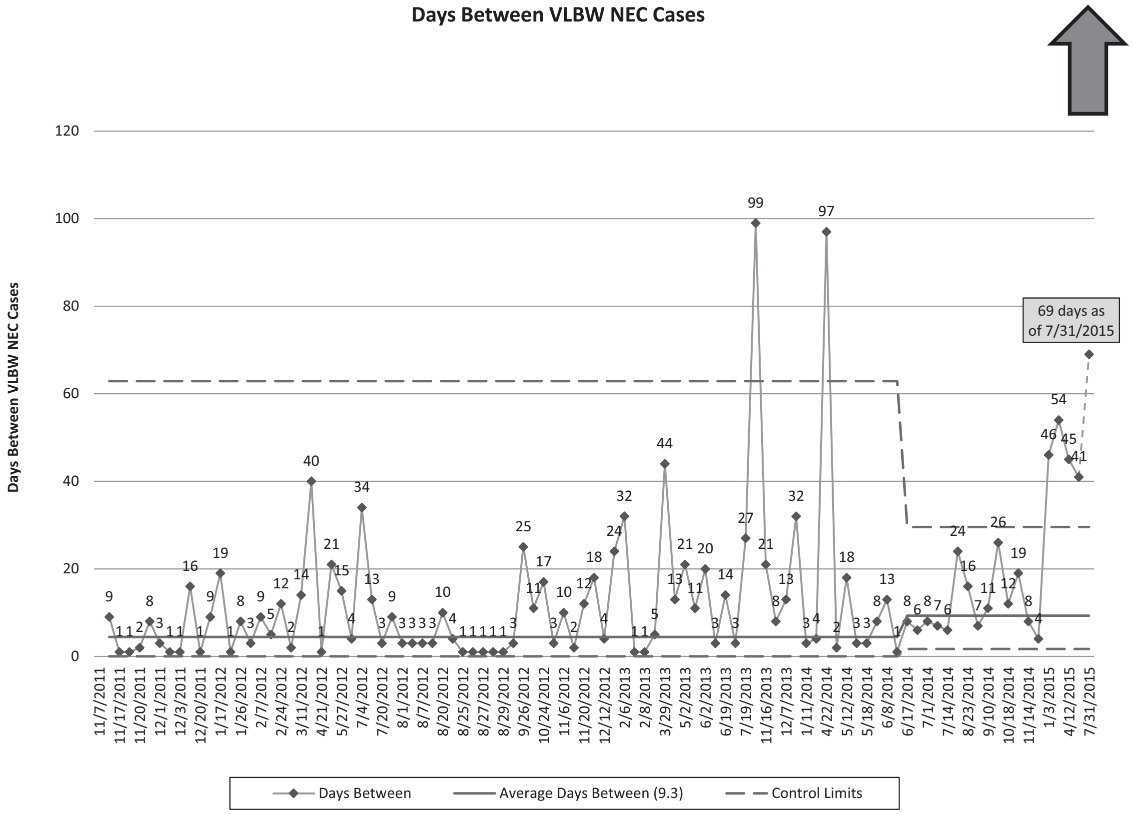


Fig. 3 Days between cases of NEC

and spread later to NICU Z. NICU Y already had an effective antibiotic stewardship program in place, and therefore did not actively work on this intervention.

The first-line treatment for PDA using ibuprofen instead of indomethacin was tested, with eventual change in the hospital formulary. Implementation of optimal cord clamping protocols were spread between hospitals.

Discussion

Through reliable implementation of evidence-based practice changes, this project reduced the regional rate of NEC by 83% from baseline. This translates to lives saved for premature infants, and the reduction of associated morbidities, including impaired neurodevelopment, and catastrophic complications, such as short gut syndrome requiring small bowel transplant.

By decreasing cases of NEC, the project provided substantial cost savings to families, health plans, and hospitals. It is estimated that each case of NEC treated medically costs an additional $74,004 over and above the average costs incurred for extremely premature infants without NEC. NEC requiring surgical intervention costs an additional $198,040 [26]. Project results demonstrated that 49 cases of NEC were prevented over a 5-year period. Using the published financial estimates and data that approximately 35% of cases of NEC require surgery, cost savings for surgical NEC cases is calculated to be $3.3 M. Patients treated medically would have incurred costs of $2.4 M. This translates to a total reduction in cost over the 5-year period of the project of $5.7 M.

The major financial investment in this project was the extension of the donor human milk program to four weeks (instead of two). This represents a logarithmic increase in cost, as the volumes of milk needed increased exponentially with the growth of infants. However, the return on this investment has been significant and is consistent with other studies [27, 28].

The key outcome and the primary driver of project success was the standardization of care across multiple NICUs resulting in the consistent application of best practices and the reduction in variation. Our neonatology group now provides clinical care in five Level III/IV NICUs, each belonging to a different hospital system. Three of the five were a part of the original multidisciplinary group formed to reduce NEC through QI methodology, and the central intervention of a standardized feeding protocol was developed together. However, the implementation was carried

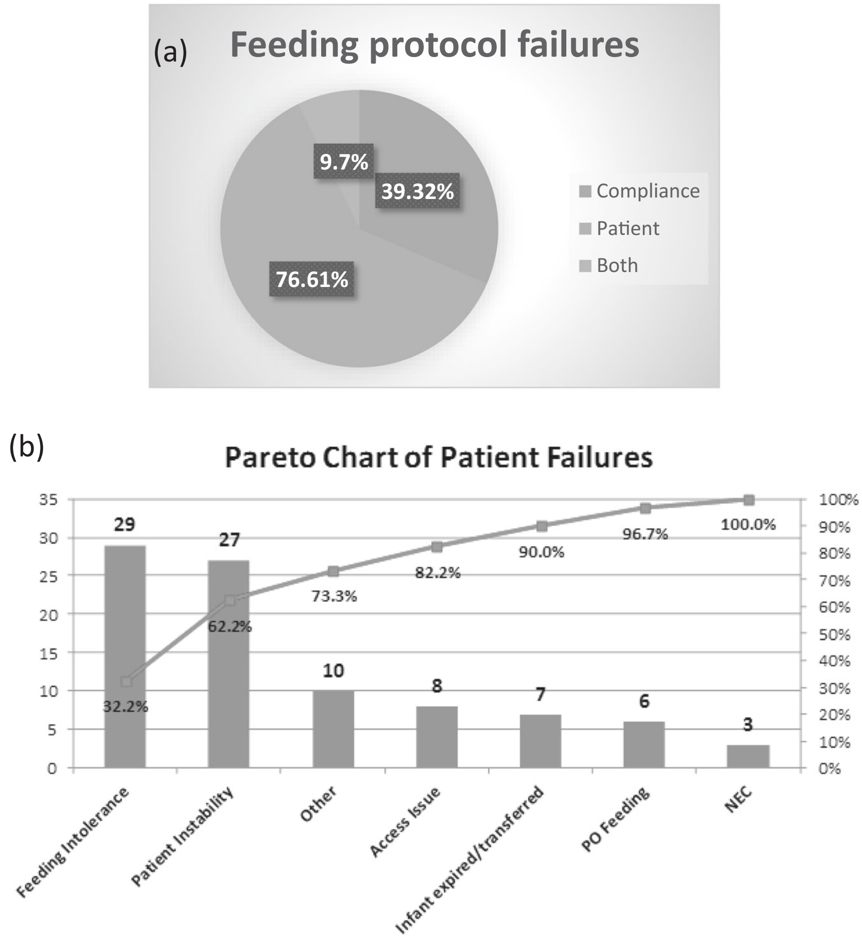


Fig. 4 **a** Comparison of staff (compliance)-related failures of adhering to the feeding protocol with patient-related factors **b** Pareto chart of patient-related factors leading to failure to follow the feeding protocol

out in a site-specific manner testing various approaches in unique cultural contexts.

The spread process for interventions was also a key element of the project design and resulted in rapid adoption of process changes and buy-in among staff at the participating NICUs. If a NICU-specific testing group decided to adopt a particular change, it was then systematically spread to the other NICUs. As this process continued, data were analyzed in relation to the timing of the change adoption. This enabled the project to have greater confidence in the impact of the interventions, while spreading at the same time. This process also facilitated more efficient testing and progress monitoring of key drivers, as simultaneous testing occurred for different drivers at multiple sites.

Examining the data in a frequent and accurate manner was crucial to the success of this and any QI project. Our work illustrates the limitations of national benchmarking networks to fulfill data needs. Although these networks and databases have utility in comparing performance of NICUs across the country, the ability to relate cases temporally to changes being tested was not met until the adoption of a novel method to express cases of NEC (cases per 100 VLBW days). A unique aspect of the project was the conscious decision to track NEC cases in a manner analogous to cases of central line associated bloodstream infection (CLABSI)—with patient days as a denominator—rather than as a simple rate. This was crucial to link the temporality of NEC cases with ongoing improvement efforts, while allowing the monitoring of change with more rapid testing cycles.

Another novel aspect of our project is the application of the model for improvement across different hospital systems. This approach facilitated cross-hospital collaboration and integration, with concurrent independent initiatives, accelerating learning and progress. Although working with nursing and dietary personnel from different hospital systems with different reporting structures was challenging, particularly in securing the time for front-line staff to participate, this collaboration and the relationships that developed from the ongoing interactions has helped lay important groundwork in the region benefiting the health of newborns impacted by future projects. Another barrier in working with competing hospital systems was a reluctance to share data and concerns about transparency. Other multicenter learning collaboratives (such as Solutions for Patient Safety) have addressed this issue with a

Memorandum of Understanding signed by the participating centers, and a culture that "network hospitals will not compete on safety."

Prior studies have documented reduction in NEC cases when feeding practices are standardized [29–32], and when human milk is the preferred substrate [33, 34], thus these approaches were the foundation of our work. Standardization of feeding practices was beneficial, despite a lack of evidence of each step of the feeding protocol. The published literature demonstrates that adherence to a feeding protocol, irrespective of the details of that protocol, has been shown to decrease NEC rates [35]. Although the details of a feeding protocol have been shown to be less important than actually having a standardized protocol, reaching consensus on the feeding protocol was one of the most challenging aspects of the project, and took more than 6 months to accomplish. However, once the consensus was established and reliable compliance was achieved, our results supported the previously published finding that adherence to a protocol can decrease rates of NEC.

A major strength of this project is generalizability, as three different NICUs participated, each with a unique patient population and local context/microsystem. The interventions applied are practical and transferrable to other groups, and with the exception of a Donor Milk program, are not costly to the hospital. We believe that all components of our bundle of care are important in reducing NEC. Some of our NICUs already had consistent protocols around the bundle elements in place; therefore, decisions about where to focus improvement efforts may be NICU-specific, in order to achieve care practices that address all of the key drivers of NEC.

Limitations to these findings include the fact that our NEC rates were higher than the average to begin with (though they had been high with little variation for several years). Another weakness of this project is the fact that we did not track the surgical NEC cases separately from medically managed cases. Although the general impression of neonatology and the surgical teams is that we have seen a more dramatic decrease in surgical NEC cases, we do not have data over time to demonstrate this conclusively. Finally, the length of the project also introduces the possibility that other practices changed over time, and could have had an impact on this outcome. Our current rate of NEC is now lower than the national average [36], but there continues to be room for improvement, and we did observe some rebound in NEC rates when the project was moved from active improvement to sustain mode. Learning from the best-performing centers may provide insight into further key drivers and interventions to test.

In summary, NEC is a complex disease with multiple risk factors and pathophysiology that is not yet clearly defined. To impact this major clinical outcome, simultaneous improvement strategies addressing a variety of key drivers were used to approach the problem. Learnings from this project, over a number of years, have shown that multiple interventions may be necessary to effectively reduce NEC, and should be chosen based on context-specific details of the care environment and the population.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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