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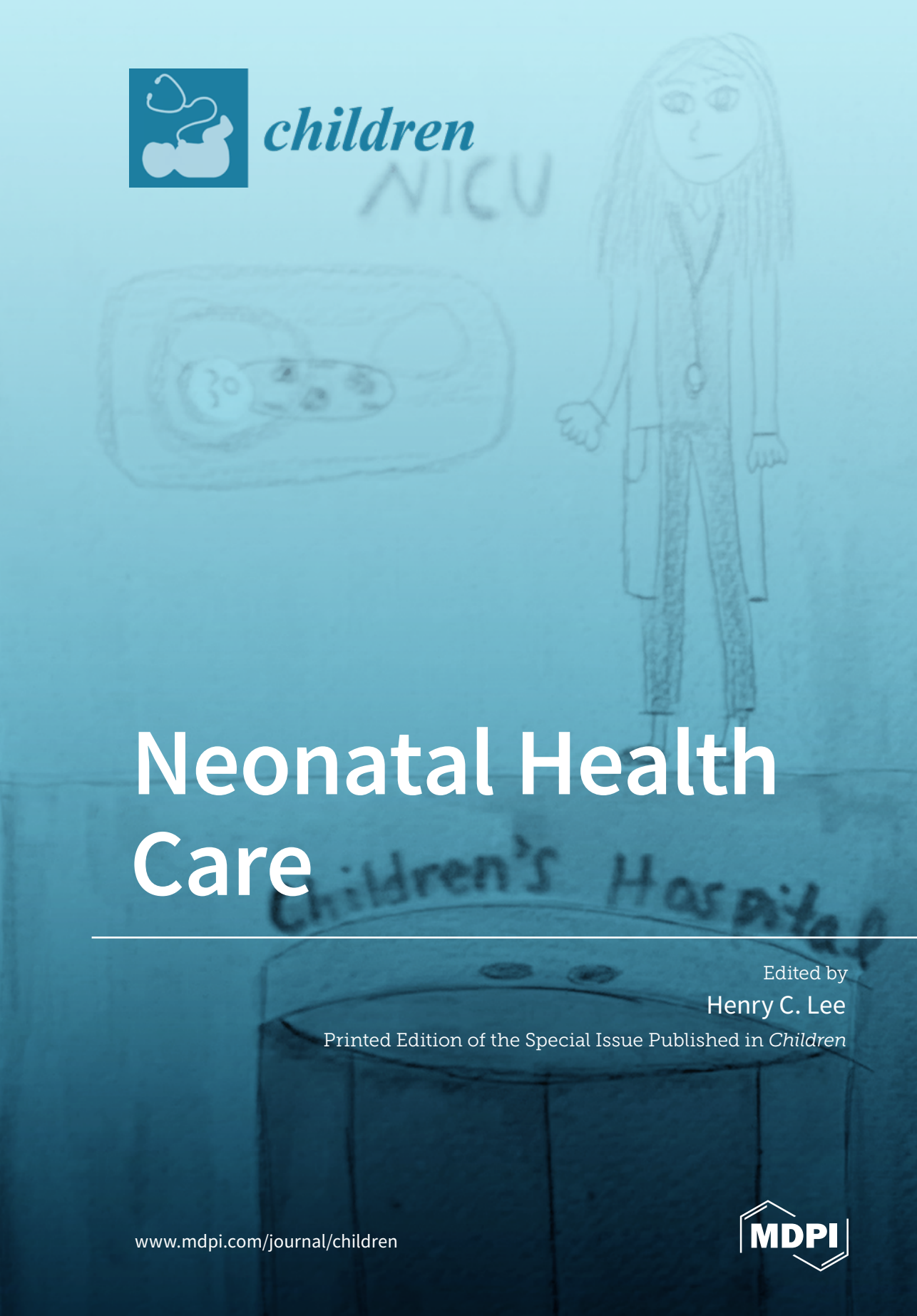

Neonatal Health Care

Edited by
Henry C. Lee

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About the Editor

Henry C. Lee is Associate Professor of Pediatrics (Neonatology) at Lucile Packard Children's Hospital Stanford and Chief Medical Officer of the California Perinatal Quality Care Collaborative.

Preface to "Neonatal Health Care"

This issue of Children concerns healthcare delivery and research in neonatology. Several articles concern the work of the California Perinatal Quality Care Collaborative, including a history by founder Dr. Jeffrey Gould, and recent quality improvement work. Other articles concern methodological issues in neonatal research and findings of recent clinical studies.

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Commentary

Building the First Statewide Quality Improvement Collaborative, the CPQCC: A Historic Perspective

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Abstract: The California Perinatal Quality Improvement Collaborative (CPQCC), founded in 1997, was the country's first statewide perinatal quality improvement collaborative. Our goal was to improve the quality and outcomes of perinatal healthcare in California by developing a collaborative network of public and private obstetric and neonatal providers, insurers, public health professionals, and business groups to support a system for benchmarking and performance improvement activities for perinatal care. In this presentation, we describe how viewing the CPQCC as a complex value-driven organization, committed to identifying and addressing the needs of both its stakeholder partners and neonatal intensive care unit (NICU) members, has shaped the course of its development.

Keywords: collaborative quality improvement; perinatal healthcare; neonatology

1. Introduction

An essential factor in the success of any innovative endeavor is to have a clear picture of what you want to achieve, its potential benefits, and even more importantly, the identification of factors that may block innovation, and potential strategies to overcome them. When we first entertained the possibility of California as the site to create the country's first statewide perinatal quality improvement collaborative, we were told that especially in California, it would be impossible. In the late 1990s, California was known for the competitive fragmentation of the perinatal provider community. Deregionalization had led to competition and distrust between the traditional academic centers and the emerging community-based neonatal intensive care units. Within community providers, there was competition between emerging large-scale multisite provider groups and the more traditional hospital-based neonatal programs. Geographically, there was even open competition between academic referral centers based in northern and southern California.

Engaging the state health systems as essential partners proved to be another challenge. Although it was imperative to recruit California Maternal and Child Health, California Children's Services, California Vital Records, and Office of State Health Planning and Development (OSHPD) as working partners, these groups tended to exist within independent silos and initially viewed the creation of a statewide, data-driven, provider-based quality improvement organization as trespassing into their specific territories. However, within perinatal medicine, a call for health provider accountability was also emerging both nationally and locally. California's Pacific Business Group on Health, an essential potential partner representing the interests of payers and by extension, the healthcare of their families, supported the idea of building an organization to assess the quality of care. However, this group's motivation was consumer advocacy rather than quality improvement. They were gathering, assessing, and report carding their own outcomes data without provider input and were viewed almost as an enemy by the provider community—an enemy whose goal was not to promote quality improvement but to bring about the elimination of low performing institutions. Given the many disparate interests

that existed in the mid-1970s, the creation of a statewide California perinatal collaborative built upon the essential partnership of perinatal providers, state health organizations, and consumer advocates seemed all but impossible.

There was, however, a series of events that suggested the possibility of developing a statewide collaborative. Dr. David Stevenson and colleagues had recently developed the California Association of Neonatologists (CAN). Dr. Stevenson felt that, to strengthen CAN's foundation, it would be important to involve its members in an important and far reaching project. In a conversation with David, I proposed that developing a quality improvement collaborative to serve as its action arm represented an important enterprise for this new organization. He agreed and became instrumental as a cofounder of the California Perinatal Quality Care Collaborative (CPQCC). Another essential partner, the California Maternal, Child, and Adolescent Health (MCAH) branch, was charged with understanding how well California was meeting the needs of pregnant mothers and their newborns.

In the early 1970s, California MCAH developed and published a risk-adjusted neonatal mortality report for every delivery facility in California. The approach created by Dr. Ronald Williams at the University of California, Santa Cruz utilized the paradigm that outcome was a function of risk, care, and chance. After adjusting for differences in case mix and taking chance into account, one could develop an estimate of risk-adjusted neonatal mortality for each California delivery hospital that could be benchmarked against all California facilities. Although well-intentioned, the report was highly technical in its format and its public release was controversial. This led to its being abandoned due to unfavorable acceptance by the provider community. However, by the mid-1990s, in large part due to the publications of the risk-adjusted variation on surgery in New England by Wennberg and Gittelson [1] and outcome variation in chronic lung disease across eight neonatal intensive care units (NICUs) attributed to variation in practice effectiveness by Avery [2], the traditional notion that quality could be assured on the basis of institutional reputation was rapidly being replaced by an emerging need to assess the quality of care based on timely, case mix-adjusted outcome data. Responding to this emerging need, several California hospital systems convinced MCAH to reinitiate these reports. Working in the Maternal Child Health program at the University of California, Berkeley School of Public Health, I had developed for California MCAH one of the country's first perinatal geographic information systems that combined sociodemographic US census data with data from state birth and death certificate records to profile perinatal risks and outcomes for each zip code in California [3]. Because of the success of this utility in identifying hot spots for adolescent pregnancy intervention [4] as well as other indicators of perinatal need, I was asked to develop and recreate William's yearly risk-adjusted rates of neonatal mortality for each of California's ~280 delivery hospitals. Because neonatal mortality is an uncommon event, I felt that collecting data on neonatal morbidity would provide a more sensitive measure of the quality of care and was able to explore the feasibility and approach to risk-adjusted neonatal morbidity analysis as part of the work scope. The big stumbling block in developing this approach was how to obtain morbidity data to perform the analysis.

Dovetailing California's need for outcomes assessment and CAN's need for a significant project, we proposed the development of a statewide collaboration of neonatal intensive care and obstetric care providers to both assess and improve perinatal morbidity. We were able to enlist Dr. Rugmini Shah, Director of California's MCAH, as a cofounding partner. Dr. Shah put us in contact with Dr. Maridee Gregory, the director of California Children's Services (CCS). CCS paid for the majority of neonatal intensive care in California and had the responsibility to assure that this care was of high quality. In order to do this, they had created a multipage report form that each NICU was required to submit each year. Compliance was extremely poor and even when reports were turned in, the workload at the state did not allow for a careful analysis of these reports. The possibility of an organization that would collect outcomes data and provide risk-adjusted benchmarked estimates of quality care brought CCS on board. The leadership of MCAH and CCS helped to enlist state vital statistics and the OSHPD as members of our executive leadership committee.

At this point, we had enough enthusiastic support for a collaborative to collect risk-adjusted perinatal morbidity data. The remaining challenge was how to build a statewide perinatal database. Once again, serendipity came to the front. The Vermont Oxford Network (VON) was established in 1989 with the primary goal of conducting volunteer-based randomized clinical trials in the NICU following the model developed at Oxford in England. Their first step was to build a multi-institutional database. I was fortunate to be involved as a consultant with Drs. Jerold Lucey and Jeffrey Horbar at VON's inception and had followed their expansion to NICUs across the US. Although the development of VON had been largely funded by California's Lucile Packard Foundation, the number of VON NICUs in California in 1996 was only 12. In discussions with Drs. Horbar and Lucey, we explored the possibility of developing a statewide expansion of the VON database as the backbone for the development of the California Perinatal Quality Care Collaborative (CPQCC). Our goal was to focus on quality improvement rather than randomized clinical trials.

In 1997, we applied to the Packard Foundation and were able to put together funding from Packard, state MCAH, and CCS to establish the CPQCC. The plan was to develop the CPQCC as the action arm of CAN with the goal of developing a collaborative *network* of public and private obstetric and neonatal providers, insurers, public health professionals, and business groups to support a system for benchmarking and performance improvement activities for perinatal care. It is important to note that the purpose of the collaborative was not the passive documenting and reporting of outcomes. Our mission was to collect the data needed to inform activities designed to improve perinatal outcomes for all of California. We were fortunate to recruit Dr. David Wirtschafter, one of neonatology's pioneer quality improvement advocates who stated our task as (1) collecting high-quality reliable data, (2) transforming the data into information by the development of fair risk adjustment and timely reports that inform and organize work, and most importantly, (3) to promote action by supporting perinatal providers in their work of improving perinatal care and outcomes. In addition, we also had an organizational philosophy: (1) That quality improvement was an essential part of perinatal practice, (2) that the collaborative should be bottom-up and provider-driven, and (3) that all aspects of the collaborative should be value-driven. With these as our founding principles and Stanford University School of Medicine agreeing to serve as our administrative intermediary, the CPQCC was launched.

2. Ideating the Creation of a Complex Organization

At this point, we had all of the foundational pieces in place: overall objective, initial funding, administrative home, database platform—the big problem was getting our potential partners to work together as an effective executive committee. That is, how do we get these essential partners not only on board but working together to create an enterprise that had both benefits with respect to their strategic mission but also could potentially threaten their autonomy? Although California's perinatal scene was often described as a hotbed of rivals, the one unifying factor was that all of the potential partners were strongly committed to the goal of improving the health and outcomes of all California mothers and their newborn infants. It is important to note that, in creating the CPQCC's executive committee, we did not want to recruit members as passive stakeholders but as working partners. The overwhelming challenge at this point was how to get them to work together.

I described both the vision and the difficulties I was facing over dinner to friends who were highly successful specialists in organizational development. They responded that what I was trying to develop was a highly complex organization and asked if I had training or experience in this area. I answered that even though my training in Maternal and Child Health had emphasized the importance of putting together multi-stakeholder committees and initiatives, and how to identify stakeholders whose participation would be essential, guidance on how to actually build a complex organization was not part of the curriculum. Their guidance on how to proceed was essential. Thefirst step was to develop the organization's groundwork: (1) craft an initial mission statement that aligns with each stakeholder's strategic goals, (2) craft initial key organizational policies that would not only drive the collaborative but would be acceptable to potential partners, and (3) select who to invite as members of

the executive committee and issue the invitations. The second step was to conduct face to face meetings with each of the potential executive committee members: (1) rank the potential members with respect to their enthusiasm, and (2) begin one-on-one meetings to present and refine the CPQCC's mission and organizational policy. In these discussions, we sought to address the question, "what is your strategic mission and how will partnering with CPQCC advance your strategic mission?"—that is, what are the benefits of your organization's joining the CPQCC? However, it was important to appreciate that while describing all the benefits, the candidate would be thinking about and rarely openly sharing all of the potential downsides. An important but often neglected and absolutely essential part of this discussion is to jointly identify the potential risks that their participation might engender. This will allow understanding of potential risks and begin to construct a risk/benefit "equation" for participation. By understanding their concerns, one will then be in a position to jointly figure out how to maximize benefit and minimize risk. The goal of the face-to-face meeting is to negotiate an agreement with respect to the organization's name, mission statement, policy, their role as a partner, and most importantly, what specific value their partnership can bring to their organization. In building a complex organization, one needs to move the executive committee from passive stakeholders to active partners. To accomplish this, participation must bring value. A fundamental concept especially germane to a quality improvement collaborative is that value is essential for both the initial behavioral change and maintaining the new behavior. A successful quality improvement organization must be obsessed with continuously identifying ways to provide value for its members and partners. Figure 1 shows our founding partners and the value that their participation would provide.

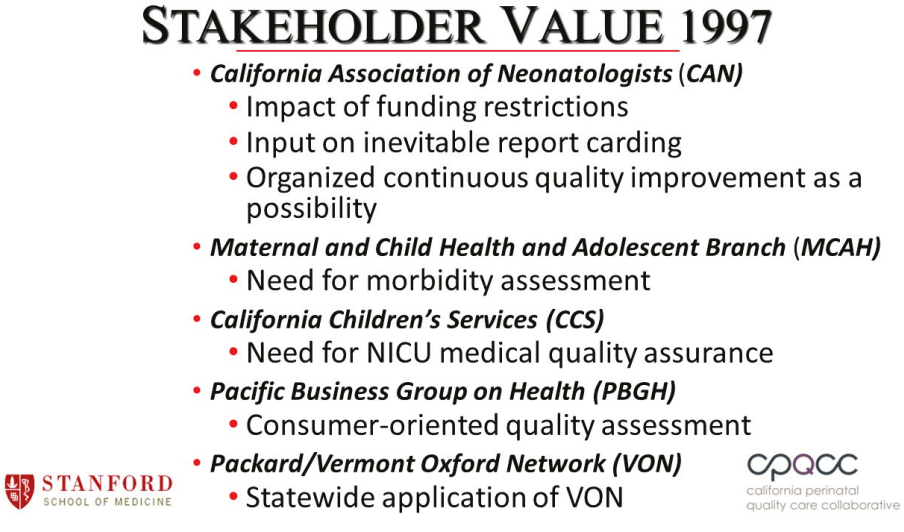

Figure 1. Founding partners and stakeholders involved in the launch of the California Perinatal Quality Improvement Collaborative (CPQCC).

3. Building the Network

3.1. Even More Face to Face

After the first round of meeting individually with each potential partner, the next step was to meet with groups of two potential partners who have a history of not working well together. Again, the task was to jointly modify, as needed, the mission statement and organizational policy and to get them to work together to craft how the CPQCC would facilitate reaching their common strategic goal of improving the health of California's pregnant women and their newborns. We then put together

several groups of three potential partners. This was a very time-consuming process. At this point, we were almost a year from the initial invitation to join the executive committee and folks were asking when we were actually going to meet. We had our first meeting a little over a year from issuing the invitations.

Although the initial meetings described above were with state agency and neonatal practice decisionmakers, when we had our first meeting, many of the participants from state agencies were lieutenants rather than leaders with the power to make decisions essential to partnership. In terms of developing a complex organization, this was a huge setback. Fortunately, we were able to identify several powerful advocates who were able to stress the importance of the enterprise and get the agency decision makers to attend.

3.2. Building the California Database

An important strategy in building a complex quality improvement organization is to solicit participation from the membership and to assure that their participation results in timely action. We recognized that there were many California neonatologists who were interested in data and its analysis. One of our first quality improvement committees was our database advisory group. We carefully recruited so as to have geographic (north, central, and southern California) as well as academic and private practice representation. Beginning with the VON data format, their first role was to identify what we wanted to know and what constituted the minimal data we needed to gain this knowledge. An additional concern was how to ensure that our data were accurate. To this end, we adopted three strategies. The first was the traditional approach of building range and logic checks into the database. Our second approach was to develop an executive committee of data entry personnel. In California, data entry personnel ranged from professional data entry personnel to neonatologists and NICU nurses. In addition, California NICUs varied widely with respect to census and resource. To assure that we had the needed depth of frontline expertise required having broad-based representation on our committee. Their role was to assure that the data element definitions and data entry procedures were clear, that our entry formats were optimally sequenced and presented so as to minimize data entry errors, and to assess the feasibility of extracting and unambiguously defining suggested new data elements. This committee remains a mainstay even to this day. All database and data collection changes must be approved by the committee. Our third approach to assuring high-quality data is to hold yearly data trainings at several locations throughout California. An essential part of these meetings is to identify problems that members are experiencing in data entry and data closeout as well as to present any new data elements that are scheduled for inclusion. Beginning in 2006, each year, several hundred data entry folks attend these meetings. In addition, we made our database team available on a daily basis to answer data entry questions as well as to reach out to centers that had a high number of missing data items.

3.3. The Quest for Value

A successful complex organization must constantly search for ways to increase the value of participation for its members and partners. An early example of identifying ways to provide value was seen with our executive committee whose state participants were in leadership positions within their organizations. We noticed that during the lunch break and at even at the end of the formal executive committee meeting, there would be private conversations among them. Clearly, they were using the meeting for backchanneling. To build value, we stopped the meeting at 2 h rather than the traditional 3.5 h, giving the participants time to do their private business. The result was that we had exceptional attendance, not only to do the work of creating the CPQCC, but also for them to take advantage of the setting for backchanneling.

3.4. CPQCC Database Development Proceeded in Several Stages

Phase 1 (VON in California): At its initiation, we used the standard VON designed paper forms, and scanned them into a data file that we cleaned and submitted to the VON. The VON then provided the CPQCC with a custom yearly standard aggregated VON report for California members and provided the members with yearly individual standard VON paper-based performance reports. This had several limitations. Scanning the paper forms into digital format, running error detection, and then having to have the NICUs make corrections to be re-entered was very labor intensive. Our members also wanted to expand the database.

Phase 2 (Addressing California's needs): The data committee felt that the VON database was a good foundation. They felt the need to include more information on some of the items and to include infants readmitted to the NICU as well as high-risk infants that had birth weights greater than 1500 g. The latter was felt to be essential because in most NICUs, these infants make up the majority of the infants cared for. They also wanted more timely reports and to be able to compare their NICU not only with all California NICUs, but also with California NICUs with the same level of care designation. When we considered all of these new requirements, our systems developer, Dr. Beate Danielson at Health Information Solutions, realized that doing this would require online data submission and real-time report generation. In 2000, we began to process our paper data entry forms, report our expanded database to our members, and submit the "small babies" (birth weight less than 1500 g) subset to the VON. Because the CPQCC is a regional member of the VON, our CPQCC members are also full members of the VON and receive data reports from the CPQCC, enabling comparison with California benchmarks, as well as from the VON, enabling comparison with national benchmarks. This dual source of benchmarking provided additional value to our members. By 2006, our data entry was completely online, and our online data reports were in real time. We also began to compile the yearly mandated CCS NICU activity and outcomes report. Following each NICU's review and at their request, we submitted the report to CCS. To gain a more complete picture of perinatal risks and outcomes, in 2007, we began to collect and include information and a quality assessment on the approximately 7000 acute neonatal transports [5]. In 2009, we worked with CCS to develop and link NICU data to an all California database that assessed the completeness of NICU registration as well as the social/medical needs and developmental outcomes of NICU graduates until age three in California's statewide High-Risk Infant Follow-Up program [6,7]. Because the CPQCC had narrowed its focus to NICU care, there was a need to address California's maternity care. Our sister collaborative, the California Maternal Quality Care Collaborative (CMQCC), was established in 2006 to assess the outcomes of all of California's 500,000+ births using near-real-time administrative data to facilitate rapid cycle quality improvement [8]. This maternal data was then linked to our NICU data. Figure 2 shows the yearly data that are available to support perinatal quality improvement in California.

Phase 3 (Enhancing support for our quality improvement activities). Table 1 shows the development of our data system. As we grappled with how to obtain an overall picture of a NICU's quality, we incorporated the Baby-MONITOR developed by Dr Jochen Profit [9]. In order to support our rapid cycle quality improvement activity, we incorporated control charts as a standard element of our real time online report (Figure 3).

As we continued to focus on and emphasize our work on health equity, we created a disparity dashboard (Figure 4). We plan to assess how our current efforts in incorporating equity goals into quality improvement may lead to reduced disparities. In addition to the quantitative approach outlined above, over the last several years, we realized that although we could identify NICUs that were challenged or highly successful, identifying the factors that held them back or allowed them to succeed required a qualitative approach. We believe that our developing mixed methods approach can greatly accelerate quality improvement interventions by informing both the where there is need (quantitative) as well as the factors that are important drivers of the need (qualitative) [10–14].

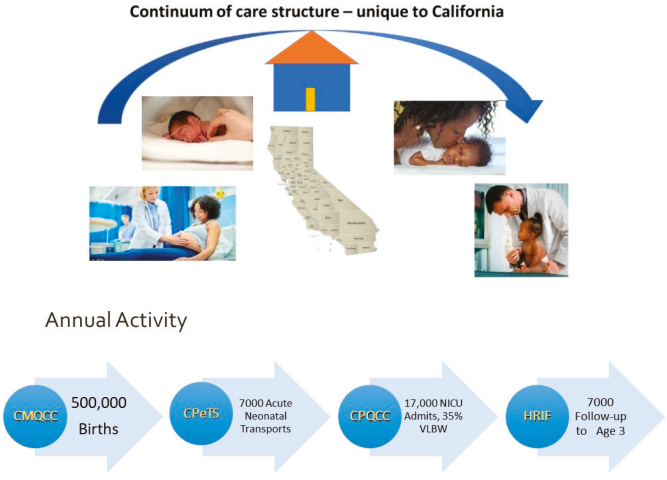

Figure 2. Data to support perinatal quality improvement in California from the CPQCC and California Maternal Quality Care Collaborative (CMQCC) data centers. Images in this figure are licensed for use from iStock.com. NICU: neonatal intensive care unit; VLBW: very low birth weight.

Table 1. CPQCC Database Development.

Year	Data/Feature
1998	VON < 1500 g
2000	High-risk > 1500 g
2007	Real time reporting + neonatal transport
2008	Infants linked across NICUs
2009	Statewide high-risk follow-up until age 3
2013	NICU based follow-up records
2017	Real-time control charts
2019	Baby-MONITOR
2019	Health equity dashboard

VON: Vermont Oxford Network.

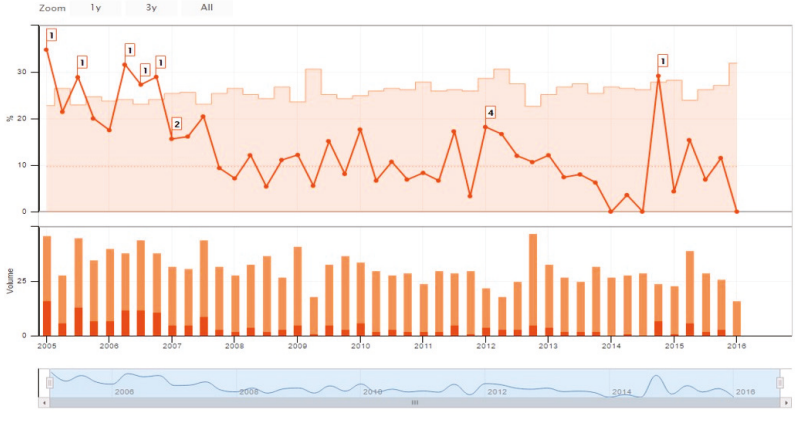

Figure 3. Sample control chart feature for nosocomial infection of a member hospital.

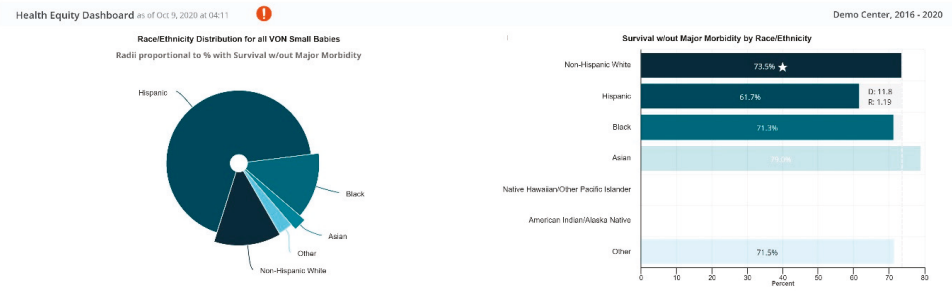

Figure 4. Sample disparity dashboard report.

4. Turning Data into Action

Three elements are essential to any quality improvement enterprise: Collecting high-quality reliable data, presenting real-time risk-adjusted reports that effectively inform opportunities for quality improvement, and most importantly, providing support to perinatal providers in their work of improving perinatal care and outcomes. Our quality improvement arm of the CPQCC was initiated by Dr David Wirtschafter at the inception of the CPQCC in 1997. A key strategy was to create a Perinatal Quality Improvement Panel (PQIP) to design and manage continuous quality improvement (CQI) cycles. Members were chosen to ensure representation from neonatologists (eleven), perinatologists (four), nursing clinical experts (four), administrators of the Regional Perinatal Programs of California (six), and a health plan physician with expertise in quality improvement (QI). Appointments to the PQIP were designed to balance both academic and private practice constituencies as well as to ensure regional representation. The PQIP guides all of the CPQCC's quality improvement activities including choosing collaborative topics, creating toolkits, and designing innovative QI models. The PQIP's subcommittees serve as action arms for the panel by creating and disseminating tools and information that help CPQCC members implement the PQIP's QI recommendations. From its modest beginning, the PQIP has grown to include four committees on Analysis (to identify quality improvement needs), Education, Research (analyze and publish results from our QI collaborative projects), and QI Infrastructure. These committees meet monthly and are made up of physicians, nurses, and other NICU personnel who, together, contribute more than 100 hours a month as volunteers. Each committee develops a yearly strategic plan and timetable of accomplishments and their status in meeting these goals is presented at each of the quarterly all PQIP meetings. We believe that strategically and when appropriate, rapidly moving from plan to action has been a key to success.

The PQIP began to develop and release quality improvement toolkits that were freely available on the CPQCC's website [15] from its inception with a commitment to review and update regularly. Our first toolkit, which concerned administration of antenatal steroids prior to preterm delivery, was developed and released within a year of the CPQCC's inception. Believing in the essential importance of rapidly moving from plan to action, we launched our first full-scale quality improvement initiative on improving the use of antenatal steroids in 1999 [16]. The format of our approach to formal statewide QI initiatives has also evolved over time. Our highly successful initial approach developed by Dr. Wirtschafter was based on identifying topics with improvement potential, assessing the validity of potential improvement strategies, and then developing readily available web-based toolkits and launching statewide educational lectures, webcasts, and workshops across California and at the CAN annual meeting. These sessions included small group discussions addressing implementation goals, barriers faced, and ways to overcome them. NICUs registered to participate. However, the actual implementation was conducted individually at each NICU without formal oversight. Although the toolkit/workshop approach was highly successful [17], CPQCC shifted to the Institute for Healthcare Improvement (IHI) Model [18].

The goals of adapting the IHI model were to build practical improvement capacity based on the science of improvement into every CPQCC NICU, healthcare executive, and clinician, while driving innovation to dramatically improve performance at all levels of the health care system. The advantages of the IHI model include commitment to a specific level of improvement within a specified timeframe; accelerating achievement from a community of learning approach; the use of Plan Do Study Act (PDSA); cycles of intervention monitored by recording agreed upon process, outcome, and balancing measures on a run chart; and each NICU's reporting of their progress to the group on monthly meetings. Movement to several elements of this approach was successfully demonstrated by Dr. Wirtschafter with the statewide CCS/California Children's Hospital/CPQCC catheter-related infection initiative. As the final report points out, it was clear that the participants that routinely conducted multiple audits during the course of their projects (a precursor to the IHI PDSA-run chart approach) were the most successful. To fully integrate the IHI approach into the CPQCC, the leadership of CPQCC's quality improvement arm transferred to Dr. Paul Sharek in 2008. Although not a neonatologist, Dr.'Sharek was highly experienced with the IHI breakthrough approach. He also introduced the use of quality improvement approaches to the work conducted by the PQIP committees. A difficulty with many committees is the disconnect between discussion and action. By employing yearly strategic goals, a timetable for their accomplishment, and monthly reporting of progress, members of our committees experience their discussions and plans actually leading to timely action. This approach is not only important to the membership who will benefit from the action but is highly motivational to the members who volunteered to participate in the committees. As shown in Table 2, the CPQCC has conducted six highly successful QI Collaborative based on the IHI model over the past 10 years. The first collaborative using this approach, Healthcare-Associated Infections was from February 2008 to January 2009. The 19 NICUs in the Healthcare-Associated Infections Collaborative decreased catheter-associated bloodstream infections (CABSIs) by 75% in infants with birth weights ≤ 1500 g.

In October 2018, leadership was transferred to Courtney Breault, a neonatal nurse with expertise in quality improvement who had served as codirector of the Quality arm since its inception, and Dr. Jochen Profit, a neonatologist and health services researcher expert in quality improvement. Several challenges that they faced were how to effectively reach out to vulnerable NICUs who had not participated or rarely participated in our formal QI programs, how to address racial and socioeconomic equity into our quality improvement work, and how to meet the data and quality improvement needs unique to certain CPQCC NICUS. These include addressing the specific needs of NICUs of our high-volume children's hospitals with their many surgical cases and also addressing the needs specific to our small low-volume NICUs. To identify their specific needs, the PQIP recommended that two workgroups be created. Based on their feedback and input, the CPQCC has created QI initiatives tailored to their needs.

In order to better meet the quality improvement needs of our diverse NICUs, we have moved away from the biannual all-NICU formal initiative approach of the past to several concurrent initiatives specifically designed to meet the diverse needs of our member NICUs. In 2021, in addition to an all-newborn ICU offering neuroprotective care, we will have two growth and nutrition initiatives, one designed to meet the needs of smaller low-volume NICUs, and a second to meet the needs of postoperative surgical infants cared for in our Children's Hospital NICUs. In addition, we are incorporating the use of vignettes to identify the extent and areas of decision-making variability. This approach, which has been led by Dr. Kurlen Payton, allows our QI facilitators to identify and work on those areas of decision-making that require greatest attention. A further advance in our approach to QI is the incorporation of the ECHO model that will be piloted by a team that includes Dr. Payton and Dr. Henry Lee in our upcoming Optimizing Antibiotic Stewardship Initiative.

Table 2. CPQCC Quality Improvement (QI) collaborative projects based on the Institute for Healthcare Improvement (IHI) Model for Improvement.

Project	Dates	Number of NICUs	Summary	Result
Healthcare-Associated Infections	Feb 2008–Jan 2009	19	Aim to decrease catheter-associated bloodstream infections in very low birth weight infants	Reduction of 75% in infection rates
Breastmilk Nutrition Collaborative	Sep 2009–Apr 2011	11	Increase breastmilk feeding rates for very low birth weight infants	Participants increased breastmilk feeding rates at discharge to home from 54.6% to 64% and decreased necrotizing enterocolitis rates from 7% to 2.4% [19]
Delivery room management	Jun 2011–Nov 2012	20	Improve management for high-risk deliveries with focus on thermal management, reducing invasive ventilation, and supporting teamwork	Collective decrease in admission hypothermia, delivery room intubation [20]
Optimizing length of separation	Jun 2013–May 2015	20	Reduce length of stay for infants born between 27–32 weeks gestational age	Participants decreased length of separation by average of 3 days and increased early discharge (before 36 weeks, 5 days) from 41.9% to 31.6% [21]
Antibiotic stewardship	Jun 2016–Nov 2017	28	Reduce antibiotic utilization rates through bundle including antibiotic "time-outs"	Estimated to have reduced antibiotic days by 11,700 and decreased antibiotic utilization rate by 13.8%

5. Quality Improvement Research and Training

It is important to note that the principle focus of a quality improvement collaborative and its database should always be quality improvement. As many CPQCC members are academic centers and all neonatologists receive research training during fellowship, research using the infrastructure of the CPQCC has always been a consideration. However, as the primary mission of the CPQCC is quality improvement, the efforts of research need to be considered an important but secondary goal. In that context, we also recognize that as a large statewide QI organization, there are opportunities to advance science in several ways. First, we have aimed to lead the efforts of QI science. It is important to evaluate the effectiveness of QI interventions and learn from past projects in order to inform future QI work. We consider it an obligation to formally study QI in order to benefit both CPQCC members and the larger QI community. Second, the infrastructure of data collection in the CPQCC allows for opportunities in both observational and prospective clinical research. These have included supplemental data collections, epidemiologic studies, health services research, and the facilitation of clinical trials.

6. Conclusions

We end with some of the lessons learned from the development of the CPQCC:

1. Perinatal Quality Collaboratives (PQCs) are complex organizations that rely on the effective contribution of partners who may have differing agendas and approaches to the common goals

of the collaborative. Engaging an expert in organizational development can greatly facilitate developing a coherent, productive collaborative.

2. Identifying and increasing value is the essential driver of participation, behavioral change, and maintaining the new behaviors. An ongoing task for successful PQCs is to continuously look for ways to increase value for members and stakeholders.
3. Rapidly moving from committee discussion to action creates dynamic energy for the membership as well as a sense of accomplishment for the members of the committees. Avoid spending lots of time to plan the perfect intervention. The IHI approach of multiple tests of change will refine the project as it proceeds by incorporating approaches that work and rapidly abandoning approaches that do not.
4. Using the smart aim approach [22] to define specific goals within a specified timeframe, and formally reviewing progress on a quarterly basis, at a minimum, is an essential strategy across the enterprise. This is especially important for volunteer committees as it facilitates reaching their defined objectives within a reasonable timeframe. This provides not only a useful product for the members but also instills a sense of motivating accomplishment to the volunteers.
5. Seek the expertise needed for success in your front line. Whereas the leadership can set out the destination, it is the frontline folks who have the working experience to understand what has to be changed and how it might most efficiently be changed to reach the destination.
6. When designing a quality improvement initiative, make sure that all of the elements required by the SQUIRE publication criteria will be met. A critique of this sort will often strengthen final intervention design, data collection, and analytic strategy.

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Review

The Denominator Matters! Lessons from Large Database Research in Neonatology

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Abstract: Observational studies from large datasets are becoming more common in neonatology. In this review, we highlight the importance of the denominator in study design and interpretation including examples of bias from source data, weight-based categories, age-related bias, and diagnosis-based denominators.

Keywords: infants; infant; neonatal intensive care; health service research; statistics; study interpretation

1. Introduction

Observational studies from "big data" sources are important for generating hypotheses and for doing comparative effectiveness studies when randomized controlled trials are not feasible. In neonatology, we are fortunate to have several high-quality datasets, including from National Institute of Child Health and Development [1], the Canadian Neonatal Network [2], the Children's Hospitals Neonatal Consortium [3], the Vermont Oxford Network (VON) [4], the California Perinatal Quality Care Collaborative [5], and our own dataset—the Pediatrix Clinical Data Warehouse (CDW) [6].

Clinically relevant insights have been reported from all of these sources, and these studies are becoming more common every year. Therefore, we must be intentional in the design and interpretation of findings from these sources. Critical review of these studies tends to focus primarily on the observational numerator—such as how the exposure or outcome is defined or how to account for confounding factors. We feel that the denominator deserves similar scrutiny.

Our goal with this review is to demonstrate how the denominator can be a hidden source of bias in retrospective observational research. A better understanding of these issues can help both clinicians and researchers in applying appropriate context to this type of data.

2. Ascertainment Bias in the Source Population

Ascertainment bias refers to bias that results from the sampling method. All of the neonatal databases have specific enrollment criteria for an infant to be included in the dataset. Notably, these criteria are unique to each dataset, and these differences can have important ramifications on study design.

In 2015, Rysavy et al. [1] published an insightful observation about mortality at periviable gestations. He found that "differences in practices regarding the initiation of active treatment in extremely preterm infants appear to explain a large portion of the between-hospital variation in survival among such patients". Although we would have liked to validate this observation across our ~300 centers, this study would not have been possible using the Pediatrix CDW, which only collects data on infants that are admitted to the neonatal intensive care unit (NICU). None of the infants

who died in the delivery room could be included in the denominator in a CDW study examining the same relationship.

This issue extends to the other end of the gestational age spectrum as well. The criteria for inclusion of larger and more mature infants in many of these datasets select for infants who are also ill enough to require critical or intensive care. This is a minority of term infants (Figure 1), and so, studies evaluating less severe diseases in term infants (such as neonatal hypoglycemia or hyperbilirubinemia) sourced from the CDW (or other NICU-based datasets) are likely to under-report disease incidence.

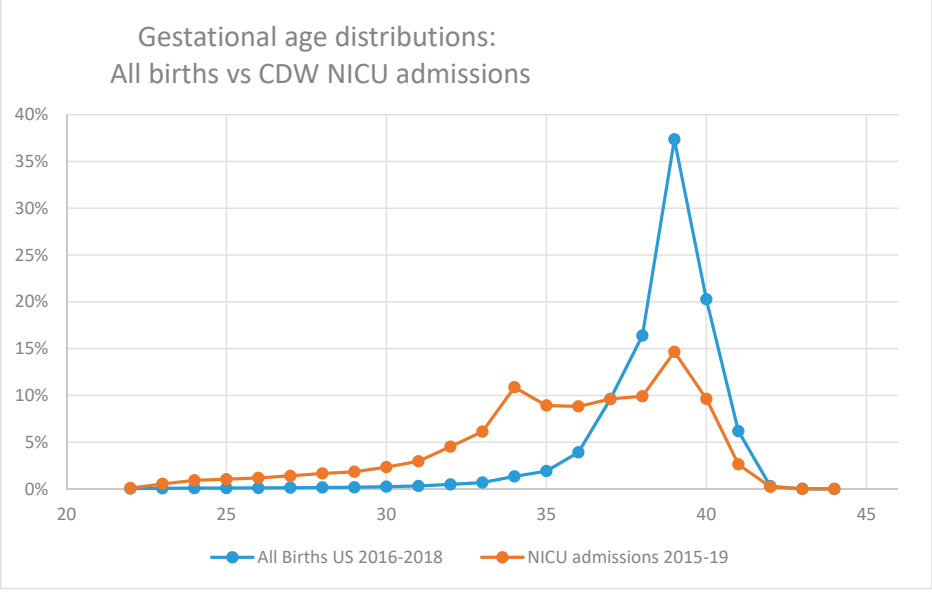


Figure 1. Gestational age distributions: all births vs. neonatal intensive care unit (NICU) admissions. Data derived from the Centers for Disease Control and Prevention and the Pediatrix Clinical Data Warehouse (CDW).

One method to account for this is to include an unrelated but similar diagnosis that can act as an internal control. When we reviewed the changing prevalence of gastroschisis, we used the prevalence of patients with omphalocele to act as an internal control. We assumed two similar gastrointestinal anomalies would vary in a similar way if referral or care parents explained the changes. We found that the prevalence of gastroschisis changed in significant ways but the prevalence of omphalocele was much more consistent [6].

Gestational age is not the only cause of bias in source data. Cohorts derived from Children's Hospital NICUs have a referral bias in that the infants admitted to their sites are more likely to have complex diagnoses or require specialized care [3]. The effect of referral bias goes both ways. A level 2 NICU may have a zero mortality rate if that NICU consistently refers all of its critically ill infants to a regional level 4 NICU. Transferred patients are sometimes included in the denominator, but because their final outcome is not known, their data are not included in the numerator.

Studies of infants with a poor prognosis (such as hydrops fetalis or genetic anomalies) can have ascertainment bias from several sources: prenatal diagnosis may result in pregnancy termination, and infants who are receiving palliative care may receive care in the NICU. These factors complicate comparisons between datasets and can limit overall study generalizability, so it is essential to understand the context of source data.

3. Selection Bias from Weight-Based Cohort Selection

In neonatology, it is common to define infant categories based on birth weight. Study cohorts will select for very low birth weight (VLBWs) or extremely low birth weight infants (ELBWs). Although these definitions are based on objective measures that are accurate, reliable, and easily reproducible, we find this classification a problematic source of bias for several reasons.

First, VLBW infants represent an extremely heterogeneous group (Figure 2). The mortality rate varies from 47% in the infants <500 g to <1.9% in the infants who weigh 1251 to 1499 g at birth. Mortality is obviously a principal outcome, but even when it is not the primary outcome, its role as a competing outcome or in immortal time bias can greatly influence study validity in a group of infants with such heterogeneity.

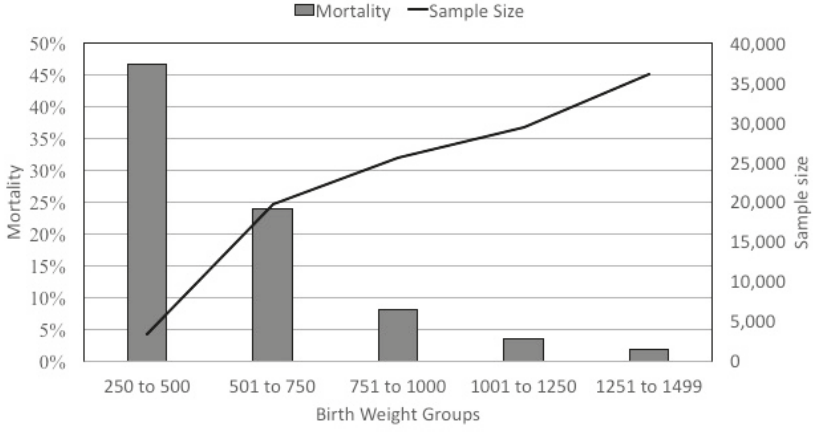


Figure 2. Mortality rate and sample size in very low birth weight infants stratified by birth weight in the Clinical Data Warehouse (CDW) from 1997–2019.

Second, the gestational age at birth VLBW infants is not normally distributed. Because of this, more mature and larger infants are over represented in VLBW cohorts. For example, in a VLBW cohort from the Pediatrix CDW, almost half of infants are greater than 29 weeks and the ratio of 28 week infants to 23 infants is 3:1 (Table 1). One method used to mitigate this effect is to bracket VLBWs by gestational age; VON allows reports to be restricted to ≥23 weeks and ≤29 weeks. However, applying that filter to the CDW would exclude 35% of the sample, and there would be no impact on the 3:1 ratio of infants at 28 weeks to 23 weeks. The ELBW classification is also problematic, in that it also skews the data but in a different way. Because of changes in the relative distribution of gestational ages, an ELBW cohort actually includes more 23 week infants than 28 week infants.

A third concern with weight-based classification for premature infants is bias introduced by small-for-gestational-age infants. Older studies suggested that growth restriction, presumably caused by some process that accelerates fetal maturity, may actually improve some morbidities such as respiratory distress syndrome [7]. However, within each birth weight group, infants with growth restriction were significantly more advanced in gestational age, potentially giving rise to the impression that these infants do better than expected for their birth weight as opposed to their gestational ages. More recent work was verified that a prenatal history of intrauterine growth restriction (IUGR) and being born small for gestational age (SGA) are associated with an increased risk of mortality and morbidity and poor long term outcomes both in term and preterm infants [8–10].

Table 1. The distribution of gestational ages in infants in the CDW from 2008–2018.

	All VLBW Infants		VLBW Infants ≥ 23 and ≤ 29 Weeks		All ELBW Infants	
GestAge	**N**	**%**	**N**	**%**	**N**	**%**
22	879	0.77%	0	0.00%	879	1.81%
23	4855	4.26%	4855	6.54%	4853	10.00%
24	8320	7.30%	8320	11.21%	8308	17.12%
25	9264	8.13%	9264	12.49%	9066	18.68%
26	10,589	9.29%	10,589	14.27%	8915	18.37%
27	12,407	10.89%	12,407	16.72%	6856	14.13%
28	14,465	12.69%	14,465	19.50%	4561	9.40%
29	14,294	12.54%	14,294	19.27%	2429	5.00%
30	13,238	11.62%	0	0.00%	1391	2.87%
31	9880	8.67%	0	0.00%	681	1.40%
32	7548	6.62%	0	0.00%	379	0.78%
33	3867	3.39%	0	0.00%	129	0.27%
34	2595	2.28%	0	0.00%	54	0.11%
35	959	0.84%	0	0.00%	18	0.04%
36	454	0.40%	0	0.00%	13	0.03%
37	176	0.15%	0	0.00%		
38	73	0.06%	0	0.00%		
39	48	0.04%	0	0.00%		
40	30	0.03%	0	0.00%		
41	13	0.01%	0	0.00%		
42	8	0.01%	0	0.00%		
43	1	0.00%	0	0.00%		
44	5	0.00%	0	0.00%		
All	113,968	100.00%	74,194	100.00%	48,532	100.00%

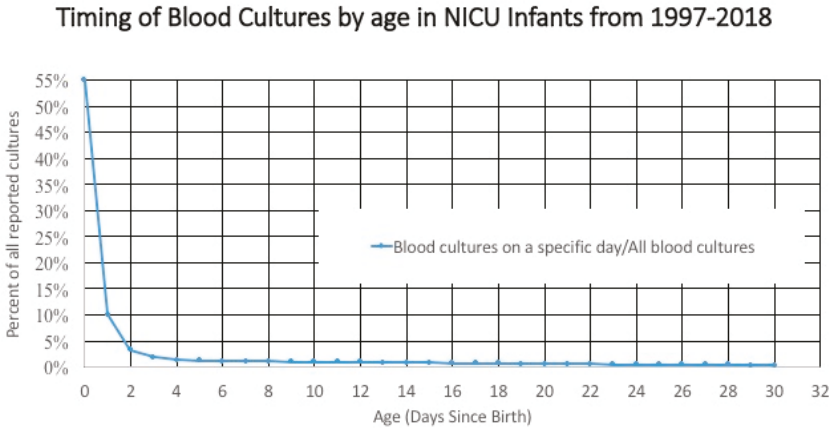
For these reasons, we prefer to use gestational-age-based categories (such as last completed week or the extremely low gestational age newborns or ELGANs [11]), despite the intrinsic imprecision in measurement of gestational age.

4. How Age Influences the Denominator

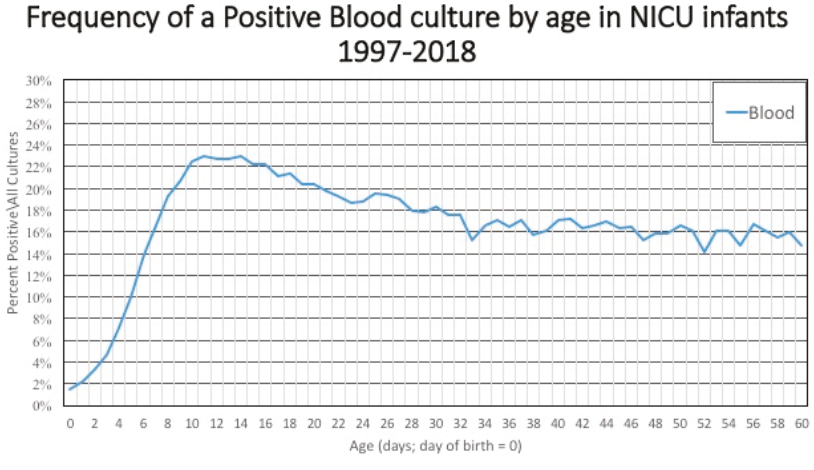
Complications can also arise in any denominator that is age-dependent due to skews in distribution of NICU stay and/or timing of death.

The characteristics of the study cohort included in an age-based study cohort changes dramatically with duration of NICU stay. For example, the incidence of early onset sepsis is dependent on the denominator. Most blood cultures are done in the first 3 days after birth (Figure 3a), and that large denominator, which includes term and late preterm infants at low risk for having a positive blood culture means that the incidence of a positive culture is low early in the hospital course (Figure 3b). After 3–5 days, these larger, healthier, lower-risk infants are discharged and the infants that remain in the hospital are less mature, sicker, and at higher risk of having a positive blood culture related to their illness, environmental exposures, and invasive procedures. The numerator/likelihood of a positive culture is also changing. The measured incidence of early onset sepsis will be higher if the cohort of

infants includes infants in the hospital for ≤7 days instead of limiting the study cohort to include only infants who were discharged before ≤3 days of age.



(**a**)



(**b**)

Figure 3. (**a**) Timing of blood cultures by age in neonatal intensive care unit (NICU) infants. (**b**) Frequency of a positive blood culture by age in NICU infants.

Mortality poses a similar problem. In premature infants, mortality rates are the highest in the first few days after admission and every day that these babies survive, they are more likely to go home alive [12]. As a result, cohorts that are derived from older premature infants (which seems reasonable when the exposure of interest occurs late in the hospital stay) will have a survival bias compared to a cohort that includes all premature infants. This effect may help explain the wide variation in rates of retinopathy of prematurity described in a recent publication that compared international experiences of the disease [13].

5. Beware the Dynamic Denominator

Sometimes, in order to further explore disease incidence of progression, investigators will define their cohort as infant with a specific diagnosis. However, bias can be introduced by changes in the evaluation or classification of the disease of interest. This leads to a denominator that changes over time or among studied groups.

We recently described changes in the frequency of patent ductus arteriosus (PDA) diagnosis in premature infants [14]. In that same paper, we also described changes in PDA treatment patterns in all NICU infants. Because of the underlying changes in PDA diagnosis, a study that evaluated treatment changes over time with a denominator limited to infants with a PDA would have led to different results. We illustrate this in Figure 4, which shows changes in PDA treatment over time in two different denominators: all infants or those infants diagnosed with a PDA. Although the general trend is similar, the decrease in treatment among the cohort of all infants was 23% compared to a 28% decrease among infants diagnosed with a PDA. Notably, the relative difference in treatment rates in these two cohorts varied over time as well, from 17% in 2010 to 11% in 2019.

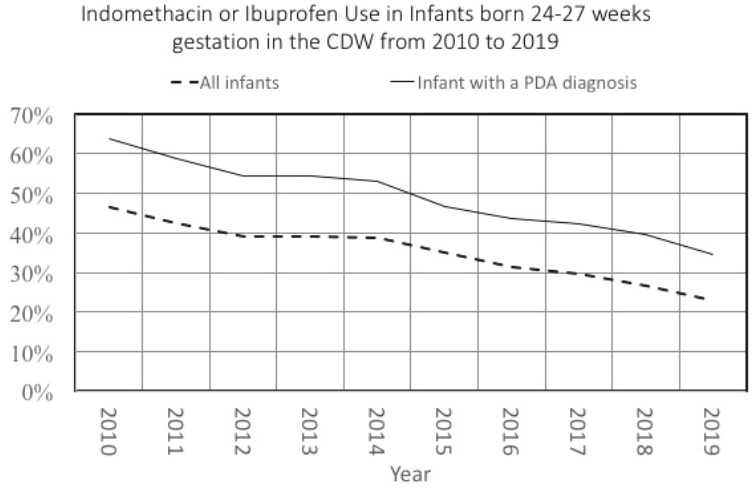


Figure 4. Treatment with Indomethacin or Ibuprofen in infants diagnosed with a patent ductus arteriosus (PDA) or in all infants 24–27 weeks.

Another example comes from disease incidence of intraventricular hemorrhage (IVH) in preterm infants. There is substantial variation in diagnostic cranial ultrasound (CUS) in higher gestational age groups [15] (29 weeks through 32 weeks), and some authors have suggested a risk-based screening approach [2]. We sought to understand how the rate of screening CUS might influence the incidence of IVH, so we calculated the rate of screening of these infants by center and then stratified centers into three groups based on each center's rate of CUS in this population. We found that the disease incidence of IVH was higher in the centers with greater rates of CUS (Table 2).

As these two cases illustrate, changes in disease incidence or measurement must be considered potential sources of bias when the denominator is based on a diagnosis.

Table 2. Rates of cranial ultrasound screening and intraventricular hemorrhage in infants 29–32 weeks from infants in the CDW from 2008–2017.

Centers Stratified by Screening Rate (Number of Infants)	Screening Rate	Rate of Any IVH
29 Lowest Third (n = 1449)	63%	4.97%
29 Middle Third (n = 11185)	92%	7.66%
29 Highest Third (n = 4185)	94%	8.84%
30 Lowest Third (n = 1789)	47%	3.24%
30 Middle Third (n = 14412)	87%	5.16%
30 Highest Third (n = 5279)	93%	6.14%
31 Lowest Third (n = 2489)	35%	1.93%
31 Middle Third (n = 17945)	76%	3.19%
31 Highest Third (n = 6596)	90%	3.87%
32 Lowest Third (n = 3907)	14%	0.64%
32 Middle Third (n = 27220)	47%	1.59%
32 Highest Third (n = 9906)	78%	2.28%

6. Summary

Big data research is important. The large sample sizes are almost always able to discern statistically significant relationships. Randomized trials are not available or feasible for many pressing clinical questions in our field. These examples come from the Pediatrix Clinical Data Warehouse [16]. The source of CDW data is medical records from approximately 350 NICUs that are managed by MEDNAX, Inc. (Sunrise, FL, USA)—approximately one fourth of NICU admissions in the United States. Despite its size, the CDW has several limitations. It is not geographically representative. The data are generated from physicians' documentation, and some information might be better obtained via a standardized case report form (a method used by the Vermont Oxford Network). Similarly, each neonatal dataset has its own set of unique limitations [17]. There are addition limitations to all United States NICU data that is currently collected [18]. How one defines the denominator when using these sources can introduce bias and influence the study results, validity, and generalizability. For this reason, we urge everyone to think critically about both the numerator and denominator—they both matter.

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children

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Review

Examining the Relationship between Cost and Quality of Care in the Neonatal Intensive Care Unit and Beyond

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Abstract: There is tremendous variation in costs of delivering health care, whether by country, hospital, or patient. However, the questions remain: what costs are reasonable? How does spending affect patient outcomes? We look to explore the relationship between cost and quality of care in adult, pediatric and neonatal literature. Health care stewardship initiatives attempt to address the issue of lowering costs while maintaining the same quality of care; but how do we define and deliver high value care to our patients? Ultimately, these questions remain challenging to tackle due to the heterogeneous definitions of cost and quality. Further standardization of these terms, as well as studying the variations of both costs and quality, may benefit future research on value in health care.

Keywords: health care costs; quality; neonatal intensive care; value

1. Introduction

The Institute for Healthcare Improvement (IHI) launched the term Triple Aim in health care [1] to encourage institutions to focus on improving the experience of care, improving the health of populations, and reducing per capita costs of health care. Inherent within Triple Aim is the understanding that more spending does not necessarily equate improved experience and population health.

From 1996 to 2013, total health care spending on children increased from USD 149.6 billion to USD 233.5 billion (2015 U.S. dollars). In 2013, the largest health condition leading to health care spending for children was well-newborn care in the inpatient setting [2], yet the United States (U.S.) ranks last among eleven high-income countries in infant mortality [3], highlighting the paradox of "spending more and achieving less" [4].

Through this article, we explore what is known about the relationship between costs and outcomes in the adult and pediatric literature. We will then review the costs associated with neonatal intensive care and the current efforts toward reducing unnecessary spending. We will discuss value in health care and the complex interplay between value in the context of costs and outcomes.

2. Health Care Spending

The Commonwealth Fund [3], a private U.S. foundation that supports independent research on health care issues to promote high-performing health care systems with improved quality and efficiency, develops a report every three to four years that compares the health care system performance of the U.S. and ten other, similar, high-income countries. The report is developed using data from Commonwealth Fund International Health Policy Surveys, reports of the Organization for Economic Cooperation and Development, the European Observatory on Health Systems and Policies, and the World Health Organization. Seventy-two measures relevant to health care systems performance were identified and organized into five main performance domains (care process, access, administrative

efficiency, equity, and health care outcomes). The report summarizes quality of care in these main aforementioned performance domains and the costs as the per capita spending. According to the Commonwealth Fund *Mirror*, *Mirror* 2017 report [3], the U.S. ranks last in the overall ranking and either last or second to last in four of the five domains. A specific example cited within health care outcomes domain is infant mortality. According to their raw data, the U.S. has 6.0 deaths per 1000 live births, performing well below even the next lowest performing country (Canada at 4.8 per 1000 live births) and a stark contrast to the top-ranking country, Sweden, with 2.2 deaths per 1000 live births. Although there is variability among each of these health care systems, despite performing poorer, as the report highlights, the U.S. spends more money on health care than any of the other included ten counties, and this amount continues to rise at a steeper slope.

3. Stewardship Campaigns: Reducing Waste

One method of reducing costs is with health care stewardship campaigns such as *Choosing Wisely*, where specialties have created lists of tests, treatments and procedures within their respective fields to avoid because they are considered low value (i.e., unnecessary and/or increase costs without improving outcomes) [5,6]. Since its beginning in 2012, *Choosing Wisely* has expanded from the "top five" lists of nine specialty societies to more than seventy societies in 2020. A variety of initiatives have focused on this list with promising improvements such as a reduction in repetitive laboratory testing which not only increases costs, but also can lead to poor patient outcomes [7]. Other interventions to reduce costs and waste capitalize upon the power of electronic health records (EHR), such as including price display in computerized physician order entry or *incorporating Choosing Wisely* recommendations into clinical decision support tools in the EHR. A systematic review of 19 studies by Silvestri et al. [8] found that price display interventions for laboratory tests, imaging studies, or medications likely reduces order costs to a modest degree; however, there was limited evidence related to patient safety outcomes, although it appeared unchanged. Utilization of clinical decision support tools have been found to impact physician behavior and reduce costs, improve length of stay (LOS), and reduce complication rates [9]. These findings suggest that reducing low-value interventions does not harm patient safety outcomes and may even improve them.

In joining with other specialties, Ho et al. [10] utilized national surveys and an expert panel through the American Academy of Pediatrics Section on Neonatal Perinatal Medicine to develop the "*Choosing Wisely* Top Five" list for newborns consisting of "(1) avoid routine use of antireflux medications for treatment of gastroesophageal reflux disease or apnea and desaturation in preterm infants, (2) avoid routine continuation of antibiotic therapy beyond 48 h for initially asymptomatic infants without evidence of bacterial infection, (3) avoid routine use of pneumograms for pre-discharge assessment of ongoing and/or prolonged apnea of prematurity, (4) avoid routine daily chest radiographs without an indication for intubated infants, and (5) avoid routine screening term-equivalent or discharge brain MRIs in preterm infants [10]". This set of interventions and procedures adds to the list of other pediatric *Choosing Wisely* topics, has helped to escalate and continue the conversation of being health care stewards within Neonatology, and has led to large initiatives, such as *Choosing* Antibiotics *Wisely* by the Vermont Oxford Network (VON)—a national quality improvement initiative focused on reduction in unnecessary antibiotic exposure in newborns [11,12]. Amongst the next steps for health care stewardship within Neonatology is to figure out how to utilize neonatal care "more wisely" [13] to help combat the increasing trends in neonatal intensive care unit (NICU) admissions over time [14].

4. Defining Cost and Quality of Care

While interventions to reduce waste and cost focuses first on "do no harm", others may hypothesize that reducing costs may inevitably lead to decreased quality of care. Some describe a framework of comparative costs and quality to define high and low performers (Figure 1).

Figure 1. Framework used to evaluate the association between cost and quality hospitals can be classified as high or low performers based on their costs and quality of care.

A systematic review by Hussey et al. in 2013 [15] looked at 61 studies published between 1990 and 2012 to review the evidence of the association between health care quality and cost in the adult literature. However, the review is limited due to the variability in the type of cost and quality measures reported by the individual studies. Cost measure type included accounting costs, care intensity index, charges, and expenditures; while quality measure type included access, composite measure, outcome, patient experience, process, and structure. Associations between quality and spending were categorized as "positive", "mixed-positive", "negative", "mixed-negative", "mixed", "no difference", and "imprecise or indeterminate". Overall, there was heterogeneity in the results without a clear direction or magnitude of association between measures of cost and quality. The authors concluded that the association between health care costs and quality remains poorly understood. This challenge of comparing the body of literature repeatedly occurs as there is a wide range of definitions for cost and quality (Table 1). For example, some studies use length of stay as a marker of cost of care while others use it as a measure of quality. In addition, costs are also reported as adjustments to a certain year to account for inflation.

Table 1. Examples of defining cost and quality in the literature.

Cost	Quality
Expenditure (hospital, staffing, pharmacy, etc.)	Morbidity
Charges *:	Mortality
- facility and professional fees	Patient Safety
Charges * (with or without cost adjustment using Cost to Charge Ratios)	Outcomes
Payments collected *	Complications
Length of Stay	Composite Measures
Resource tallies with applied costs from literature	Post-Acute Care
	Length of Stay

* Sources include hospital records, payers, all claims databases.

Looking at the link between costs and quality of care of a specific example within adult medicine, there has been a substantial amount of work focused on adult acute myocardial infarctions (AMI). Globally, there have been contradictory data on whether costs and quality of care for AMI are related. Nuti et al. [16] completed a cross-sectional study looking at outcomes among Medicare beneficiaries ≥65 years hospitalized with AMI and concluded that increased costs in the in-hospital setting were not associated with differences in mortality or reduced cost of post-acute care. They also did not see improved outcomes related to increased costs, suggesting that higher cost hospitals could reduce spending and resource utilization without reducing quality of care [16]. A large study compiling data from Finland, France, Germany, Spain, and Sweden found that, specifically for AMI patients in Sweden,

the costs were higher in hospitals with the highest quality of care [17]. However, there was not a clear cost–quality tradeoff when comparing cost and in-hospital mortality in the other countries. Further, a study using data from the Korean National Health Insurance Program also found no significant trade-off between cost and quality as related to AMI [18]. Of note, a significant limitation of the above studies in adult AMI data focused on mortality, whether in-hospital or 30-day post-discharge as a measure of quality of care.

5. Cost of Pediatric Care

The lack of evidence for a clear correlation between cost and quality is also seen in the pediatric literature. Using the Pediatric Health Information Systems (PHIS) database, which includes data compiled from 47 participating children's hospitals across the U.S., Gupta et al. [19] evaluated the relationship between hospital costs and patient outcomes in pediatric critical care. They used in-hospital mortality as their primary quality metric with a secondary analysis using prolonged hospital length of stay (>75th percentile) as a quality metric. Using hospital costs rather than hospital charges, they compared quality outcomes among high-performance hospitals (low costs, low mortality) and low performance hospitals (high costs and high mortality) and did not find any relationship between costs and patient outcomes in children with critical illness. They found that even among patients with the same condition, hospital costs vary widely across the included children's hospitals and the highest costs of care were associated with utilization of high-cost resources such as extracorporeal membrane oxygenation (ECMO) and inhaled nitric oxide [19].

A study using combined data from the Society of Thoracic Surgeons Congenital Heart Surgery (STS-CHS) and the PHIS database looked at the relationship between quality and cost in 27 hospitals among children undergoing congenital heart surgery between 2004 and 2010. The authors divided the hospital costs by tertiles and found that most hospitals in the lowest adjusted cost tertile delivered the highest quality of care, defined as the lowest rate of inpatient mortality, and also reported out the shortest LOS and fewer major complications [20]. However, a study from the Kids' Inpatient Database (KID) came to the opposite conclusion—using a hospital charge-to-cost approach, authors found that higher cost hospitals had decreased mortality [21]. Despite studying similar populations (children undergoing congenital heart disease surgery), the two studies came to opposite conclusions, highlighting the difficulties in studying this very important topic due to the heterogeneity of approaches.

In efforts to find methods to decrease resource utilization without affecting patient outcomes, Lion et al. [22] studied the implementation of evidence-based, standardized clinical pathways at Seattle Children's Hospital. They studied their fifteen clinical pathways in aggregate, tracking hospital charge-to-costs and length of stay, using patient physical functioning scores and readmission rates as balancing measures. After implementation of their pathways, they had a significant halt of rising costs with a post pathway slope difference of USD 155 per patient per month [95% confidence interval (CI)−USD 246 to −USD 64] and significantly decreased length of stay with a post pathway slope difference −0.03 days per admission per month (95% CI −0.05 to −0.02). This study is a powerful reminder of using quality improvement and standardization of care to improve patient outcomes, all while reducing costs and utilization.

6. Cost of Neonatal Care

The costs of health care in Neonatology are known to be large, especially for very low birth weight (VLBW, birthweight < 1500 g) infants and those with significant comorbidities of prematurity. In addition, term infants admitted to the NICU are inherently sicker than their uncomplicated counterparts in the mother–baby units and thus appropriately require a longer length of stay and incur more costs [23]. According to a cross-sectional study by Russel et al. [24], of the 4.6 million infant hospital stays in the U.S. in 2001, 8% had a diagnosis of preterm birth/low birth weight, yet the costs for this group represented 47% of the costs for all infant hospitalizations, which equates to USD 5.8 billion dollars. In contrast, 10% of the costs were for uncomplicated newborns, which comprised

of 42% of total hospitalizations. Of these preterm/low birth weight infants, 25% had one of more complications (respiratory distress syndrome, bronchopulmonary dysplasia, intraventricular hemorrhage, or necrotizing enterocolitis), with total estimated costs of USD 3.1 billion for these conditions. Johnson et al. [25] estimated increased costs from development of morbidities in VLBW infants as USD 12,048 (in 2009 US dollars) for brain injury (including intraventricular hemorrhage, periventricular leukomalacia, acquired hydrocephalus), USD 15,440 for necrotizing enterocolitis (NEC), USD 10,055 for late onset sepsis, and USD 31,565 for bronchopulmonary dysplasia (BPD), controlling for sociodemographic characteristics and the presence of other morbidities.

Similar to adult and pediatric medicine, Neonatology too has demonstrated variation in costs across centers without a link to an improved outcome. Massaro et al. [26] conducted a study utilizing linked data between the Children's Hospitals Neonatal Database (CHND) and PHIS to quantify inter-center cost variation for perinatal hypoxic ischemic encephalopathy (HIE) treated with therapeutic hypothermia. These data were reviewed in the context of favorable (defined as survival with normal magnetic resonance imaging) or adverse (death or need for gastric tube feedings at discharge) in order to examine the relationship between costs and outcomes. They found marked inter-center cost variation associated with treating HIE. Interestingly, they found that although the widest cost variation across centers was electroencephalogram (EEG) use (10-fold cost variability between centers), hospitals with low cost and favorable outcomes (highest value) ranked higher in regard to EEG costs. They also found that centers with the highest frequencies of adverse outcomes had lower relative costs [26]. By delving deeper into where the differences in spending were between centers, the study was able to tease out potential drivers for cost and how that might impact outcomes. As discussed by Clark and Spitzer in an accompanying editorial, these points highlight the importance of understanding what drives the differences in costs between centers and using this information to improve outcomes and decrease costs. As we begin to understand more of what drives cost variation, we can move towards improving value.

In addition to inter-center cost variation within neonatal care, variation for outcomes has been well established and persists even with overall improvement in quality of care. Both California Perinatal Quality Care Collaborative (CPQCC) [27] and VON [28] have demonstrated a reduction in major morbidities in VLBW infants over time, yet a variation between centers persists. CPQCC noted a nearly 20% center variation over time (2008–2017). The exact reasons for such wide variation in outcomes are multi-factorial and not fully understood. Practice patterns, such as 40-fold antibiotic utilization across NICUs without a difference in positive blood stream infections [29], may help address some of it. Racial/ethnic disparities in perinatal health, which result in part from structural racism and social determinants of health such as poverty, food insecurity, socioeconomic status, and environmental toxicity (i.e., pollution), certainly contribute to both inter and intra-NICU variability. The assessment of costs and outcomes together is common practice for economic evaluations such as cost effectiveness, cost benefit and cost consequence analyses. There are many examples in Neonatology literature that evaluate the financial impact of a new therapy or program in order to globally assess what is the incremental gain in outcome for the incremental dollar amount spent, including the use of antenatal corticosteroids in preterm [30] and late preterm infants [31], the use of surfactant in respiratory distress syndrome [32], the use of exclusive human milk and human milk fortifiers in prevention of NEC in VLBWs [33–37], the use of probiotics in prevention of NEC in VLBWs [38], routine screening for retinopathy of prematurity [39,40], among others. These assessments are important to understand the financial impact of tests, treatments and programs. Yet similar to quality improvement and outcomes assessment at the center level, it is also important to look at costs and outcomes together in order to help understand the variation that exists and identify opportunities to reduce unnecessary spending without affecting the outcomes.

7. How Do We Evaluate Value in Neonatal Care?

As we continue to strive to reduce costs in medical care through quality improvement efforts or initiatives such as *Choosing Wisely*, it is important to measure the impact that these changes have on patient outcomes and strive for a focus on high-value care. In the literature, value is defined as "health outcomes achieved per dollar spent" [41]. Although value can be difficult to study well in medicine, there are multiple discussions and approaches to value in neonatal care in the literature [41–45].

One approach attempts to simplify the interrelationship of value, quality improvement, evidence-based medicine, and evidence-based economics with a "value equation". In the neonatal value equation, Dukhovny et al. describe that value is determined by the outcomes (the numerator) divided by cost (the denominator) (Figure 2) [42]. The outcomes represent the interplay between quality, efficacy and safety while costs represent resource tallies as well as dollars. Ho et al. [43] build on this and describe the importance of using value and cost measures within the SMART aim (specific, measurable, attainable, relevant, time-bound) for quality improvement initiatives. With this equation, an increase in value can also be derived from improving outcomes without increasing resource utilization.

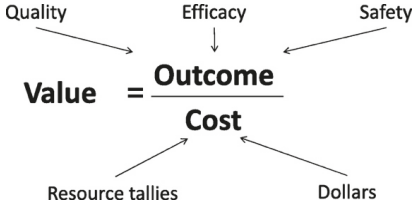

Figure 2. The neonatal value equation. Reproduced with permission from *Pediatrics* Vol. 137, Issue 3, e20150312. Copyright © 2016 by the American Academy of Pediatrics (AAP).

Another formula proposed by Kaempf et al. [44] calculates value in their "benefit and value metric", which assesses quality as a composite of major neonatal morbidities and mortality as tracked by VON. Kaempf uses length of stay (LOS) as a proxy for costs, which is reasonable in the NICU population given the discussion by both Kaempf [44] and Ho et al. [43] as it represents costs and resource utilization incurred over time. Similarly, in this metric, efforts to improve morbidities and mortality would increase the value of care; however, it does not specifically address how value might be increased by decreasing LOS.

When value is studied in medicine, we are attempting to answer the question: Is it worth the investment? As addressed by Flanagan [46], the value calculations in pediatric (and neonatal) care vary from the adult value calculations in that the pediatric value calculations require a longer time course as "adult health depends on child health". Hospitalization costs, whether for birth or within the first year of life, have discrete timepoints, but do not encompass the entirety of costs that extend beyond what can be truly reasonably studied. Even a single disease can have significant long-term impacts to the family and incur continuous costs that cannot be accounted [47]. Kaempf et al. [44] also highlight the importance of the interplay between all points of the value equation, if there is an increase in the "costs" (LOS in this case), yet it results in a significantly improved outcome (lower morbidities among VLBW infants), our overall value has improved despite the increased LOS.

While these formulas neatly summarize and conceptualize that there is a close relationship and interplay between value, cost, quality and outcomes, the question of value of care can be so complex and nuanced to study since either part of the equation: costs (whether in dollars or LOS) and quality (what defines quality and what is the right outcome to look at) each have their own challenges. Quality and outcomes can have different definitions depending on whether it is from the perspective of a health care provider, health care institution, insurance company, family, patient, or society. For example, LOS, as used in the Kaempf metric, is often simplified to be a marker for cost.

However, it does not account for the significant non-medical costs to the family, fixed costs of care in the NICU, including space and staffing, as well as expected LOS for the physiologic maturation [42,43,48].

There are other considerations when trying to study value. First is the impact on family—with the potential discordance between the value from the hospital perspective and the value from the family perspective [42]. Occasionally, there exists a trade-off between family costs and health care cost. Second, there is the difficulty of proper attribution of outcomes and costs to specific hospitals, should the infant be transferred. Third, attempts to understand value from a health disparity lens are extremely complicated. One of the five domains evaluated by the Commonwealth Fund is equity and, to our knowledge, none of the cost-effectiveness and value literature specifically addresses disparities in neonatal care. Furthermore, the focus on the link between cost and quality is often focused on inpatient medicine, in particular for newborns. Some of that is inherent to the U.S. health care system that has multiple payers, and even with the introduction of the medical homes and Accountable Care Organizations, has silos of episodes of care that frequently are financially rewarded for each episode. Such an approach limits the capture of outpatient services and community-based programming that focuses on both pre-conception, pre-natal and post-natal support. Although these programs are also associated with costs, investment pre- and post-birth may have substantial improvement on both cost reduction during the inpatient stay, as well as quality of care, including closing the racial disparity gap.

Recently, there has been a growing body of literature looking at disparities in neonatal care demonstrating that there is variation in terms of clinical outcomes. Using data from the CPQCC, Profit et al. developed a validated tool (Baby-MONITOR) to assess the quality of care at different hospitals and demonstrated hospital-to-hospital variation [45]. Furthermore they compared the quality of care among different races and ethnicities between and within individual NICUs and found significant variation in care when comparing white, African American, Hispanic and Asian American populations within and between individual NICUs [49]. Their study highlights an important piece of high value care that can be overlooked when populations are evaluated as a whole. As we strive to improve value in our NICUs, we have not truly achieved this goal if such disparities persist.

8. Next Steps

The large variation in both costs and outcomes coupled with limited evidence in health care to demonstrate the link between spending more money (higher health care costs) and better outcomes (higher quality) presents a dilemma when it comes to investing additional resources in a system that is already constrained. In order to reduce unnecessary health care spending, we must couple cost analyses with outcome studies and evaluate the relationship between the two. While quality improvement initiatives are often used as a tool to improve outcomes, there is also the necessary investment of resources (Figure 3). Therefore, trying to study the delicate balance between what costs are important and necessary and the quality of care delivered inherently comes with many confounders. It is possible to imagine that with greater investment of resources and thus increased costs, the quality of care delivered may be improved. Conversely, higher quality of care could also lead to decreased health care costs due to lower rates of complications, morbidities, and length of stay. Furthermore, utilizing mortality as a marker for quality of care can be problematic in and of itself, as mortality could also arguably decrease cost by reducing the length of stay and reducing resource utilization (in particular in the NICU population).

There is already a model that exists in collaborative quality improvement for centers to learn from best and worst performers in order to learn opportunities for improvement. The same approach should routinely incorporate costs into the conversation in order to allow tools such as *Choosing Wisely* and EHR to drive down unnecessary spending without affecting outcomes. There are both micro and macro-economic opportunities for cost reduction while allowing additional financial investments as new technologies, drugs and programs are introduced.

Figure 3. The relationship between quality improvement, outcomes, and costs.

9. Conclusions

The link between health care cost and quality of care is inconsistent across the spectrum of ages and disease processes. Much of the struggle lies in the heterogenous definitions of cost, quality, and value of care. While some studies (e.g., Kaempf Benefit Metric [44]) support a correlation between increased LOS (proxy for cost) and improved outcomes (neonatal morbidities), the literature either fails to look at the cost and quality in the same analysis or does not demonstrate a correlation. In addition, health care stewardship campaigns such as *Choosing Wisely* are built on the premise that eliminating services that are not necessary will not worsen outcomes (and potentially would improve them). Coupled with comparative reports such as *Mirror Mirror* [3], where the U.S. spends double or triple per capita on health care compared to economic equivalents yet has worse outcomes, this combination suggests that there is room to reduce costs without negatively affecting outcomes (as has been demonstrated by multiple studies). The next steps for us to improve value in health care is to better define how we look at quality and costs in order to consistently study them together. As we strive to understand the variation in clinical outcomes, we must also strive to understand the variation in costs and embrace the opportunity to reduce each rather than assume that one hospital has better outcomes because they are resource rich and allocate higher dollars. In addition, we should include a "health equity lens" to ensure that our value-based care works to eliminate disparities between groups in health care and we are truly achieving improved outcomes for all of our patients.

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children

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Article

Learning from Wildfire Disaster Experience in California NICUs

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Abstract: Wildfires have been affecting California greatly, and vulnerable patients in neonatal intensive care units (NICUs) are not exempt. Our aim was to learn how personnel working in NICUs of California hospitals handled issues of neonatal transfer during wildfire disasters in recent years, with an ultimate goal to share lessons learned with healthcare teams on disaster preparedness. We identified California fires through newspaper articles and the CalFire.gov list. We determined which hospitals were affected and contacted members of the healthcare team through connections via the California Perinatal Quality Care Collaborative (CPQCC) database. We audio recorded interviews over phone or remote conferencing software or by written survey. We coded and analyzed transcripts and survey responses. While describing disaster preparedness, equipment (such as bassinets and backpacks), ambulance access/transport and documentation/charting were noted as important and essential. Teamwork, willingness to do other tasks that are not part of typical job descriptions, and unconventional strategies contribute to the success of keeping NICU babies safe when California wildfire strikes. Healthcare teams developed ingenious and surprising ways to evacuate NICU babies.

Keywords: NICU; perinatal care; California; wildfire; disaster preparedness; evacuation

1. Introduction

"The 2018 wildfire season was the deadliest and most destructive wildfire season on record in California with a total of 8,527 fires" [1]. These wildfires led to various evacuations in healthcare settings including neonatal intensive care units (NICUs), and evacuation protocol reevaluation. Perinatal patients may be critically ill and highly dependent on medical staff and technology for care [2]. Babies cared for in NICUs are most likely to be impacted by acute evacuation from their units [3].

In addition to wildfires, it is inevitable that other types of disasters will also impact California healthcare systems in the future. The California Association of Neonatologists (CAN) resource, the "Neonatal Disaster Preparedness Toolkit," addresses a plethora of forms of disaster preparedness from bioterrorism to an active shooter [2]. With the purpose of "provid(ing) guidance to NICU leadership in developing comprehensive disaster response plans that are in compliance with Joint Commission Standards and based on community, best-practice models" [2], the toolkit delves into the command center, six critical elements of disaster response [4] and the TRAIN™ tool (triage by resource allocation for in-patients).

The TRAIN™ tool is a way that NICU leaders categorize the infants under their care every day to prepare for evacuation if needed [5]. TRAIN™ tool assigns ambulance asset needs but not NICU level [2]. The assignments for transport can be car, BLS (basic life support), ALS (advanced life support), CCT (critical care transport), or Specialized with the categories being life support, mobility (car/car seat, stretcher, incubator, immobile), nutrition, and pharmacy [2]. The TRAIN™ tool provides a more subjective and efficient way to transport inpatients during a disaster evacuation [5]. We utilized the

TRAIN™ tool because it has been studied and researched in its original form, as well as modified to be applicable to all neonatal and pediatric inpatients [5]. It is also a triage tool that meets the three needs of evacuation, surge capacity, and communication [5] and is endorsed by the CAN and the District IX AAP (American Academy of Pediatrics) section on Perinatal Pediatrics. Unlike the TRAIN™ tool, other available triage tools do not meet the three needs [5]. For this reason, our study exclusively used and focused on the TRAIN™ tool (Table 1).

Table 1. Triage by resource allocation for inpatients (TRAIN) tool. (Adapted from Dr. Lin's *Triage by Resource Allocation for Inpatients: A Novel Disaster Triage Tool for Hospitalized Pediatric Patients*, 2018) [5].

Transport	Blue/Car	Green/BLS	Yellow/ALS	Orange/CCT	Red/Specialized
Life Support	Stable	Stable +	Minimal	Moderate	Maximal
Mobility	Car/Car seat	Wheelchair or Stretcher	Wheelchair or Stretcher	Transport rig	Incubatoror Immobile
Nutrition	All PO	Intermittent Enteral	Continuous Enteral or Partial Parenteral	TPN Dependent	
Pharmacy	PO Meds	IV Intermit meds	IV Fluids	IV Drip ×1	IV Drip ≥2

PO: Per os (taken orally); TPN: Total parenteral nutrition; IV: Intravenous medication.

Although guidelines have been published both in and out of California for various disasters, there is a gap in our knowledge in how these guidelines are implemented in actual disaster settings, particularly in the context of the recent wildfires in California. Additionally, we wanted to study the experiences and the practices of NICU personnel during evacuation or acceptance of babies. What are some of the barriers in healthcare delivery for NICUs, especially if needing evacuation, that we may have learned from recent California wildfire experiences? What have healthcare team members and leaders learned about how to improve patient safety during a crisis like a wildfire that is encroaching on the hospital's door? What new ways have healthcare workers discovered and are enacting to effectively and efficiently evacuate NICUs? We answered these questions in an open-ended fashion as we wished to learn what health care team members were doing. These questions do not have absolute requirements based on certain guidelines.

In order to answer these questions, we researched NICUs that evacuated or accepted babies due to a California wildfire, contacted key members of the healthcare team (NICU medical directors, neonatologists, nurse managers/directors, neonatal clinical nurse specialists, NICU nurses, patient care manager, and NICU department managers), and conducted interviews from April 2019 to May 2020. The purpose of this study was to learn more about the issues faced by NICU healthcare providers during wildfire disasters, with the longer-term goal of improving NICU patient safety. We focused on NICUs that evacuated, as they made more of our sample pool of interviews.

2. Materials and Methods

We researched California fires using CALFire, newspaper articles, and internet search engines. Through newspaper articles and internet search engines, fifty-nine NICUs were investigated and a total of seven hospitals' health care worker(s) were interviewed. The NICUs were spread out geographically and included parts of Northern and Southern California where the wildfires happened. Two interviewee's NICUs are located in Southern California. Eight interviewee's NICUs are located in Northern California, with six in the same city of Northern California. Of the six in the same city, hospital A had two interviewees, hospital B had one interviewee, and hospital C had two interviewees/three interviews, as one health care team member was interviewed twice due to two separate wildfires in different years affecting the same hospital.

We obtained contact information for the health care team members at these NICUs through contacts from the California Perinatal Quality Care Collaborative (CPQCC), referrals from previous participants that were interviewed, and other relevant sources. CPQCC is a California network of NICUs and HRIF (high risk infant follow-up) clinics, whose goal is to improve care for California's mothers and most vulnerable infants [6]. We did not obtain contact information from HRIF clinic sources.

Once the informant was identified, we audio recorded approximately 60-min interviews over phone or remote conferencing software. We also gained additional information through online surveys. Of the ten interviews conducted from April 2019 to May 2020, three were obtained only through online survey. The online survey questions on Google Form were the same as the questions asked by phone or remote conference software and were reserved for participants with scheduling conflicts.

This qualitative study consisted of ten questions. By interviewing key members of the health care team, we were able to assess key components of patient safety in the hospital related to wildfire disaster response, specifically in regard to improving newborn care. A semi-structured interview process was used (Appendix A—interview guide). The interview questions contained four major sections: Participant's Background, Institutional Perspective, Evacuation Experience, and Lessons and Insights. Please see Appendix A for the interview protocol.

Data were analyzed using qualitative research methods. The audio recordings were transcribed and read iteratively to find common themes in the interviews. We used a grounded theory approach based in "data systematically gathered and analyzed" but primarily focused on practical aspects that could be potentially generalizable to further work in the area of NICU preparedness for disaster experiences [7].

Before interviewing participants, interviewees filled out a consent and demographic form. All questions on the demographic form were optional. After the interviews, we emailed each participant a USD 25 gift card in appreciation for their time and effort. This study was approved by the Stanford University Institutional Review Board.

3. Results

Of the ten interviews, roles included NICU medical directors (n = 1), neonatologists (n = 2), nurse managers/directors (n = 2), neonatal clinical nurse specialists (n = 1), NICU nurses (n = 1), patient care managers (n = 1), and NICU department managers (n = 2). Overall, there were seven phone/remote conferencing software interviews and three online survey interviews. One participant was interviewed twice as their institution's NICU was evacuated twice in different years.

While NICU level of care was not a focus of the questioning, the level of care came up in three of the interviewee's responses. One was Level II, one Level III, and one Level IV. Each interviewee was interviewed on their own. However, as stated in the Materials and Methods section, two people were interviewed from the same location for two of the locations in Northern California.

3.1. NICU Redundant Systems

As seen in Figure 1, redundant systems were in place for power in 90%, medical gas in 90%, water in 70%, wall suction in 70%, and information technology in 70%.

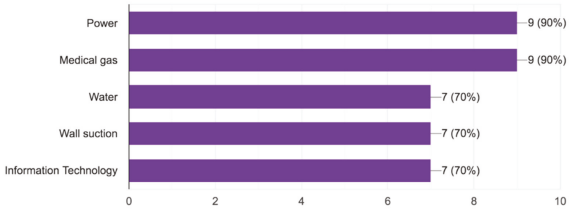

Figure 1. Neonatal intensive care units (NICU) redundant systems.

3.2. Use of TRAIN™ Tool Nomenclature to Categorize Infants and Evacuation Preparedness

Table 2 shows the prevalence of TRAIN™ tool nomenclature in NICUs, hospitals, and regions to categorize infants. It also depicts evacuation preparedness including having necessary supplies and an established evacuation plan.

Table 2. Use of TRAIN™ tool nomenclature to categorize infants and evacuation preparedness.

	Yes (%)
The California Association of Neonatologists and the District IX AAP section on Perinatal Pediatrics have endorsed TRAIN™ tool (triage by resource allocation for in-patients). Did your NICU use TRAIN™ tool nomenclature to categorize the infants under their care?	60%
Did your hospital use TRAIN™ tool nomenclature to categorize the infants under their care?	30%
Did your region use TRAIN™ tool nomenclature to categorize the infants under their care?	30%
Did your NICU have the necessary supplies for safe evacuation (including equipment stockpile such as emergency transport devices, backpacks, portable pulse oximeters, etc.)?	70%
Did your NICU have an established evacuation plan (including knowledge of how to stage the two types of evacuation—horizontal and vertical, determining priorities, established clear roles and responsibilities, rehearsal of these roles and ensuring quick and easy access to emergency equipment, supplies and documentation forms, emergency medication administration, and transport)?	80%

AAP: American Academy of Pediatrics; NICU: Neonatal Intensive Care Unit.

3.3. Please Describe Your Experience with [The Fire Incident] and the NICU Evacuation

When participants were asked about their NICU Evacuation Experience, 50% of participants declared that smoke and air quality were an issue. Two participants alleviated the bad air quality by using air scrubbers to pull the particulates out of the air.

In terms of transport, 40% used ambulances, with three participants using bassinets in the back of ambulances to transport babies. Other babies were triaged by bus or private car transport. One participant spoke of evacuating babies that could be feasibly transported in a car seat to be transferred in that way, in order to increase the capacity of the transport system for sicker babies.

For supplies, two participants spoke of the use of backpacks; one participant was putting together a small backpack per baby bedside including formula, wipes, diapers, and feeding tubes.

Communication to alleviate confusion was lacking in some NICUs. In one instance, babies showed up at the receiving hospital without a call from the evacuating NICU asking for permission or providing warning. Internet and phone call issues did not help. One participant had to text or text someone else who had access to the other person to communicate.

Furthermore, delegation of responsibilities was problematic. One participant said if they could have changed one thing, it would be to have a clear command structure in the unit.

Documentation of baby's care was sometimes nonexistent by the receiving hospital. Compatibility of the electronic medical record (EMR) made a difference because it forced some medical professionals to have to chart on paper or wait for the nurse from the receiving hospital to chart for them. EMR incompatibility is an existing inefficiency even outside of a disaster context and is amplified even further when wildfire disaster strikes.

Forty percent of hospitals solved the problem of getting numerous babies out of the hospital at a time by using evacuation Med Sleds®. The Med Sled® Infant 6 can fit up to six babies in the pockets (Figure 2) and another can fit three babies on a sled (Figure 3) and quickly get them out the door into an ambulance. The sleds lock in place, removing worry about the babies falling out. One hospital

even noted how they could place the ventilator in the sled for a baby that needed it. This is one of other potential solutions to navigating babies going down the stairs, if the elevators are not working, an important component to evacuation.

Figure 2. Med Sled® Infant 6 insert.

Figure 3. Med Sled® infant insert that can hold up to three infants.

Some participants took away getting as much supplies as they could if a disaster were to strike again and cause a NICU to evacuate; one hospital specified grabbing formula bottles and nipples. Two participants spoke of backpacks, with one putting together a daypack, a small backpack for each baby in case of emergency with formula, wipes, diapers, and feeding tubes and another revamping their backpacks.

Important to note in one hospital is that even though they tried ensuring people working in the NICU went through a streamlined vetting process, this did not happen for a number of people. This was an identified gap for future implementation work.

Infant identification was another concern by some of the hospitals. Ways to solve this problem that arose were making sure babies had ID bands on and stickers on their abdomens. A backup baby identification strategy may be important for local policies.

A theme from two informant interviews was limited storage space in the unit. One hospital did not keep the bassinets and incubators at hand, instead storing them in a couple of vacant patient rooms. Another hospital found it difficult to get equipment and supplies, including emergency food storage (formula), when the elevators are being used constantly and the hospital is chaotic.

Additionally, some participants explained the experience as traumatic or emotional with four participants relaying personal family issues including being evacuated or their house burning down as they were simultaneously helping NICU babies during the fire incident. Health care workers are resilient and selfless. Even though their own homes were burning down, they helped NICU babies stay safe and healthy.

3.4. Can You Describe Any Changes That Your NICU Implemented in Your Evacuation Procedures after the Experience with This Incident?

In terms of changes the participant's NICUs implemented in their evacuation procedures after the experience with their corresponding fire incident, equipment was important to 50% of participants.

Two participants cited bassinets for the perinatal patients, some with the ability to have oxygen attached to them. Another two participants spoke of aprons to carry babies, with one hospital realizing that they did not work well during their own evacuation.

3.5. Are There Other Aspects of Disaster Preparedness That You Think Are Gaps in Your NICU? (Source: NICU Disaster Preparedness Survey—Gap Analysis)

When asked of gaps still existent in their NICU's disaster preparedness, two respondents said it was staffing. There were minimal or skeleton staff during the wildfire, and they could not rely on people on call because those workers could not always get to the hospital. Furthermore, a common theme was the evacuation plan. One hospital noted that they had a pretty solid evacuation plan while another said that they are working on an evacuation plan and need two plans: one for horizontal for issues in NICU only (fire, structural issues, etc.) and one for vertical (out of building).

Two participants were confident in their disaster preparedness as the previous incident went smoothly and there were no gaps in protocols or procedures. Among the other 80%, one respondent explained how you identify gaps as you go and adapt. Big gaps included not using all resources to the fullest extent, getting patients out, getting equipment, not using the TRAIN™ tool for a live event or not having the TRAIN™ tool work, and making sure people were participating in drills and training for these disasters even though it is "not that likely for evacuation to happen again." Another interesting insight was that the participant learned that they should have called the operation center instead of calling other potentially receiving NICUs themselves for better regional coordination and overlap prevention.

3.6. Can You Share Any Insights on How to Better Prepare for Future Disasters That Can Inform Neonatal Transport?

The insights that participants had on how to better prepare for future disasters that can inform neonatal transport include 30% declaring practicing is important, for example by doing live drills every year. One participant has not started doing drills yet. Two participants specified coordinating with their county/region with the county or statewide drills and spoke of having necessary equipment. Safety was something that one participant brought up, citing the fact that their use of open cribs in the ambulance could have been safer, so the babies do not have the chance of sliding around, even though their open cribs did not slide around in their fire experience.

A major insight brought up by one respondent was about being flexible in terms of what you are doing even though it does not meet your job description. Being open minded and thinking outside the box about how to transport babies, even putting them in car seats for example, is very important. Staying calm was another important insight by a participant who said that their neonatologist and nurses were very calm and acted fast.

3.7. Is There Anything Else That You Would Like to Share?

When asked for additional things to share, three spoke of community and a culture of team, with two specifying that even though the experience was personally traumatic with two of the team's main people: their neonatologist and manager's houses burning down, they still stepped up and showed up for their priorities. Staff did everything that needed to be done, some staying 48 h or longer. One participant is looking for the best models and is trying to teach that model to other areas, even implementing that model statewide as a possibility.

4. Discussion

With climate change, the incidence of wildfires that may lead to NICU evacuations are likely to increase. Therefore, it is important to be prepared and have effective plans in place to keep the most vulnerable population of babies, their caregivers, and medical staff as safe and healthy as possible [8].

Gaps in disaster preparedness exist and need to be identified, addressed and closed [9]. An example of a logistical gap is the inability to access temporary hospital privileges to "continue to take care of

his or her patients in the receiving NICU" [10]. Congress and President George W. Bush saw gaps in disaster preparedness as a significant problem and established The National Commission on Children and Disasters in 2007 to try to close these gaps through a "cohesive national strategy . . . to protect children during disasters" [9].

These disasters include hurricanes. In August of 2005, Hurricane Katrina necessitated evacuation of NICUs as well. Dr. Barkemeyer explained what happened to the babies, hospital, city, trainees, and family while he was "on duty in the NICU of a flooded downtown New Orleans hospital" [11]. As a result of Katrina, babies were triaged and transported to other hospitals and a preterm baby girl was born four days after Katrina's landfall and cared for using equipment on a portable generator [11]. Similar to our interviews focused on wildfires, communication methods following Hurricane Katrina was an issue [11].

Clearly, disaster preparedness also applies to events that are not wildfires, which is further shown in published guidelines and resources with hopes of keeping the NICU population safe [8]. The Illinois Department of Public Health released the "Neonatal Intensive Care Unit (NICU) Evacuation Guidelines," planning in advance for transporting the NICU population and focuses on tornados, winter storms, flooding, and earthquakes (Illinois). The Illinois Guidelines suggest identifying infants in multiple ways, such as standard ID bands and direct patient marking, as well as performing horizontal evacuation before vertical evacuation [12]. The New York City Pediatric Disaster Coalition and New York City Department of Health and Mental Hygiene made a broad template available online titled the *Neonatal Intensive Care Unit Surge and Evacuation Plan* in 2018 [4]. However, descriptions of evacuation plans are adapted in the moment, including "using a smartphone to take pictures of patient arm bands" to facilitate tracking [13].

Common themes of our study are shown below in Figure 4. This figure answers the leading questions we posed in the introduction: "What are some of the barriers in healthcare delivery for NICUs, especially if needing evacuation, that we may have learned from recent California wildfire experiences? What have healthcare team members and leaders learned about how to improve patient safety during a crisis like a wildfire that is encroaching on the hospital's door? What new ways have healthcare workers discovered and are enacting to effectively and efficiently evacuate NICUs?"

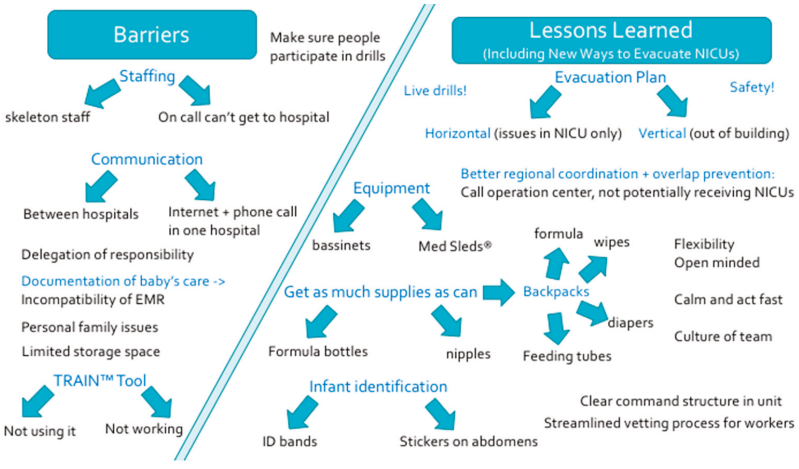

Figure 4. Barriers and lessons learned from wildfire disaster experience in California NICUs.

A limitation of our study is that we did not have knowledge of actual transfer of babies to which hospitals as this was a qualitative study, and we did not have patient data. There may also have been recall bias given the amount of time that had elapsed since the disasters that the interviewees

discussed. Interviews were conducted from April 2019–May 2020. It is important to give health care members time to recover from crises and grieve, as these disasters can exert a heavy burden not only professionally but in personal lives. We aimed to have a balance in order to interview participants at a reasonable time in order to allow for an optimal recounting of the wildfire event while not causing undue stress.

Disaster resources for center internal evaluation of their own processes include the California Association of Neonatologists' Neonatal Disaster Preparedness Toolkit and Stanford's Disaster Planning Toolkit, both linked below.

1. https://www.cpqcc.org/sites/default/files/pdf/toolkit/CAN_Neonatal%20Disaster%20Preparedness%20Toolkit_02.2015.pdf
2. https://obgyn.stanford.edu/divisions/mfm/disaster-planning.html

5. Conclusions

Overall, the recent history of neonatal intensive care unit (NICU) evacuations due to wildfires in Northern and Southern California provided an opportunity to learn from past disaster experience and to be better prepared for the future. NICU teams have solved some issues faced during wildfire disaster, improving future disaster response. However, there is much more improvement that needs to be done. We hope our findings aid and inspire NICUs to reevaluate and possibly change their disaster preparedness protocol for evacuating due to a California wildfire. Health care team members are heroes. We need the system of disaster preparedness to improve, so our selfless medical community and vulnerable NICU patients have hope, resources, and practices to stay safe and healthy.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A : Interview Protocol

Participant's Background

1. Please describe your role.
2. How long have you been in your present position?
3. How long have you been at this institution?
4. Briefly describe your role as it relates to the NICU evacuation that you will be describing?

Institutional Perspective

5. Please describe the procedures that were in place in your NICU prior to the event:

Probes (Refer to NICU Disaster Preparedness Survey—Evacuation Planning):

a. Did your NICU have redundant systems for:

Power?
Medical gas?
Water?
Wall suction?
Information Technology?

b. The California Association of Neonatologists and the District IX AAP section on Perinatal Pediatrics have endorsed TRAIN™ tool (triage by resource allocation for in-patients). Did your **NICU** use TRAIN™ tool nomenclature to categorize the infants under their care? No (1), Yes (2), Don't Know (3).
c. Did your hospital use TRAIN™ tool nomenclature to categorize the infants under their care? No (1), Yes (2), Don't Know (3)
d. Did your region use TRAIN™ tool nomenclature to categorize the infants under their care? No (1), Yes (2), Don't Know (3)
e. Did your NICU have the necessary supplies for safe evacuation (including equipment stockpile such as emergency transport devices, backpacks, portable pulse oximeters, etc.)? No (1), Yes (2), Don't Know (3)
f. Did your NICU have an established evacuation plan (including knowledge of how to stage the two types of evacuation—horizontal and vertical, determining priorities, established clear roles and responsibilities, rehearsal of these roles and ensuring quick and easy access to emergency equipment, supplies and documentation forms, emergency medication administration, and transport)? No (1), Yes (2), Don't Know (3)

Evacuation Experience

6. Please describe your experience with [the Fire Incident] and the NICU Evacuation.

Lessons and Insights

7. Can you describe any changes that your NICU implemented in your evacuation procedures after the experience with this incident?
8. Are there other aspects of disaster preparedness that you think are gaps in your NICU? (Source: NICU Disaster Preparedness Survey—Gap Analysis)
9. Can you share any insights on how to better prepare for future disasters that can inform neonatal transport?
10. Is there anything else that you would like to share?

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Article

Lessons Learned from a Collaborative to Develop a Sustainable Simulation-Based Training Program in Neonatal Resuscitation: Simulating Success

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Abstract: Newborn resuscitation requires a multidisciplinary team effort to deliver safe, effective and efficient care. California Perinatal Quality Care Collaborative's Simulating Success program was designed to help hospitals implement on-site simulation-based neonatal resuscitation training programs. Partnering with the Center for Advanced Pediatric and Perinatal Education at Stanford, Simulating Success engaged hospitals over a 15 month period, including three months of preparatory training and 12 months of implementation. The experience of the first cohort (Children's Hospital of Orange County (CHOC), Sharp Mary Birch Hospital for Women and Newborns (SMB) and Valley Children's Hospital (VCH)), with their site-specific needs and aims, showed that a multidisciplinary approach with a sound understanding of simulation methodology can lead to a dynamic simulation program. All sites increased staff participation. CHOC reduced latent safety threats measured during team exercises from 4.5 to two per simulation while improving debriefing skills. SMB achieved 100% staff participation by identifying unit-specific hurdles within in situ simulation. VCH improved staff confidence level in responding to neonatal codes and proved feasibility of expanding simulation across their hospital system. A multidisciplinary approach to quality improvement in neonatal resuscitation fosters engagement, enables focus on patient safety rather than individual performance, and leads to identification of system issues.

Keywords: neonatal resuscitation; simulation; debriefing; quality improvement

1. Introduction

Neonatal resuscitation is one of the most critical events in neonatal-perinatal medicine requiring a high level of individual skill and team performance. Resuscitation of a critically ill newborn cannot occur

in a silo—it requires a team effort. Ineffective communication has been noted to play a role in almost 75% of cases of neonatal mortality or severe neonatal morbidity reported to the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) [1,2]. Studies of real-life delivery room resuscitations have elucidated opportunities for improvement in behavioral skills, as well as lack of adherence to the recommended steps of the Neonatal Resuscitation Program (NRP) algorithm [3,4]. Simulation-based training for neonatal resuscitation in an immersive environment replicating a real clinical scenario provides an opportunity to improve behavioral and communication skills [5,6]. Notably, health care professionals (HCPs) who have completed simulation-based training in Adult Cardiopulmonary Life Support (ACLS) better adhere to resuscitation guidelines in the real-life clinical environment [7]. Thomas et al. translated principles of communication and teamwork behavior to neonatal resuscitation practice and developed a framework for assessing teamwork behavior using video recordings [8]. In a randomized trial testing the addition of teamwork training to NRP, those who received the teamwork training intervention exhibited more teamwork behavior than the control group [9,10]. NRP training has increasingly incorporated simulation-based training in these cognitive, technical, and behavioral skills with the aim of improving the quality of newborn resuscitation [11].

Neonatal resuscitation is complex and occurs infrequently. Team training aims to teach and support knowledge acquisition, and skills and attitudes that lead to optimal team performance. Simulation and debriefing methodology provide the tools to conduct team training with the primary goal of patient safety [2,12]. Simulations can be conducted in a simulation center or in situ (i.e., actual setting where participants work, for example Labor and Delivery). There are several benefits for health care teams to conduct simulations in situ [13]: adding realism; ability to identify systems errors or latent safety threats (LSTs) that could lead to changes in practice; and filling of gaps between knowledge and practice [14,15]. California Perinatal Quality Care Collaborative's (CPQCC) Simulating Success program was designed to help participating hospitals implement an on-site, simulation-based neonatal resuscitation training program. In this report, we describe the experience of the first cohort of three hospitals to participate in the program. The structure of the remainder of this paper is such that the three institutions' aims are each presented in the Methods along with the local context in which the project occurred, and the results of the project are then presented for each institution separately in the Results in corresponding order.

2. Materials and Methods

Simulating Success engaged hospitals over 15 month long periods that included three months of preparatory training followed by 12 months of implementation (Figure 1). Simulating Success was offered by CPQCC in partnership with the Center for Pediatric and Perinatal Education (CAPE) at Stanford University. Preparatory training consisted of an online didactic program followed by a 1.5 day, face-to-face training program at CAPE in the core principles of developing and conducting simulation-based training. The online didactic program was made available to an unlimited number of staff members at each site. Face-to-face training was attended by a maximum of three staff members from each site (referred to as the 'multidisciplinary champion team' for the remainder of this manuscript). Implementation at each site entailed ongoing in situ simulations followed by debriefings and monthly online check-ins with CAPE faculty, in addition to two site visits, for continued feedback and support.

The first cohort of three sites began in April 2018. Principles of quality improvement were incorporated throughout the collaborative with a focus on implementing Plan Do Study Act (PDSA) cycles. A quality improvement expert helped each site develop their Specific, Measurable, Applicable, Realistic, and Timely (SMART) Aim statements to target unit-specific needs. The resulting aim statements reflect the Simulating Success program goals of incorporating quality improvement tools and developing sustainable programs. Performance of the implementation teams as well as the clinical staff were used as potential measures of

sustainability. This manuscript details the experience of these sites in implementing a simulation program at their respective hospitals (Children's Hospital of Orange County (CHOC), Sharp Mary Birch Hospital for Women and Newborns (SMB) and Valley Children's Hospital (VCH)).

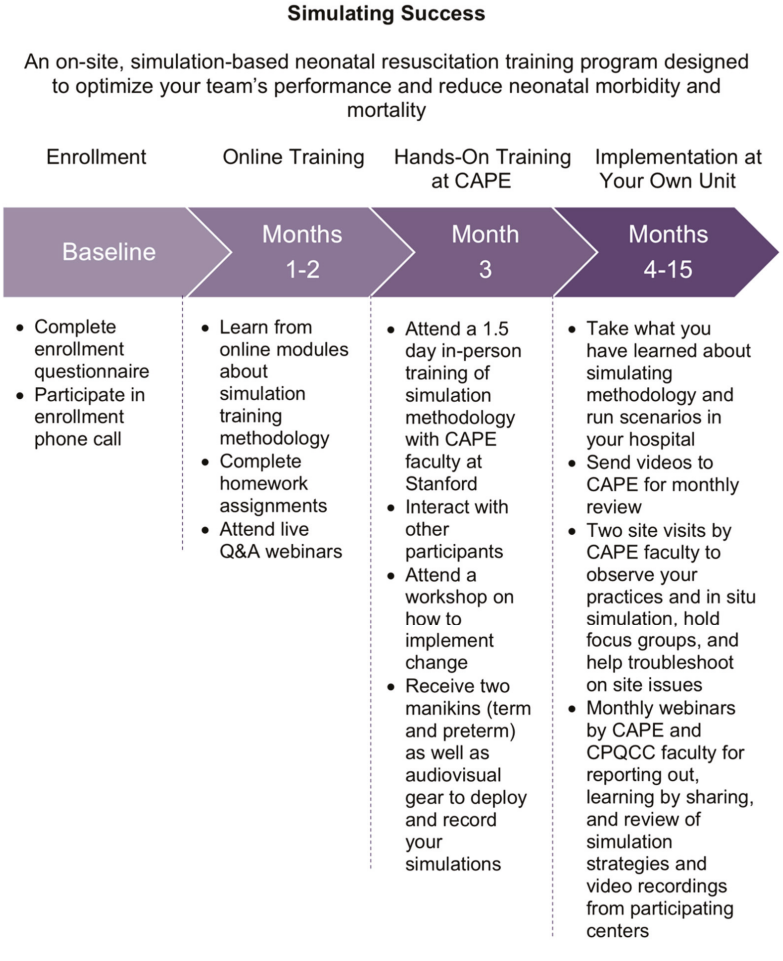

Figure 1. Timeline for CPQCC's Simulating Success collaborative.

2.1. CHOC

The CHOC Neonatal Intensive Care Unit (NICU) is a level IV, 104-bed NICU with a Surgical NICU, Small Baby Unit, Neuro NICU and Cardiac NICU within a free-standing Children's hospital that also has a Pediatric Residency and Neonatal Fellowship program. Participation in Simulating Success was intended to enhance positive team behaviors during neonatal resuscitation that impact patient outcomes. The SMART aims were to (1) increase staff participation in at least one multidisciplinary simulation team

training in the NICU from baseline of 0% to a target of 75% by June 2019; and (2) to improve patient safety through simulation exercises as demonstrated by a decrease in LSTs identified from a baseline of 4.5 per simulation to one over a period of six months, from January to June 2019.

LSTs are improvement goals identified during simulation exercises that have an impact on delivery of optimal care to the patient [14,16,17]. In situ simulations can help identify these knowledge gaps and reinforce positive team behaviors [18]. Knowledge gaps were further categorized as cognitive, technical, or behavioral. The CHOC instructor team used these debriefings to help identify LSTs. The CAPE Real-Time Debriefing Evaluation (DART) tool was used to assess the effectiveness of the debriefer(s) and participation of the learners during debriefing (Appendix A). Using the DART tool, a goal ratio of trainee responses to instructor questions plus statements is ideally >3:1. Participants were also asked to submit post-simulation surveys which included 13 questions related to understanding scenario learning objectives, duration and realism of the simulation, facilitators' ability to encourage participation and knowledge base, participants' confidence and psychological safety (Appendix A). The purpose of these were twofold: (1) to ideally increase the value of the program for trainees; and (2) to generate continuous data collection and share it with the Patient Safety Committee and hospital administration to engender support. The data was collected electronically via a QR code and entered into Research Electronic Data Capture (REDCap)—an existing data collection platform used by the hospital.

2.2. SMB

SMB is a hospital delivering nearly 8000 newborns each year in San Diego. The SMB NICU is a level III 84-bed unit with specialty care including a small baby program, neuro-intensive care program, and an advanced life support team that attends high-risk deliveries. The SMB NICU chose to participate in Simulating Success to address team competencies related to changing patient conditions and to improve communication skills in managing neonatal resuscitations. The team's primary SMART aim was to implement and conduct monthly simulation and debriefing exercises in the NICU at SMB while increasing multidisciplinary participation by the end of the 18 month collaborative. Nursing and respiratory departments added a requirement for each person to participate in at least two simulation and debriefing events per year for their annual performance evaluation. Historically, "mock codes" in this NICU did not focus on behavioral competencies required for improving teamwork, collaboration, and communication. In addition, the team wanted to improve staff confidence in managing changing patient conditions including appropriate use of positive pressure ventilation to avoid an unnecessary full resuscitation leading to intubation and/or chest compressions.

2.3. VCH

The Neonatal Service Line of Valley Children's Healthcare includes an 88-bed level IV Regional NICU located at the free-standing children's hospital in Madera, a 14-bed level III community NICU in Fresno, an 8-bed level II community NICU in Merced, and a second 6-bed level II NICU in Hanford. Given the complexity of multiple locations, staff composition and size, and critical nature of the patient population, VCH chose to participate in Simulating Success with the goal of improving team clinical and communication skills through simulation-based training. The team's goal was to increase the number of simulations offered and to improve the comfort level and skill set of staff performing resuscitation for infants in all units through effective simulation and debriefing. The first SMART aim was to run two simulation events per month at Regional NICU, two simulation events per month at one of the level II NICUs, and one quarterly simulation event at the other level II NICU by October 2020. The second SMART aim was to have each member of the core simulation team perform two debriefs per quarter and participate in two of the monthly simulation events.

3. Results

The following is a report of results by each site to date. Each hospital is discussed separately since each had different SMART aims. It is important to note that this analysis does not include analyses of patient outcomes, which continues to be tracked at the time of this writing.

3.1. CHOC

The multidisciplinary champion team at CHOC was comprised of a neonatologist, nurse educator and respiratory therapist. A total of 10 HCPs (four physicians, three nurses, three respiratory therapists) completed the online video training. Video-recorded simulations and debriefings were started in July 2018. The first 10 recordings served as a baseline to inform the creation of the first simulation improvement bundle which included (1) use of standardized briefings prior to simulation; (2) NRP education classes and skills workshops; (3) consistent use of the debriefer rating tool from CAPE; (4) use of debriefing the debriefer; and (5) addition of a simulation specialist to help conduct these team exercises. This bundle was implemented in January 2019 with modifications during multiple PDSA cycles. A total of 38 simulation exercises were completed in situ on Labor and Delivery and the NICU or in a simulation lab.

3.1.1. SMART Aim #1

Increase staff participation. A total of 73% of physicians, 48% of nurses, and 100% of respiratory therapists were exposed to at least one simulation exercise through June 2019.

3.1.2. SMART Aim #2

Decrease LSTs. After implementation of the simulation improvement bundle, LSTs decreased and there was a shift in the median to two LSTs per simulation (Figure 2). Of the LSTs identified, 57% were found to involve technical (e.g., lack of knowledge on usage of laryngeal mask) and 31%, behavioral issues (e.g., lack of role assignment) while 6.4% were attributable to cognitive issues (e.g., knowledge about delayed cord clamping) and 5.4% to system errors (e.g., failed pages).

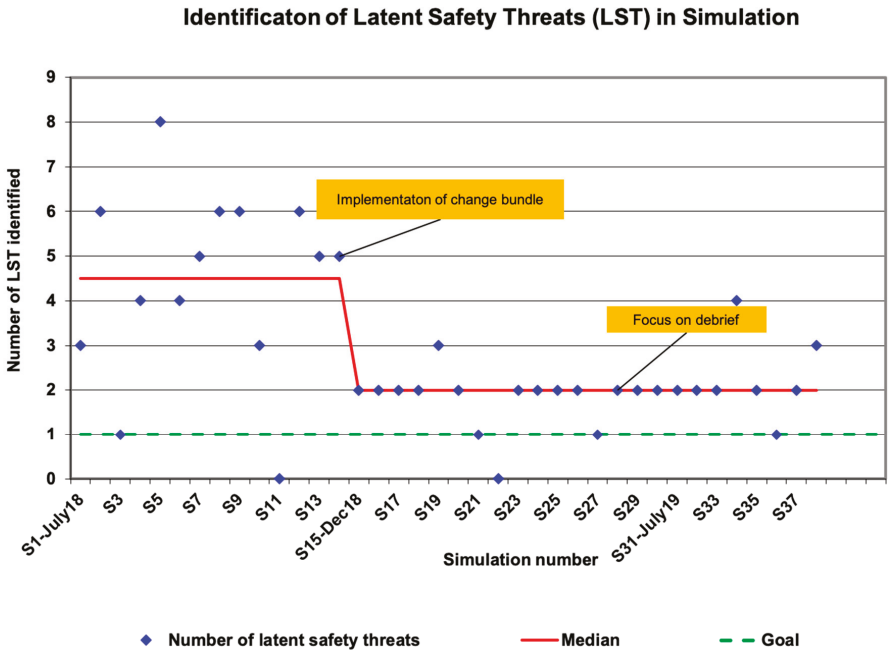

Figure 2. LSTs identified during CHOC simulations over time. Of note, there was a significant shift in the median (>8 consecutive data points below the median) during PDSA cycle 2 towards the goal of ≤1.

3.1.3. Other Notable Results

DART scoring revealed improvement over time towards the goal ratio of 3:1 [trainee responses: instructor questions + statements] (Figure 3). Of the 61 post-simulation surveys sent, 56 were completed; 90% of participants strongly agreed or agreed with the objectives of the program. These objectives were to provide a realistic simulated multidisciplinary team training experience in a constructive and psychologically safe learning environment and with ongoing feedback for improvement from participants. Notably, 89% of the participants believed the debriefing was constructive, 92% felt safe participating in the debrief and 90% wanted to experience more simulation sessions. In response to early qualitative feedback on sessions sometimes being overly long, subsequent sessions were adjusted by having a set time for debriefing.

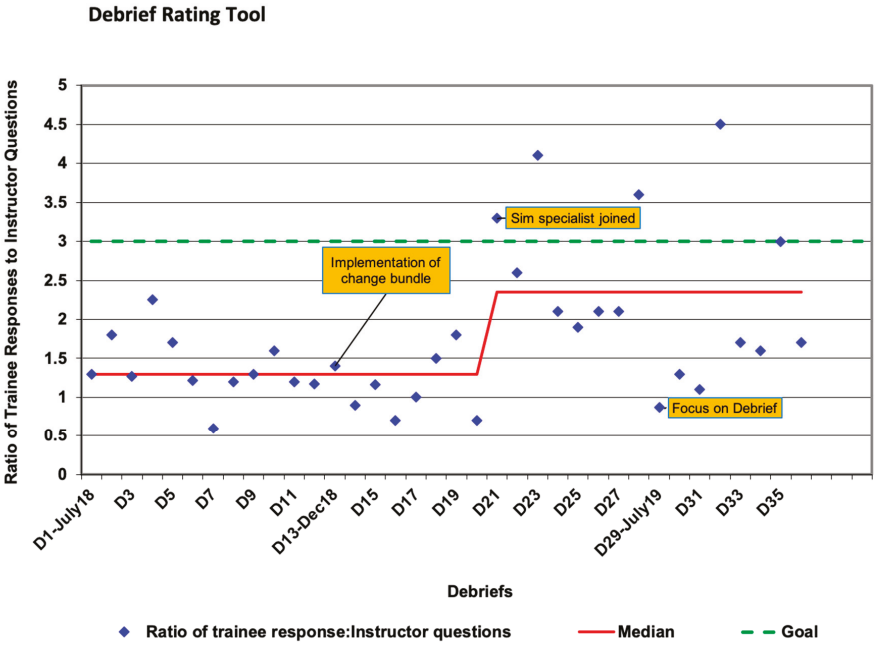

Figure 3. CAPE Real-Time Debriefing Evaluation (DART) scores for CHOC simulations over time. Of note, median shows improvement over time with a shift in median towards a goal ratio of >3:1.

3.1.4. Lessons Learned

The collaborative process of CPQCC's Simulating Success Program provided many benefits including the opportunity to: (1) learn from national experts; (2) share challenges and successes; (3) learn from and adapt to different settings; (4) share tools such as confidentiality agreement, surveys and clinical scenarios amongst the sites. This enabled participating sites to appreciate the power of learning from one another. The collaborative approach also helped the team to develop an urgency for change at the institutional level, encouraged friendly competition and fostered accountability. Monthly review of video recordings of the simulation and debriefings with our mentors at CAPE gave the team several opportunities to improve. Systems issues identified during these exercises led to process changes in how codes were called overhead in the NICU and replacing pagers to phones for Labor and Delivery to eliminate missed calls from failed pages.

3.1.5. Challenges Faced

Common difficulties in implementing CHOC's simulation program included time allocation, turnover of trained staff, and achieving the desired number of simulation sessions per month. There were several competing projects in the unit that made it difficult for the facilitators to allocate time for the goal number of sessions per month. This also made the growth of the team difficult to achieve. High census during October through December 2019 limited the team's ability to continue with a goal number of simulation sessions. Monthly webinars and face to face meetings helped CHOC's team trouble shoot some of these hurdles.

3.2. SMB

The multidisciplinary champion team at SMB was comprised of a neonatologist, clinical nurse specialist, a NICU supervisor and respiratory therapist. A total of 15 HCPs completed the online video training. The team developed a variety of custom NICU scenarios based on actual code events that occurred in Labor and Delivery and in the NICU. Beginning in July 2018, the team began video recording of simulations and debriefings. A timeline of the progression of the project is depicted in Figure 4. Simulation and debriefing events were held monthly for both day shift and night shift. Neonatologists and neonatal nurse practitioners were encouraged to participate in at least one simulation. Initial survey results demonstrated overwhelmingly positive results from HCPs who participated in these simulation and debriefing events. Forty-two HCPs responded to the initial survey; nurses and respiratory therapists represented 85% of the respondents. These respondents had moderate level of experience in their specialty (14.0 years + 11.7). Results demonstrated that participants had increased confidence in communicating during an emergency, increased ability to function as an essential team member during a code, and increased ability to voice a concern during a critical situation (Appendix B).

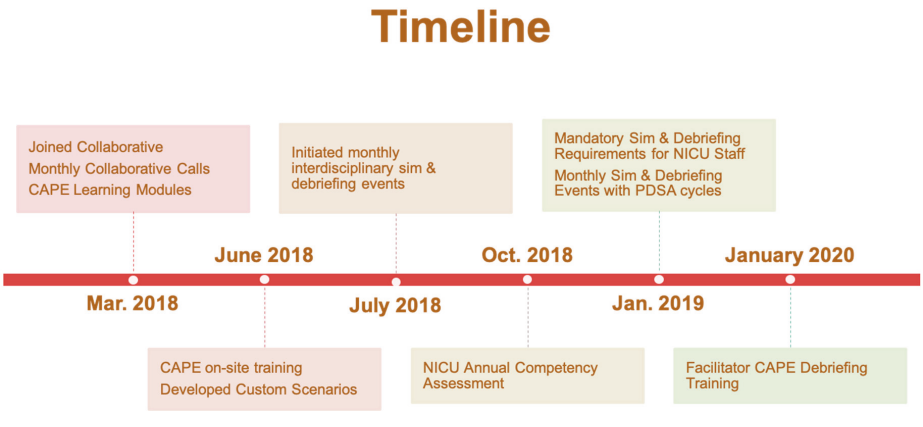

Figure 4. SMB Simulating Success project timeline.

Early in the implementation phase, the core team realized the need for additional simulation/debriefing facilitators and champions. The core team used a "train-the-trainer" approach to onboard additional facilitators. The train-the-trainer approach was not sufficient—additional preparation specific to effective debriefing was necessary. NICU nurses and respiratory therapists, mostly NRP instructors and advanced life support nurses who attend high-risk deliveries, volunteered to participate as champions. They each completed the CAPE online training course, "Strategies for Debriefing Health Care Scenarios".

3.2.1. SMART Aim #1

SMART Aim #1: Increase participation. A total of 100% of nurses (n = 205) and respiratory therapists (n = 40) participated in at least two simulation events within the first year. Participation in a minimum number of simulation and debriefing events were added to the annual competency requirements for both nurses and respiratory therapists which enabled achievement of this SMART aim. Throughout the 18 month participation in the collaborative, SMB utilized the PDSA process for the quality improvement framework.

3.2.2. Lessons Learned

The use of video to enhance CAPE's debriefing techniques allowed everyone to speak up and recognize areas for improvement. The debriefing technique which was new to SMB involved a flipped approach where the debriefers ask prompting questions or statements to elicit discussion from the participants thereby allowing the participants to identify strengths and opportunities for themselves. As a team, they critique their own performance and identify behaviors that they should reinforce and opportunities for improvement. Building effective, realistic scenarios using real-life events that have occurred at SMB helped staff identify and intervene with changing patient conditions. Strategies were identified to increase interdisciplinary team participation including adaptations to various provider schedules.

Effective debriefing has been key for successful learning. Some focus areas identified were the need for increased communication, consistently designating a team leader, knowledge of when to call for help and closed loop communication. Less experienced staff, especially on night shift, have expressed an increased confidence in ability to respond during an emergency. They have also increased their ability to recognize patient deterioration through simulation. Staff comments have been very positive. For example, staff comments include "This is the best mock code I have ever participated in; it is so realistic"; "This is such a great learning environment"; and "I really like how realistic this mock code is." In addition to the monthly simulation and debriefing sessions, newly learned debriefing skills have been incorporated into the review and evaluation of video-recorded neonatal resuscitations.

For more than 15 years, the SMB NICU team has used video resuscitation review as an ongoing quality improvement project to improve delivery room resuscitation. Using the debriefing model to discuss areas for improvement identified by the team has been highly effective. This process has proven beneficial in identification of a team leader, effective communication, and delegation of tasks. It has created an atmosphere that focuses more on team processes as opposed to individual performance. Given the technical components of simulation and debriefing (running video equipment, high-fidelity mannequin, and time commitment for set up and tear down), the goal was to have at least two facilitators at each debriefing. After initial experience, three facilitators were found to be ideal: one to direct the scenario and debriefing, one to control the high fidelity simulator, and one that manages the technical aspects of the debriefing with video equipment. In addition, the third person acted as a confederate as needed or as an additional debriefer.

3.2.3. Challenges Faced

Identified challenges with in situ simulation included (1) lack of dedicated space to conduct simulations and debriefings and inadequate space to store all the equipment; (2) technical and time consuming challenges of setting up for each simulation and debriefing; (3) interruption of simulations/debriefings by events occurring in the unit (i.e., high census, high acuity); (4) ensuring adequate participation. Monthly multidisciplinary simulation and debriefing sessions were offered on each shift. Initially, they were offered on weekends as well, but there was less participation on weekends. Varying days and times simulation/debriefing sessions were offered throughout the month encouraged staff participation. Dates and times of all scheduled simulation and debriefing sessions were emailed and posted in advance allowing staff to plan ahead. Early in the process, it was difficult to achieve physician and nurse practitioner participation since scheduled times mostly occurred in the afternoon or evenings when HCPs had already completed their shift for the day. In order to increase physician and nurse practitioner participation, session times were moved to accommodate rounding schedules and ensure multiple physicians were present on the unit to attend simulations and provide patient care as needed. They were also timed around typical breaks for nurses and respiratory therapists to enable them to participate.

3.3. *VCH*

The multidisciplinary champion team at VCH was comprised of two clinical nurse specialists and a neonatologist.

3.3.1. SMART Aim #1

Increasing number of simulations. The global aim of increasing the number of simulations conducted in the Neonatal Service Line of Valley Children's Healthcare was achieved although the monthly and quarterly targets for the number of simulations per month were not always met. The team has been able to significantly improve the quantity and quality of simulation training. The average compliance with the aim of four simulations per month was 40% (Figure 5).

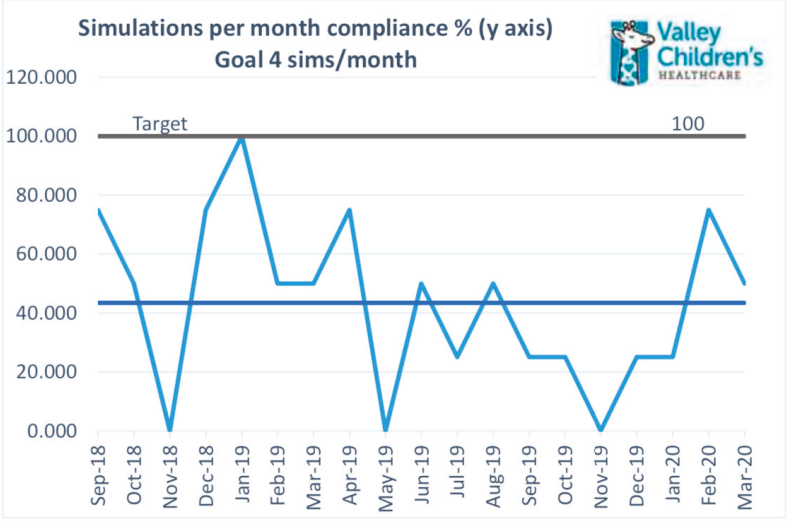

Figure 5. Average compliance with the goal of four simulations at VCH.

3.3.2. SMART Aim #2

Performing debriefings. Due to core team turnover, only the five consistent team members for compliance with number of simulations conducted per month and the number of debriefs per quarter have been tracked. The compliance of team members conducting two simulations per month ranges from 0% to 80% with a median of 40%. The compliance of team members conducting two debriefs per quarter ranges from 0% to 80% with a median of 60%. Areas of improvement have been identified and the team is continuing with data gathering and analysis. A follow-up staff survey in fall of 2020 will be conducted.

3.3.3. Other

As a part of the first PDSA cycle, the team identified a need to elicit baseline satisfaction and self-assessment of skill and confidence in code situations; therefore, the team developed a survey to be completed by all clinicians in the NICU (physicians, neonatal nurse practitioners, nurses and respiratory therapists). Based on the survey results, the team developed the following aims (Appendix C):

- Increase participation in 2–3 simulations/year from 18% to 40%;
- Decrease dissatisfaction with simulation experience to <10%;
- Decrease lack of confidence in the ability to participate in a neonatal code blue to <10%;
- Decrease lack of confidence in the ability to lead a neonatal code blue to <10%;
- Decrease lack of comfort with communication skills required during a neonatal resuscitation to <5%.

3.3.4. Lessons Learned

By careful scenario design and planning, a major component of Simulating Success, the VCH team has been able to capitalize on two other major quality improvement initiatives—reduction in unplanned extubations and implementation of Golden Hour Guidelines for premature infants. Simulation expanded into several other arenas of staff development and training, including competency assessment in resuscitation, transport and clinical skills. CAPE simulation techniques and scenarios have been used to deliver resuscitation training at multiple referring facilities as well. The debriefing model taught by CAPE and use of video for debriefing was new to the VCH team. Over the course of the collaborative, team members have grown from being unsure to developing real confidence in their ability to effectively debrief. A robust multidisciplinary team (clinical nurse specialist, nurse, respiratory therapists, neonatologist, and neonatal outreach coordinator) has enabled them to fine tune the different aspects of the simulation scenarios. Simulation training aligns with the safety goals of VCH which has facilitated leadership support in both equipment purchases, staff time, and designated space.

3.3.5. Challenges Faced

First, high census/acuity impacts the team's ability to conduct scheduled simulations thereby making it difficult to ensure team availability and staff participation. Second, the logistics of conducting simulations at four locations (Regional NICU and three satellite NICUs) with one simulation staff remains a challenge. Third, the team experienced turnover in several key roles requiring the onboarding and training of new simulation team members which was time consuming. Finally, constantly moving equipment due to a lack of dedicated space to conduct simulations/debriefings contributed to the inability to fully achieve the team's goals.

4. Discussion

As with any team event, the more that team members practice together, the better they perform together [19]. When the core principles for simulation and debriefing are followed, it is possible to deliver safe, effective and efficient patient care [20]. Simulation improves neonatal resuscitation and patient safety [21]. Participation in CPQCC's Simulating Success has shown that a multidisciplinary approach to quality improvement creates more engagement, enables focus to be directed towards patient safety rather than individual performance and leads to identification of system issues. To highlight one example, in the CHOC experience, a major systems issue identified through simulations was the paging method by which codes were called in the NICU. This led to inconsistencies in staff response. This issue was referred to leadership in CHOC's Code White Committee which recommended the change to overhead code white calls, consistent with hospital wide code white calls, for appropriate staff response. Similarly, missed pages during simulation sessions were documented in Labor and Delivery which led to a change to iPhones for teams to respond and communicate in real-time.

4.1. Future Directions: CHOC

In 2020, with ongoing simulation exercises, our aim is to improve (1) long-term outcomes including decreasing the rate of chronic lung disease (CLD) from 25% to 20% and severe intraventricular hemorrhage (IVH) from 15.9% to 12%; and (2) short-term measures of decreasing the frequency of Apgar score <8 at five minutes, decreasing the number of intubation attempts in the delivery room, decreasing the frequency of cardiopulmonary resuscitation in the delivery room, and decreasing the time to leave the delivery room to the NICU. Simulating Success has been an impetus to expanding the simulation program at CHOC to involve other specialties including emergency medicine, pediatric intensive care, cardiovascular intensive care and hospital medicine. A temporary simulation center with basic infrastructure for a simulation room and a debriefing room with audiovisual capacities was built to conduct simulation lab exercises. The program at CHOC is able to use the space for procedural skill training for incoming attendings, residents, and fellows. The team at CHOC continues to collect data on resource utilization to emphasize the demand for this program to hospital leadership. A core simulation team has been established which meets monthly. A website for the simulation program has been created that can be accessed through the hospital intranet that contains the mission, training modules, confidentiality agreement, liability and request forms, and a list of facilitators and mentors. A three-tier facilitator program is being developed to help facilitators advance their skills in order to become mentors and grow the program. A tiered approach was created so as to ensure the quality of the program. Several facilitators have completed the online debriefing program through CAPE. Currently, neonatal and pediatric critical care are the main specialties involved in simulation with a plan to develop a simulation task force for both of these divisions. There will be ongoing education through reviews and webinars for facilitators on simulation methodology similar to the CAPE online debriefing course in order to further hone skills. A common debriefing language will be used for all simulations performed in the organization to integrate it as part of our culture of care.

4.2. Future Directions: SMB

In 2020, the SMB core team of facilitators will meet quarterly to review videos of their debriefings with the intent to improve facilitating effective simulation scenarios and debriefing using a "debriefing the debriefer" model. The process used by CAPE and CPQCC of providing insightful feedback during face to face sessions has helped to train the team's facilitators. A train-the-trainer model has been implemented whereby experienced debriefers are scheduled with newly trained debriefers. Finally, in order to continue to enhance the program and assess its effectiveness among each of the disciplines, a pre–post-survey to elicit ongoing feedback has been created.

4.3. Future Directions: VCH

The team at VCH is working on budget planning to schedule simulations six months in advance, assess for feasibility to schedule staff and conduct multiple simulation events in a day. They aim for shared accountability amongst all simulation team members for set up, planning and implementation. They hope to train additional team members to replace those that have moved into other roles and continue the professional development of existing members. The team is eager to continue its work with their partners in Simulating Success through the sharing of experiences, scenarios and best practices.

4.4. Limitations

Our paper is limited in that these are the experiences of three institutions, presented as case studies, with differing aims and outcome measures. This limits the conclusions that can be drawn regarding the value and impact of the program; however, we hope that the narrative descriptions of these experiences can be helpful to institutions working on simulation and debriefing implementation for neonatal resuscitation.

5. Conclusions

In situ simulation aids in identifying system issues and focuses on improving patient safety [22]. Our paper describes the experiences of three sites with some similar, but also different contexts and results of implementing in situ simulation programs for neonatal resuscitation. Lessons learned will inform each institution's continued progress, but may also be useful for others embarking on similar implementation projects. A goal of the implementation for all three institutions was to potentially affect systems change, and ultimately lead to improved patient care and outcomes. Each hospital in this collaborative had their own set of challenges and approached their simulation training and implementation methods based on the unique needs and goals of their unit. However, there were commonalities in barriers, such as adapting to fluctuations in clinical acuity and census and having consistent, dedicated team members with time allotted for the program. Establishing a strong foundation in simulation methodology, developing debriefing skills, ensuring multidisciplinary champions for implementation, and following a quality improvement framework are key components in order to achieve the goals of enhancing teamwork in neonatal resuscitation in order to improve clinical outcomes.

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Institutional Review Board Statement: This study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Stanford University Institutional Review Board, protocol 38601.

Informed Consent Statement: Informed consent was obtained prior to recorded simulations. No protected health information was included.

Data Availability Statement: The data presented in this study may be available on request from the corresponding author. The data are not publicly available due to privacy concerns and some data not consented to be shared.

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Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

v2011-01-01

CAPE Real Time Debriefing Evaluation©2011

Instructor:_____ **Scenario:**_____ **Date:**_____

Before scenario: ■ Reviews learning objectives and anticipated actions.
During scenario: ■ Takes notes re: performance of cognitive, technical, and behavioral skills.
After scenario: ■ Briefs re: performance issues/items on debriefing checklist.
Debriefing: ■ Determines whether trainees share same mental model of patient.
■ Facilitates self-reflective learning.

Scenario Start Time:	Debriefing Start Time:
Scenario End Time:	Debriefing End Time:
Scenario Length:	Debriefing Length:

Time between end of scenario and start of debriefing: _____ min

Time when tape first rolls during debriefing: _____ min

Percentage of scenario covered during debriefing: _____ %

Percentage of learning objectives covered during debriefing: _____ %

Length of debriefing : Length of scenario ratio: _____

Number of times tape paused during debriefing: _____

Length of tape segments played: _____

Instructor Questions:	Instructor Statements:	Trainee Responses:
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Instructor question : Instructor statement ratio: _____

Trainee responses : Instructor questions+statements ratio: _____

Figure A1. DART tool.

Appendix A

Table A1. CHOC post-simulation evaluation and survey results.

1a. I clearly understood the purpose and objectives of this simulation exercise:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	59	33
Agree	32	18
Disagree	2	1
Strongly Disagree	7	4
Total		56
1b. The scenario represented a real-life situation:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	59	33
Agree	34	19
Disagree	0	0
Strongly Disagree	7	4
Total		56
1c. The debriefing discussion after the simulation was constructive:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	68	38
Agree	21	12
Disagree	4	2
Strongly Disagree	7	4
Total		56
1d. I felt that the learning environment was safe:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	71	40
Agree	21	12
Disagree	0	0
Strongly Disagree	7	4
Total		56
1e. I would like to participate in another simulation experience:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	52	29
Agree	38	21
Disagree	2	1
Strongly Disagree	7	4
Total		55
2a. As a result of the simulation experience, I have increased my ability to anticipate the needs of other team members:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	52	29
Agree	39	22
Disagree	2	1
Strongly Disagree	7	4
Total		56
2b. As a result of the simulation experience, I have increased my ability to communicate efficiently with other team members:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	50	28
Agree	41	23
Disagree	2	1
Strongly Disagree	7	4
Total		56

Table A1. *Cont.*

3a. The facilitators were knowledgeable about patient care in the scenario:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	64	36
Agree	29	16
Disagree	0	0
Strongly Disagree	7	4
Total		56
3b. The facilitators were well prepared for the session:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	68	38
Agree	21	12
Disagree	4	2
Strongly Disagree	7	4
Total		56
3c. The facilitators encouraged active participation during the debriefing session:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	70	39
Agree	23	13
Disagree	0	0
Strongly Disagree	7	4
Total		56
4a. The scenario was presented in a realistic environment:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	59	33
Agree	36	20
Disagree	0	0
Strongly Disagree	5	3
Total		56
4b. The location and time worked for me:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	46	26
Agree	36	20
Disagree	13	7
Strongly Disagree	5	3
Total		56
4c. The session lasted about the right time:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	54	30
Agree	36	20
Disagree	5	3
Strongly Disagree	5	3
Total		56
5. What were the positive aspects of the experience?		
6. What changes would you recommend to improve future simulation experiences?		
7. Additional Comments: Examples below: "Created a great learning environment and the multidisciplinary aspect was helpful and made it more realistic." "I liked the discussion of the medical aspect and the crisis resource management for each simulation." "Non-judgmental, Informative." "The situation was more real than other simulations I have been a part of in the past 3 years." "Being able to work through common hiccups with critical situations, work through the and debrief afterwards improved confidence in being at bedside."		

Appendix B

Table A2. SMB post-simulation evaluation and survey results.

1. What is your current role in the NICU:		
Answer Choices	**Percentage %**	**Responses**
Advanced Life Support Nurse	3.6	2
Registered Nurse	67.3	37
Respiratory Therapist	20.0	11
Physician	3.6	2
Nurse Practitioner	1.8	1
Other	3.6	2
Total		55

	Mean	**SD**
2. # Years in Current Role	14.02	10.6
3. # Years in Current Role at SMB	9.82	8.5
4. # Sim & Debrief sessions in past year	2.33	1.9
5. # Code Pink Events in past year	0.68	1.1

6. Since participating in NICU Simulation and Debriefing, I have become more confident in my ability to communicate effectively during an emergency:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	50	27
Agree	50	27
Disagree	0	0
Strongly Disagree	0	0
Total		54

7. Since participating in NICU Simulation and Debriefing, I am able to recognize and intervene in a rapidly changing patient situation:		
Answer Choices	**Percentage %**	**Responses**
Strongly Agree	46.3	25
Agree	53.7	29
Disagree	0	0
Strongly Disagree	0	0
Total		54

8. I am able to voice my concerns during a critical situation:		
Answer Choices	**Percentage %**	**Responses**
Strongly agree	63.0	34
Agree	37.0	20
Disagree	0	0
Strongly disagree	0	0
Total		54

9. Overall, I am confident in my ability to participate as an essential team member in a neonatal code:		
Answer Choices	**Percentage %**	**Responses**
Strongly agree	40.7	22
Agree	59.3	32
Disagree	0	0
Strongly disagree	0	0
Total		54

10. The debriefing process is effective in aiding the team and learner to reflect on team performance and identify potential learning opportunities:		
Answer Choices	**Percentage %**	**Responses**
Strongly agree	70.4	38
Agree	29.6	16
Disagree	0	0
Strongly disagree	0	0
Total		54

Appendix C

Table A3. VCH post-simulation evaluation and survey results.

1. Number of simulations (excluding NRP) you have participated in during the last year:		
Answer Choices	**Percentage %**	**Responses**
0–1	79	110
2–3	18	24
4+	3	4
Total		139
2. I am satisfied with simulation experience:		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	7	9
Disagree	14	19
Agree	61	83
Strongly agree	19	26
Total		137
3. I am confident in my ability to participate in a neonatal code blue:		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	4	5
Disagree	11	15
Agree	56	77
Strongly agree	30	41
Total		138
4. I am confident in my ability to be a team leader during a neonatal code blue:		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	8	11
Disagree	28	38
Agree	38	53
Strongly agree	26	36
Total		138
5. I am confident with my ability to perform skills of neonatal resuscitation (i.e., positive pressure ventilation, chest compression, dosing and administering medications):		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	1	2
Disagree	7	9
Agree	59	82
Strongly agree	33	46
Total		139
6. I am confident in my ability to anticipate clinical changes and interventions needed at bedside:		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	1	2
Disagree	2	3
Agree	57	79
Strongly agree	40	55
Total		139
7. I am comfortable with my communication skills required during a neonatal resuscitation:		
Answer Choices	**Percentage %**	**Responses**
Strongly disagree	2	3
Disagree	8	11
Agree	58	80
Strongly agree	32	45
Total		139

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Article

A Neonatal Intensive Care Unit's Experience with Implementing an In-Situ Simulation and Debriefing Patient Safety Program in the Setting of a Quality Improvement Collaborative

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Abstract: Extensive neonatal resuscitation is a high acuity, low-frequency event accounting for approximately 1% of births. Neonatal resuscitation requires an interprofessional healthcare team to communicate and carry out tasks efficiently and effectively in a high adrenaline state. Implementing a neonatal patient safety simulation and debriefing program can help teams improve the behavioral, cognitive, and technical skills necessary to reduce morbidity and mortality. In *Simulating Success*, a 15-month quality improvement (QI) project, the Center for Advanced Pediatric and Perinatal Education (CAPE) and California Perinatal Quality Care Collaborative (CPQCC) provided outreach and training on neonatal simulation and debriefing fundamentals to individual teams, including community hospital settings, and assisted in implementing a sustainable program at each site. The primary Aim was to conduct two simulations a month, with a goal of 80% neonatal intensive care unit (NICU) staff participation in two simulations during the implementation phase. While the primary Aim was not achieved, in-situ simulations led to the identification of latent safety threats and improvement in system processes. This paper describes one unit's QI collaborative experience implementing an in-situ neonatal simulation and debriefing program.

Keywords: neonatal simulation; simulation; debriefing; quality improvement; collaborative; neonatal intensive care unit; in-situ simulation; patient safety

1. Introduction

During the last couple of decades, literature suggests there is ongoing patient morbidity and mortality associated with avoidable harm and medical errors, including errors that can be prevented with improved communication and systems design [1,2]. Healthcare is a complex, dynamic process involving many disciplines collaborating in an effort to provide optimal care. In the U.S., most births do not require advanced resuscitation (i.e., positive pressure ventilation, chest compressions, or medication administration); however, about 10% of infants born do require some resuscitative efforts [3]. Approximately one percent will require extensive resuscitation following birth, including chest compressions and medication administration [3]. Because extensive neonatal resuscitation is infrequent,

resuscitation can be compromised because of cognitive and task overload, poor communication, and lack of teamwork. In-situ simulation provides a realistic context and opportunity for staff to practice problem-solving, decision-making, teamwork, and critical thinking skills in the actual delivery care setting [4]. Additionally, interprofessional in-situ simulation is a useful tool to help promote quality in neonatal care [5] and has been shown to identify latent safety threats (LSTs) [6]. This is in contrast with simulations conducted in a simulation center, in which there may be incomplete teams or healthcare professionals, who may not necessarily work with each other [6].

LSTs are errors in design, organization, training, or maintenance that can lead to medical errors [7]. LSTs are categorized into medication errors, equipment malfunction/misuse, inadequate teamwork, and other findings [8]. The relatively low frequency of neonatal resuscitation (especially extensive resuscitative interventions) creates an opportunity for LSTs to occur. In a retrospective study examining LSTs in a pediatric intensive care unit through an in-situ simulation program, 41% of the LSTs that were identified had the potential to cause harm. Category analysis showed that the majority of these LSTs were due to either a lack of resources (36%) or lack of education and training (27%) [9]. In-situ simulation training can help identify LSTs in the real-life clinical setting where maternal deliveries and neonatal resuscitations actually occur. As a result, this type of training can test systems and uncover gaps in processes that may delay timely care. In-situ simulations can assist in detecting LSTs and minimize the risk of a serious safety event [7]. For example, the simulation of a placental abruption followed by neonatal hypovolemia and perinatal depression can test the system and processes that are in place to include the blood bank, laboratory, respiratory therapy, and the maternal and neonatal teams. One metric to evaluate the effect of this simulated scenario is to measure the time required to obtain emergency O-negative blood from the hospital blood bank. Timely recognition and mitigation of LSTs are essential to reducing preventable harm during neonatal resuscitation.

Quality improvement (QI) collaboratives have grown increasingly popular. As such, there has been an exponential rise in perinatal and neonatal collaboratives across the United States, including California, Massachusetts, Florida, Tennessee, Ohio, New York, and Oregon. Since the inception of collaboratives in many states and regions throughout the United States, QI projects have covered various topics such as antenatal corticosteroid administration, antibiotic stewardship, and neonatal abstinence syndrome [10]. QI collaboratives create an environment for shared learning among healthcare organizations and professionals. In this shared learning environment, QI collaborative participants are supported by a faculty of experts who identify better practices and help facilitate implementation strategies to improve care [11]. Through monthly webinars and face-to-face interactive sessions, shared learning among different healthcare organizations and professionals occurs. Teams come together to learn, apply, and share not only their approaches to QI but also their data, successes, and barriers to improved performance [11].

We describe our unit's experience participating in *Simulating Success*, a QI collaborative hosted by California Perinatal Quality Care Collaborative (CPQCC) and the Center for Advanced Pediatric and Perinatal Education (CAPE) through Stanford. CPQCC, established in 1997, is a non-profit quality improvement organization dedicated to improving the delivery of care and outcomes for California's mothers and vulnerable infants. CAPE, the world's first simulation center founded in 2002, is dedicated to neonatal and pediatric simulation-based training and research. The QI collaborative focused on implementing an in-situ neonatal simulation and debriefing program. Although the collaborative had common principles of implementation across centers, each individual center had their own Aims and process for implementation. We were provided ongoing assistance throughout the collaborative with a QI specialist that helped our team create Aim statements, identify metrics to assess progress in the collaborative, and review the concepts and assist core team members with the development of plan-do-study-act (PDSA) cycles.

2. Materials and Methods

2.1. Training and Preparation

Our Neonatal Intensive Care Unit (NICU) is a 14-bed, community Level III NICU located in Southern California. In 2019, there were 2354 deliveries and 211 NICU admissions with an average daily census (ADC) of six. Training and preparation to implement an in-situ neonatal simulation program consisted of identifying three core team members from our unit: a neonatologist/NICU Medical Director; a clinical nurse IV (the highest position on the clinical ladder for a staff nurse) that works the day shift; and a clinical coordinator (charge nurse) for the NICU on the night shift.

Participation in *Simulating Success* lasted 15-months, including three months of pre-implementation work prior to the 12-month active implementation phase (Figure 1). During the three-month pre-implementation phase, from July 2018 to September 2018, the core team members viewed nine online modules developed by CAPE. This series of modules covered a broad scope of simulation and debriefing techniques developed by the CAPE faculty. Homework assignments were included with each module; these involved the development of simulated clinical scenarios that our NICU experienced on a daily basis (high-risk, high volume) and scenarios that were not as frequently encountered (high-risk, low volume). During this same timeframe, monthly webinars were conducted with CAPE, CPQCC faculty, and a QI specialist in preparation for the simulation and debriefing course conducted at CAPE. In October 2018, our three-person team attended a 1.5-day intensive CAPE simulation and debriefing course and had the opportunity to engage with CAPE and CPQCC faculty and perform simulated clinical scenario followed by debriefings. During this intensive 1.5-day training, these same core team members also had the opportunity to debrief another NICU team's simulated clinical scenario and have our debriefing critiqued by the CAPE team, essentially a debriefing of our debriefing. During the months of November and December 2018, our team solidified simulation team members, developed Aim statements for the project, procured simulation materials and supplies, and discussed space allocation for simulations and debriefings.

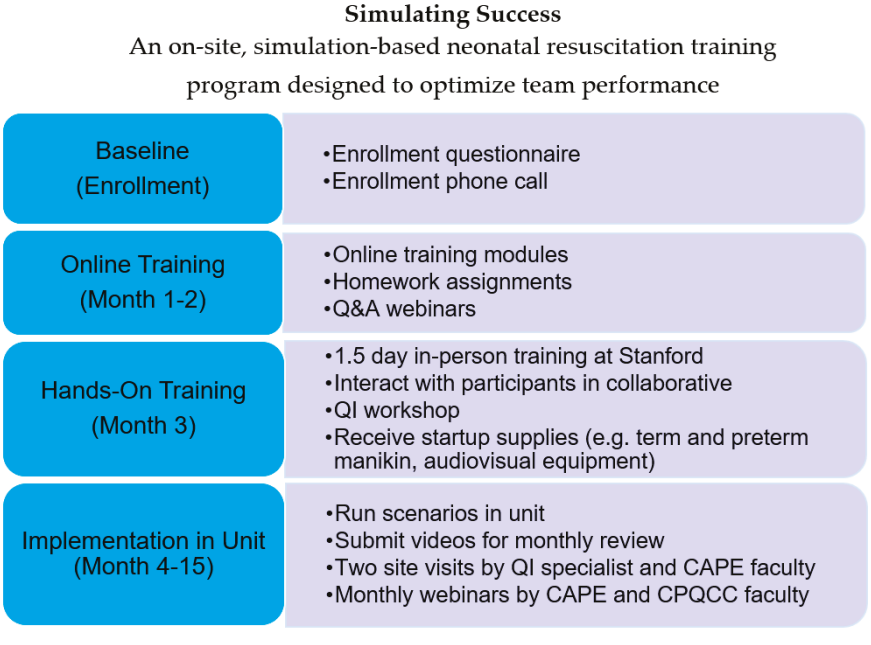

Figure 1. *Simulating Success* Project Timeline.

Our core team was provided ongoing assistance throughout the collaborative with a QI specialist that helped our team create Aim statements, identify metrics to assess progress in the collaborative, and review the concepts and assist core team members with the development of plan-do-study-act (PDSA) cycles. CPQCC and CAPE had two patient outcome-related Aims for the overall collaborative. As a small NICU, we were concerned that we would not have enough patient data to demonstrate improved patient care outcomes. Without accurate and timely data evaluation and feedback to staff, we were concerned that this could impact short and long-term staff buy-in. Our NICU's overall goal and reason to participate in this collaborative were to implement a multidisciplinary in-situ simulation program to improve team performance and debriefing skills. Therefore, our primary Aim statement indicated that the training team would conduct two video-recorded in-situ simulations and debriefings in the NICU every month from January 2019 through December 2019. Our second Aim statement declared that 80% of NICU staff would participate in two in-situ simulations and debriefings on an annual basis by December 2019. The QI specialist also worked with our team and provided suggestions on how to implement the simulation and debriefing program.

2.2. In-Situ Simulation Implementation Process

Our team decided to implement an in-situ simulation and debriefing program in which simulations and debriefings are conducted in labor and delivery or the NICU. Leadership in nursing and respiratory therapy supported and promoted the project through budgetary and personnel resources. A presentation explaining *Simulating Success* and the collaborative's goals and objectives were presented at a Maternal Newborn Services Division and Respiratory Services Department meeting. Additional communications occurred via email and during shift change reports.

Initially, the two nurse (RN) members of the core team set up and facilitated the first in-situ simulations utilizing simulations previously developed at CAPE. The neonatologist/medical director and respiratory care professional (RCP) members assisted by fulfilling different roles necessary to make the simulated scenarios realistic. In-situ simulations were held approximately two times per month, starting in January 2019. After a few months of becoming familiar with the simulation-based and audiovisual technologies and gaining practice with debriefing, the core team presented an in-person, interactive in-service training session based on CAPE's simulation and debriefing principles. This learning session was open to NICU RCP and RN clinical coordinators (charge nurses) and the goal was to integrate the CAPE debriefing methodology into routine simulations and utilize the debriefing techniques with real-life events. The in-service was also designed to incorporate other staff as part of succession planning for core team leaders. Training additional staff allows for the sustainability and expansion of in-situ simulations and debriefings at our institution.

Each month during the one-year implementation phase, January 2019 through December 2019, we submitted our in-situ simulation and debriefing videos to the team at CAPE for their review and critique. Additionally, CAPE and CPQCC faculty hosted monthly webinars attended by our core team members and another NICU participating in Group 2. In June 2019, Group 2 (n = 2) combined with Group 3 (n = 3) for the monthly webinars. The two groups were combined to enhance the shared learning environment and unit experiences. During these webinars, CAPE faculty offered suggestions on scenario design and implementation as well as techniques for enhancing realism. In addition, the CAPE team critiqued our recorded debriefings. Participating NICUs were also afforded the opportunity to share the barriers to implementation and strategies for success that each experienced.

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Stanford (Project identification 38601).

3. Results

Aim 1: Between January 2019 and December 2019, the team conducted 15 in-situ simulations (goal 24) in our Maternal and Newborn Services Division, averaging roughly one simulation per month.

The main challenge to conducting in-situ simulations was a persistently high census in the NICU that limited the ability of staff to participate without potentially compromising the care of actual patients.

Aim 2: In 2019, 70% of our staff (goal 80%) attended two or more simulated scenarios. Seven of the staff (26%) attended only one simulation during that time. We fell short of our goal primarily due to medical leave or per diem schedules.

Latent Safety Threats

Participation in *Simulating Success* revealed a total of four LSTs in our unit. The first LST identified involved the administration of epinephrine. Although the team was able to ascertain and give the correct dose of epinephrine utilizing the standard preprinted, weight-based drug calculation sheet, trainees reported that it took longer to find the right dose since that form contained multiple other drugs. One trainee suggested that because epinephrine is one of the drugs that is most commonly administered during resuscitation, the dosages for intravenous (IV) and endotracheal tube (ETT) administration should be listed on a laminated card and placed inside the NICU emergency tackle box. This tackle box is taken to all deliveries attended by a NICU nurse. The use of this card has allowed for more timely identification of the correct dose by weight and administration route, reducing time to administration (Figure 2).

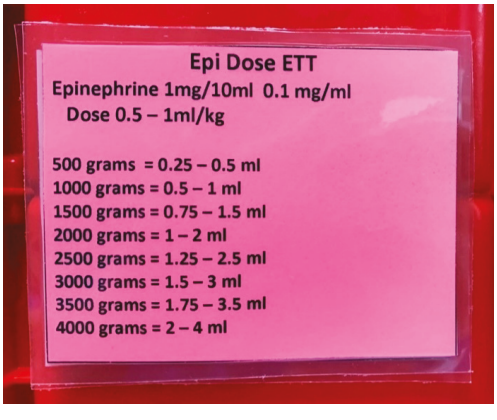

Figure 2. Epinephrine Administration via Endotracheal Tube Dosing Card Inside the Tackle Box.

The second LST identified concerned the performance of neonatal resuscitation and initiation of oxygen therapy. Throughout multiple simulated scenarios, trainees had difficulty in assessing the extent to which the simulated newborn required assistance with ventilation and displayed uncertainty as to the need for oxygen as guided by the Neonatal Resuscitation Program (NRP) algorithm. To assist trainees with timely evaluation and management, the simulation team placed laminated cards on the radiant warmers in Labor and Delivery that address the target hemoglobin oxygen saturation levels by minutes of age according to NRP guidelines [12]. Furthermore, cards depicting the mnemonic MRSOPA (used to indicate the six steps recommended to address inadequate ventilation) were placed on the radiant warmer (Table 1).

The third LST identified pertained to the resuscitation equipment. One of our simulated scenarios involved the response to a newborn in the normal newborn nursery in the Mother–Baby Unit who became dusky during a lab draw. The newborn needed to be moved from a crib to the radiant warmer for resuscitation. Trainees participating in the scenario noted that the equipment and supplies that were needed to treat the simulated newborn were scattered haphazardly in the drawer of the radiant warmer, making it difficult to find them in a timely manner and potentially producing a negative impact on neonates requiring resuscitation (Figure 3).

Table 1. The Steps of MRSOPA (modified from the Textbook of Neonatal Resuscitation [12]).

MRSOPA	ACTION
M:	adjust **M**ask
R:	**R**eposition mask
S:	**S**uction mouth and nose
O:	**O**pen mouth
P:	increase **P**ressure
A:	**A**lternate airway

Figure 3. Mother–Baby Radiant Warmer Drawer Before Simulation.

As a result, the NICU team assisted the clinical coordinators in that unit with reorganizing supplies and equipment and developing a checklist to ensure that everything needed to resuscitate a newborn is present (Figures 4 and 5).

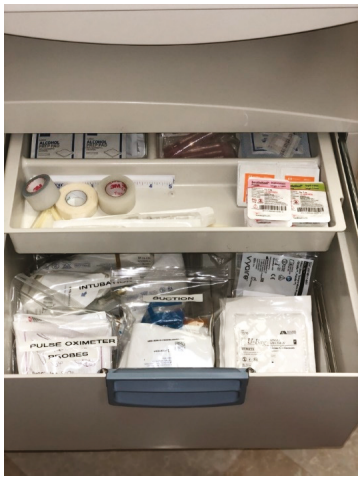

Figure 4. Mother–Baby Radiant Warmer Drawer After Simulation.

5SW NURSERY INFANT WARMER SUPPLY LIST

MONTH_____

DATE														
	7A	7P	7A	7P	7A	7P	7A	7P	7A	7P	7A	7P	7A	7P
ON WARMER: (checked & connected)														
T-piece														
Suction tubing														
TOP SHELF:														
Skin temp probe														
Pulse ox probe														
Suction catheters 8 & 10 FR.														
INSIDE DRAWER:														
LAB COLLECTION SUPPLIES														
2 heel warmers														
Lancets (Gentlefeet) 2 newborn & 2 preemie														
5 spot bandaids														
5 sterile 2 x 2's														
10 alcohol pads														
1 plastic tape														
Miscellaneous Supplies														
2 urine collection bags														
5 cotton balls														
2 pulse ox probes														
2 temp probes														
1 cord clamp														
3 saline bullets														
2 tape measures														
3 KY jelly														
Anesthesia bag & mask														
Airway supply bag (content label on bag)														
TIME:														
INITIALS:														

Figure 5. Mother–Baby Radiant Warmer Checklist.

The fourth LST involved the process of stabilizing a newborn with gastroschisis. This scenario truly reflects a high-risk, low-volume situation for our teams as a newborn with gastroschisis has not delivered at our hospital in more than five years and few of our staff have practical hands-on experience in managing a newborn with this condition. During the review of this recorded scenario, the CAPE team noted that other hospitals manage the stabilization of newborns with this congenital malformation in a different manner. This prompted us to contact the pediatric surgeons at the children's hospital to which we typically transfer our surgical patients and inquire as to what procedure they prefer that we follow. This led to a change in our stabilization process to reflect these updated recommendations. We also modified our supplies and equipment based on that information and communicated these changes to all NICU staff via email, as well as during the staff huddles held prior to each shift. We also noted that our debriefings of this scenario provided an opportunity for staff to engage in rich discussions (essentially "debriefing themselves"); this activity has been shown to improve clinical reasoning that may translate to replicating debriefings in a real-life situation [13].

4. Discussion

While the *Simulating Success* QI project involved experienced neonatal healthcare professionals, much of the literature that describes debriefing, centers on training relatively inexperienced learners, not practicing healthcare professionals. Most authors convey the need for four phases of debriefing: reaction, description, analysis, and summary [14–23]. This is done primarily because of a belief that psychological distress is frequent during participation in simulated clinical events and, without first having an opportunity to "ventilate" pent up emotion, trainees being debriefed will not be able to participate effectively in a debriefing. Henricksen et al. examined the expression of psychological distress in 3900 subjects undergoing debriefing after simulated healthcare scenarios and found that <1% were perceived to manifest such distress [24]. Finally, patient outcome is not routinely emphasized and some authors state that discussion of patient outcome should be avoided, especially when outcome is poor [25]. These aspects of debriefing in healthcare conflate the difference between a technical performance debriefing (used to critique human and system performance) and a critical incident stress debriefing (conducted to provide psychological support after an emotionally and/or psychologically challenging event). A fundamental difference with CAPE's Guiding Principles for Healthcare Debriefings [26] emphasizes that learning is better achieved through facilitated trainee discussions rather than didactic teaching provided by the facilitator. This facilitated discussion can be best achieved using a series of four "drill-down" questions [26]. CAPE's debriefing principles also guide trainees to develop approaches to replicate actions that strengthen human and system performance and avoid activities that are ineffective or harmful [26]. Integrating CAPE's Guiding Principles for Healthcare Debriefings was a change from our unit's previous style of debriefing. There was a learning curve for the core team members to adapt and incorporate various elements of CAPE's debriefing principles. Additionally, participants commented on the differences they experienced themselves and that utilizing CAPE's debriefing principles opened more opportunities for discussion and active learning.

CPQCC's *Simulating Success* collaborative was designed to assist participating NICUs implement a patient safety neonatal simulation and debriefing program. In the context of this QI collaborative, our community NICU benefitted from the expertise of CAPE and CPQCC faculty, and the QI specialist who helped critique our processes and support our goals. At its foundation, CPQCC utilizes the Institute for Healthcare Improvement (IHI) improvement framework—the Model for Improvement—which focuses on three questions and conducting Plan-Do-Study-Act (PDSA) cycles during the implementation phase of a collaborative [10]. The three questions are: What are we trying to accomplish? How will we know that a change is an improvement? What change can we make that will result in improvement? To address these questions, we conducted PDSA cycles that developed the change (plan), implemented the change (do), evaluated the change (study), and determined whether any modifications or revisions were needed (act) [27]. To answer the IHI's three questions:

1. What are we trying to accomplish? *We sought to implement a simulation and debriefing program.*
2. How will we know that a change is an improvement? *We aimed to conduct two simulations and debriefings monthly and achieve an 80% participation rate by our nursing staff in two simulations during the yearlong implementation phase.*
3. What change can we make that will result in improvement? *We sought to identify LSTs, make changes to various resuscitation processes, and train additional team members in order to sustain the simulation and debriefing program.*

It is worthwhile to note that, from a QI collaborative perspective, a unit's readiness for change is assessed before embarking in a QI collaborative. This assessment of the readiness for change can be evaluated by various unit and/or organizational context factors. Relevant stakeholders who can effect change, especially from a financial and human resource standpoint, should assess and understand the unit's culture, leadership and financial support, and evaluation capabilities [28]. We have been involved with past CPQCC collaboratives; however, those collaboratives focused on reducing variation

in the performance of healthcare professionals and/or standardizing changes in practice (e.g., antibiotic stewardship and increasing the frequency of breastmilk feedings). With *Simulating Success,* our goal was to implement and develop processes to sustain a simulation and debriefing program. To achieve this goal, we needed to ensure the significant financial resources necessary to support personnel, assistance from information technology services, allocation of sufficient time to allow core team members, nurses and respiratory therapists to participate in the simulated clinical scenarios. We were fortunate that our hospital's nursing, respiratory, and physician leadership recognized the importance of a simulation and debriefing program to neonatal care. This support facilitated buy-in with the program by our staff.

Undertaking a QI project also means having the ability to collect and evaluate data, and then provide feedback to team members to advance QI improvements. While we acknowledge that our project's Aim statements did not focus on patient outcome data, the LSTs identified by the trainees and the resultant process improvements did act to foster staff buy-in. We cannot underscore the importance of evaluation and feedback in quality improvement work—they are the foundations of "study" and "act" in PDSA cycles.

Implementation Barriers

One of the concerns of the core team involved videotaping staff during the simulation and debriefing. In the past, videotaping simulated scenarios had not been a positive experience, as expressed by many NICU staff. We used a handheld iPad for recording and moved it around to attempt to capture the best views; this served to constantly remind staff that they were being filmed. The staff also expressed concern that mistakes made during simulation would be highlighted during playback during debriefings. For all these reasons, we had ceased recording simulated scenarios. At the beginning of *Simulating Success,* the core team was concerned that the videotaping and playback could make staff resistant to participating in this QI collaborative. These issues were addressed with staff members by the core team via one-on-one discussions and presentations to groups of professionals working in the NICU and Labor and Delivery. The core team assured staff that recordings would be used only as a debriefing tool to enhance training and not as a formal critique of their abilities. We also emphasized that our core team's debriefing technique was backed by CPQCC and CAPE as a recommended technique. Nursing Leadership also approved the purchase of a "GoPro" camera (which has a small physical footprint) making recording less noticeable to the staff. As a result, many staff commented that they actually forgot that they were being videotaped during the scenarios. As the months progressed, the staff learned to "debrief themselves" as they watched the playback and became comfortable with CAPE's debriefing methodology.

Another barrier was the challenge of a limited number of staff present during the simulations and the inability to bring on-duty NICU staff to Labor and Delivery for the simulated scenarios. We therefore utilized areas in the NICU such as a back corner or the isolation room and simulated as if we were in the labor and delivery area. We also ensured that each simulation and debriefing was completed in 30 min or less at the end of each shift. This allowed staff to complete all or most of their work prior to participating.

As with any QI project, there were barriers to participation. We, therefore, established that unit and organizational stakeholders shared our mental model as to how the program should proceed prior to its start. This shared mental model involved various context factors, such as financial and staff resources, in order to effect change and provide overall accountability for the implementation process and simulation program. To help with the program's sustainability, we also actively engaged and started initial training with other interprofessional team members.

5. Conclusions

This manuscript describes our unit's experience with implementing a simulation and debriefing program in a NICU QI collaborative setting. Our overall objective was to integrate an in-situ simulation

and debriefing program in the context of our local unit and achieve widespread interprofessional simulation and debriefing experiences. Once we achieve consistent and sustained in-situ simulations and debriefings (conducting two simulations monthly for six months), our future goals include: (1) integrating CAPE's debriefing techniques into debriefings following actual clinical events; (2) continuing to train the current members of our simulation team and recruit new members; and (3) using patient outcome data from the CPQCC database to inform future QI projects, using simulation as a method for evaluation and feedback.

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Article

Association between Regional Tissue Oxygenation and Body Temperature in Term and Preterm Infants Born by Caesarean Section

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Abstract: Body temperature (BT) management remains a challenge in neonatal intensive care, especially during resuscitation after birth. Our aim is to analyze whether there is an association between the BT and cerebral and peripheral tissue oxygen saturation ($crSO_2$/cTOI and $prSO_2$), arterial oxygen saturation (SpO_2), and heart rate (HR). The secondary outcome parameters of five prospective observational studies are analyzed. We include preterm and term neonates born by Caesarean section who received continuous pulse oximetry and near-infrared spectroscopy monitoring during the first 15 min, and a rectal BT measurement once in minute 15 after birth. Four-hundred seventeen term and 169 preterm neonates are included. The BT did not correlate with $crSO_2$/cTOI and SpO_2. The BT correlated with the HR in all neonates ($\varrho = 0.210$, $p < 0.001$) and with $prSO_2$ only in preterm neonates ($\varrho = -0.285$, $p = 0.020$). The BT was lower in preterm compared to term infants (36.7 [36.4–37.0] vs. 36.8 [36.6–37.0], $p = 0.001$) and prevalence of hypothermia was higher in preterm neonates (29.5% vs. 12.0%, $p < 0.001$). To conclude, the BT did not correlate with SpO_2 and $crSO_2$/cTOI, however, there was a weak positive correlation between the BT and the HR in the whole cohort and a weak correlation between the BT and $prSO_2$ only in preterm infants. Preterm neonates had a statistically lower BT and suffered significantly more often from hypothermia during postnatal transition.

Keywords: body temperature; hypothermia; hyperthermia; neonates; term; preterm; postnatal transition; oxygenation; tissue oxygenation; near-infrared spectroscopy

1. Introduction

Maintaining optimal body temperature remains a challenge in neonatal intensive care. In 1997, the World Health Organization (WHO) defined the normal range of body temperature in newborn infants between 36.5–37.5 degrees Celsius (°C) [1]. However, Knobel et al. observed that the maximized normal heart rate (HR) observations occurred when the neonates body temperature was 36.8–37.0 °C [2], and Lyu et al. described the lowest rates of adverse neonatal outcomes in preterm infants with body temperatures of 36.5–37.2 °C [3]. Generally, the body temperature of newborn infants varies widely and depends on different variables such as postnatal age, location of measurement, and the method to determine body temperature [4–6]. Both hypothermia and hyperthermia are associated with increased

mortality and morbidity [3,7]. The incidence of neonatal hypothermia is up to 84% in developing countries [8] and up to 53% in Europe [9], whereby preterm neonates are more often affected compared to term neonates because of differences in body temperature management [10]. Pichler et al. reported that body temperature correlated with peripheral muscle tissue oxygenation, measured by near-infrared spectroscopy (NIRS), in newborn infants who were admitted to the neonatal intensive care unit [11]. Whether body temperature affects both peripheral and cerebral tissue oxygenation in newborn infants during fetal-to-neonatal transition remains unclear.

The primary aim of this study is to analyze whether there is an association between (i) body temperature and cerebral ($crSO_2$/cTOI) and peripheral regional tissue oxygen saturation ($prSO_2$) and between (ii) body temperature and the HR and arterial oxygen saturation (SpO_2) in neonates born by Caesarean section during fetal-to-neonatal transition. Our secondary aim is to (iii) describe and compare body temperatures between term and preterm neonates of the same cohort in minute 15 after birth. We hypothesize that body temperature will not affect $crSO_2$/cTOI, due to auto-regulative processes. For $prSO_2$, we expect a negative correlation with body temperature, due to a consequently increased metabolic rate. Further on, we hypothesize that the HR and SpO_2 will correlate positively with body temperature.

2. Materials and Methods

This study is a post-hoc analysis of secondary outcome parameters of five prospective single-center observational studies that were performed between 2008 and 2016 at the Division of Neonatology, Department of Pediatrics and Adolescent Medicine, Medical University of Graz, Austria. All studies were approved by the Ethics Committee of the Medical University of Graz, Austria (EK-numbers: 19-291ex07/08, 23-302ex10/11, 25-342ex12/13, 25-592ex12/13, and 27-465ex14/15), with written parental consent being obtained prior to study inclusion.

2.1. Participants

Term and preterm neonates who received continuous NIRS and pulse oximetry monitoring during the first 15 min after birth as well as body temperature measurements in minute 15 after birth were included. Due to logistical reasons, measurements were performed only in neonates delivered by elective, interactive, or emergency Caesarean section. Exclusion criteria were vaginally delivered newborns and presence of congenital malformations that could potentially affect cardiorespiratory or neurological function.

2.2. Postnatal Stabilization and Temperature Management

Cord clamping was performed within 30 s after birth. After that, all neonates were immediately placed in supine position under the resuscitation table's (CosyCot™, Fisher & Paykel Healthcare, Auckland, New Zealand) pre-warmed manually regulated overhead heater. Standardized room temperature in the delivery suite was 23–25 °C. If the neonate was below 28 weeks of gestation, it was put in a polyethylene bag. More mature preterm neonates were dried and had their bodies covered with warm towels. All neonates received elastic cotton caps to reduce heat loss from the head and were kept under the overhead heater for the measurement period of 15 min. Postnatal stabilization was performed according to current resuscitation guidelines [12,13]. SpO_2 and HR were measured routinely using pulse oximetry on the right wrist or palm (IntelliVue MP50, Philips, Amsterdam, The Netherlands). Blood pressure was measured non-invasively at least once during postnatal stabilization. Respiratory support (continuous positive airway pressure [CPAP] and/or positive pressure ventilation [PPV]) was provided by using a silicone face mask (LSR Silicon mask no. 0/0 or 0/1; Laerdal Medical, Norway) and the Neopuff Infant T-Piece Resuscitator (Perivent, Fisher& Paykel Healthcare, Auckland, New Zealand). Requirement of respiratory support (CPAP and/or PPV or intubation) was documented. Non-heated and non-humidified gases were used for initial respiratory

support. In minute 15 after birth, the rectal body temperature was measured once using a standard temperature probe (IntelliVue MP50, Philips, Amsterdam, The Netherlands).

2.3. Near-Infrared Spectroscopy

For cerebral NIRS measurements, the sensor was attached to the neonates' right forehead, and for peripheral NIRS measurements, the sensor was placed on the right forearm by a member of the research team. The sensors were fixed with a gauze bandage. $crSO_2$/cTOI and $prSO_2$ were measured continuously during the first 15 min after birth. $crSO_2$/cTOI was measured either with the INVOS 5100C device (Somanetics Corporation, Troy, Michigan, USA) or the NIRO 200-NX tissue oxygenation monitor (Hamamatsu Photonics, Hamamatsu-city, Japan). $prSO_2$ was measured with the INVOS 5100C device. The peripheral fractional oxygen extraction (pFTOE) was calculated as follows: $pFTOE = [(SpO_2 - prSO_2)/SpO_2]$.

2.4. Data Collection

Vital parameters such as $crSO_2$/cTOI, $prSO_2$, HR, and SpO_2, were saved automatically every second in a polygraphic data management system (Alpha-trace digital MM, BEST Medical Systems, Austria). These data were extracted and saved in a Microsoft Excel 2015 (Microsoft Corporation, Redmond, Washington, USA) database together with documented non-invasive blood pressure, rectal body temperature, need for respiratory support (CPAP and/or PPV or intubation), as well as prenatal and demographic information. Diagnoses (intraventricular hemorrhage [IVH], periventricular leukomalacia [PVL], NEC, and bacterial infection/sepsis) were extracted from electronic medical records (openMEDOCS, Version 6.5, SAP Business Client, Baden-Wuerttemberg, Germany).

2.5. Group Stratification

In a first step, the neonates were stratified into term neonates ($\geq 37^{+0}$ weeks of gestation) and preterm neonates ($<37^{+0}$ weeks of gestation). In a second step, sub-groups for preterm neonates were generated: (i) extremely preterm infants (EPI) born $\leq 28^{+0}$ weeks of gestation, (ii) very preterm infants (VPI) born between $>28^{+0}$ and $<32^{+0}$ weeks of gestation, and (iii) late preterm infants (LPI) born between $\geq 32^{+0}$ and $<37^{+0}$ weeks of gestation. According to the WHO, body temperature stages were defined as follows: hyperthermia (>37.5 °C), normothermia (36.5–37.5 °C), mild hypothermia (36.0–36.4 °C), moderate hypothermia (32.0–35.9 °C), and severe hypothermia (<32.0 °C) [1].

2.6. Statistics

To detect and eliminate artifacts from the raw data, the following quality criteria for NIRS measurements were used. For physiological reasons, the SpO_2, which is a measure of arterial hemoglobin oxygen saturation, should not be equal to or below the regional tissue saturation, which is a measure of hemoglobin oxygen saturation in the tissue including the arterial, capillary, and venous compartments [14]. If this was observed within the raw data, both arterial and regional oxygen saturation values were excluded from the analyses for abovementioned physiological reasons [14]. Data are given as mean ± standard deviation or as median (interquartile range) in dependency of distribution. Data were analyzed using IBM SPSS Statistics 24 Software (PSS Inc., Reston, VA, USA). Data distribution was tested using the Kolmogorov-Smirnov test. Mean values of $crSO_2$/cTOI, $prSO_2$, HR, and SpO_2, were calculated for each minute after birth. For the statistics, we used $crSO_2$/cTOI, $prSO_2$, HR, and SpO_2, values from minute 15 after birth. To investigate potential differences between groups, non-parametric tests (Mann-Whitney-U test and Kruskal Wallis test) were performed, and for the comparison of categorical variables, the χ^2 test was used. For correlation analyses, we used Spearman's correlation. A p-value of <0.05 was considered statistically significant.

3. Results

3.1. Characteristics

In a total of 587 neonates, continuous NIRS measurements and a single body temperature measurement within 15 min after birth were performed during the observation period. One neonate had to be excluded due to implausible data. Thus, 586 neonates (99.8%) were included in the present study. All 586 neonates received body temperature measurements, and in 492 neonates (84%), regional oxygen saturation values were available in minute 15 after birth. Four-hundred seventeen neonates (71.2%) were born at term and 169 neonates (28.8%) were born preterm. Demographic data are presented in detail in Table 1. Three-hundred two neonates (51.5%) were male, 50 neonates (8.5%) were twins, and six (1%) were triplets. One-hundred ninety-four neonates (33.1%) required respiratory support, thereof 188 neonates (32.1%) received CPAP and/or PPV, and 13 neonates (2.2%) were intubated during the observation period. Four of the included neonates (0.7%) needed cardiopulmonary resuscitation.

Table 1. Demographic data of the whole cohort, preterm and term born neonates, as well as of the subgroups EPI (extremely preterm infants $\leq 28^{+0}$ weeks of gestation), VPI (very preterm infants $>28^{+0}$ and $<32^{+0}$ weeks of gestation), and LPI (late preterm infants $\geq 32^{+0}$ and $<37^{+0}$ weeks of gestation). Data are expressed as mean ± standard deviation or median (interquartile range). Gestational age (GA), birth weight (BW), umbilical arterial pH (pHa), mean arterial blood pressure (MABP), arterial oxygen saturation (SpO_2), heart rate in beats per minute (bpm), body temperature in degrees Celsius (°C), cerebral tissue oxygen saturation ($crSO_2$/cTOI), peripheral tissue oxygen saturation ($prSO_2$), and peripheral fractional tissue oxygen extraction (pFTOE) in minute 15.

	Total (n = 586)	**Term (n = 417)**	**Preterm (n = 169)**	***p*-Value**	**EPI (n = 10)**	**VPI (n = 38)**	**LPI (n = 121)**
GA (weeks)	39 (36–39)	39 (38–39)	34 (32–35)	<0.001	26 (24–27)	31 (30–31)	34 (33–36)
Apgar 1	9 (8–9)	9 (9–9)	8 (8–9)	<0.001	8 (8–9)	8 (7–8)	8 (8–9)
Apgar 5	10 (9–10)	10 (10–10)	9 (8–10)	<0.001	8 (6–8)	9 (8–9)	9 (9–10)
Apgar 10	10 (10–10)	9 (9–10)	10 (10–10)	<0.001	9 (9–10)	9 (9–10)	10 (9–10)
BW (grams)	3088 (2380–3460)	3290 (2996–3590)	1830 (1438–2260)	<0.001	700 (626–906)	1330 (1054–1564)	2040 (1756–2400)
pHa	7.30 (7.28–7.32)	7.30 (7–28-7.32)	7.31 (7.28–7.34)	0.004	7.33 (7.31–7.39)	7.32 (7.29–7.34)	7.30 (7.27–7.33)
MABP (mmHg)	45 ± 10	47 ± 9	40 ± 9	<0.001	31 ± 7	38 ± 8	41 ± 9
SpO_2 (%)	95.1 (91.7–97.7)	95.7 (92.7–97.9)	93.5 (88.5–96.8)	<0.001	92.6 (72.1–96.1)	90.4 (86.9–93.8)	94.5 (91.1–97.3)
Heart rate (bpm)	154 ± 18	153 ± 18	156 ± 18	0.015	159 ± 17	161 ± 16	154 ± 18
Body temperature (°C)	36.8 (36.6–37.0)	36.8 (36.6–37.0)	36.7 (36.4–37.0)	0.001	37.0 (36.9–37.4)	36.7(36.3–37.0)	36.7 (36.4–37.0)
$crSO_2$/cTOI (n)	458	342	116		5	22	89
$crSO_2$/cTOI (%)	78.9 (71.0–86.0)	78.4 (71.0–85.0)	79.0 (68.7–87.5)	0.853	79.6 (75.6–91.1)	71.7 (62.0–79.0)	80.0 (72.0–89.0)
$prSO_2$ (n)	355	289	66		1	9	56
$prSO_2$ (%)	74.0 (63.0–85.0)	74.0 (63.0–85.0)	73.0 (62.0–87.0)	0.728	69.0 (69.0–69.0)	65.0 (51.0–75.0)	76 (63–87.5)
pFTOE	0.23 (0.12–0.34)	0.22 (0.12–0.34)	0.23 (0.11–0.30)	0.596	0.28 (0.28–0.28)	0.24 (0.16–0.40)	0.23 (0.09–0.29)

3.2. Oxygenation

There was no association between body temperature and $crSO_2$/cTOI and SpO_2, a weak positive correlation between body temperature and HR in the whole cohort as well as a weak negative correlation between body temperature and $prSO_2$ only in preterm infants. Correlation coefficients and *p*-values of body temperature and $crSO_2$/cTOI, $prSO_2$, pFTOE, HR, and SpO_2 are demonstrated in detail in Table 2, Figures 1 and 2. In neonates with hypothermia, we did not find any significant correlation between body temperature and $crSO_2$/cTOI, $prSO_2$, HR, and SpO_2, ($crSO_2$/cTOI: $\varrho = -0.02$, $p = 0.867$; $prSO_2$: $\varrho = -0.05$, $p = 0.672$; HR: $\varrho = -0.177$, $p = 0.127$; SpO_2: $\varrho = 0.199$, $p = 0.069$), respectively. In hyperthermic neonates, the body temperature did also not correlate significantly with $crSO_2$/cTOI, $prSO_2$, HR, and SpO_2 ($crSO_2$/cTOI: $\varrho = 0.111$, $p = 0.642$; $prSO_2$: $\varrho = 0.232$, $p = 0.658$, HR: $\varrho = 0.300$, $p = 0.186$; SpO_2: $\varrho = -0.335$, $p = 0.118$).

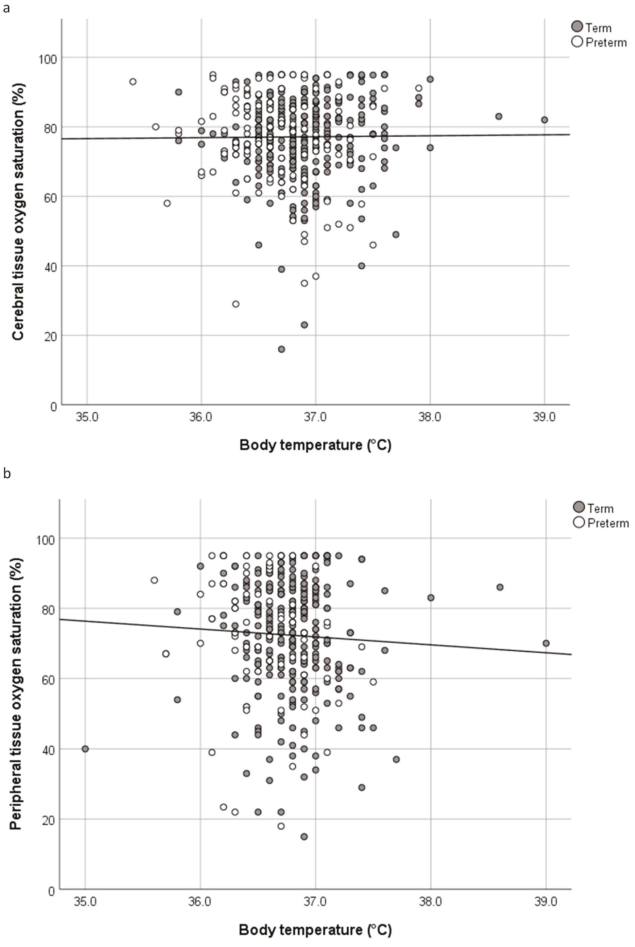

Figure 1. (**a**) Scatter plot of cerebral tissue oxygen saturation (%) and body temperature (°C) in term and preterm neonates. (**b**) Scatter plot of peripheral tissue oxygen saturation (%) and body temperature (°C) in term and preterm neonates.

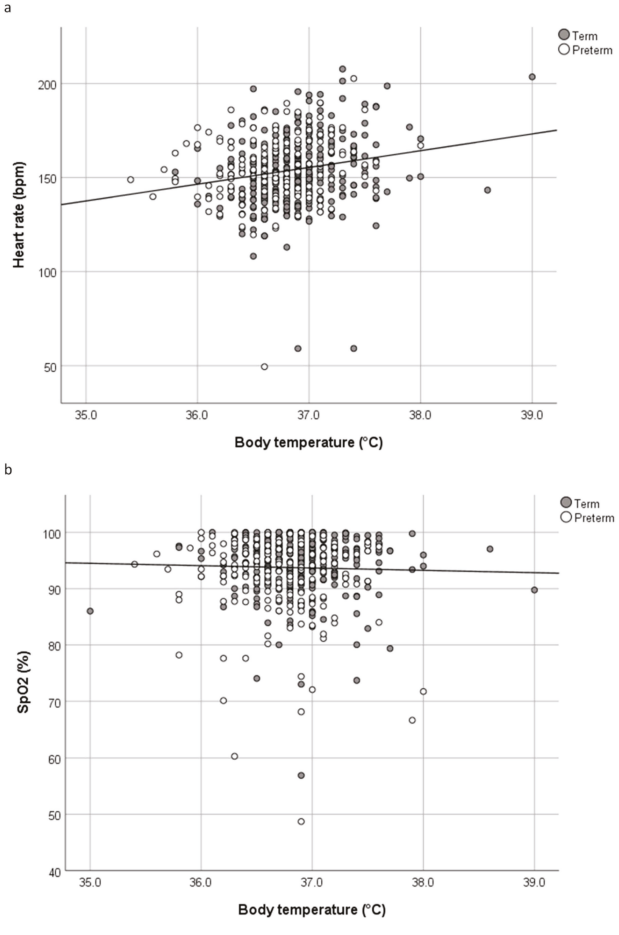

Figure 2. (**a**) Scatter plot of heart rate in beats per minute (bpm) and body temperature (°C) in term and preterm neonates. (**b**) Scatter plot of arterial oxygen saturation (SpO_2)% and body temperature (°C) in term and preterm neonates.

Table 2. Correlation analyses of body temperature in degrees Celsius (°C) and cerebral tissue oxygen saturation ($crSO_2$/cTOI), peripheral tissue oxygen saturation ($prSO_2$), peripheral fractional tissue oxygen extraction (pFTOE), heart rate in beats per minute (bpm), and arterial oxygen saturation (SpO_2).

	Total Cohort (n = 586)		**Term (n = 417)**		**Preterm (n = 169)**	
	Body Temperature (°C)	***p*-Value**	**Body Temperature (°C)**	***p*-Value**	**Body Temperature (°C)**	***p*-Value**
$crSO_2$/cTOI (%)	$\varrho = 0.018$	0.701	$\varrho = 0.077$	0.155	$\varrho = -0.102$	0.275
$prSO_2$ (%)	$\varrho = -0.092$	0.084	$\varrho = -0.044$	0.461	$\varrho = -0.285$	0.020
pFTOE	$\varrho = 0.042$	0.443	$\varrho = 0.011$	0.852	$\varrho = 0.165$	0.195
Heart rate (bpm)	$\varrho = 0.210$	<0.001	$\varrho = 0.236$	<0.001	$\varrho = 0.222$	<0.006
SpO_2 (%)	$\varrho = -0.015$	0.741	$\varrho = -0.013$	0.805	$\varrho = -0.125$	0.111

3.3. Body Temperature

The body temperature was statistically lower in preterm neonates compared to term neonates (median [IQR] 36.7 [36.4–37.0] °C vs. 36.8 [36.6–37.0] °C, $p = 0.001$). EPI had the highest body temperature (median [IQR] 37.0 [36.9–37.4] °C) and VPI (median [IQR] 36.7 [36.3–37.0] °C, $p = 0.039$) and LPI (median [IQR] 36.7 [36.4–37.0] °C, $p = 0.017$) had the lowest mean body temperature compared to the other groups 15 min after birth (Figure 3). There were significant differences in body temperature between LPI and term born infants (median [IQR] 36.7 [36.4–37.0] °C vs. 36.8 [36.6–37.0] °C, $p = 0.004$). There were no differences between LPI and VPI ($p = 1.000$), between VPI and term born infants ($p = 0.279$), as well as between EPI and term born infants ($p = 0.293$). In general, the prevalence of hypothermia was significantly higher in preterm neonates compared to term neonates (29.5% vs. 12.0%, $p < 0.001$). The prevalence of normothermic, hypothermic, and hyperthermic neonates within the groups and sub-groups is presented in detail in Table 3. None of the included neonates suffered from severe hypothermia. Four infants (0.7%) had a body temperature of >38.0 °C.

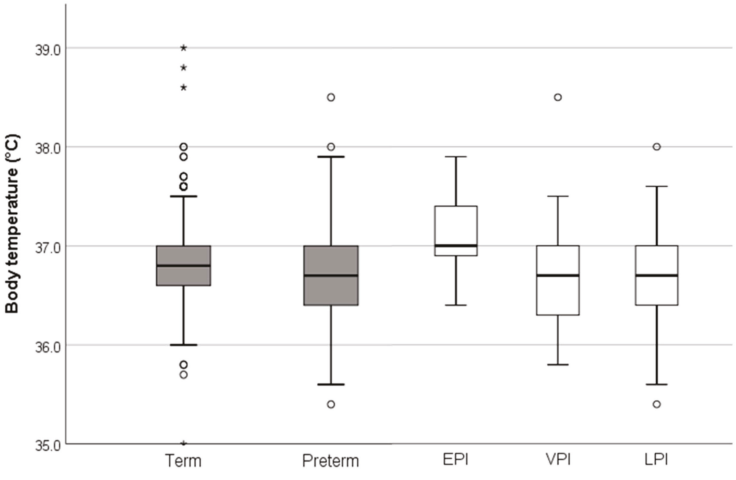

Figure 3. Boxplot (box: median, 1st and 3rd quartile; whisker: lower and upper extreme within 1.5 times the inter-quartile range from the upper or lower quartile; O: outliner >1.5 to <3 times the interquartile range from the upper or lower quartile, *: extreme outliner ≥3 times the interquartile range from the upper or lower quartile; highest and lowest extreme outliner demonstrate minimum and maximum range) of body temperature (°C) according to gestational age: term (≥37^{+0} weeks of gestation), preterm (<37^{+0} weeks of gestation) and subgroups EPI (extremely preterm infants ≤28^{+0} weeks of gestation), VPI (very preterm infants >28^{+0} and <32^{+0} weeks of gestation), and LPI (late preterm infants ≥32^{+0} and <37^{+0} weeks of gestation).

Table 3. Prevalence of normothermia (36.5–37.5 °C), mild hypothermia (36.0–36.4 °C), moderate hypothermia (32.0–35.9 °C), and hyperthermia (>37.5 °C) in the study sample (term [≥37^{+0} weeks of gestation], preterm [<37^{+0} weeks of gestation], and subgroups EPI [extremely preterm infants ≤28^{+0} weeks of gestation], VPI [very preterm infants >28^{+0} and <32^{+0} weeks of gestation], and LPI [late preterm infants ≥32^{+0} and <37^{+0} weeks of gestation]). Data are expressed in *n* (%).

	Total (*n* = 586)	**Term (*n* = 417)**	**Preterm (*n* = 169)**	**EPI (*n* = 10)**	**VPI (*n* = 38)**	**LPI (*n* = 121)**
Normothermia	461 (78.7)	347 (83.2)	114 (67.5)	7 (70.0)	23 (60.5)	84 (69.4)
Mild hypothermia	89 (15.2)	46 (11.0)	43 (25.4)	1 (10.0)	11 (29.0)	31 (25.6)
Moderate hypothermia	11 (1.9)	4 (1.0)	7 (4.1)	0 (0.0)	3 (7.9)	4 (3.3)
Hyperthermia	25 (4.3)	20 (4.8)	5 (3.0)	2 (20.0)	1 (2.6)	2 (1.7)

3.4. Respiratory Support

There was no difference in body temperature of the neonates who received respiratory support compared to those without need for respiratory support (mean 36.8 ± 0.4 °C vs. 36.8 ± 0.4 °C; $p = 0.067$). Among the term neonates, seventy-three (17.5%) needed respiratory support (CPAP and/or PPV). We found no significant difference in the body temperature of term neonates when comparing those with and those without the need for respiratory support (mean 36.8 ± 0.3 °C vs. 36.9 ± 0.4 °C, $p = 0.544$). One-hundred twenty-one preterm neonates (71.6%) required respiratory support, with no significant difference in body temperature between those who received respiratory support and those who did not (mean 36.7 ± 0.5 °C vs. 36.7 ± 0.4 °C, $p = 0.764$).

3.5. Short-Term Outcome

Of the 586 included neonates, 26 (4.4%) suffered from proven early or late bacterial infection/sepsis and one neonate (0.2%) suffered from NEC. Thirteen neonates (2.2%) were diagnosed with IVH grade one and two neonates (0.3%) with IVH grade three. Five neonates (0.9%) developed PVL. Three patients (0.5%) died during the neonatal period. There was no difference in body temperature between neonates with one of the abovementioned adverse outcomes neither when testing for the combined endpoint ($p = 0.238$) nor for individual testing.

4. Discussion

In the present study, we described the association between body temperature and regional tissue oxygenation, HR, and SpO_2 of term and preterm neonates born by Caesarean Section 15 min after birth. The main findings can be summarized as follows: (i) no association between body temperature and cerebral tissue oxygenation in term and preterm infants, (ii) no association between body temperature and peripheral tissue oxygenation in term infants, (iii) a weak negative correlation between body temperature and peripheral tissue oxygenation in preterm infants, (iv) a weak positive correlation between body temperature and HR in term and preterm infants, and (v) no association between body temperature and SpO_2 in term and preterm infants.

The absent association between body temperature and cerebral tissue oxygenation may be explained by the neonatal brain's autoregulation ability and by the only mild deviation of body temperature in our cohort. This assumption is supported by a recently published porcine model study, investigating the changes of cerebral autoregulation during induction of deep hypothermia [15]. A rapid induction of deep hypothermia was performed to simulate the clinical scenario of accidental hypothermia. It was demonstrated that the analyzed autoregulation indices (pressure reactivity index, oxygen reactivity index, brain tissue oxygen tension, and the cerebral oximetry index) reflected normal cerebral autoregulation and did not change until a brain temperature of 34 °C. Cerebral tissue oxygen saturation increased not before a brain temperature of 29 °C [15]. However, cerebrovascular autoregulation varies between term and preterm neonates. Pressure reactivity and autoregulation to systolic and MABP are not observed until 26 to 28 weeks of gestation due to the on-going vascular development and anatomical features of the premature cerebral vasculature [16]. The very small number of EPI in our cohort may explain the absent association between body temperature and cerebral tissue oxygen saturation.

We found a weak, but significantly negative correlation between peripheral tissue oxygen saturation and central body temperature only in preterm neonates. However, as cardiac function, blood gases (e.g., carbon dioxide), hemoglobin levels, and especially peripheral temperature all influence peripheral blood flow, tissue oxygenation, and oxygen extraction, interpretation of this finding is challenging [17]. The weak negative correlation may be explained by the fact that hyperthermia causes a higher metabolic rate, resulting in higher tissue oxygen extraction and a consequent decrease in peripheral tissue oxygen saturation. Furthermore, microvascular perfusion in preterm infants may be more affected by temperature variations than peripheral perfusion in term neonates, due to their

higher body surface to weight ratio, higher heat loss by evaporation due to skin immaturity, deficiency of subcutaneous adipose tissue, and limited ability to regulate cutaneous blood flow [18,19].

Physiologically, the HR of neonates should decrease when suffering from hypothermia, at least initially [20]. Thereafter, norepinephrine gets released and the HR increases [20]. This matches our finding of a significantly positive correlation between body temperature and HR for the whole cohort as well as in preterm and term neonates individually. This was also observed in other studies [2,21], whereby Davies et al. reported the increase in HR per added degree of temperature is approximately 10 bpm based on observations in 31851 children, attending the pediatric emergency department [21]. On the other hand, we did not find a correlation between body temperature and SpO_2, which was independent from gestational age. Literature about the association between body temperature and SpO_2 in neonates is scarce. Mitra et al. demonstrated that SpO_2 dropped briefly at the start of induced therapeutic hypothermia in neonates, but it was mostly above 95% [22]. When the body temperature was raised to 37 °C, SpO_2 remained stable [22], suggesting no clinically relevant association between body temperature and SpO_2. This was confirmed in a recent study by Wu et al., where SpO_2 remained stable during the rewarming phase after induced hypothermia in neonates with hypoxic-ischemic encephalopathy [23].

Regarding our secondary aim, we observed statistically lower body temperature in preterm neonates; however, the difference was small (mean of 0.1 °C) and we expect that its clinical relevance is negligible. Nevertheless, preterm neonates suffered from hypothermia significantly more often compared to term neonates. There are only limited data about hypothermia in term neonates. We reported hypothermia only in 12% of term born infants, whereas Takayama et al. observed that 17% of the included healthy term born infants suffered from hypothermia 34 min after birth [6]. In contrast to term born infants, several studies have investigated body temperature in large cohorts of preterm infants. The incidence of hypothermia in preterm neonates ranged between 38–53% [9,24,25], and in EPI the incidence of hypothermia below 35.0 °C was found in a worrying 9.6% [25]. In contrast, Lyu et al. reported that only 12% of the investigated preterm infants had an admission temperature of below 36.0 °C, and only 2% had an admission temperature lower than 35.0 °C [3]. This suggests that temperature management varies between institutions and may have a profound impact on postnatal body temperature.

We observed a distinctly lower rate of hypothermia in our cohort compared to the results of the abovementioned studies, as a body temperature of below 36.0 °C was only found in 4.1% of preterm infants. The highest rate of hypothermia occurred in VPI (7.9%), but even this rate is considerably lower than in other studies. Interestingly, none of the EPI had a body temperature of below 36.0 °C. We speculate that attention to body temperature management was paid mostly to EPI and to a lesser extent to more mature preterm neonates. Only Lyu et al. published an incidence of hypothermia in preterm infants similar to our results, but it has to be acknowledged that their hypothermia thresholds were lower than ours [3]. The number of included infants, the earlier body temperature measurement, and the fact that this is a mono-centric study may explain the differences between our results and those of other studies. In the present study, all included infants were born by Caesarean section. The birth mode may have an impact on vascular reactivity, peripheral oxygenation, and thermal homeostatic mechanism. Additionally, vaginally delivered newborns often benefit from postnatal skin-to-skin contact, whereas infants born by Caesarean section are regularly placed on a resuscitation table after birth, resulting in a different body temperature management. Additionally, in all included infants, early cord clamping (<30 s) was performed. Timing of umbilical cord clamping has an impact on neonatal hemodynamics and may affect both body temperature and cerebral tissue oxygenation. Whereas studies reported no differences in cerebral tissue oxygenation six to 12 h after birth when comparing immediate and delayed cord clamping [26], Pichler et al. demonstrated that delayed cord clamping caused lower initial cerebral tissue oxygen saturation in spontaneously breathing preterm neonates compared to preterm neonates without immediate cord clamping [27,28]. Furthermore,

we observed a high rate of normothermic infants and, therefore, temperature differences may have been more pronounced in other studies.

Several studies demonstrated that the number of preterm infants suffering from hypothermia could be decreased (without increasing hyperthermia rates) by using a practice plan including consistent head and torso wrapping, warmed blankets, a transwarmer mattress, and maintaining a consistent operating room temperature (between 21 °C and 23 °C) [29,30]. In consideration of our observations, we assume that our standardized postnatal temperature management concept seems to be beneficial for body temperature preservation in preterm infants.

Besides hypothermia, also iatrogenic hyperthermia is a complication with detrimental neonatal outcomes [3]. Overheating can be caused by the use of plastic wraps, radiant warmers, incubators, or excessive environment heating [10,31]. Studies described hyperthermia incidences in preterm infants at admission between 1–2% [3,7,25]. In comparison to these studies, the prevalence of hyperthermia was higher in our study, yet the difference was small. According to the WHO, we defined hyperthermia as a body temperature of above 37.5 °C, which is in contrast to the abovementioned studies, defining hyperthermia mostly ≥38.0 °C. This different definition may explain the higher rate of hyperthermia in our cohort. Nevertheless, it has to be considered that two of the included ten EPI suffered from hyperthermia. This may have been caused by the use of polyethylene bags [32,33]. However, Lenclen et al. demonstrated that a higher admission body temperature may be achieved in preterm neonates without increasing the risk for hyperthermia by using polyethylene bags [34]. Additionally, maternal fever and/or infections such as chorioamnionitis may have contributed to the rate of neonatal hyperthermia, but these data were not available in our database. Nonetheless, it should be kept in mind that excluding neonates from mothers with signs of infection would have increased the incidence of neonates suffering from hypothermia.

The use of heated humidified gases for respiratory support to avoid hypothermia in newborn infants is an important concept. A recent meta-analysis investigating heated humidified gases for respiratory support in preterm neonates during resuscitation could only include two studies [35]. Still, the authors concluded that heating and humidification of inspired gases immediately after birth improves admission temperature in preterm infants [35]. In the present study, we did not find any differences between newborn infants without respiratory support and those who received respiratory support using non-heated unconditioned gases. This raises the question whether the use of heated humidified gases offers a substantial advantage during immediate postnatal stabilization and resuscitation in a cohort of newborn infants in whom the hypothermia rate was generally low.

Limitations and Strengths

There are some limitations associated with this study. Firstly, this is a single center study. Secondly, we performed only one body temperature measurement in each patient and therefore have no data about the course of body temperature. Thirdly, we only recorded the need for respiratory support, but data about the fraction of inspired oxygen were not available in our data base. All infants were born by Caesarean section, which should be considered when interpreting the results. The small number of both extremely premature neonates and of adverse clinical outcomes may have contributed towards some expected or apparent associations having reached no statistical significance. Finally, a bias might be that all of the included neonates participated in clinical studies and as a result more attention may have been paid to body temperature management and preservation.

This is the first study investigating the relationship between cerebral and peripheral tissue oxygen saturation and central body temperature in neonates 15 min after birth, thus adding important novel data to the field. Further strengths of the study are the direct comparison between term and preterm neonates, the sub-group analysis of the preterm neonates, and the consistent use of rectally measured, i.e., central, body temperature. Several studies have shown that axillary body temperature measurements tend to be lower than those gained rectally [5,36,37] and that the rectal body temperature is a more accurate measure of body core temperature [1].

5. Conclusions

Body temperature neither correlated with $crSO_2$/cTOI nor with SpO_2 and this finding was independent from gestational age. We found a weak negative correlation between $prSO_2$ and body temperature in preterm neonates and a weak positive correlation between HR and body temperature in the whole cohort, as expected. Body temperature during immediate postnatal transition was statistically lower in preterm neonates compared to term neonates, but the difference was small and probably clinically irrelevant. Nevertheless, hypothermia was significantly more often observed in preterm neonates than in to term neonates. Preterm infants $>28^{+0}$ and $<32^{+0}$ weeks of gestation had the highest prevalence of hypothermia, whereas hyperthermia was most frequent in preterm infants born below 28^{+0} weeks of gestation. Therefore, attention to stringent body temperature management should be paid not only to extremely preterm neonates but also to very and late preterm infants.

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children

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Article

Non-Contact Video-Based Neonatal Respiratory Monitoring

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Abstract: Respiratory rate (RR) has been shown to be a reliable predictor of cardio-pulmonary deterioration, but standard RR monitoring methods in the neonatal intensive care units (NICU) with contact leads have been related to iatrogenic complications. Video-based monitoring is a potential non-contact system that could improve patient care. This iterative design study developed a novel algorithm that produced RR from footage analyzed from stable NICU patients in open cribs with corrected gestational ages ranging from 33 to 40 weeks. The final algorithm used a proprietary technique of micromotion and stationarity detection (MSD) to model background noise to be able to amplify and record respiratory motions. We found significant correlation—r equals 0.948 (p value of 0.001)—between MSD and the current hospital standard, electrocardiogram impedance pneumography. Our video-based system showed a bias of negative 1.3 breaths and root mean square error of 6.36 breaths per minute compared to standard continuous monitoring. Further work is needed to evaluate the ability of video-based monitors to observe clinical changes in a larger population of patients over extended periods of time.

Keywords: neonatal monitoring; respiratory rate; clinical alarms; video recording; biomedical technology

1. Introduction

The drive and control of breaths is an intricate system involving the circulatory, pulmonary, and central nervous systems. Chemoreceptors throughout the body monitor for hypoxia and hypercarbia, altering respiratory rate (RR) to maintain organ perfusion and optimal pH. Evidence has shown RR to be a better predictor of cardio-pulmonary deterioration than blood pressure and pulse rate [1]. In the neonatal population, ventilation and appropriate pulmonary support is critical. Effective ventilation is the key objective in neonatal resuscitation, and RR is included in all early warning systems for neonatal sepsis and necrotizing enterocolitis [2,3].

Traditionally, the gold standard for measuring RR is counting breaths for a minute while auscultating the patient or palpating for chest rise. While this is the most accurate, it is time consuming and not practical for an intensive care unit where continuous vital signs monitoring is required. Since the late 1800s, multiple innovations have been developed to automate measurements of respiration [4]. Early inventions measured breaths by airflow into a device, spirometry, or by attaching a circumferential strap around the chest, respiratory inductance plethysmography (RIP). Spirometry, however, is designed to measure lung volumes, and RIP is currently used in neonates to detect airway obstruction and for sleep apnea monitoring as it accurately records respiratory waveforms over time [5]. While RIP does measure RR, it requires bulky chest straps and interpretation from a pulmonologist or somnologist.

Similar to RIP, impedance pneumography (IMP) measures changes in electrical signal secondary to the movements of the chest and diaphragm and has been widely adapted to multiple clinical settings. IMP uses mathematical algorithms to convert other electronic signals such as pulse oximeters and electrocardiograms (ECGs) to a respiratory wave form and RR, while RIP is derived directly from the attached straps. IMP can be integrated into standard continuous monitoring systems used by most hospitals [6]. While any manipulation of data or signal can introduce error, studies have shown strong correlation between RR gathered from RIP and IMP [6,7].

Nevertheless, there are several limitations of IMP. Information has to be gathered from electronic leads attached directly to the skin, and the signal needs to be amplified to be measured, making it susceptible to artifacts or noise. Artifacts and signal noise can originate from inadequate attachment of the electronic leads as well as any movement of the patient not related to breathing. In the neonatal population, these limitations are particularly apparent and produce several unique adverse outcomes. The frequency of false alarms secondary to the frequent movement of newborns is associated with provider alarm fatigue, infant hearing loss, and a disruptive environment for development [8–12]. Additionally, the humid environment of neonatal incubators and the infant's thin, underdeveloped skin cause the adhesive in electric leads to fail and require frequent changing. The recurrent application of adhesive to the fragile premature skin causes breakdown and inflammation of their dermal barrier, introducing possible sources for infection [11].

Several innovations have been developed for non-contact monitoring in neonatology to minimize risk of dermal injury and alarm fatigue in infants. A variety of techniques have been studied from radio wave signaling, ultrasound, imaging photoplethysmography (PPG), and video-based respiratory monitors. In controlled environments, they have been shown to correlate with ECG monitoring with correlation coefficients from 0.79 to 0.92 [13–16]. Video-based respiratory monitors are particularly versatile due to the accessibility of cameras. These systems could be easily integrated into current monitoring systems and potentially used in clinics and at home for virtual medical appointments. However, due to the subtle motion of neonatal respiration, these technologies have struggled to accurately determine RR as the amplification of movement also increases signal noise, making it difficult to obtain an accurate measurement.

We conducted a course of study focused on a video-based respiratory monitoring system that extracts a respiratory waveform and rate without augmenting the infant's surrounding or attire. Unlike past studies, this system extracts data on fully clothed or swaddled infants in a neonatal intensive care unit (NICU) with a variety of lighting and camera orientations. Through an iterative approach, we demonstrate a proprietary technique that is able to compensate for background signal noise while amplifying and measuring RR.

2. Materials and Methods

This study was performed at a single center, Lucile Packard Children's Hospital at Stanford University. Patients in the neonatal intensive care unit (NICU) and step-down intermediate care nursery were enrolled in this study. Institutional Review Board (IRB) approval was obtained through the Stanford University Institutional Review Board. All monitoring was performed with written informed consent from parents and guardians in the NICU. Patients who were in an open crib, without significant complications, and not already enrolled in another study were eligible to enroll. Convenience sampling was used, with subjects recruited based on attending physician referral of eligible patients. Infants with concern for active infection, need for supplemental oxygen therapy, or vasopressors were excluded. To ensure patient safety, routine medical care and protective measures were not altered during monitoring sessions. Data being obtained from the study were not made available to clinicians during the course of their care for patients.

2.1. Study Design and Measurements

This manuscript describes an iterative design process. The objectives of the design were to identify and measure the respiratory rate of a preterm infant within an open crib through the analysis of camera footage and comparison to current hospital monitoring standards. The iterative process involved sequential algorithm design and application on recorded data. The principle analysis of the study investigated the consistent ability to identify patients within the frame and ability to extract the subjects' respiratory rate. The secondary analysis compares respiratory rate from our non-contact monitoring to that recorded into the electronic medical record (EMR) by the current hospital standard of respiratory monitoring by ECG impedance pneumography. Any design that could not identify the patient, extract an RR for a majority of subjects, or did not correlate with the current standard was determined to be unsatisfactory, and the study would return to the previous design phase.

Data were collected at the bedside as continuous 48-h video recordings from each infant. Footage was recorded on off-the-shelf IP cameras from Wansview with 320X180 resolution at ten frames per second and provided raw frames in YUV format. Cameras were placed approximately 4–6 feet from the bassinet (Figure 1). Simultaneously, vital sign data were collected for usual patient care from the ECG contact-based sensors and were extracted through the hospital's Research Data Export system. No changes were made to the patient's care while enrolled in this study.

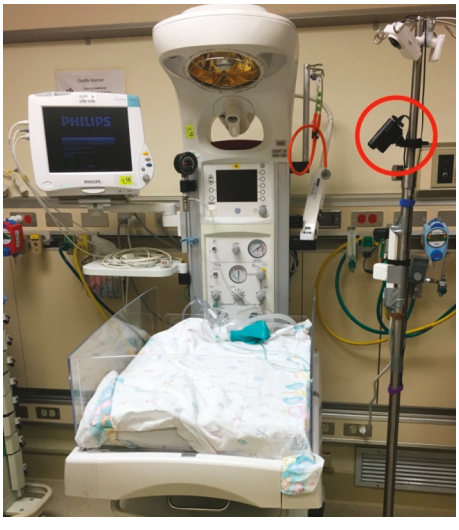


Figure 1. Study setup. Red circle shows camera set up above an open neonatal intensive care units (NICU) crib. The hospital-standard monitor can be seen on the opposite side of the crib as the camera.

2.2. Analysis

In the initial analysis, algorithms were assessed for consistent ability to identify the location of the patient in the crib, whether the patient was breathing, and finally if the monitoring could track respiration long enough to generate a respiratory rate.

Analysis was based on the assumptions that the camera or crib did not move or sway and that the only moving element in the frame was the patient (i.e., no mobiles, moving toys or moving devices were in the frame of the recording).

In the secondary analysis, RR measured by the algorithm was compared to that extracted from standard monitoring data at the same moment in time. Agreement between the two modes of measurements was analyzed using a Bland–Altman plot. The extent and significance of correlation between the algorithm and standard monitoring were performed via linear regression. Finally,

assuming complete accuracy of the ECG impedance pneumography measurement of respiratory rate, errors of algorithm measurements were determined by calculating the root mean square error.

3. Results

3.1. Subject Demographics

Eighteen subjects were enrolled and recorded in the study for the period of 2016–2017; one was excluded from final analysis due to conflicting documentation. At the time of recording, all infants were under the chronologic age of 10 weeks and had corrected gestational ages of 33–40 weeks. The mean age of patients at time of recording was 5 weeks and 35.5 weeks adjusted. The mean gestational age at birth was 30 weeks and 3 days. The population was 65% male and included a variety of racial backgrounds, with the largest group being White at 35%. Race was defined per electronic medical record with Asian including individuals of Indian and Southeast Asian descent. All subjects had various comorbidities of prematurity, with the prevalence of the most pertinent—apnea of prematurity, history of respiratory distress syndrome, chronic lung disease, and anemia of prematurity—demonstrated in Table 1.

Table 1. Demographics of enrolled subjects.

	Number	**Proportion**
Sex		
Male	11	0.65
Female	6	0.35
Race		
White	6	0.35
Hispanic/Latino	4	0.24
Asian	2	0.12
Native Hawaiian or Other Pacific Islander	2	0.12
Other	3	0.18
Medical Issues		
Apnea of Prematurity	13	0.76
History of Respiratory Distress Syndrome	11	0.65
Chronic Lung Disease	4	0.24
Anemia of Prematurity	15	0.88
	Mean	**SD** [1]
Age at Recording (weeks)	5.3	3.1
Corrected GA [2] at Recording (weeks)	35.5	1.9
Birth GA [2] (weeks)	30.5	2.5
Height at Birth (cm)	40.4	3.8
Weight at Birth (kg)	1.4	0.4

[1] Standard Deviation (SD); [2] Gestational Age (GA).

3.2. Interval Processing

The design process went through three cycles creating and testing three different algorithms: Eulerian video magnification followed by motion extraction, principal flow field, micromotion and stationarity detection. The final algorithm, micromotion and stationarity detection, achieved the design goals of consistently providing an RR for the subject and went on to the secondary analysis, comparing it to the continuous vital signs recorded into the subject's EMR.

3.2.1. Eulerian Video Magnification Followed by Motion Extraction

The initial technique for extracting RR from footage was an Eulerian video magnification (EVM) algorithm to amplify movement, followed by a motion history image (MHI) algorithm to extract the motion.

EVM amplification has been described in other fields [17]. Our algorithm decomposes the video into pyramids of Laplacian images of different spatial frequencies to allow for greater accuracy and large

amplification of minute motion. Laplacian pyramids are commonly used in motion magnification [18]. After pyramids were made, a low pass filter was performed and pixel intensity was increased based on each pyramid level. The amplified reconstructed frame was then superimposed on the original frame.

The MHI algorithm then generated the motion between frames by referencing successive binary silhouette images of the baby. The motion gradient between frames was used to calculate the amplitude for the inspiration/expiration signal of the baby's breath and generate a continuous respiratory waveform. The respiratory rate could then be calculated from the waveform. The process of quantifying motion in a MHI is a unique process and has not been studied to our knowledge.

The benefits of the EVM and MHI approach was its ability to magnify small motions, with minimal processing and few artifacts. The critical deficits were the high rates of false positive signals. This was primarily from amplification of noise generated by changes in lighting and infant movement.

3.2.2. Principal Flow Field

Principal flow field (PFF) methodology was used in hopes of decreasing the impact of noise and increasing processing speed. Flow fields are a common way to evaluate movement in engineering. To optimize processing speed, our PFFs were performed on segments instead of full frames. This was accomplished by calculating optical flow fields by generating pixel movement gradients between frames. Knowing that inhalation and exhalation would be in the opposite direction allowed us to form flow field matrices localized to pixels representing respiration rather than noise.

PFFs were computed using the flow field matrices on the initial frame and adapted for each sequential frame. The PFF was used to generate a continuous respiration signal, which again was used to generate RR.

The benefit of PFF was its localized respiratory movements which decreased processing times while picking up similarly minute movements as the EVM algorithm. However, this algorithm was limited due to recurrent false positive readings with no infant present in the crib. This was due to the optical flow fields picking up the best plausible signal that represented respiratory movement even if this motion was actually noise from video capture, video compression, movement artifacts, or lighting changing. As there is always some level of noise, this algorithm would generate respiratory signals and rates even if a baby was not breathing or even if not present in the frame.

3.2.3. Micromotion and Stationarity Detection (MSD)

The final algorithm utilized micromotion and stationarity detection (MSD) and has not previously been studied for this application. To overcome the challenge of finding respiratory motion at a frame-to-frame level without incidentally measuring noise, the MSD analyzed and modeled the noise instead of trying to eliminate it.

In order to model noise characteristics, the image was divided into small sub-regions where changes in pixel intensity were measured over time. The model of the noise consisted of standard deviation (SD) measures of the changes in pixel intensity.

Assuming that the SD of the change in pixel intensity over a series of frames, with no motion and only noise, would remain relatively small and equal from frame to frame, then a large change in the SD of pixel intensity would indicate a micro movement. This is how imperceptible movements of chest rise and fall could be located and measured.

Pixel intensities, or breathing motions, were calculated by taking SD measures of the SD measures. This generated heat maps that represented motion (Figure 2). To determine an RR, the number of peaks were counted and averaged over 100 frames of SD measured values.

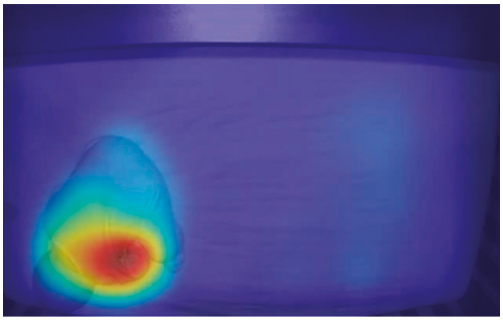


Figure 2. Heat map derived from standard deviation (SD) measures of SD measures showing motion due to breathing. The red region represents high SD measures and the blue region represents low SD measures. The red region was concentrated near the baby's chest, indicating that the measurement showed motion associated with breathing.

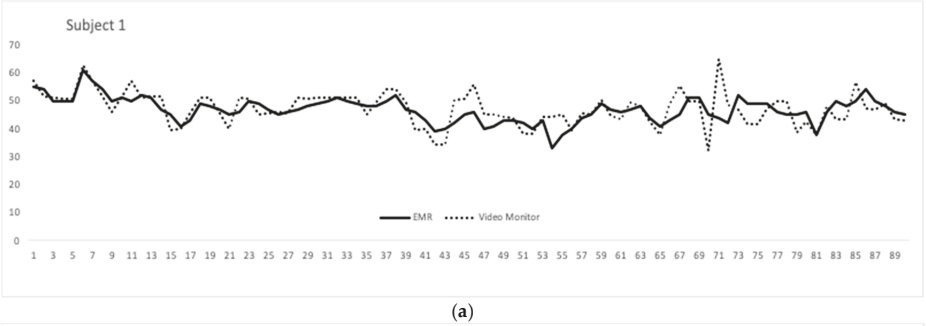
A significant benefit of the MSD is its insusceptibility to noise and capability to detect whether or not an infant is in the frame and if that infant has had an apneic event, defined as a pause in breathing for greater than 20 s. The MSD algorithm had difficulty with measuring RR while the patient had gross or macro movements, such as movement of arms, leg, or torso with crying or shifting while sleeping. After such movements, the algorithm needs to recalibrate over 100 frames, or 10 s at 10 frames per second, to ensure it has located the subject and is measuring the correct signal. ECG impedance pneumography also cannot extract RR with large patient movements, but recovers more quickly after only a couple of seconds.

3.3. Respiratory Rate Correlation between ECG and MSD Video-Based Monitoring

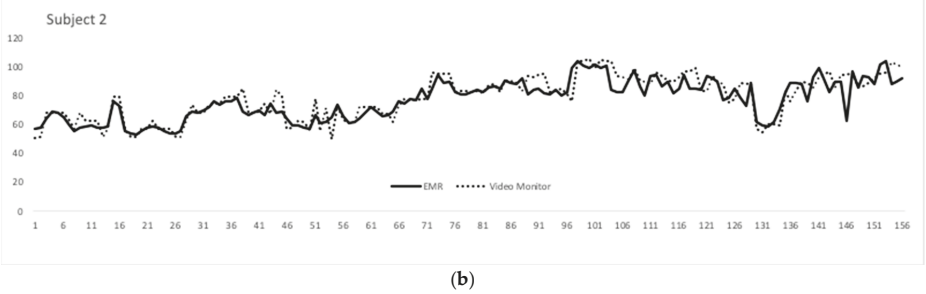
The secondary analysis was completed by running the MSD analysis on two patients. Their 48 h of video recording was scanned for continuous time frames where the patient remained asleep, relatively still, and unobstructed by staff or parents providing care. The combined continuous uninterrupted video consisted of 21 min and 50 s and contained 246 time points.

The MSD algorithm takes 10 s to calibrate, as described above, and then populates an RR every 5 s. The EMR produced a time point every 1 s as long as there was no interruption in the signal. To assure the two data sets represented the same points in time, the RR of 10 sequential timestamps from the video algorithm were assessed against the same time stamp from the EMR, and if there was a large discrepancy, then that series would be considered inaccurate and would not be included in the final data set. After confirmation that the time stamps matched up, respiratory rates from the MSD algorithm were compared to the RR from the EMR at the same corresponding time stamp until there was another interruption in either signal that prevented the two RRs from being generated at the same time. This assessment would then repeat to find the next usable segment of data.

The average RR over the approximately 22 min was 65 breaths per minute (BPM) in the EMR data and 67 in the video monitor group. The standard deviations were 18.4 and 19.7, respectively. Both patients recorded were male and Caucasian. Their mean gestation age at birth was 29 weeks and 5 days. Their mean adjusted age at recording was 36 weeks and 2 days. Overlying tracings between the EMR and video monitor over the recording time (in seconds) for both subjects are shown in Figure 3.



(**a**)



(**b**)

Figure 3. (**a**) Respiratory rate (RR) (y-axis) from the video monitoring system compared to that of the extracted Electronic medical record (EMR) data over a 8.4 min recording made up of 90 time points (x-axis); (**b**) RR (y-axis) from the video monitoring system compared to that of the extracted EMR data over a 13.4 min recording made up of 155 time points (x-axis)

Comparison between the EMR and MSD respiratory rate via the Bland–Alterman method showed that the video monitoring system had a bias of 1.3 less breaths per minute, and 94.3% of all time point comparisons were between the upper and lower limits of agreement (Figure 4).

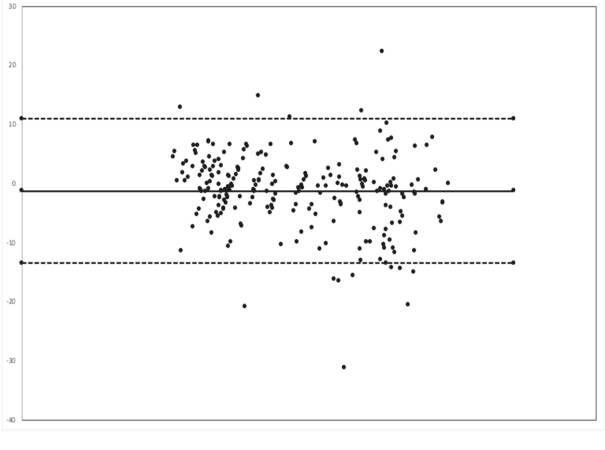


Figure 4. Bland–Altman plot. The central dark line represents a bias of −1.3 breaths per minute (BPM). The dashed lines represent the upper limit of agreement (10.9 BPM) and lower limit of agreement (−13.5 BPM).

A linear regression between the EMR data and those of the camera-based non-contact monitor showed a correlation coefficient or multiple R of 0.948, with a p value of 0.001. The regression showed an R squared of 90%. Assuming that the EMR data were representative of the true respiration rate, the error of the video-based monitoring system was calculated as 6.36 breaths per minute via a root mean square analysis (Figure 5).

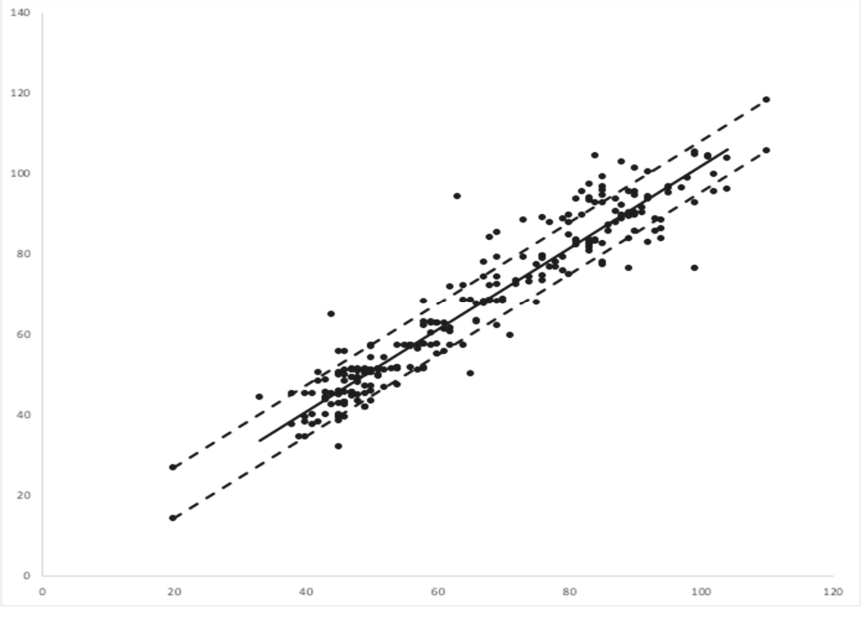


Figure 5. Linear regression comparing video-based monitoring respiration rate (RR) (y-axis) vs. electronic medical record (EMR)- RR (x-axis). The dashed lines represent upper and lower boundaries of root mean square error between the modes of measurement.

3.4. Limitations

The main limitation of this study is the relatively small sample size, short recording time, and lack of gold-standard comparison. While correlations are encouraging for the 246 time points recorded, the data were limited to a small population and short time period. As the patients in the secondary analysis were both Caucasian, the lack of diversity potentially limits the generalizability of the technology on a broader population level. This limitation may be mitigated by the technology's capacity to detect RR through varied infant attire and different color swaddles. Lastly, by selecting relatively stable infants for 48 h of monitoring, our study was not designed to assess whether video monitoring systems can track clinically significant trends in respiratory rate. As this monitor was not available for the clinical team, it could not be assessed whether it had more or less false alarms or missed apneic or tachypnea events.

4. Discussion

Video-based respiratory monitoring is at the earliest stages of development. However, our study shows the potential for MSD, making this technology equivalent to induction pneumography for at least a stable neonate in an open crib. While there are still a lot of qualifiers to its comparison, it is a major step toward a future without contact respiratory monitoring. Video-based monitoring could be integrated into incubator designs and attached to preexisting hospital cribs. With further validation, this technology could decrease the need for cardiac leads in more stable infants and be an

adjunct monitoring tool for critically ill patients as a means to possibly decrease false alarms from patient movement.

A next major step for video-based respiratory monitoring systems is to validate the technology in a large cohort study inclusive of a diverse population with varying skin tone, race, sex, age, and clinical stability. Once validated, conducting studies that allow providers to view RR in real time would demonstrate the ability of video-monitoring to screen for apneas and tachypnea in infants. To be trusted in clinical settings, this technology must be shown to be as sensitive as induction pneumography. While preliminary data from this study suggest that it is as sensitive and specific as ECG-based systems, a longer and larger study focused on comparing significant events between the two systems is needed. There may also be opportunities for this technology to reduce false positive alarms, a known issue for hospitalized patients, either by being a more accurate monitor or by providing negative feedback to current monitors.

As MSD amplifies and tracks movement by averaging background noise, it has an advantage over induction pneumography which often falls short because of increased noise with faster respiratory rates. A future study comparing video-based respiratory monitoring and ECG induction pneumography to the gold standard of counting breaths for a minute in clinically ill and tachypneic patients could potentially show superiority of video-based systems in monitoring RR.

With the majority of pediatric illnesses being respiratory-related and the accessibility of high-quality cameras, such as those present in most personal cell phones, a video-based monitoring system could also have a large impact on outpatient medicine. It is conceivable that this technology could allow healthcare providers to measure RR throughout a telehealth video visit. This would provide valuable information that would aid in the decision-making process of whether or not a patient needs to go to an emergency room or would be safe to be cared for at home. With the SARS-CoV-2 pandemic increasing demand and showing the value of telemedicine visits, this technology could be invaluable.

5. Conclusions

Video-based monitoring using an MSD algorithm is a promising method to measure RR in the neonatal population. This preliminary study shows the arc of development and potential equivalency to the current industry standard of ECG induction pneumography. Further work is needed to continue to evaluate the ability of video-based monitors to record clinically relevant apneic events and other sudden physiological changes in comparison with current monitoring standards.

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Conflicts of Interest: Authors Chandan Basavaraju and Pavan Kumar were members of a startup company designing a consumer baby monitor with the goal of utilizing the final design of this study. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Article

Randomized Longitudinal Study Comparing Three Nasal Respiratory Support Modes to Prevent Intermittent Hypoxia in Very Preterm Infants

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Abstract: Nasal continuous positive airway pressure (NCPAP) devices using variable (vf-) and continuous (cf-) flow or synchronized nasal intermittent positive pressure ventilation (s-NIPPV) are used to prevent or treat intermittent hypoxia (IH) in preterm infants. Results concerning which is most effective vary. We aimed to investigate the effect of s-NIPPV and vf-NCPAP compared to cf-NCPAP on the rate of IH episodes. Preterm infants with a gestational age of 24.9–29.7 weeks presenting with IH while being treated with cf-NCPAP were monitored for eight hours, then randomized to eight hours of treatment with vf-NCPAP or s-NIPPV. Data from 16 infants were analyzed. Due to an unexpectedly low sample size, the results were only reported descriptively. No relevant changes in the rate of IH events were detected between cf- vs. vf-NCPAP or between cf-NCPAP vs. s-NIPPV. Although limited by its small sample size, s-NIPPV, vf- and cf-NCPAP seemed to be similarly effective in the treatment of IH in these infants.

Keywords: very low birthweight infant; nasal respiratory support; s-NIPPV; NCPAP; intermittent hypoxia

1. Introduction

Nasal continuous positive airway pressure (NCPAP) is effective for treating apnea of prematurity (AOP) and preventing intermittent hypoxia (IH) [1]. It helps to keep the airways open [2] and improves oxygenation [3] as well as lung function [4]. NCPAP may also reduce the work of breathing, at least if applied via devices with variable gas flow (variable flow = vf-NCPAP) [5,6]. In addition to NCPAP, nasal intermittent positive pressure ventilation (NIPPV) is used to treat AOP or IH. In a meta-analysis, the latter was found to be more effective than NCPAP in preventing re-intubation, but only if synchronized with the infant's own breathing efforts (s-NIPPV) [7–9].

In an earlier study, we compared continuous flow (cf-) with vf-NCPAP and NIPPV concerning the rate of hypoxemic episodes and observed less such episodes with vf-NCPAP. NIPPV in that study, however, was not synchronized to the infants' own breathing efforts [10]. In the present study, we aimed to investigate the effect of s-NIPPV on the rate of IH episodes comparing cf-NCPAP with vf-NCPAP and s-NIPPV.

2. Materials and Methods

2.1. Patients

Between October 2014 and September 2019, infants admitted to the neonatal intensive care unit at Tuebingen University Children's Hospital site were evaluated for their eligibility to participate in this study. Inclusion criteria were (i) gestational age (GA) at birth ≤34 weeks (w), (ii) postmenstrual age at study ≤38 w, (iii) persistent AOP, and (iv) frequent apneas, expressed as an apnea score ≥5 on a rating scale used in the unit [11], despite treatment with hospital pharmacy-produced caffeine base and cf-NCPAP. The apnea score assigned points depending on the response of the nursing staff to events involving bradycardia (heart rate < 80/min) or hypoxemia (SpO_2 < 80%). If no intervention was needed, one point was given; two points if tactile stimulation was applied or a manual inspiration via the ventilator, and three points if the baby had to be turned over in preparation for bagging; eight points were given if the baby was felt to briefly need positive pressure ventilation to recover. The respective points were added up. Exclusion criteria were severe congenital malformations, neuromuscular conditions or chromosomal abnormalities, the presence of symptomatic apnea (e.g., due to sepsis, hypoglycemia or cerebral hemorrhage), or the lack of written informed parental consent.

2.2. Study Design

The study design included two different before–after studies involving one control and two test interventions (Figure 1). After having entered the study, infants continued on their standard cf-NCPAP device (Sophie, Fritz Stephan, Gackenbach, Germany; control intervention) to acquire at least eight hours of recording time. Only if they had reached a value of ≥10 on the above apnea score, they were randomized using sequentially numbered opaque concealed envelopes prepared by an assistant not involved in patient care to either vf-NCPAP (test intervention 1, Infant Flow Plus (Vyaire Medical Inc., Chicago, IL, USA) or s-NIPPV via a standard neonatal ventilator (test intervention 2, Sophie, Fritz Stephan). Starting with this initial eight hour run-in phase, infants had their heart rate and arterial oxygen saturation (measured by pulse oximetry; SpO_2) recorded on a standard infant monitor (Vitaguard VG 3100, GeTeMed, Teltow, Germany) in 3–4 s averaging mode; these recordings continued without delay after the infants had been switched to their respective study ventilator. Otherwise, the infants received their routine care, including treatment with a fixed dose of caffeine base (5 mg/kg/day). No infants received doxapram.

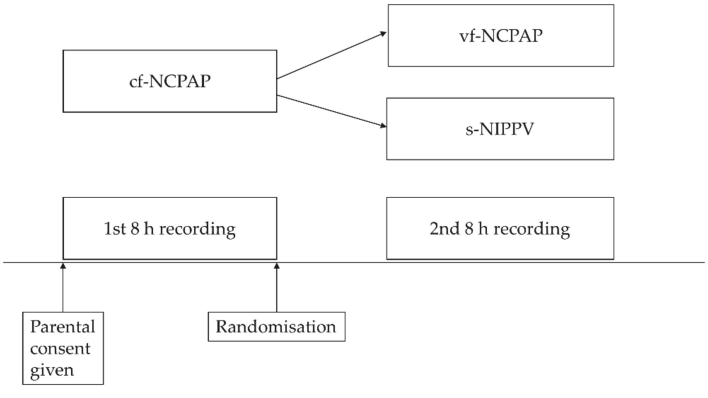

Figure 1. Study design; NCPAP: nasal continuous positive airway pressure; cf: continuous flow; vf: variable flow; s-NIPPV: synchronized nasal intermittent positive pressure ventilation.

2.3. Recordings of Physiological Signals

The above monitor stored the pulse rate and SpO_2, as well as the pulse waveforms, perfusion index and signal quality (Signal IQ®: Signal Identification and Quality, Masimo, Irvine, CA, USA) continuously. These recordings were analyzed using proprietary software (VitaWin®, version 3.3, GeTeMed, Teltow, Germany) after completing the study recruitment, thus not influencing any clinical decisions. Recordings were evaluated manually and periods with an artifactual signal, defined as a signal IQ <0.2, excluded [12]. IH was defined as a decrease in SpO_2 to <80% for >1 sec, bradycardia as a fall in heart rate to <80 beats per minute for more than one beat. The fraction of inspired oxygen (FiO2) and transcutaneous partial pressure of carbon dioxide ($tcpCO_2$) were recorded via the unit's patient data management system (PDMS; IntelliSpace, Philips, Eindhoven, Netherlands) that also included electronic documentation of the above apnea score as entered by the nursing staff. Average FiO_2 and $tcpCO_2$ were calculated as the mean of the values documented every 30 min by the PDMS.

2.4. Ventilators

While a standard neonatal ventilator (Sophie) was used to generate cf-NCPAP or s-NIPPV; vf-NCPAP was delivered using the Infant Flow Plus. The NCPAP level was set to 5 cmH_2O throughout. S-NIPPV was delivered at a rate of 20 breaths/min and a peak pressure of 15 cmH_2O. Synchronization with the infants' breathing efforts was achieved by an abdominal pneumatic trigger capsule (Respiration Sensor, Fritz Stephan, Gackenbach, Germany). Respiratory support was delivered via binasal prongs of appropriate size (EasyFlow, Fritz Stephan, Gackenbach, Germany, or Infant Flow LP, Vyaire Medical Inc., Chicago, IL, USA).

2.5. Statistical Analysis

The primary endpoint was the rate of IH events per hour. Secondary endpoints were the rate of bradycardia events per hour, mean FiO_2 and mean $tcpCO_2$. Based on our previous study [10], we estimated that 26 patients per before–after study were required to detect a paired group difference of 30%, i.e., a reduction by 0.85 IH events per hour. However, patient recruitment took much longer than expected, so that the study ultimately had to be terminated after 27 infants had been recruited over five years (see below). Thus, the results were reported descriptively stratified by before–after study (median, minimum, maximum) and the treatment effects were estimated based on the mean of the individual differences (paired samples) and its corresponding 95% confidence interval (95%CI). No statistical hypothesis testing and no comparisons between vf-NCPAP and s-NIPPV were performed on this smaller-than-expected sample size.

2.6. Ethics Approval and Consent to Participate

The study was approved by the ethics committee of the medical faculty at the study site (No. 433/2014BO1). Written parental consent was obtained upon patient recruitment. This study was registered with the German Clinical Trials register DRKS00005387.

2.7. Supplementary Materials

The study protocol, CONSORT checklist and CONSORT flow chart are available online as Supplementary Materials.

3. Results

Patient flow is shown in Figure 2, and patient demographics in Table 1. Regarding our primary endpoint, no clinically relevant changes in the rate of IH events were detected between cf- vs. vf-NCPAP or between cf-NCPAP vs. s-NIPPV (Table 2). The treatment effects (95%CI) were estimated to be 0.25 events per hour (−0.23–0.73; $n = 10$) for vf-NCPAP and −0.33 events per hour (−1.07 to 0.40; $n = 6$) for

s-NIPPV. Treatment failure on the allocated device did not occur, i.e., no infant had to be intubated during the study period for apnea or bradycardia.

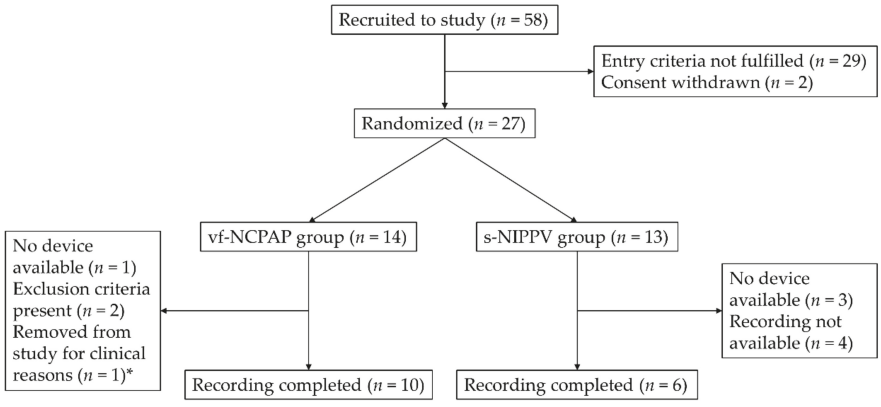

Figure 2. Patient flow; vf-NCPAP: variable flow nasal continuous positive airway pressure; s-NIPPV: synchronized nasal intermittent positive pressure ventilation; * the attending physician decided that changing the ventilator was not advisable.

Table 1. Patient demographics expressed as median (minimum–maximum).

	Total Group (*n* = 16)	**vf-NCPAP (*n* = 10)**	**s-NIPPV (*n* = 6)**
Male sex (n)	4	3	1
GA at birth (w)	27.5 (24.9–29.7)	27.0 (24.9–29.7)	28.4 (27.0–29.1)
Birth weight (g)	755 (590–1050)	718 (590–987)	940 (620–1050)
PMA at study (w)	30.5 (27.3–31.9)	30.2 (27.3–31.9)	30.5 (29.4–31.1)

GA: gestational age; PMA: postmenstrual age.

Table 2. Primary and secondary endpoints expressed as median (minimum–maximum).

Before–After Study 1 (*n* = 10)		**Before–After Study 2 (*n* = 6)**	
cf-NCPAP	**vf-NCPAP**	**cf-NCPAP**	**s-NIPPV**

Comparing both continuous positive airway pressure (CPAP) modes, $tcpCO_2$ was 3–4 mmHg lower during the vf-NCPAP or s-NIPPV support compared to cf-NCPAP, while FiO_2 remained unchanged (Table 2).

4. Discussion

In this comparison of the effectiveness of vf-NCPAP and s-NIPPV in reducing IH rates in very preterm infants with AOP compared to standard treatment with cf-NCPAP, we found only a little difference between these three nasal respiratory support systems.

We had planned this study for a total recruitment of 52 infants. This proved impossible for several reasons: there were competing large interventional multicenter studies ongoing on the unit with recruitment taking place in the first one to two postnatal days, reducing the number of infants eligible for the present study. In addition, many infants who had initially reached an apnea score of ≥5 subsequently did not reach the score of 10 required for randomization to another nasal respiratory support system, so that they never qualified for randomization. The slow patient recruitment in part was also due to a lack of external funding, so that no dedicated research personnel was available to supervise the study. Thus, after extending the original recruitment period by more than two years, the

study was eventually terminated prematurely, because recruitment would have lasted another eight years had it continued at the pace observed. This decision prohibited applying any statistical testing; nonetheless, the results showed only minor differences at a descriptive level, suggesting that either intervention had similar effectiveness.

Further limitations included the fact that we did not record apneas. However, in line with previous work from our group, we do not see this as a relevant limitation, as it is not the apnea, but its consequences, i.e., IH and to a lesser extent, bradycardia, that are relevant to the long-term outcome of preterm infants [13]. Regarding the effectiveness of s-NIPPV, synchronization between infant and ventilator depended on the nurses attaching the trigger capsule correctly. This was not systematically checked, but nurses on the unit were very experienced in using these capsules ensuring optimal placement and minimal trigger delay. Additionally, we used only a set level of pressure 5 cmH_2O during the CPAP application. This reflected the unit policy, but may not have been sufficient to open the airway during obstructive apneas. Finally, infants' postmenstrual age at the study was already 30.5 w, i.e., their apnea rate may already have decreased spontaneously.

Perhaps due to these limitations, the differences seen between the various nasal ventilator support systems were smaller than in other studies. For example, Gizzi et al., using a pneumotachograph-based system to synchronize the ventilator with the babies' breathing efforts and focusing on both bradycardia and IH, found a 50% reduction in the rate of IH episodes during s-NIPPV compared to cf-NCPAP (median, 2.9 vs. 5.9/h, respectively) [9]. In our earlier study comparing vf- with cf-NCPAP, the differences in bradycardia–/IH-rates were also larger (2.8 vs. 5.4/h [10]). Thus, although the gestational age at birth and postmenstrual age at study were similar in all three studies, cardiorespiratory event rates were lower in the present study, but s-NIPPV again seemed to be more effective than vf-NCPAP. As averaging times on the pulse oximeters used were identical and apneas are still a common occurrence at the mean postmenstrual age of our study population [14], we have no explanation for the lower overall event rates other than this being a chance finding related to our small sample size. Moreover, the comparatively low IH rate and an overall low average oxygen demand may indicate a higher clinical stability in participating infants, which also may have hampered the detection of notable differences between interventions.

A different approach to nasal respiratory support for preterm infants has recently been introduced by the nasal application of the neurally adjusted ventilatory assist (NAVA) technique in preterm infants. Using this technique in eight preterm infants studied at a median post-menstrual age of 29 w, a 40% reduction in the number of episodes with $SpO_2 < 80\%$ was found; episodes were also of significantly shorter duration while the infants received NAVA [15]. This may thus be a valuable addition to treating AOP via nasal respiratory support systems, but still requires further study.

Thus, although our data showed a smaller decrease in the rate of IH events than observed previously, they were in line with these previous studies in that we also found less IH and fewer bradycardias during s-NIPPV compared to cf-NCPAP.

5. Conclusions

Given the above limitations of our study, particularly its small sample size, the comparatively small differences observed between the three different modes of nasal respiratory support investigated should not prevent clinicians from preferring s-NIPPV or vf-NCPAP over cf-NCPAP when trying to prevent or treat IH episodes in very preterm infants.

Supplementary Materials: The following are available online at http://www.mdpi.com/2227-9067/7/10/168/s1, Figure S1: Study protocol CPAP study, Figure S2: CONSORT flow chart, Table S1: CONSORT checklist.

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