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The unfinished work of neonatal very low birthweight infants quality improvement: Improving outcomes at a continental level in South America

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ABSTRACT

Neonatal mortality rate varies between 4.2 and 18.6 per thousand by country in South America. There is little information regarding the outcomes of very low birth weight infants in the region and mortality rates are extremely variable ranging from 6% to over 50%. This group may represent up to 50–70% of the neonatal mortality and approximately 25–30% of infant mortality. Some initiatives, like the NEOCOSUR Network, have systematically collected and analyzed epidemiological information on VLBW infants' outcomes in the region. Over a 16-year period, survival without major morbidity improved from 37 to 44%. However, mortality has remained almost unchanged at approximately 27%, despite an increase in the implementation of the best available evidence in perinatal practices over time. Implementing quality improvement initiatives in the continent is particularly challenging but represents a great opportunity considering that there is a wide margin for progress in both care and outcomes.

1. Introduction

There are more than six million births in South America (SA) annually and neonatal mortality rate (NMR) varies between 4.2 and 18.6 per thousand among SA countries. There is little information regarding the outcomes of very low birth weight (VLBW) infants in the region but some initiatives, like the SA NEOCOSUR Network, are the source for valuable reports on the outcomes of this vulnerable population in this part of the world.

The importance of collaborative neonatal networks lies in that they can prospectively collect standardized data on a high-risk population such as VLBW infants. Thus, they can provide a standardized registry for observational research, describe trends in perinatal care and adjusted morbidity and mortality for benchmarking purposes and therefore motivate centers for care improvement, facilitate the execution of controlled trials, and perform collaborative quality improvement projects.

Worldwide, the number of deaths of children under 5 years of age fell from 12.7 million in 1990 to 6.3 million in 2013. The first 28 days of life – the "neonatal period" – represent the most vulnerable time for a child's survival. In 2013, around 44% of under-five deaths occurred during this period, up from 37% in 1990 [1]. Strategies that countries have implemented to reduce infant and childhood mortality have not necessarily impacted neonatal mortality. Within neonatal mortality, prematurity plays an important role. In SA, prematurity as a cause of death represents between 18 and 28% of the mortality rate in children under 5 years of age and between 29 and 45% in newborns [2] (Table 1).

The relevance of VLBW infant outcomes is that although they represent only 1%–2% of total births, their outcomes contribute significantly to neonatal and infant mortality rates. In SA, VLBW infant mortality may represent up to 50–70% of neonatal mortality and approximately 25–30% of the total infant mortality [3]. Larger and increasing amounts of resources are consumed for their short- and long-term care and this is crucial in a limited-resources area like our region. The good news about VLBW infant registries is that all cases are immediately and easily identified in hospitals, making this group of

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Table 1
Child Mortality Estimates, global and regional child deaths by cause, 2018. Data from: UNICEF GLOBAL DATABASES, http://data.unicef.org [2].

Country	2017 - PCM <5 years (%)	2017 - PCM newborns (%)
Argentina	28.1	44.9
Bolivia	19	31
Brazil	18.7	29.3
Chile	27.6	38
Colombia	21	34.1
Ecuador	24.8	42.4
Guyana	19.7	31.5
Paraguay	23.1	39.4
Peru	20.2	38.7
Suriname	24	43.3
Uruguay	21.9	35.8
Venezuela	26.3	39.6
Latin America & Caribbean	20.5	34.4

PCM: Prematurity as cause of mortality.

patients suitable for all kinds of analyses and follow-up. For these reasons, VLBW infants have been described as a "sentinel" population that may be representative of general neonatal and infant care.

Important variability in outcomes, such as those found in our region, might entail differences in multiple variables besides clinical practices or therapeutic interventions. Moreover, the association between potentially better practices and outcomes proven in high income countries might not hold uniformly across different populations, health systems, and organizations [4]. Designing and implementing quality improvement (QI) initiatives in the region might require the identification of specific shortcomings that should be approached differently. As recently stated regarding safety and efficacy of antenatal steroids in low resource countries, providing a minimum standard of care appears essential in achieving benefits and preventing harm and should be incorporated into future QI strategies [5].

This review will provide an overview of actual regional neonatal and VLBW infant outcomes, the changes in antenatal and neonatal VLBW infant care practices over time and will give an insight into their outcome's variability. It will also provide and propose QI interventions for their improvement.

2. A South-American overview

SA includes countries sharing many socio-cultural and historical features that provide a certain identity to their population. On the other hand, there is an enormous heterogeneity in the organization and administration of health in each country that weighs in the great variability in their public health indicators. When looking at global indicators of perinatal health, SA as a group ranks below the industrialized countries of Europe/North America, Oceania and Southeast Asia, but surpasses countries from Africa and the rest of Asia.

Within SA, the variability is evidenced by the NMR values, which ranged from 4.2 per thousand live births in Uruguay to 18.6 in Guyana in 2019 [6] (Table 2). NMR represents between 59% and 76% of infant mortality in the region, highlighting that policies should focus primarily on reducing neonatal mortality [6]. The reasons for this disparity are beyond the scope of this paper but deserve to be studied and analyzed. Interestingly, it appears to be not only a matter of allocating resources to perinatal health in these countries, but also its good utilization, since the percentage of gross domestic product that goes to this sector in half of the countries of SA, shows similar values to those in high income countries [7] (Fig. 1). Although there has been some improvement in perinatal health results in recent years, the rate of decline in important indicators such as infant mortality is far from optimal. Despite the work of several local and international organizations (CLAP, CREP, PAHO and Neonatal Networks, such as NEOCOSUR, EPIC Latino, SIBEN) it appears

Table 2
Neonatal and infant mortality rate (per 1000 live births) in SA countries. Data from World Bank [6]. NMR: neonatal mortality rate; IMR: infant mortality rate.

Country	2019 NMR	2019 IMR	NMR/IMR (%)
Argentina	6.1	8.2	74.4
Bolivia	14.6	21.2	68.9
Brazil	7.9	12.4	63.7
Chile	4.6	6	76.7
Colombia	7.5	11.8	63.6
Ecuador	7.1	12	59.2
Guyana	18.6	24.4	76.2
Paraguay	10.9	16.6	65.7
Peru	6.4	10.3	62.1
Suriname	11.2	16.1	69.6
Uruguay	4.2	6.1	68.9
Venezuela	14.6	21	69.5
Latin America & Caribbean	9.1	13.9	65.5

that perinatal health may have been left behind other priorities in many SA countries.

Several countries in SA report persistent profound social inequities that need to be addressed urgently. The 2014 Lancet series on perinatal health stated that every year 2.9 million newborn infants die from largely preventable causes [8]. The series focused on facility-based care around the time of birth, as this is the time when most deaths occur. To significantly improve these disturbing numbers requires health systems that are up to the task. While certainly it is necessary to have modern equipment, facilities, and well-trained professionals, this is far from enough. Political leadership is crucial as is the conscience of local communities to demand optimal care for mothers and neonates. Societies should not accept maternal and neonatal deaths as inevitable, as it was in the past. Perinatal health must be prioritized in every country's agenda.

Chile has been a model for successful strategic initiatives to reduce infant mortality over the last 27 years (1990–2016). The under-5 years mortality rate in Chile came down from 19.9 to 8.1 deaths per 1000 live births (59.3% reduction). In almost all categories of birth weight, mortality risk dropped by at least half, except for extremely low birth weight, which experienced a more modest 26% reduction. To achieve these results, public efforts have focused on early mortality by improving the access to specialized neonatal care [9].

Uruguay has also shown great improvements in the last 10 years in terms of infant mortality rate and NMR. The first dropped from 13.2 in 2004 to 6.8 per 1000 live births in 2019, while NMR has accompanied this downwards trend reaching 4.2/1000 births in 2019 [10]. These promising outcomes can be attributed to the increasing efforts to strengthen social and health policies at a governmental level. The largest maternity hospital in the country, the Pereira Rossell, covers 25% of births in Uruguay, has an actual NMR of 22% in VLBW infants (NEOCOSUR's's database). One remarkable strength of the Uruguayan health system is the importance attributed to enhancing breastfeeding, together with the development in 2003 of a human milk bank which is located at the mentioned public hospital. This bank meets the demands of VLBW infants across the country.

The Brazilian Neonatal Research Network published in 2015 results from a cohort of 2646 VLBW infants born at 20 centers between 2012 and 2013. They reported an overall mortality rate of 30% and survival without major morbidity of 47% [11].

Regarding Argentina, data from the National Ministry of Health is available and usually published yearly albeit covering only partially the governmental sector and providing very scant information on VLBW morbidity and mortality [12]. Tavosnanska et al. published in 2012 data from 15 public hospitals in the City of Buenos Aires reporting a VLBW infant mortality rate of 29.2% and a relatively low antenatal steroids utilization of 52,6% [13].

The National Ministry of Health in Peru reports a NMR of 26,2% in neonates under 1 kg and 17.8% between 1001 and 1499 g in 2019 [14].

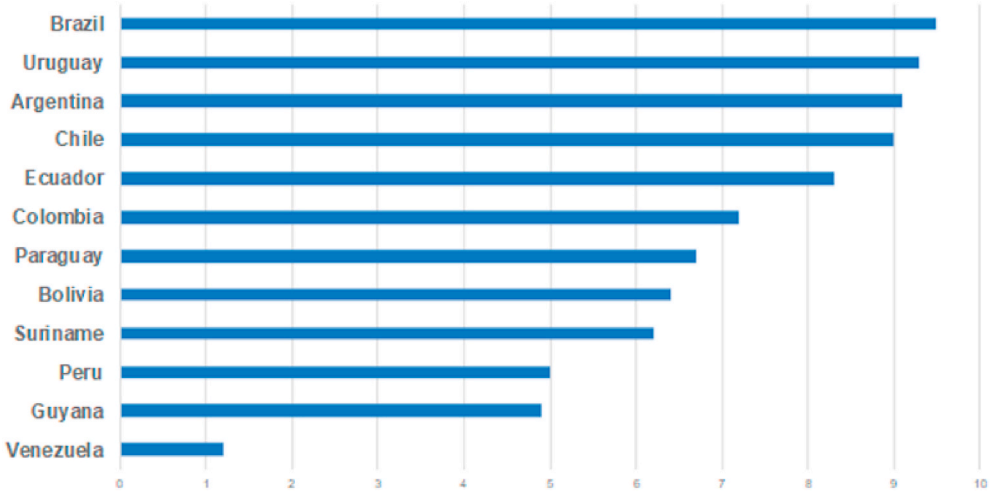

Fig. 1. Health expenditure as percentage of gross domestic product (%). Data from World Health Organization, 2017 [7].

Other countries such as Colombia, have focused on research collaborations to promote improvement in care and obtaining reliable information [15]. Similarly, the participation of several SA centers in international networks such as the Vermont Oxford Network (VON) must be acknowledged.

Overall, one of the difficulties that countries in SA face is the scarcity of adequate data, particularly on VLBW infants' outcomes, that is essential to develop public health strategies and QI initiatives. This lack of consistent regional data is challenging for researchers and clinicians as preterm birth remains a crucial issue in child mortality [16]. In this context, we provide NEOCOSUR's data in this review as a reference for SA, albeit acknowledging some limitations in its representativeness.

3. Quality improvement

QI in healthcare has been defined as "the combined and unceasing effort of everyone – healthcare professionals, patients and their families, researchers, payers, planners and educators – to make the changes that will lead to better patient outcomes (health), better system performance (care) and better professional development (learning)" [17].

The foundations for a successful QI model require reaching a profound knowledge of every NICU's perinatal results, therefore, enabling the clinicians to identify weak performing areas where most efforts should be made to improve outcomes. Monitoring the burden of VLBW infants across each country or region is vital, not only to assess their impact, but also for parental counseling, clinical decision-making, developing targeted strategies to reduce preterm birth, and fostering implementation of evidence based-high quality medicine to enhance results in areas where clinicians know that have worst performance [18].

Neonatal collaborative QI (CQI) methodology emerged in the late 1980s with VON [19]. Thereafter, several Neonatal CQI projects have been successful in improving perinatal practices and neonatal outcomes [20–23], the majority coming from well recognized neonatal networks from developed countries [24]. Neonatal intensive care unit (NICU) networks that embrace regions or countries offer the perfect platform for implementing collaborative quality improvement (CQI) initiatives to advance the health care provided to vulnerable neonates [24]. Benchmarking and feedback of outcomes, combined with mutual collaborative learning in cycles of identification and implementation of best available evidence, leads to a better performance of health care systems and neonatal outcomes. For this purpose, it is pivotal to generate standardized databases [25]. Data must be able to be analyzed and compared with previous results or with other NICU's. The most advanced level is the creation of national or international networks to share and expose multicenter data under a standardized criterion [26,27]. VON has paved the way in the QI area and has encouraged NICUs to develop four key habits for improvement: 1) the habit for change, 2) the habit for practice as a process, 3) the habit for collaborative learning, and 4) the habit for evidence-based practice. Information generated by VON can be used for comparisons among hospitals providing similar levels of care [19].

3.1. The South American NEOCOSUR network: achievements and challenges

Since 1997, NEOCOSUR has prospectively monitored the care and outcomes of VLBW infants across six SA countries using standardized collection of data on morbidity and mortality as well as antenatal and postnatal care practices. It is a voluntary non-profit, collaborative neonatal network (including 5 countries and 32 Neonatal Units from Argentina, Brazil, Chile, Paraguay, Peru, and Uruguay). All participating centers are university-affiliated tertiary-care institutions that belong to both public and private health systems [28]. It comprises units with diverse health systems, heterogeneous population, and variable resources, and consequently shows a very high variability in outcomes. Despite these differences, it provides high quality data on the outcomes of VLBW infants cared for in NICUs from a region composed of middle-income countries. Over the years, NEOCOSUR has systematically collected and analyzed epidemiological information on VLBW infants' outcomes in an effort to fulfill its primary mission of improving neonatal care in the region [29–31].

The standardization of data collection that allows for benchmarking and feedback of outcomes, combined with mutual collaborative learning, has been successful. Identification and implementation of the best available evidence in perinatal practices have increased over time. As recently published, over a period of 16 years, survival without major morbidity in VLBW infants improved from 37 to 44% [29]. This was mainly driven by an improvement in the outcomes of moderately preterm infants >29 weeks gestational age. The percentage of antenatal steroids (ANS) use increased from 70.2% to 82.3% in a 16-year period; the use of CPAP increased from 41.3% to 64.3%, and mechanical ventilation decreased from 67.7% to 63.9% [29]. Although mortality has remained unchanged at 26.8%, variability among centers has decreased. Mortality rates among centers ranged from 6 to 53% in the early 2000s and in the last 4 years ranges between 5 and 38%.

Variability in the main outcomes of mortality, and survival with and without major morbidity, in the last 10 years period (2010–2019) in each center is shown in Fig. 2. Overall mortality rate is 27.1% (ranging 10.7–46.4% among centers).

Mortality rates according to BW and gestational age stratification in

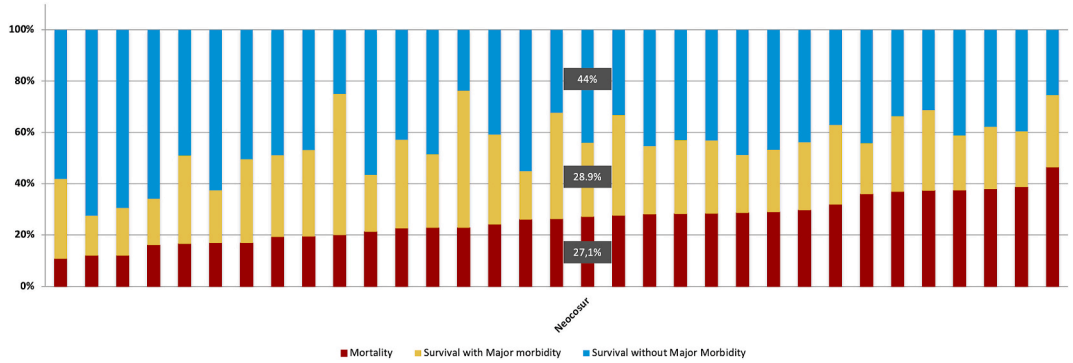

Fig. 2. Mortality and survival with and without Major Morbidity by Center- 2010–2019. Ranges between centers: Mortality 10.7–46.4%; survival with mayor morbidity 15.5–55%; survival without mayor morbidity 23.7–72.5%. Each bar represents a different center. The mean of the network is represented by NEOCOSUR. Major morbidity is defined as the presence of bronchopulmonary dysplasia, necrotizing enterocolitis with intestinal perforation, periventricular leukomalacia, severe intraventricular hemorrhage (grades III-IV), severe retinopathy of prematurity (grades 3–5) and/or late onset neonatal sepsis.

the last 19 years (2001–2019) are shown in Fig. 3. As expected, mortality decreases with increasing BW, and decreases with advancing gestational age up to 33 weeks; thereafter, it increases as the severity of intrauterine growth restriction increases.

The voluntary and persevering work of its members has been crucial. Participant centers receive confidential annual reports that document their performance and compare practices and outcomes at each NICU along with those in other units within the Network.

Taking over differences and barriers present in our region, NEOCOSUR has developed various strategies that allow comparing the results of different centers over time. Adjusting mortality and morbidity by risk, allows to compare the center's performances looking at the observed/expected (O/E) incidences [32] (Fig. 4).

These reports provide centers opportunities for specific improvement and monitor their own successful or failed efforts. Benchmarking is presented after risk adjustment to evaluate the center 's performances. Predictive models for severe intracranial hemorrhage and bronchopulmonary dysplasia (BPD) have also been developed [33,34]. A few controlled trials have also been accomplished. In one of these trials the use of early prophylactic CPAP in infants with a birthweight 800–1500g was associated with a significant reduction in the need for surfactant (46.4%–27.5%) and for mechanical ventilation (50.4%–29.8%) [35].

Although information is necessary for improvement to take place, it is not enough to produce lasting effects in time. Thus, information must

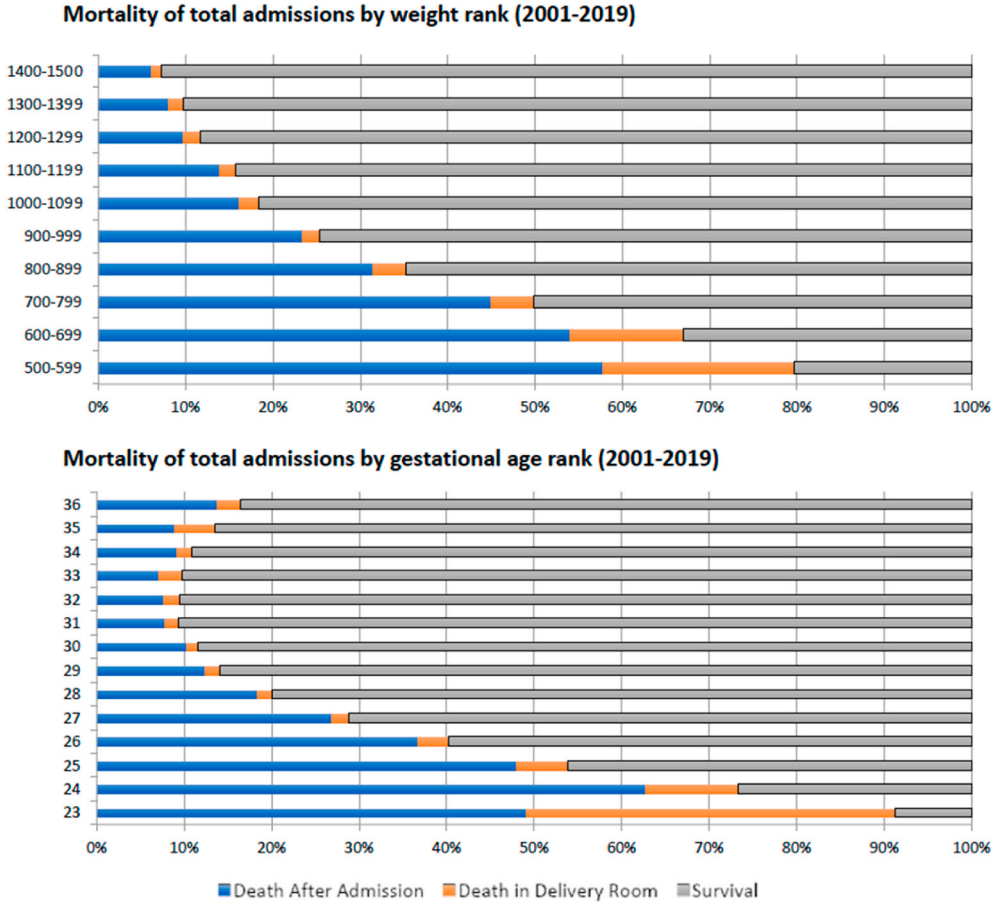

Fig. 3. Mortality by birth weight (g) and gestational age (weeks) 2001–2019, NEOCOSUR Network.

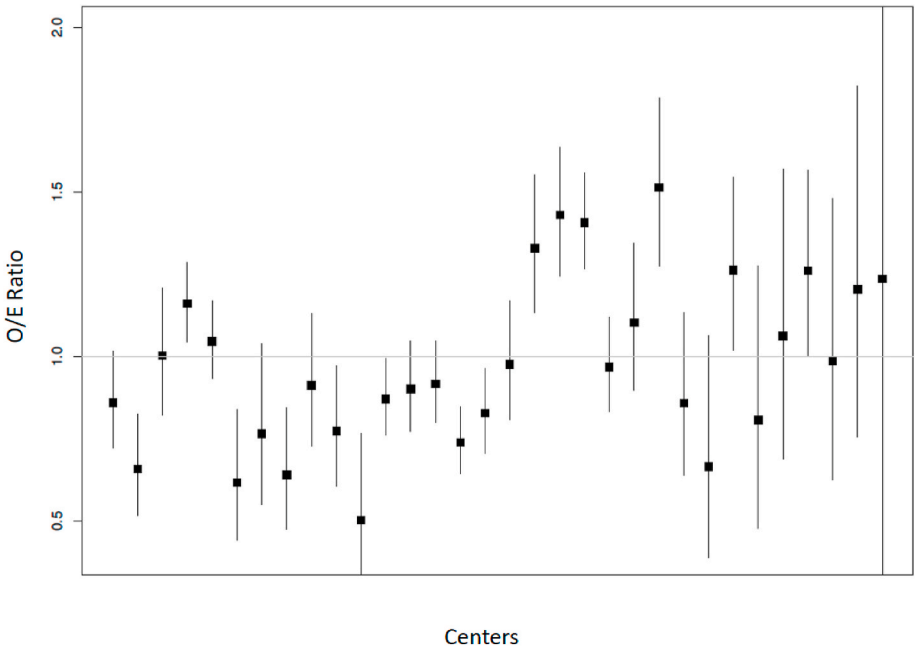

Fig. 4. Mortality adjusted by risk in NEOCOSUR centers from 2001 to 2019. O/E ratio: observed/expected ratio.

lead to specific actions [26]. Although NEOCOSUR has been a robust network for the past 23 years, it has not been able to implement formal multicenter QI strategies. This is clearly our "pending task", and without the shadow of a doubt the following step is to successfully achieve the implementation of QI strategies that might lead us to a path of major improvements in our VLBW infants' outcomes.

3.2. Regional barriers to implement QI strategies

Various obstacles and problems can be easily identified in most developing countries [36,37]. Several barriers have limited the implementation of QI strategies to improve outcomes of VLBW infants in SA. Great inequities can be recognized regarding state of health development, public health policies, and funding directed to perinatal care. Furthermore, neonatal outcomes can be quite different within the same country. This is partly due to the differential investment in resources between the public and private health systems. In addition, the geographical barriers and centralization of care also plays an important role in increasing the gap of inequality in neonatal care across the different regions of the same country.

On the other hand, each country's health system places a different priority on health investment. During the last decades, resources have been directed mainly to improve access to health assistance (universality) and decreasing mortality. The decrease in morbidity associated with conditions such as prematurity has not been a health priority in the countries of the region; consequently, fewer resources have been channeled to this objective.

Human resources are also a growing need in the region. For most countries, there is a great shortage of neonatologists and fundamentally specialized nurses. This causes large differences between referral centers and the rest of health institutions. In addition, due to the continuous interaction between different cultures and increase regional migration, divergences could be deepened, adding new barriers to the development of QI strategies. Human resources are also scarce when it comes to devoting dedicated time to research in the field of medicine. There has not been investment in having full time neonatologists in the region. Moreover, the majority must work part time in private practice as pediatricians or attend more than one institution. In this inhospitable land it seems difficult for research and QI strategies to blossom.

3.3. NEOCOSUR QI initiative

The Network's first formal QI project is a proposal applying the methods of benchmarking and collaborative improvement with two specific aims: reduction in the composite outcome of BPD/Death and reduction of late onset sepsis. After analyzing our data, a starting point has been established by selecting 5–6 centers for each intervention, in an intervention period of 12–18 months. Respiratory and infectious diseases have been the main causes of death in our population after NICU admission [38]. The centers targeted for intervention are those with the highest observed to expected ratio for the adverse outcomes of interest.

The Network coordinators for these projects will support centers with a preparatory program including surveys (already carried out); interviews, particularly with front line health professionals; and written and visual material. The Network will continue to support these efforts by developing and providing improved tools and resources for the practice of evidence-based neonatology. These projects are only possible because of the voluntary efforts of the Network members.

A permanent monitoring of the interventions must be assured. This can be done with internal facilitators in each NICU and an external support from the network. The supervision can be done remotely through virtual meeting platforms and visits to the different centers by telemedicine on a regular basis will be programmed. Visits to centers (if feasible), together with audiovisual material and checklist will be scheduled. Change in specific clinical practices should be stimulated, but more importantly, spreading a QI culture in the network has proven to be effective in other parts of the world [39].

Enthusiasm of each center to improve, support of the network, and the willingness of the governments to invest in QI strategies to improve the results of our premature population are the keys to generating successful programs in our region.

3.4. A path to QI in South America

A first step in provision of high-quality healthcare is establishing infrastructure for monitoring of outcomes and processes in developing countries [40]. Healthcare facilities and governments should invest in collection and analysis of reliable data to inform both quality assurance and QI activities. Creation of QI teams have shown not only to improve results but also to have a significant effect on reducing total health costs.

Although QI might seem unaffordable, the monetary advantages that the implementation of QI programs can bring in the long run must tilt the scale towards it [40]. QI strategies must consider best evidence-based practices adjusted to the culture and reality of our region and to what are the main outcomes to improve. Actual available evidence strongly supports incorporating QI interventions to increase the consumption of human milk by our VLBW infants and parental education; therefore, their implementation should be reinforced [41].

The SA continent represents a big challenge but at the same time a great opportunity for improvement, because of its high outcome variability and a wide margin for progress. An important obstacle has been the lack of resources. Large inequities are also present in current research funding support for the amounts invested in newborn health in comparison to other diseases globally [42]. We urge governments, international organizations, and other stakeholders to support initiatives that may improve outcomes in these vulnerable infants that should be included among the world's Public Health priorities.

4. Conclusions

There is an urgent need for standardized data collection of premature and VLBW infants' outcomes in SA. Countries and centers should work along with governments, and local health authorities for this purpose. NEOCOSUR may serve as a model of a successful network in the region and provides data and models for risk adjustments and benchmarking. We feel that the unfinished labor for VLBW QI in the region is just beginning.

Practice Points.

From our Network's experience, we can suggest some practice points for regional CQI implementation and organization:

1. Seek individuals for leadership positions who represent both private and public academic institutions.
2. Search for models from other networks and successful CQI initiatives that are implementable in your own context.
3. Implement a trustable Data Base Unit (DBU), where all the information is maintained safely. This information is confidential to centers and patients and overseen by an informatics service. Health professionals including trained nurses, physicians, and statisticians in our setting audit and validate online data entry from each center.
4. Predefined standardized information is prospectively registered and sent to the DBU. Variables should include main perinatal epidemiological characteristics, main perinatal practices, and main clinical outcomes. Examples for core variables suggested are easily available from several neonatal networks.
5. Risk adjustment is critical for benchmarking and center performances. Models are available on-line.
6. At least a yearly report should be given to centers describing their performances and that of the rest of the centers.
7. Promote low cost proven beneficial interventions like antenatal steroids, CPAP, human milk, kangaroo care.
8. Promote controlled trials initiatives or participation.
9. Design CQI initiatives that are feasible in the local context.
10. Involve parents and families and promote breast milk production.

Future directions.

From NEOCOSUR.

- Continue prospectively registering standardized data, analysis of which is crucial to track prevalence, risk factors, and trends in therapies and morbimortality.
- Promote more RCT trials in critical issues in VLBW infants' management and interventions.
- Implement specific QI interventions to improve the survival without major morbidities of VLBW infants.
- Build capacity to coach and conduct QI projects that may serve the region.
- Nurse and parental care matter: promote their education and contribution.
- Funding availability is a key unsolved issue that remains a barrier

Funding sources

None.

Declaration of competing interest

None declared.

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