


# BMJ Open Impact of secondary and tertiary neonatal interventions on neonatal mortality in a low-resource limited setting hospital in Uganda: a retrospective study

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## ABSTRACT

**Objective** To assess the impact of secondary and tertiary level neonatal interventions on neonatal mortality over a period of 11 years.

**Design** Interrupted time series analysis.

**Setting** Nsambya Hospital, Uganda.

**Interventions** Neonatal secondary interventions (phase I, 2007–2014) and tertiary level interventions (phase II, 2015–2020).

**Participants** Neonates.

**Primary and secondary outcome measures** Primary outcome: neonatal mortality. Secondary outcome: case fatality rate (CFR) for prematurity, neonatal sepsis and asphyxia.

**Results** During the study period, a total of 25 316 neonates were admitted, of which 1853 (7.3%) died. The average inpatient mortality reduced from 8.2% during phase I to 5.7% during phase II ( $p=0.001$ ). The CFR for prematurity reduced from 16.2% to 9.2% ( $p=0.001$ ). There was a trend in reduction for the CFR of perinatal asphyxia from 14.9% to 13.0% ( $p=0.34$ ). The CFR for sepsis had a more than a twofold increase (3%–6.8%  $p=0.001$ ) between phase I and phase II.

**Conclusion** Implementation of secondary and tertiary neonatal care in resource-limited settings is feasible. This study shows that these interventions can significantly reduce the neonatal mortality, with the largest impact seen in the reduction of deaths from perinatal asphyxia and prematurity. An increase in sepsis related deaths was observed, suggesting emphasis on infection control is key.

## BACKGROUND

Each year, an estimated 2.4 million neonates die, mainly from complications of prematurity, neonatal infections and intrapartum-related events.<sup>1–3</sup> In Uganda, the neonatal mortality rate (NMR) of 27 deaths per 1000 live births has not changed over the past 10 years.<sup>4</sup> There has been a rapid reduction in neonatal mortality in countries that have scaled up neonatal special care units.<sup>5</sup> The introduction of neonatal special care units

## STRENGTH AND LIMITATIONS OF THE STUDY

- ⇒ The relatively long duration of our study, of 11 years, improved our ability to accurately evaluate the impact of the interventions.
- ⇒ Our study was also able to report case fatality rates for prematurity, asphyxia and infections.
- ⇒ The retrospective design was a key limitation to our study, a many of the hospital records had incomplete data.

in India led to a 22.5% reduction in neonatal mortality between 2011 and 2016.<sup>6</sup> Reducing the NMR in low-income countries (LICs), such as Uganda, will require improved access to good quality care at birth and better-quality inpatient care for small and sick newborns.<sup>7,8</sup>

It is believed that 90% of preterm deaths could be averted through the implementation of both level 2 care (nasogastric tube feeding, infection prevention and treatment, phototherapy, oxygen, pulse oximetry and kangaroo care) and level 3 care (continuous positive airways pressure (CPAP), artificial surfactant, mechanical ventilation, 24-hour monitoring, specialised neonatal nurses and neonatologists).<sup>5</sup> Growing evidence suggests that by combining effective neonatal interventions together can lead to successful reductions in mortality in sub-Saharan Africa.<sup>9</sup> In Tanzania, the implementation of a preterm care bundle that included antenatal corticosteroids, maternal intrapartum antibiotics, neonatal antibiotics and avoidance of hypothermia at birth, reduced preterm mortality by 26%.<sup>10</sup> Similarly, in eastern Uganda, the implementation of both level 1 and level 2 neonatal care led to a reduction in mortality from 48% to 21%.<sup>3,11,12</sup> However, despite this growing body of evidence, very

**Table 1** (A) Phase I—secondary level interventions (2007–2014). (B) Phase II - —Tertiary level interventions (2015–2018)

<b>(A) Phase I—secondary level interventions (2007–2014)</b>	
<b>Year</b>	<b>Description of the intervention</b>
2008	Perinatal audit: weekly multidisciplinary team audits began in 2008. Gaps identified in care were discussed and proposed actions were followed up monthly
2008	Basic neonatal resuscitation: training in basic neonatal resuscitation was provided every 3 months in labour ward, obstetric theatre and neonatal units. A resuscitation corner (heat bulb) and flat surface was created in each of these areas
2008	Feeding and intravenous fluid administration guidelines for preterm and sick neonates. All staff working in the neonatal unit were trained in lactation support and breast milk expression. Nasogastric feeding was done for all sick infants and all preterm infants less than 33 weeks. Cup feeds were commenced for well preterm infants above 33 weeks. Feeds were advanced as the neonates tolerated at a rate of 24 mL/kg/day from the 2nd day after birth until attainment of full feeds (200 mL/kg/day). Intravenous 10% dextrose was started for all preterm infants less than 1500 g and neonates who were critically ill. If the mother's own milk was not enough then formula milk was supplemented
2008	Bubble CPAP (bCPAP) for neonates with respiratory distress. Staff were trained on how to set up and use bCPAP. An oxygen cylinder or oxygen concentrator was used as the oxygen source and the flow was set at 5 L/min and the expiratory tube was placed underwater at 5 cm H <sub>2</sub> O. Pressure could be gradually increased to 7 cm H <sub>2</sub> O if there was worsening respiratory distress. The oxygen saturation was monitored every 3–4 hours for neonates on bCPAP
2008	Nurse-to-patient ratio 1:10: nurse-to-patient ratio of 1:10 facilitated monitoring of the temperature, oxygen saturation every 4 hours
2008	Infection control: proper cleaning of the surfaces and incubators using 5% chlorine, kangaroo care and cleaning of the feeding equipment with soap and water, safe administration of injections and intravenous fluids
2009	Kangaroo mother care for stable low weight infants: kangaroo care training was provided for all the neonatal unit staff and a dedicated space for kangaroo care was created. Intermittent kangaroo care was initiated for all neonates >800 g if the neonate is stable on oxygen or CPAP. A kangaroo care scoresheet was adopted to assess the adherence to KMC and was used to assess readiness for discharge. A neonate was discharged once score >15 and included a weight ≥1200 g or gestational age >34 weeks, evidence of weight gain, stable thermoregulation, spontaneous breathing, full oral feeding by breast or cup feeding and normal vital signs for at least 48 hours before discharge
2009	Use of antibiotics for sick neonates and infection control: Antibiotics were initiated according to the WHO guidelines; however, blood cultures and infection markers were not available. The first-line antibiotics were ampicillin and gentamicin and the second line was ceftriaxone
2009	Anticonvulsants for neonatal seizures: phenobarbitone was used to control convulsions
2007–2012	Phototherapy: bilirubin was assessed clinically and using laboratory methods and those with hyperbilirubinemia were managed with phototherapy. Florescent tubes were used initially, and later LED lights were introduced in 2012
<b>(B) Phase II—tertiary level interventions (2015–2018)</b>	
2015	A 10-bed neonatal intensive care unit (NICU) was set up and equipped with 2 neonatal ventilators, 3 radiant warmers, 6 incubators, 6 monitors, 8 CPAP machines. Training in management of critically ill newborns included: neonatal intubation and mechanical ventilation, infection control, monitoring, advanced neonatal resuscitation, cooling, administration of surfactant, standardised fluid and feeding protocols. Nurses were taught admission and monitoring of sick neonates, infection control, the use of CPAP and safe use of oxygen and feeding of extremely low birth weight neonates, capillary blood sampling, thermoregulation and use of incubators. Two hourly monitoring of the heart rate, oxygen saturation, temperature and blood pressure (peripheral) was done
2015	Artificial surfactant. guidelines on surfactant administration were adopted from the South African neonatal care book. <sup>13</sup> Surfactant (Survanta) was administered for infants with an FiO <sub>2</sub> >40%, or Silverman Anderson Score of more than 6 within 2 hours after delivery <sup>14</sup>
2015	Infection control: training and use of guidelines on infection control, antibiotic stewardship: infection control was further improved to include alcohol hand gel on every incubator and cot, thorough scrubbing of the floor done on a weekly basis, a protocol for cleaning of equipment was introduced. In addition, autoclaving of feeding utensils for those less than 1 kg and surveillance for late onset sepsis was done. A protocol for antibiotics use was created based on the local sensitivity patterns. Biomarkers such as a C reactive protein and CBC and blood cultures preceded the initiation of the antibiotics

Continued

**Table 1** Continued

<b>(B) Phase II—tertiary level interventions (2015–2018)</b>	
2015	Use of donated breast milk and use of breast milk only for preterm neonates Breast milk was available to all Preterm neonates and pasteurised donated human breast milk was introduced
2016	Cooling for moderate-to-severe hypoxic ischaemic encephalopathy (HIE). Newborn infants ( $\geq 36$ weeks and $\geq 1800$ g), with moderate-to-severe HIE at age $< 6$ hours, evidence of intrapartum asphyxia, with each infant satisfying the following criteria: a 10 min Apgar Score of $< 7$ , and Thompson Score of more than 7 at 6 hours were cooled using cool gel packs (at $7^{\circ}\text{C}$ – $10^{\circ}\text{C}$ ) applied to the head and upper body and replaced hourly. The core temperature is servo controlled by an overhead radiant warmer (Servocrib, Servocare Medical Industries cc, Cape Town), capable of controlling to a low target temperature of $33.5^{\circ}\text{C}$ . A heat shield is placed over the head to prevent local head heating. After 72 hours, the cold gel packs are removed and the temperature of the radiant warmer is increased every hour by $0.2^{\circ}\text{C}$ , until a core temperature of $36.5^{\circ}\text{C}$ – $37^{\circ}\text{C}$ is achieved. During the cooling a daily follow-up form is filled by the nurses and doctors and it includes: temperature, Thompson Score, clinical characteristics, serum electrolytes and coagulation
2017	Warm Transportation: warmth was provided during transportation from labour ward using exothermic mattress (Warmilu) in a small transport infant bed. Neonates could be transported with oxygen, bCPAP or Neopuff
2017	CPAP in the delivery room for all neonates with immediate respiratory distress. CPAP was initiated in labour ward for all neonates who were high risk, including those delivered by caesarean section or any neonate with respiratory distress soon after birth and with Silverman Anderson Score of 3 and above
2015–2017	Improved human resource: the nurses in the neonatal unit were increased to a nurse-to-patient ratio 1:4 in the NICU and 1:7 in the other units. The number of doctors also improved from one to five doctors, including a neonatologist in the NICU and one paediatrician in the observation/kangaroo care unit and a trained medical officer leads the neonatal resuscitation team

CBC, cell blood count; CPAP, continuous positive airways pressure; KMC, kangaroo mother care.

few regional and district hospitals in Uganda have implemented these interventions. Here, we report the development and implementation of two levels of evidence-based and low-cost neonatal care and their associated impact on neonatal inpatient mortality in a private-not-for-profit hospital in Uganda.

### Objectives

1. To describe the stages of implementation of secondary (level 2) and tertiary (level 3) interventions in a resource-limited setting.

2. To describe the associated impact on overall inpatient mortality and disease case fatality.

### METHODS

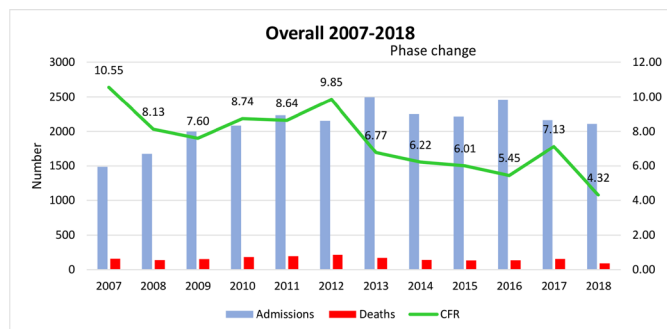
An interrupted series study design was used for assessing the impact of the implementation of secondary and tertiary neonatal care on inpatient outcomes in a private-not-for-profit hospital in Uganda over an 11-year period. Two distinct phases were studied: phase I (2007–2014) consisted of ten secondary level interventions and phase II (2015–2018) consisted of eight tertiary level interventions. The primary and secondary outcome measures were: impact on overall mortality and the disease-specific case fatality rates (CFRs) for prematurity, asphyxia and infections.

### Study site

This study was conducted at Nsambya Hospital, a private not-for-profit tertiary hospital in Kampala, Uganda, which serves as a tertiary referral centre for Makindye division with a total population of 398 800. The following services are available: obstetrics, paediatrics, internal medicine and surgery. Each of the departments have specialists and medical officers and nurses. It conducts 7000 deliveries per year and provides 24-hour comprehensive emergency obstetric and neonatal care services. The obstetric department has 9 obstetricians, 12 postgraduate doctors and 40 midwives. The neonatal unit admits 2500 neonates annually, has a bed capacity of 50 and 1 neonatologist, 1 paediatrician, 2 medical officers, 25 nurses and 7 postgraduate

**Table 2** Number of neonatal admissions and inpatient deaths from 2007 to 2018 at Nsambya Hospital

Year	Total of admissions	Total number of deaths (%)
2007	1488	157 (10.5%)
2008	1673	136 (8.1%)
2009	1999	152 (7.6%)
2010	2083	182 (8.7%)
2011	2234	193 (8.6%)
2012	2152	212 (9.8%)
2013	2496	169 (6.7%)
2014	2 250	140 (6.2%)
2015	2214	133 (6.0%)
2016	2459	134 (5.4%)
2017	2161	154 (7.1%)
2018	2107	91 (4.3%)



**Figure 1** Overall mortality for phase I and phase II (phase I—2007–2014 and phase II—2014–2018). CFR, case fatality rate.

students. The unit is currently divided into three levels: (1) neonatal intensive care unit, (2) neonatal observation unit and (3) kangaroo and isolation unit. The neonatal intensive care unit was opened in 2015 and includes 10 beds with access to oxygen therapy, artificial surfactant, low-cost bubble CPAP and mechanical ventilation. The neonatal observation unit opened in 2006 and has a total capacity of 30 beds with access to phototherapy and bubble CPAP. Together, the kangaroo and isolation unit have a total capacity of 10 beds.

### Intervention

A neonatal package consisting of level 2 and level 3 interventions was implemented from 2007 to 2018. Details of each of these phases are described in detail in [table 1](#).

### Data collection

A register for all admissions and causes of death was created in 2007. This was completed daily by the nurse in charge. Initially, all information was collected using a paper-based registry. In 2014, an electronic registry was introduced (Microsoft Excel) and this is reviewed monthly by the head of department for accuracy and completeness. All the paper-based data collected prior to 2014 were transferred to the electronic register by a data entrant.

### Statistical analysis

All the data were entered in Excel and exported to STATA V.14 for analysis. Admission and causes of death were summarised and presented with corresponding

proportions for each year. CFR was computed for each cause of death per phase; differences in the proportions were assessed using the immediate two-sample test of proportions. Mortality trends by each cause of death were computed, disaggregated by phase and cause of death. The trend analysis was done using the non-parametric test for trend across ordered groups (in this case, each cause of death by year). The analysis of interrupted time series was estimated using the Newey-West standard errors for coefficients which used the ordinary least squares regression. P values were presented and a value of  $<0.05$  was considered statistically significant.

### Public patient involvement

Individual patient consent was not applicable as the research team extracted anonymised data from case notes. Patients and the public were not involved in this study. The findings of this study shall be disseminated to different forums in the country, in the department, conferences and the local newspapers and preterm patient follow group among the survivors in the hospital. The patients/mothers/parents will guide what interventions they thought benefited them or may have led to a reduction in neonatal mortality.

### RESULTS

A total of 25 316 neonates were admitted, of which 1853 (7.3%) died during the study period. Annual admissions increased from 1488 in 2007 to over 2000 from 2010 onwards ([table 2](#)). Overall mortality decreased from 10.5% in 2007 to 4.3% in 2018. There was a mortality reduction from 10.5% to 6.7% (phase I) and from 6.7% to 4.3% (phase II) ([figure 1](#)).

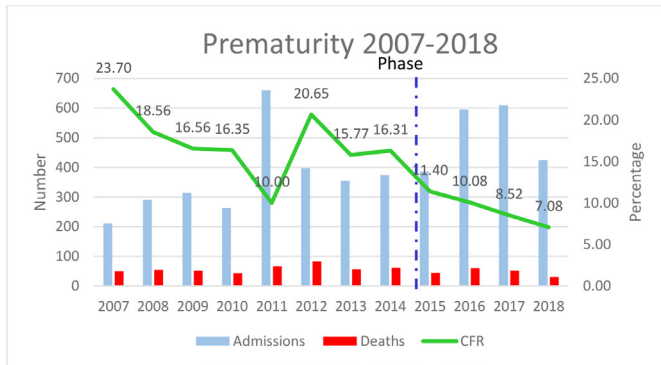
There was a 30% reduction in the overall number of deaths from phase I (8.2%) to phase II (5.7%) ( $p=0.001$ ). The CFR for prematurity reduced from 16.2% to 9.2% ( $p=0.001$ ), the CFR for asphyxia also reduced from 14.9% to 13% ( $p=0.34$ ) while that of other causes reduced from 5.6% to 2.4% ( $p=0.001$ ). Sepsis, on the other hand, had more than a twofold increased (3.0% to 6.8%,  $p=0.001$ ) ([table 3](#), [figures 2–4](#)).

The overall mortality reduced at an annual rate of 7.7 deaths per year (95% CI, 10.5 to  $-4.9$ ,  $p=0.002$ ) after implementation of phase II. Interrupted time series

**Table 3** Case fatality rate by condition

	Phase I (2007–2014) secondary level			Phase II (2015–2018) tertiary level			P value
	Admissions	Deaths	CFR	Admissions	Deaths	CFR	
Asphyxia	2438	363	14.9	885	115	13.0	0.34
Prematurity	2865	464	16.2	2015	186	9.2	0.001
Sepsis	4195	127	3.0	1504	102	6.8	0.001
Other	6877	387	5.6	4537	109	2.4	0.001
Total	16375	1341	8.2	8941	512	5.7	0.001

CBC, Cell Blood Count ; CFR, case fatality rate; KMC, Kangaroo Mother Care.



**Figure 2** Case fatality for prematurity phase I (2007–2014) and phase II (2015–2018). CFR, case fatality rate.

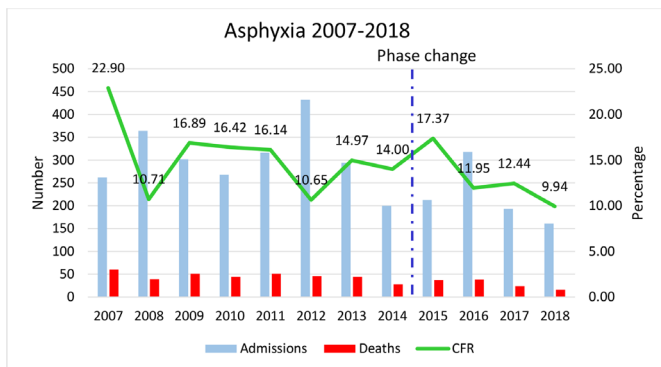
analysis using regression with Newey-West standard errors was performed. The number of asphyxia deaths decreased by 2.5 deaths per year during phase I ( $p=0.064$ ) and by 5.2 ( $p=0.028$ ) during phase II. Deaths due to prematurity had an increasing trend of 2.4 per year ( $p=0.082$ ) in phase I and had a decreasing trend of 7.4 deaths per year in phase II. Mortality due to sepsis increased by 0.3 deaths per year in phase I and increased by 7.2 deaths per year in phase II,  $p=0.0037$  (table 4 and figure 5).

## DISCUSSION

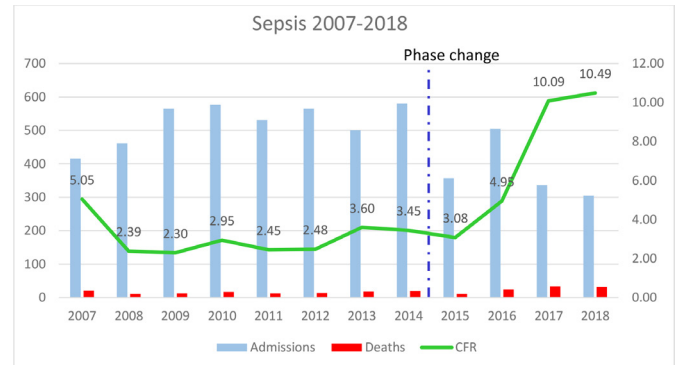
Evidence for the effectiveness of packages of hospital-based care for sick and preterm infants is scarce, both high-income countries and in low income and middle-income countries, since trials tend to focus on the incremental gains of single interventions. This is one of few studies to evaluate the trends in inpatient mortality and case fatalities for prematurity, asphyxia, sepsis following the implementation of a package of secondary and tertiary interventions in a low-resource setting in Uganda.

### Overall mortality reduction

Our approach led to a significant reduction in mortality of the small and sick newborns by over 30% over the eleven-year period. Reducing these deaths required high coverage of good quality care at birth, and inpatient care for small and sick newborns. This included: provision of warmth, feeding support, safe oxygen therapy and



**Figure 3** Case fatality rates for asphyxia in phase I (2007–2014) and phase II (2015–2018). CFR, case fatality rate.



**Figure 4** Case fatality for sepsis phase I (2007–2014) and phase II (2015–2018). CFR, case fatality rate.

effective phototherapy with prevention and treatment of infections. Inpatient care for newborns requires dedicated ward space, staffed by health workers with specialist training and skills. A delphi exercise estimated that optimal supportive care in a hospital special care baby unit could avert 70% of neonatal deaths due to preterm birth complications, and that 90% could be averted with availability of hospital neonatal intensive care units.<sup>5</sup> Another study reported that neonatal deaths would be reduced by half if there was appropriate investment in special care units and the neonatal intensive care an appropriate respiratory support to preterm.<sup>6</sup> A similar study in eastern Uganda, that used a phased approach including improving infrastructure, staff skills and equipment, showed a significant reduction in neonatal mortality from level 1 to level 2 neonatal care.<sup>11</sup> Studies from Congo and South Africa reported improvement in care newborns following training and mentorships; however, they reported they were not able to improve infrastructure and equipment.<sup>13 14</sup>

Lack of neonatal nursing skills has been identified as one of the major challenges in improving the management of small and sick newborns. The recommended nurse-to-patient ratio is 1:1 in neonatal intensive care units.<sup>15</sup> In our study, the nurse-to-patient ratio improved from 1:10 to 1:4 in the neonatal intensive care unit. The improved ratio improved monitoring and facilitated earlier detection of sick neonates. Additionally, there was improvement in the nursing skills through bed side teaching. The skills included: monitoring of critically neonates, use of bubble CPAP (bCPAP), infection control, advanced neonatal resuscitation, management of hypothermia, improved feeding of sick neonates and more frequent monitoring.

The other explanation for reduction in the mortality is that the interventions implemented addressed the first 24 hours of birth. The highest risk for mortality is the day a neonate is born.<sup>16</sup> According to studies conducted in the Gambia and Uganda, over 50% of the neonates died in the first 24 hours.<sup>17 18</sup> Furthermore, hypothermia on admission was reported to be as high as 45% in both studies.<sup>17 18</sup> Hypothermia at admission increases neonatal mortality by 28%–75% among preterm neonates.<sup>19</sup> It is

**Table 4** Annual trend comparing the period before and after institution of the tertiary care package using interrupted series

Condition	Deaths, 2007	2007–2014		2015–2018	
		Annual trend	P value	Annual trend	P value
Asphyxia	56.5	-2.5 (-5.1 to 0.2)	0.064	-5.2 (-9.8 to -0.7)	0.028*
Prematurity	47.3	2.4 (-0.4 to 5.1)	0.082	-7.4 (-18 to 3.2)	0.147
Sepsis	14.4	0.3 (-1.3 to 1.9)	0.657	6.9 (2.7 to 11.0)	0.005*
Other	36.8	2.6 (-5.5 to 10.7)	0.484	-7.7 (-18.7 to 3.3)	0.145

also known to reduce surfactant production thus increase the incidence of respiratory distress syndrome in preterm infants. In our study, we reduced hypothermia at admission, by provision of radiant warmers in the delivery rooms and training of the health workers to use them. Skin-to-skin care was implemented for the stable neonates. Additionally, all the high-risk neonates were transported to the newborn unit from the labour ward or theatre using a low-cost warm transport cot and exothermic mattress. Studies using exothermic mattresses for transport have reported reduced incidence of hypothermia compared with plastic wraps alone.<sup>20</sup> Hypothermia increases respiratory distress, hypoglycaemia and metabolic acidosis.

According to studies from Mulago and the Gambia, over 50% of preterm infants died within the 48 hours and the majority had respiratory distress.<sup>17 18</sup> Initiation of CPAP in the delivery room has been found to reduce mortality and need for mechanical ventilation by 50%.<sup>21</sup> Combining this with improvement in thermal management at birth may explain the drop in mortality in 2018 (4.3%).

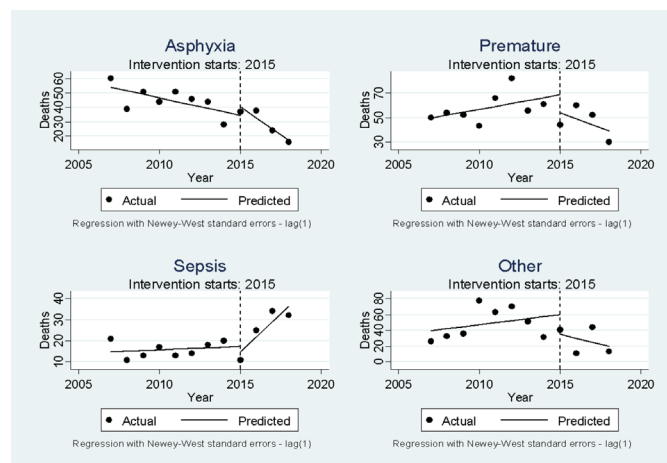
### Prematurity-related mortality

The CFR for prematurity was reduced by more than half. One of the major interventions was the introduction of kangaroo care, which has been shown to reduce mortality and morbidity in low-resource settings by 40% and 34%, respectively.<sup>22</sup> In our setting, the facilitators for implementation of KMC (Kangaroo Mother Care) were strong leadership, training and mentorship, availability of space

and algorithms to guide when to initiate and discharge neonates in KMC.

CPAP for preterm infants with respiratory distress syndrome reduces both intensive care admissions (by 53%) and mortality (48%) and when used effectively, can reduce the need for mechanical ventilation by 30%–50%.<sup>23 24</sup> In resource-limited settings, CPAP has been reported to improve survival of preterm neonates by 27%.<sup>25</sup> The introduction of CPAP in the delivery room has been shown to reduce need for surfactant and mechanical ventilation by 56% in high resource settings.<sup>21</sup> In our study, improved staffing, frequent mentorship and training and the use of clinical algorithms were key factors that likely facilitated the appropriate use of bCPAP. Other studies have also reported mentorship, frequent training and the use of clinical algorithms can improve the use of CPAP in low-resource limited settings.<sup>26–28</sup>

The use of animal derived surfactant in preterm infants with established respiratory distress syndrome is associated with substantial decreases in risks of pneumothorax (by 58%), pulmonary interstitial emphysema (55%) and neonatal mortality (32%).<sup>29</sup> The introduction of surfactant administration in 2014 in our hospital likely contributed to the further reduction in prematurity-related deaths. Although surfactant is not yet available in many LICs, as demonstrated in this study, it can be given safely under the supervision of experienced personnel. Other interventions that may have improved our preterm mortality include; the exclusive use of breast milk and donor human breast milk for preterm infants and the improvement of infection control measures.



**Figure 5** Interrupted series analysis for asphyxia, prematurity, sepsis and other causes of neonatal deaths.

### Asphyxia-related mortality

In our study, asphyxia related mortality was 15.9% before the intervention and 13.9% after the intervention. This is similar to other studies where reduction in neonatal mortality fell among 15%, 30% and 47% after introduction of neonatal resuscitation programmes.<sup>30–32</sup> In another study from the National Referral Hospital in Uganda, where midwives were trained and attended all the deliveries, a reduction in asphyxia admissions but not mortality was reported.<sup>33</sup> Additionally, evidence from high-income settings, suggests that therapeutic hypothermia could reduce neonatal mortality by 25% and major neurodevelopmental disabilities by 23%.<sup>34</sup> Although high rates of infection have been noted in LICs, in our unit there was a reduction in the asphyxia

related mortality after introduction of therapeutic hypothermia.

### Sepsis-related mortality

There was a relative increase in the case fatality of sepsis from 3.6% to 6.8% in our neonatal unit and may represent an increase in hospital acquired infections. The increment could be explained by the increasing numbers of preterm admissions 500 (phase II) compared with 358 (phase I) annually, this may have led to overcrowding. The recommended spacing in between neonatal cots is 1 m; this was not achievable in our setting.

Neonatal sepsis is also difficult to diagnose, the signs can be subtle and non-specific and in settings where little or no laboratory support exists and clinical care is basic, the diagnosis is challenging.<sup>35</sup> In phase I of our study, we did not use septic markers to diagnose sepsis, and relied on clinical algorithms that may have underestimated the number of neonates that died due to sepsis. In phase II we used blood cultures and C reactive protein, hence we were confidently able to diagnose sepsis.

### Strengths and limitations

One of the strengths of this study was the large number of small and sick newborns included and were studied over a period of 11 years. It highlights the steps taken to implement both secondary and tertiary interventions over time and the impact of these on mortality. It also highlights the burden of sepsis that is sometimes not emphasised in our setting. As this is a retrospective study, we were reliant on routinely recorded information. While information on the majority of the relevant variables was available in the routine records, this information was missing for some neonates, for example, like gestational age, time of death. As this information is likely not to be missing at random, this missing information may limit the generalizability of the findings.

### Conclusion

Implementation of secondary and tertiary interventions reduces mortality from preterm and asphyxia. However, there was an increase in sepsis related deaths, therefore more attention and emphasis should be done to improve infection control and reduce the case fatalities for sepsis.

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**Contributors** VNK drafted the study protocol, design, data collection, analysis and writing up the manuscript and takes full responsibility in the publication of this work. She also acts as the guarantor. FN analysed the data and writing up of the manuscript. RNazziwa, SN, RNasiima, SR, IN, CN, GL, PP, MMA and LO took

part in writing up the study and patient care for the neonates. IN took part in data collection. KB and HB contributed to the data analysis and writing up and editing of the manuscript.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

**Patient consent for publication** Not applicable.

**Ethics approval** Permission to review these data was sought from the administration and ethical approval obtained from the local IRB council at Nsambya Hospital the Rec Number was UG REC-020.

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**Data availability statement** Data are available upon reasonable request. Data can be available from the Nsambya Hospital records department upon a reasonable request. ORCID-0000-0002-6947-9298.

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