BMJ Open Morbidity and trends in length of hospitalisation of very and extremely preterm infants born between 2008 and 2021 in the Netherlands: a cohort study

Karen de Bijl-Marcus , ¹ Manon J N L Benders, ¹ Jeroen Dudink, ¹ Kees Ahaus , ² Marijn Kahlmann, ¹ Floris Groenendaal

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¹Department of Neonatology, Universitair Medisch Centrum Utrecht-Locatie Wilhelmina Kinderziekenhuis, Utrecht, The Netherlands

²Erasmus School of Health Policy & Management, Erasmus Universiteit Rotterdam, Rotterdam, The Netherlands

Correspondence to

Dr Karen de Bijl-Marcus; k.a.marcus@umcutrecht.nl

ABSTRACT

Objectives This study investigated changes in the length of stay (LoS) at a level III/IV neonatal intensive care unit (NICU) and level II neonatology departments until discharge home for very preterm infants and identified factors influencing these trends.

Design Retrospective cohort study based on data recorded in the Netherlands Perinatal Registry between 2008 and 2021.

Setting A single level III/IV NICU and multiple level II neonatology departments in the Netherlands.

Participants NICU-admitted infants (n=2646) with a gestational age (GA) <32 weeks.

Main outcome measures LoS at the NICU and overall LoS until discharge home.

Results The results showed an increase of 5.1 days (95% Cl 2.2 to 8, p<0.001) in overall LoS in period 3 after accounting for confounding variables. This increase was primarily driven by extended LoS at level II hospitals, while LoS at the NICU remained stable. The study also indicated a strong association between severe complications of preterm birth and LoS. Treatment of infants with a lower GA and more (severe) complications (such as severe retinopathy of prematurity) during the more recent periods may have increased LoS.

Conclusion The findings of this study highlight the increasing overall LoS for very preterm infants. LoS of very preterm infants is presumably influenced by the occurrence of complications of preterm birth, which are more frequent in infants at a lower gestational age.

INTRODUCTION

Length of stay (LoS) at the neonatal intensive care unit (NICU) is an important indicator of clinical outcomes and (economic) performance of the healthcare system. 1 2 Predicting LoS is crucial for resource planning, decision-making and parental counselling. Many factors influence LoS, including infant characteristics, quality and complexity of care, management and the availability of postdischarge healthcare facilities. 1 3 4 Trends towards shorter hospital stays have been observed for many hospital populations

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ One of the first studies to provide information regarding the total duration of hospital stays for very preterm infants until discharge home, encompassing both the length of stay (LoS) at the level III neonatal intensive care department and LoS at the level II departments.
- ⇒ Examines LoS in a single, relatively large neonatal intensive care unit over a relatively long period of
- ⇒ Organisational factors such as bed capacity were not included or accounted for in the analysis. It provides no data regarding maternal or pregnancyrelated factors, foetal death, death before admission or infants for whom intensive care treatment was not initiated in the delivery room.

within developed countries, attributed to enhanced patient outcomes and the delivery of more efficient care.⁵⁻⁷ During the final decade of the previous century, the Vermont-Oxford Network and others reported similar trends of decreasing LoS at the NICU.89 In more recent years, NICUs have implemented multiple interventions to facilitate the safe and earlier discharge of (very) preterm infants. 10-14 However, despite the implementation of these interventions, recent studies conducted in multiple developed countries have shown a consistent or even increased LoS at the NICU.8 15 16 Extended hospital stays put significant pressure on healthcare resources, which may jeopardise patient safety and escalate healthcare expenses. Such prolonged periods of hospitalisation not only heighten the risk of infants encountering healthcareassociated infections but also place substantial emotional and financial strain on their families. Moreover, an increase in LoS, when combined with restricted bed availability,



may necessitate more frequent patient transfers to facilities outside the region, further complicating care continuity and accessibility.

The cause of the stabilisation or increase in LoS is unknown. It is speculated that improvements in survival may have led to higher LoS since more infants at extremely low gestational age (GA) and/or with more severe health conditions survive to discharge. ^{8 15 16} If and how these changing population characteristics are related to the LoS at the NICU has not been elucidated. Furthermore, in several neonatal healthcare systems (including the Netherlands), infants are being transferred to a level II hospital to receive convalescent care (online supplemental file 1). Limited information is available regarding the overall duration of hospitalisation for preterm infants until they are discharged home after being transferred.

With the present study, we aim to investigate changes in the overall length of hospitalisation until discharge home, encompassing both the LoS at the NICU and the level II departments, for surviving preterm infants (GA <32 weeks) between 2008 and 2021. In addition, we aim to identify key variables that influence trends in LoS. These data could facilitate predicting LoS and possibly provide deeper knowledge of developments regarding the care demands of preterm infants.

METHODS

Study design

This study is a retrospective cohort study based on data from the Netherlands Perinatal Registry (www.perined. nl), which were completed by manual medical record review of all individual records. Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Study subjects

All infants born alive below 32 weeks gestation between 1 January 2008 and 31 December 2021, admitted to the level III/IV NICU of the Wilhelmina Children's Hospital of Utrecht, were eligible for inclusion. The exclusion criteria consisted of (1) major congenital anomalies (defined as chromosomal anomalies, congenital anomalies requiring surgery within the neonatal period and/or congenital anomalies incompatible with life) and (2) infants transferred from/to another level III/IV NICU.

Study period

The study period was divided into three subgroups:

- 1. 2008–2010: period in which infants with a GA <25 weeks were admitted to the NICU only by exception.
- 2. 2011–2015: first period after the revision of the Dutch perinatal guideline, lowering the threshold to offer active treatment from 25 to 24 weeks of gestation.
- 3. 2016–2021: for trend analyses, a third period was studied.

Setting

The NICU of the Wilhelmina Children's Hospital is part of a Dutch university hospital with 24 level III/IV NICU beds and many paediatric medical subspecialists, including (neuro/cardiac) surgeons, ophthalmic and anesthesiologic subspecialists. The NICU is located in a highly regionalised area with four regional post-NICU/high care (HC) departments and three non-post-IC/HC units. A high percentage (>90%) of infants are transferred to level II hospitals for convalescent care. Infants are transferred when all of the following criteria are met: corrected GA ≥30 weeks, weight ≥1000 g, respiratory support consisting of nasal continuous positive airway pressure (nCPAP), humidified high-flow nasal cannula (HHFNC), or low flow, and no need for specialised intensive care treatment.

Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

Outcomes (of each period)

- ► Primary outcomes
 - Median LoS (days) at the NICU.
 - Median LoS (days) until discharge home (LoS NICU+LoS level II hospital).
- Secondary outcomes
 - In-hospital mortality rate, which was compared with the expected mortality rate calculated using a previously published prognostic model.^{17 18}
 - The morbidity rate of each period is defined as a composite variable of at least one of the following complications: chronic lung disease (CLD, defined as at least 28 cumulative days of oxygen therapy), intraventricular haemorrhage grade 3 (IVH-III), cerebral venous infarction (VI), posthaemorrhagic ventricular dilatation (PHVD) needing intervention, cystic periventricular leukomalacia (cPVL grade II/III), laser coagulation for retinopathy of prematurity (ROP) and necrotising enterocolitis with indication for surgery (NEC_s). 19 20
 - Type of respiratory support at the time of transfer since changing policies regarding (maximum) respiratory support at the time of transfer could affect LoS.
 - Readmission rate.
 - The association between LoS and variables such as period of birth, GA, birth weight less than the third percentile (small for GA (SGA), sex, antenatal corticosteroids, multiple pregnancies, Apgar score, outborn, caesarean section, CLD, duration of mechanical ventilation, IVH-III, VI, PHVD, cPVL, persistent ductus arteriosus (PDA) with treatment, ROP, NEC_s, late-onset sepsis, type of receiving level II department).

Efforts were made to retrieve the missing data. Hospital admission records were compared with local department

Table 1 Patient characteristics at the time of admission

Patient characteristics	Period 1: 2008–2010	Period 2: 2011–2015	Period 3: 2016–2021	
All included infants, including deceased	n=594	n=1034	n=1018	P value*
GA (weeks) at birth (median IQR) Number of infants with a GA at birth <25 weeks	30.0†‡ (28.3–31.0) 10	29.4† (27.4–30.9) 45	29.6‡ (27.7–30.9) 54	<0.001
Sex (% male)	50.8%‡	50.8%§	55.8%‡§	0.043
Birth weight in g (median IQR)	1265† (1000–1555)	1215§ (920–1475)	1263§ (970–1545)	0.001
Survivors	n=563 (94.8%)	n=969 (93.7%)	n=946 (92.9%)	P value*
GA (weeks) at birth (median IQR)	30.1†‡ (28.4–31.1)	29.7† (27.7–30.9)	29.7‡ (28.0–31.0)	0.001
Sex (% male)	51.2%	50.4%	55.3%	0.077
Birth weight in g (median IQR)	1300 (1035–1570)	1235§ (960–1498)	1285§ (1005–1573)	0.001
Birth weight percentile (median IQR)	-0.61‡ (-1.55-0.33)	-0.60§ (-1.59-0.14)	-0.43‡§ (-1.45-0.38)	0.004
Small for GA (% < 3rd percentile)	17.6%	17.5%	15.2%	0.317
Small for GA (% <10th percentile)	36.8%	37.5%	32.5%	0.054
Multiple pregnancy (%)	32.7%‡	27.9%	25.1%‡	0.006
Antenatal corticosteroids (% optimal)	53.6%‡	51.7%§	60.8%‡§	<0.001
Caesarean section (%)	54.7%	58.6%	53.9%	0.253
Inborn (%)	87.6%	86.6%	89.8%	0.081
Apgar score at 5 min (median IQR)	9†‡ (8–9)	8†§ (7–9)	8§‡ (7–9)	<0.001

^{*}Kruskal-Wallis.

databases. Missing data from level II units were corrected by letters and phone calls.

Statistical analysis

Patient characteristics and outcome variables were summarised as proportions, means and medians, where appropriate. We estimated changes in medians of primary and secondary outcomes during the study period using univariate analyses with 95% CIs. Generalised linear models were used to examine differences in LoS as a dependent variable across the three study periods, with GA, SGA, multiplicity and several neonatal complications (NEC, ROP, CLD and late-onset sepsis) as independent variables due to their well-known effect on length of hospital stay (see online supplemental appendix 2 for a complete list of tested variables based on textbook knowledge). Interactions between periods and complications were also tested. After step-by-step backwards removal of the variables that were not significant, that is, those with a p value greater than 0.05, the results of the final model, including the interactions, are presented. Statistical analyses were performed using Statistical Package for Social

Sciences for Windows V.29 (SPSS, Chicago, Illinois, USA) and R statistical software (http://www.r-project.org).

RESULTS

Overall, 2646 infants were included in the study. Of the 2776 live births below 32 weeks, 90 infants were excluded due to major congenital anomalies and 40 due to transfer from/to another NICU. Patient characteristics (potentially) affecting the LoS of the included infants during the three study periods are presented in tables 1-3. There were significant differences between study periods regarding median GA, sex, birth weight, duration of mechanical ventilation and treatment of PDA. Furthermore, the incidence of late-onset sepsis and severe ROP varied between study periods. In period 3, infants were more often transferred to a level II department while receiving intensive forms of non-invasive respiratory support, such as HHFNC or nCPAP (table 4). LoS at the NICU was available for all 2646 infants. The total duration of LoS until discharge home was available for 2256 of 2478 surviving infants (91%). Patient characteristics at

[†]Statistically significant difference between period 0 and period 1.

[‡]Statistically significant difference between period 0 and period 2.

Statistically significant difference between period 1 and period 2.

GA, gestational age.

Patient characteristics	Period 1: 2008–2010	Period 2: 2011–2015	Period 3: 2016–2021 n=1018	P value*	
All included infants, including deceased	n=594	n=1034			
In-hospital mortality number (%)	31 (5.2%)	65 (6.3%)	72 (7.1%)	0.336	
Survival rate (%)	94.8%	93.7%	92.9%	0.336	
Expected survival rate (mean survival prediction)†	92.5% ^{@#}	89.6% ‡	90.2% §	<0.001	
Survivors	n=563 (94.8%)	n=969 (93.7%)	n=946 (92.9%)	P value*	
Intraventricular haemorrhage grade 3 and/or cerebral venous infarction (%)	5.7%	4.5%	3.7%	0.196	
Posthaemorrhagic ventricular dilatation (%)	1.2%	1.0%	1.7%	0.443	
Cystic periventricular leukomalacia (%)	0.5%	0.5%	0.5%	0.999	
Necrotising enterocolitis (%)	5.7%	7.4%	5.8%	0.255	
Necrotising enterocolitis with laparotomy (%)	2.5%	3.2%	3.4%	0.611	
Mechanical ventilation (% receiving mechanical ventilation)	42.6%§	45.1%¶	35.3%§¶	<0.001	
Chronic lung disease (%)	31.6%	37.0%	32.8%	0.059	
Medication for persistent ductus arteriosus (%)	15.1%	19.6%¶	14.5%¶	0.006	
Surgical ligation persistent ductus arteriosus (%)	3.0%	4.4%¶	1.9%¶	0.006	
Late-onset sepsis (%)	23.1%§	19.1%¶	14.6%§¶	<0.001	
Retinopathy of prematurity with laser coagulation (%)	0.2%‡§	1.3%‡	2.1%§	0.007	
At least one major morbidity** (%)	34.1%	38.4%	35.4%	0.189	
No major morbidities (%)	65.1%	61.6%	64.6%		
1 major morbidity (%)	27.7%	30.3%	28.9%		

^{*}Kruskal-Wallis.

2 major morbidities (%)

>2 major morbidities (%)

3.9%

2.5%

5.6%

2.5%

the time of discharge and the effect of severe complications on LoS are presented in tables 3 and 4. LoS at the NICU and corrected GA at the time of transfer did not change significantly during the study period. However, the results approached statistical significance, indicating a trend towards longer durations of hospitalisation. Total LoS increased 5.1 days between period 1 and period 3 after accounting for confounding variables (95% CI 2.2 to 8.0, p<0.001) (table 5). LoS at the NICU, depending on GA and the occurrence of severe complications are shown in figure 1. LoS, depending on the presence or absence of various variables during the different time periods, is illustrated using boxplots (see online supplemental appendix 3). In table 5, the results of the multivariable analysis of LoS at the NICU and overall LoS are presented. Most infants with NEC were also diagnosed with CLD. In survivors, there was a difference in overall

LoS per period, adjusted for SGA, NEC, PHVD, CLD, late-onset sepsis and ROP. In the final model, some interactions were significant: the variables SGA, NEC and CLD had significantly different effects on LoS during the three time periods. In the final model of total LoS, the variables GA, mode of delivery, sex and multiple births were no longer significant. Exclusion of infants with a GA <25 weeks at the time of birth did not alter the observed results regarding trends in LoS (see online supplemental appendix 4).

4.1%

2.4%

DISCUSSION

Trends regarding overall LoS until discharge home

This study aimed to investigate changes in overall LoS, encompassing both the duration of stay at the NICU and the level II departments. After accounting for

[†]Survival prediction calculated using model described by van Beek et al.

[‡]Statistically significant difference between period 0 and period 1.

[§]Statistically significant difference between period 0 and period 2.

[¶]Statistically significant difference between period 1 and period 2.

^{**}At least one of the following neonatal complications: chronic lung disease (defined as at least 28 cumulative days of oxygen therapy), intraventricular haemorrhage grade III and IV (defined by Papile's classification), posthaemorrhagic ventricle dilatation requiring intervention, cystic periventricular leukomalacia grade II and III (defined by de Vries' classification), laser coagulation for retinopathy of prematurity and necrotising enterocolitis with indication for surgery.

GA, gestational age.



Table 3 Patient characteristics at the time of discharge during three time periods				
Discharge characteristics	Period 1: 2008–2010	Period 2: 2011–2015	Period 3: 2016–2021	P value*
All survivors	n=563	n=969	n=946	
Corrected GA (weeks) at the time of first discharge from the NICU (median IQR)	32.6 (31.9– 33.9)	32.4 (31.6– 34.1)	32.7 (31.9– 34.6)	0.051
LoS of first admission at the NICU (days) (median IQR)	18 (10–36)	17 (10–44)	20 (11–43)	0.060
Respiratory support at the time of first discharge from the NICU	None: 56%†¶ Low flow: 43% HHFNC: 0% nCPAP: 1%	None: 42%¶§ Low flow: 55% HHFNC: 1% nCPAP: 2%	None: 44%†§ Low flow: 20% HHFNC: 24% nCPAP: 12%	<0.001
Readmission rate (%)	8.0%	7.6%	5.5%	0.092
Infants transferred to level II department (%)	98%†	96%	94%†	0.002
Infants transferred home from level II hospital (%)	95%	94%	92%	0.070
Corrected GA (weeks) at the time of discharge home (from NICU or level II hospital) (median IQR)	37.4†¶ (36.6–39.0)	37.9¶ (36.7–39.9)	38.0† (36.9–40.0)	<0.001
Total duration hospitalisation NICU (days) (median IQR)	18 (11–39)	18 (10–45)	21 (11–44)	0.070
Total duration hospitalisation level II hospital (days) (median IQR)	32*¶ (27–40)	36¶ (28–45)	35†(28–45)	<0.001
Total duration hospitalisation: NICU+level II hospital (days) (median IQR)	55*¶ (44–72)	60¶ (45–84)	61† (46–82)	<0.001
Survivors without major morbidities‡	n=371	n=597	n=611	
Corrected GA (weeks) at the time of first discharge from the NICU (median IQR)	32.3¶	32.0¶§	32.1§	<0.001
LoS of first admission at the NICU (median IQR)	13¶ (8–18)	11§¶ (8–15)	13§ (8–20)	<0.001
Corrected GA (weeks) at the time of discharge home (from NICU or level II hospital) (median IQR)	37.0 (36.3–38.3)	37.1§ (36.3–38.3)	37.3§ (36.6–38.6)	0.017
Total duration hospitalisation: NICU+level II hospital (days) (median IQR)	48† (40–58)	49§ (41–59)	51†§ (42–63)	0.020
Survivors with at least one major morbidity ‡	n=192	n=372	n=335	
Corrected GA (weeks) at the time of first discharge from the NICU (median IQR)	34.1§¶ (32.7–36.2)	35.0¶ (33.0–37.6)	35.1† (33.3–37.6)	0.003
LoS of first admission at the NICU (median IQR)	45†¶ (33–60)	53¶ (38–76)	52† (38–76)	0.001
Corrected GA (weeks) at the time of discharge home (from NICU or level II hospital) (median IQR)	38.6†¶ (37.4–40.9)	39.9¶ (38.1–42.1)	40.0† (38.3–42.1)	<0.001
Total duration hospitalisation: NICU+level II hospital (days) (median IQR)	77†¶ (64–94)	90¶ (74–110)	88† (71–109)	<0.001

^{*}Kruskal-Wallis test

confounding variables, we found a median increase of 6 days in the overall LoS for surviving preterm infants born below 32 weeks of gestation between 2008 and 2021. This increase was primarily driven by extended stays at level II hospitals. Similar trends of increased LoS have been reported in other recent studies.^{8 15 16} However,

these studies did not differentiate between or include the LoS at the NICU and the level II hospitals.

Variables influencing LoS

We observed a strong association between severe complications of preterm birth and LoS at the NICU, as well as

[†]Statistically significant difference between period 0 and period 2.

[‡]At least one of the following neonatal complications: chronic lung disease (defined as at least 28 cumulative days of oxygen therapy), intraventricular haemorrhage grade III and IV (defined by Papile's classification), posthemorrhagic ventricle dilatation requiring intervention, cystic periventricular leukomalacia grade II and III (defined by de Vries' classification), laser coagulation for retinopathy of prematurity and necrotising enterocolitis with indication for surgery.

[§]Statistically significant difference between period 1 and period 2.

[¶]Statistically significant difference between period 0 and period 1.

GA, gestational age; HHFNC, humidified high-flow nasal cannula; LoS, length of stay; nCPAP, nasal continuous positive airway pressure; NICU, neonatal intensive care unit.

Table 4 Patient characteristics at the time of discharge depending on type of receiving level II department

	Non-postintensive care/high			
Discharge characteristics	care level II department n=699 (31%)	Postintensive care/high care level II department n=1606 (69%)	P value*	
GA at birth (weeks) (median IQR)	30.3 (28.6–31.1)	29.7 (28.0–30.9)	<0.001	
At least one major morbidity† (%)	33.5%	33.7%	0.899	
Corrected GA at the time of first discharge from the NICU (weeks) (median IQR)	32.9 (32.1–34.6)	32.3 (31.4–33.6)	<0.001	
Respiratory support at the time of first discharge from the NICU (%)	None: 55% Low flow: 38% HHFNC: 6% nCPAP: 1%	None: 38% Low flow: 43% HHFNC: 12% nCPAP: 7%	<0.001	
Corrected GA at the time of discharge home (weeks) (median IQR)	38.0 (37.0–39.7)	37.6 (36.6–39.4)	0.001	

^{*}Mann-Whitney U test.

GA, gestational age; HHFNC, humidified high-flow nasal cannula; nCPAP, nasal continuous positive airway pressure; NICU, neonatal intensive care unit.

overall LoS. Infants without severe complications exhibited a consistent LoS at the NICU, with a modest increase of 3 days in the overall hospitalisation during the study period. In contrast, infants experiencing at least one severe complication showed a substantial prolongation of 7 days in NICU stays and an overall hospitalisation increase of 11 days. We hypothesise that (the treatment of) severe ROP may have contributed to this extended hospitalisation, considering the observed rise in the incidence of this complication during the study period. These findings underscore and confirm the significant impact of complications on the LoS of very preterm infants.²¹ This emphasises the importance of comprehensive care and tailored interventions to address the complexities associated with these medical illnesses.

Complications of preterm birth were strongly associated with LoS when compared with GA. However, extremely preterm infants are more prone to experiencing severe complications associated with preterm birth, for example, all infants with a GA of 24 weeks developed CLD.8 Our observations indicate that the treatment of infants with a lower GA at the time of birth (related to lowering the threshold for active treatment) and treating infants with severe complications of preterm birth may have contributed to an increased LoS. This supports previous research suggesting that the treatment of extremely preterm infants has a significant impact on LoS.8 15 21-24 This is especially important considering the fact that the guideline is currently being evaluated in the Netherlands to determine whether the threshold should be lowered even further. The models described in this study can be used to predict the LoS of individual infants. Factors most strongly associated with LoS were severe complications of preterm birth occurring relatively late during the NICU stay (eg, CLD and ROP).

Trends regarding morbidity and mortality

Our findings did not show an improved survival rate, which suggests that the prolonged LoS cannot be directly attributed to more vulnerable infants surviving to discharge. However, the overall survival rate is a crude measure that might not capture all dynamic changes. A small number of vulnerable infants surviving could drive a change in LoS without changing overall survival rates. It is possible that the sample size was not large enough to investigate this aspect in more detail. Our study did reveal several improvements in outcome and care. We observed a decrease in the frequency and median duration of mechanical ventilation, as well as a decline in the incidence of late-onset sepsis. These positive changes, along with a stable mortality rate and a lower median GA at birth, are encouraging. They suggest advancements in preventive strategies and the overall care provided to these vulnerable infants. Furthermore, in all three periods, the observed mortality was lower than the mortality predicted by the model of van Beek et al. 18 The increased incidence of severe ROP was expected due to the revision of guidelines regarding saturation thresholds during the study period.²

Changing patterns of transfer

Traditionally, level II hospitals primarily received infants who were considered 'feeders' and 'growers' requiring minimal respiratory support after being transferred from a NICU.²⁶ In contrast, our study revealed a shifting trend, with more infants requiring intensive forms of

[†]At least one of the following neonatal complications: chronic lung disease (defined as at least 28 cumulative days of oxygen therapy), intraventricular haemorrhage grade III and IV (defined by Papile's classification), posthemorrhagic ventricle dilatation requiring intervention, cystic periventricular leukomalacia grade II and III (defined by de Vries' classification), laser coagulation for retinopathy of prematurity and necrotising enterocolitis with indication for surgery.

Table 5 Model most accurately describing the association between LoS and perinatal variables of surviving infants

	•	Model dependent variable LoS at the NICU (days)		Model: dependent variable verall LoS (days) hospital (NICU+level II)		
	Coefficient	of the model with 95% CI	Coefficient of th	ne model with 95% CI		
Constant	14.9	12.9 to 16.9	48.2	45.9 to 50.5		
Factors	Additional of 'constant'	days of admission on top of	Additional days of 'constant'	of admission on top of		
SGA	2.3	0.6 to 3.9	7.4	2.8 to 12.1		
Multiplet	2.0	0.6 to 3.5				
Period 2	-1.2	−3.1 to −0.8	2.0	-0.9 to 4.9		
Period 3	1.9	-0.1 to 3.9	5.1	2.2 to 8.0		
CLD	35.2	32.4 to 38.1	30.5	26.6 to 34.4		
NECs	-2.2	-11.7 to 7.8	-4.2	-15.6 to 7.3		
PHVD intervention	18.4	11.7 to 25.0	14.3	7.1 to 21.6		
ROP intervention	38.1	31.1 to 45.1	29.6	22.0 to 37.3		
Late-onset sepsis	5.2	3.5 to 6.9	5.9	3.6 to 8.1		
Discharge to post-IC/HC department	-3.2	−4.6 to −1.7				
Extra days CLD period 2	4.4	0.9 to 7.9	9.1	4.3 to 13.9		
Extra days CLD period 3	5.5	1.9 to 9.1	8.2	3.3 to 13.1		
Extra days NECs period 2	16.5	4.4 to 28.6	34.1	20.4 to 47.7		
Extra days NECs period 3	5.8	-5.9 to 17.5	-0.9	-14.8 to 12.9		
Extra days SGA period 2			-6.3	−12.0 to −0.5		
Extra days SGA period 3			-7.9	-13.91.9		

Model LoS at the NICU.

LoS (days)=14.9+(2.3*SGA)+(2.0*Multiplet)+(-1.2*Period 2)+(1.9*Period 3)+(5.2*late-onset sepsis)+(-2.2*necrotising encerocolitis with laparotomy)+(16.5*Period 2*necrotising encerocolitis with laparotomy)+(5.8*Period 3*necrotising encerocolitis with laparotomy)+(18.4*PHVD with intervention)+(35.2*CLD)+(4.4*Period 2*CLD)+(5.5*Period 3*CLD)+(38.1*ROP with intervention)+(-3.2*discharge to post-IC/HC). Model overall LoS.

LoS (days)=48.2+(7.4*SGA)+(-6.3*Period 2*SGA)+(-7.9*Period 3*SGA)+(2.0*Period 2)+(5.1*Period 3)+(5.9*late-onset sepsis)+(-4.2*necrotising encerocolitis with laparotomy)+(34.0*Period 2*necrotising encerocolitis with laparotomy)+(-0.9*Period 3*necrotising encerocolitis with laparotomy)+(14.3*PHVD with intervention)+(30.5*CLD)+(9.1*Period 2*CLD)+(8.2*Period 3*CLD)+(29.6*ROP with intervention). CLD, chronic lung disease; IC/HC, intensive care/high care; LoS, length of stay; NEC, necrotising enterocolitis with indication for surgery; NICU, neonatal intensive care unit; PHVD, posthaemorrhagic ventricle dilatation; ROP, retinopathy of prematurity; SGA, small for gestational age.

non-invasive respiratory support (HHFNC or CPAP) being transferred. This change can be attributed to the increasing demands on our NICU, operating at full capacity, due to a growing population of (extremely premature) infants with higher care needs and staffing issues.²⁷ Transferring stable, yet still vulnerable, infants who require intensive non-invasive respiratory support is necessary to optimise resource utilisation and maintain access to care. 28-30 However, the transfer of these complex infants necessitates close coordination and communication among healthcare providers to ensure patient safety. Despite the increasing complexity and higher care needs, our study did not observe an increase in readmission rates during the study period. This finding suggests that healthcare providers at level II hospitals have adapted to the changing needs of these infants and are providing effective treatment. Furthermore, our results revealed that infants transferred to post-IC/HC level II departments

more frequently were on intensive respiratory support and had a lower corrected GA at the time of transfer compared with non-post-IC/HC facilities. It is intriguing to note that despite these factors, infants transferred to post-HC departments were discharged home at a lower corrected GA. Exploring these differences in future research may help optimise care pathways and provide insights into ways to reduce LoS.

Potential consequences of increasing LoS

Despite multiple interventions aimed at reducing LoS and transferring infants to intensive non-invasive respiratory support, our study revealed an increased overall LoS and longer LoS at the NICU for infants with major morbidities. This prolonged hospitalisation has significant consequences that need to be considered. From a healthcare perspective, the increased LoS places *additional strain on resources*, especially when NICUs are already

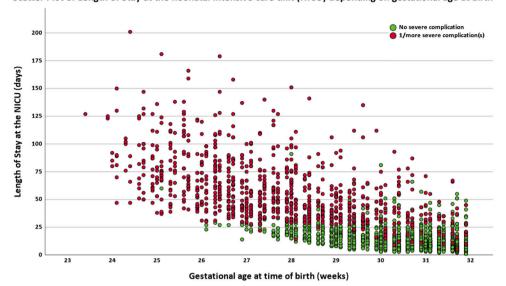


Figure 1 Scatter plot indicating the length of stay at the neonatal intensive care unit of surviving infants depending on gestational age at the time of birth and the occurrence of severe complications. The severe complication was defined as one/more of the following neonatal complications: chronic lung disease (defined as at least 28 cumulative days of oxygen therapy), intraventricular haemorrhage grade III and IV (defined by Papile's classification), posthaemorrhagic ventricular dilatation requiring intervention, cystic periventricular leukomalacia grade II and III (defined by de Vries' classification), laser coagulation for retinopathy of prematurity and necrotising enterocolitis with an indication for surgery. All infants born at a gestational age of 24 weeks and most of the infants born at 25 weeks gestation showed one or more complications.

operating at maximum capacity. 1 2 4 15 31-33 Reaching or exceeding the capacity can lead to compromised patient safety and place additional strain on healthcare providers. Moreover, reports have indicated a direct correlation between increased LoS and higher healthcare expenditure. 15 For the *infants themselves*, the extended hospitalisation may result in adverse outcomes since the NICU environment is associated with risks such as healthcareassociated infections. 1 34-36 Furthermore, the prolonged LoS influences the *families* of the infants in various ways. Parents may experience increased emotional and financial burdens due to the prolonged separation from their infants and the need to balance work and other responsibilities.³⁷ Efforts to optimise LoS are closely linked to those enhancing the quality of care and are both vital for improving patient outcomes, optimal resource utilisation and minimising healthcare costs. 15 16 Our findings indicate that focusing on reducing the occurrence of severe complications associated with preterm birth could positively impact both LoS at the NICU and overall LoS.

LIMITATIONS

This study examines LoS in a single, although relatively large, NICU. Previous research has identified variations in LoS across different healthcare systems. ^{7 16} Our NICU is located in a highly regionalised area, with a high percentage of infants being transferred. The generalisability of our findings may be limited in less regionalised areas. Additionally, organisational factors such as bed capacity were not included and accounted for in our study. In addition, we have no data regarding foetal

deaths, deaths before admission to the NICU, or infants for whom it was decided not to initiate intensive care treatment in the delivery room. Another limitation is the fact that variables such as socioeconomic status, ethnicity and pregnancy-related complications were not included.

CONCLUSION

Our findings demonstrate a significant increase in overall LoS for infants born with a GA below 32 weeks between 2008 and 2021. This increase is primarily driven by the treatment of extremely premature infants and those experiencing severe complications. The prolonged LoS could potentially have far-reaching implications for healthcare systems, families and the infants themselves. Using this information, parents could be better informed about the expected LoS of their preterm born infant. In addition, knowledge of the influence of complications on LoS could guide the benchmarking of NICUs in order to reduce these complications.

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Ethics approval The data of patients were pseudonymizsed before analysis, and stored according to European requirements. The Medical Research Ethics Committee of Utrecht granted exemption from formal approval under the Dutch Medical Research Involving Human Subjects Act for the study, using pseudonymizsed data (NedMec; number 22/588). Due to the utilisation of pseudonymizsed data, the size of the cohort and the retrospective design of the study, informed consent was noteither sought nor required from participants.

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ORCID iDs

Karen de Bijl-Marcus http://orcid.org/0000-0001-5116-6092 Kees Ahaus http://orcid.org/0000-0001-9973-3746

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