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ABSTRACT

Objective In response to the increasing focus on family-centred care, neonatal intensive care unit (NICU) environments have gradually shifted towards the single-room design. However, the assumed benefits of this emerging design remain a subject of debate. Our goal was to evaluate the impact of single-room versus open-bay care on the risk of neonatal morbidity and mortality in preterm neonates.

Design Retrospective cohort study.

Setting Level III NICU.

Patients Neonates born <32 weeks' gestation between 15 May 2015 and 15 May 2019.

Main outcome measures Mortality and morbidities of a cohort of neonates admitted to a new, single-room unit (SRU) were compared with a historical cohort of neonates admitted to an open-bay unit (OBU). Group differences were evaluated and multivariable logistic regression analyses were performed.

Results Three-hundred and fifty-six and 343 neonates were admitted to the SRU and OBU, respectively. No difference in neonatal morbidities and mortality were observed between cohorts (bronchopulmonary dysplasia: OR 1.08, 95% CI 0.73 to 1.58, p=0.44; retinopathy of the prematurity stage ≥2: OR 1.36, 95% CI 0.84 to 2.22, p=0.10; intraventricular haemorrhage: OR 0.89, 95% CI 0.59 to 1.34, p=0.86; mortality: OR 1.55, 95% CI 0.75 to 3.20, p=0.28). In adjusted regression models, single-room care was independently associated with a decreased risk of symptomatic patent ductus arteriosus (adjusted OR 0.54, 95% CI 0.31 to 0.95). No independent association between single-room care and any of the other investigated outcomes was observed.

Conclusions Implementation of single-rooms in our NICU did not lead to a significant reduction in neonatal morbidity and mortality outcomes.

What is already known on this topic

⇒ Following advances in perinatal-care management that have led to improved survival rates among preterm neonates, calls for an improved neonatal intensive care unit (NICU) environment have grown.
⇒ The architectural design of NICUs has gradually shifted away from the traditional open-bay towards single-room model of care.
⇒ Reported effects of single-room care on short-term and long-term neonatal outcomes, however, have been mixed.

What this study adds

⇒ No significant difference in neonatal morbidities and mortality was observed between neonates admitted to a single-room versus open-bay NICU.

How this study might affect research, practice and/or policy

⇒ Given that single-room care embodies not just a physical design, more research on other related factors such as staff workload and parental interaction is needed.
⇒ Our findings provide important evidence for all relevant stakeholders in neonatal care currently considering transition from open-bay to single-room unit NICUs.

INTRODUCTION

Preterm birth (<37 weeks of gestation) remains an important challenge in perinatal healthcare, accounting for approximately 8.7% of all live births in Europe.[1] As advances in perinatal-care management over the past two decades have led to improved survival rates among preterm neonates, the need for an optimal neonatal intensive care unit (NICU) environment has increased in parallel. There is increasing evidence that environmental features have a substantial impact on hospital and postdischarge outcomes in neonates.[2–4] Consequently, the architectural design of NICUs has gradually shifted away from the traditional open-bay towards single-room model of care, offering neonates and their family greater privacy and an individualised controlled environment to better meet their medical and developmental needs.[5] Despite the general paucity of clinical trial data comparing these two models of care on neonatal outcomes, several cohort studies have reported beneficial effects following NICU transformation to private-rooms, including shorter length of hospital

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stay, earlier transition to full enteral feed, fewer apnoeic events, increased breastfeeding rates and improved neurodevelopmental outcomes at 18 months of age.[2 6–8] Nevertheless, unfavourable effects have also been reported, including higher workloads, lower infant language scores at 2 years of age and increased maternal stress.[4 9 10] Moreover, results regarding the association between single-room care, hospital-acquired infection rates and colonisation with multidrug-resistant organisms likewise remain inconclusive.[6 11–15] As such, additional evidence describing the association between single-room care and a broad range of morbidity outcomes in preterm neonates is required in the decision to transition away from open-ward facilities.

On 15 May 2017, the Leiden University Medical Center (LUMC) completed the construction of a new level-III, single-room NICU to replace the previous open-bay ward. With this new construction came the opportunity to retrospectively analyse the impact of single-room versus open-bay care on a broad range of neonatal morbidity and mortality outcomes. We hypothesised that prematurely born neonates cared for in a single-room NICU have improved short-term neonatal morbidity and mortality outcomes compared with neonates cared for in a traditional open-bay NICU.

METHODS

Study design

This study was conducted as a retrospective cohort analysis comparing in-hospital medical outcomes of prematurely born neonates admitted to a new, single-room unit (SRU) with those admitted to a historical, open-bay unit (OBU) NICU. We compared two study periods of 2 years each (15 May 2015–14 May 12017 and 16 May 2017–15 May 2019), which, respectively, represent the periods prior to and after unit transition. Approval with a waiver of informed consent was granted by the institutional review board of the LUMC (G19.072).

Setting

The LUMC is a 2100-bed tertiary university-affiliated hospital located in Leiden, The Netherlands, serving Leiden and its greater surroundings. As of 15 May 2017, the hospital contains a 25-bed level-III NICU constructed as a single-room facility consisting of 17 single-patient rooms and 4 twin-rooms and annually admitting approximately 500–600 neonates. Each neonate is hospitalised in a single-room, with an average nurse-to-patient ratio of 1:1 and 1:2 for neonates with high and intermediate dependency care needs, respectively. All rooms allow parents to stay overnight and provide the space for skin-to-skin bonding and intimate involvement with daily care. Prior to the construction of the new SRU, the NICU consisted of three open-bay rooms, two of which served as 9-bed and 7-bed intensive care (IC) units and one as a 9-bed high-/post-IC unit. Depending on the complexity of care, the standard nurse-to-patient ratio was 1:2 and 1:3 in, respectively, the IC and high-/post-IC units.

Study subjects

Preterm neonates born at a gestational age (GA) of <32 weeks and admitted to the NICU between 15 May 2015 and 15 May 2019 were enrolled in this study. To eliminate overlap of care between the two nurseries, neonates born on the day of the unit transition and those admitted to both unit types were excluded from the analysis. Neonates with an admission duration <24 hours were also excluded. In line with Dutch national policy to offer full resuscitation and life support from 24 weeks' gestation onwards, neonates born below this limit were likewise excluded. Only data pertaining to first admissions were analysed.

Data collection and definitions

Data were extracted from hospital medical records covering the period from admission until hospital discharge. To determine group homogeneity, the following baseline neonatal characteristics were collected for all study participants: birth date, birth weight (BW), GA, sex, delivery mode (ie, caesarean section or vaginal delivery), multiple gestation, full or partial course of antenatal steroid treatment, postnatal steroid treatment, Apgar score at 5 min, presence of major congenital anomalies, presence of surgical pathology, surfactant treatment, exposure to invasive mechanical ventilation (ie, conventional mechanical ventilation with pressure support or high frequency oscillation) and length of hospital stay. Data pertaining to major neonatal morbidities and mortality included: symptomatic patent ductus arteriosus (sPDA) treated either medically with non-steroidal anti-inflammatory drugs or via surgical ligation, spontaneous intestinal perforation (SIP), bronchopulmonary dysplasia (BPD) including severity, retinopathy of prematurity (ROP) including stage, intraventricular haemorrhage (IVH) including timing of onset, cystic periventricular leukomalacia (cPVL), pneumothorax, hyperbilirubinemia requiring phototherapy, inotropic support, erythrocyte and thrombocyte transfusion need, (sub)clinical convulsions and in-hospital mortality. IVH was further classified into grades 1–3 (according to Volpe), with a separate notation for periventricular haemorrhagic infarction (PVHI) and/or posthaemorrhagic ventricular dilatation (PHVD).[16] High-grade IVH was defined as IVH grade 3 or any grade of IVH complicated by PVHI and/or PHVD. Necrotising enterocolitis and late-onset sepsis were not included as major morbidity outcomes as these outcomes have been previously reported on in relation to unit transition.[11] Data for neonates who were screened for BPD and ROP following discharge from the NICU were retrieved from the hospitals to which they were discharged to. Definitions pertaining to a select number of the above-mentioned outcomes are shown in online supplemental appendix 1.

Statistical analysis

Categorical variables were described as absolute numbers and percentages, and continuous variables as mean and SD or median and IQR, as appropriate. Univariate comparisons between the two units for neonatal characteristics and morbidity and mortality outcomes were examined using the χ^2 test and Fisher's exact test for categorical data and the independent *t* test and Mann-Whitney U test for continuous data, as appropriate. Multivariable logistic regression models were developed to determine the independent association between unit type and rates of sPDA, moderate-severe BPD, ROP grade ≥2, high grade IVH, in-hospital mortality and a composite of serious adverse outcomes defined as the occurrence of either moderate-severe BPD, ROP grade ≥2, high grade IVH or death. The following covariates were entered into the models as additional independent variables and potential confounding factors: GA, sex, antenatal steroid therapy and low 5 min Apgar score (<7). Results of the regression analyses are presented as crude and adjusted OR with corresponding 95% CI). P<0.05 was considered statistically significant. Data were analysed using R V.3.6.2 (R Foundation for Statistical Computing, Vienna, Austria) and SPSS V.26 for Windows (SPSS, Chicago, Illinois, USA).

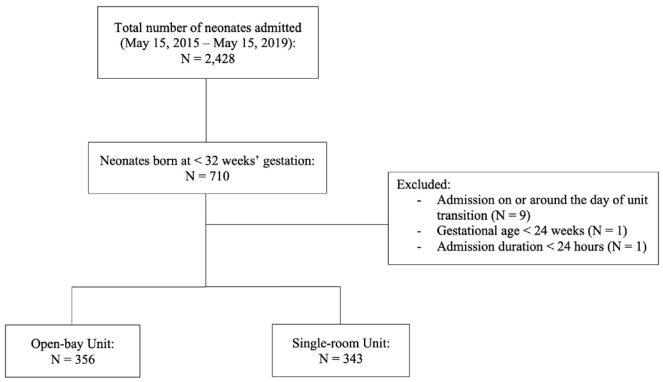

Figure 1 Flowchart of study participant enrolment.

RESULTS

Demographic characteristics

During the entire study period (15 May 2015–15 May 2019), a total of 2428 neonates were admitted to the NICU, 710 of which were born at a GA of <32 weeks (figure 1). Of the latter, 11 were excluded based on the following criteria: admission on or around the day of unit transition (n=9), birth <24 weeks' gestation (n=1) and admission duration <24 hours (n=1). Overall, 356 and 343 neonates were admitted to respectively the open-bay and SRU.

Neonatal characteristics by study group are shown in table 1. A higher number of multiples were admitted and neonates were treated with surfactant more often in the SRU cohort as compared with the OBU cohort (39.1% vs 31.7%, p=0.05 and 39.4% vs 32%, p=0.05, respectively). No further differences in baseline characteristics were found between the cohorts.

Table 1 Baseline neonatal characteristics by unit type

Characteristic	OBU (N=356)	SRU (N=343)	P value*
Birth weight (g), *mean (SD)*	1288 (377)	1239 (380)	0.09
Gestational age (weeks), *median (IQR)*	29 (4)	29 (4)	0.69
Sex, *n (%)*			0.35
Male	189 (53.1)	169 (49.3)	
Female	167 (46.9)	174 (50.7)	
Multiple gestation, *n (%)*	113 (31.7)	134 (39.1)	**0.05**
Delivery mode, *n (%)*			0.94
Caesarean section	190 (53.4)	185 (53.9)	
Vaginal	166 (46.6)	158 (46.1)	
Full or partial course of antenatal steroids†, *n (%)*	331 (92.9)	320 (93.3)	0.99
Postnatal steroid treatment, *n (%)*	19 (5.3)	20 (5.8)	0.90
Apgar score at 5 min, *median (IQR)*‡	8 (2)	8 (2)	0.19
Major congenital anomaly§, *n (%)*	9 (2.53)	3 (0.9)	0.16
Surgical pathology, *n (%)*	15 (4.2)	11 (3.2)	0.61
Exposure to invasive mechanical ventilation, *n (%)*	135 (37.9)	129 (37.6)	0.93
Duration of invasive mechanical ventilation per neonate (days), *median (IQR)*	4 (8)	5 (6)	0.96
Surfactant treatment, *n (%)*	114 (32.0)	135 (39.4)	**0.05**
Length of hospital stay per child (days), *median (IQR)*	13 (24)	13 (23)	0.55

*Statistical tests performed: independent T-test, χ^2 test of independence; Mann-Whitney U test. P-values in bold indicate statistical significance.
†Based on 350 and 339 neonates in OBU and SRU, respectively (10 missing variables).
‡Based on 354 and 340 neonates in OBU and SRU, respectively (five missing variables).
§Defined as a condition that leads to significant medical, social or cosmetic consequences and typically requires medical intervention such as oral facial clefts, cyanotic heart defects, neural tube defects and limb deficiencies.
OBU, open-bay unit; SRU, single-room unit.

Morbidity and mortality outcomes

Table 2 shows the incidences of neonatal morbidity and mortality outcomes stratified by unit type. Neonates in the SRU cohort had a non-significant greater rate of ROP stage ≥2 (20.3% vs 15.7%, OR 1.36, 95% CI 0.84 to 2.22, p=0.10). The need for a thrombocyte transfusion tended to decrease in the SRU versus OBU cohort (5.6% vs 2.6%, OR 0.45, 95% CI 0.20 to 1.01, p=0.06). No differences were found between the cohorts with respect to the rates of sPDA, SIP, pneumothorax, BPD, IVH, cPVL, hyperbilirubinemia, inotropic support, erythrocyte transfusions, (sub) clinical convulsions and in-hospital mortality.

Regression models are shown in table 3. In univariate analysis, single-room care was not associated with a decreased risk of neonatal morbidity. After adjustment for GA, sex, antenatal steroid therapy and low 5 min Apgar score (<7), single-room care was independently associated with a decreased risk of sPDA arteriosus (adjusted OR: 0.54, 95% CI 0.31 to 0.95). No independent association between single-room care and any of the other morbidity outcomes was observed.

DISCUSSION

The creation of an environment which is conducive to family-centred care and provides optimal developmental support to critically ill neonates is a key goal of modern neonatal IC. However, budgetary-related and workload-related considerations have led to a situation in which neonatal IC has become one of the last healthcare specialties to trend away from open-bay wards. The scientific evidence on the benefits of SRU is lacking and it remains controversial whether the available data justify the costs associated with the transformation from OBU to SRU. Apart from the independent association between single-room care and sPDA, our findings indicate that the SRU model is not associated with a reduced risk of severe morbidity and mortality in preterm neonates and are in line with our previous findings regarding the lack of association between single-room care, NEC (25 vs 17 episodes, p=0.36) and the incidence of nosocomial infection (13.68 vs 12.62 per 1000 patient-days, p=0.62).[11] We were thus unable to provide new evidence to support the theoretical benefits of single-room care.

Our findings are in line with a previous prospective, quasiexperimental cohort study which found no difference in the rate of BPD, IVH grade 3–4, PVL and ROP stage 3–5 between neonates admitted to a single-family room vs a conventional, open-bay NICU.[7] Similarly, a systematic review and meta-analysis investigating the association between NICU room type and a wide range of neonatal outcomes also found no difference in the incidence of BPD, ROP and mortality between preterm neonates admitted to single-family rooms as opposed to open-bay wards.[17] Although non-significant, the incidence of severe ROP in our study increased, a finding which corresponds with the reported increase in a comparative study of two national inventories on ROP in the Netherlands (NEDROP).[18] Similarly, the

Table 2 Occurrence of neonatal morbidity and mortality outcomes according to unit type

Variable	OBU (N=356)	SRU (N=343)	OR (95% CI)	P value*
sPDA, n (%)	40 (11.2)	27 (7.9)	0.68 (0.40 to 1.13)	0.89
Medical treatment	38 (10.7)	27 (7.9)		
Surgical ligation	2 (0.6)	0 (0)		
Pneumothorax, *n (%)*	17 (4.8)	11 (3.2)	0.66 (0.31 to 1.43)	0.34
SIP, *n (%)*	10 (2.8)	8 (2.3)	0.83 (0.32 to 2.12)	0.81
BPD†, *n (%)*	66 (18.5)	66 (19.2)	1.08 (0.73 to 1.58)	0.44
Mild	32 (9.0)	28 (8.2)		
Moderate	3 (0.8)	8 (2.3)		
Severe	31 (8.7)	30 (8.7)		
ROP stage≥2‡, *n (%)*	38 (15.7)	42 (20.3)	1.36 (0.84 to 2.22)	0.10
IVH§, *n (%)*	60 (16.8)	52 (15.2)	0.89 (0.59 to 1.34)	0.86
Grade 1	19 (5.3)	18 (5.2)		
Grade 2	35 (9.8)	21 (6.1)		
Grade 3	6 (1.7)	13 (3.8)		
PVHI and/or PVHD¶, *n (%)*	15 (4.2)	18 (5.2)	1.25 (0.62 to 2.53)	0.53
cPVL[6], *n (%)*	5 (1.4)	5 (1.5)	1.03 (0.30 to 3.59)	0.96
Hyperbilirubinemia, *n (%)*	264 (74.2)	265 (77.3)	1.18 (0.84 to 1.67)	0.38
Inotropic support, *n (%)*	33 (9.3)	33 (9.6)	1.04 (0.63 to 1.73)	0.89
Erythrocyte transfusion, *n (%)*	104 (29.2)	88 (25.7)	0.84 (0.60 to 1.17)	0.31
Number of transfusions, *median (IQR)*	2 (1)	1 (1)	–	0.91
Thrombocyte transfusion, *n (%)*	20 (5.6)	9 (2.6)	0.45 (0.20 to 1.01)	0.06
Number of transfusions, *median (IQR)*	1 (1)	2 (2.5)	–	0.05
(Sub)clinical convulsions, *n (%)*	4 (1.1)	3 (0.9)	0.78 (0.17 to 3.50)	1.00
In-hospital mortality, *n (%)*	13 (3.7)	19 (5.5)	1.55 (0.75 to 3.20)	0.28

*Statistical tests performed: χ^2 test of independence, Fisher's exact test or Mann-Whitney U test.
†Based on 334 and 315 neonates in OBU and SRU, respectively (43 in which BPD screening not applicable due to early death, 7 missing variables).
‡Based on 242 and 207 neonates in OBU and SRU, respectively (188 in which screening not indicated according to local protocol (online supplemental appendix 2), 43 in which screening not applicable due to early death, 19 missing variables).
§Based on 353 and 342 neonates in OBU and SRU, respectively (four in which no cerebral ultrasound was made as a result of early death).
¶Based on 352 and 342 neonates in OBU and SRU, respectively (four in which no cerebral ultrasound was made as a result of early death or transfer, 1 missing variable).
BPD, bronchopulmonary dysplasia; cPVL, cystic periventricular leukomalacia; IVH, intraventricular haemorrhage; OBU, open-bay unit; PHVD, posthaemorrhagic ventricular dilatation; PVHI, periventricular haemorrhagic infarction; ROP, retinopathy of prematurity; SIP, spontaneous intestinal perforation; sPDA, symptomatic patent ductus arteriosus; SRU, single-room unit.

observed decreased risk of sPDA may be largely explained by a trend towards the increased use of conservative management as opposed to medical and surgical treatment for sPDA at our institution, a tendency which has been reported by numerous other studies.[19–21] On the other hand, our findings challenge the results from a previous report which found a reduction in both the total length of stay and occurrence of moderate-to-severe BPD in neonates allocated to a single-room NICU (length of stay: 27.4 days vs 32.8 days, p=0.05; BPD: adjusted OR, 0.18 (95% CI 0.04 to 0.8)).[6] However, the possibility that these latter findings may have been mediated by the concomitantly reduced duration of mechanical ventilation (although not significant and unrelated to ward design), a necessary aetiological precursor for BPD, cannot be excluded.

Table 3 Crude and adjusted ORs for major morbidity outcomes associated with single-room care

	SRU*	
Outcome	Crude OR (95% CI)	Adjusted OR (95% CI)†
sPDA	0.68 (0.40 to 1.13)	0.54 (0.31 to 0.95)
Moderate to severe BPD	1.21 (0.74 to 1.98)	1.21 (0.69 to 2.12)
ROP stage≥2	1.36 (0.84 to 2.22)	1.27 (0.75 to 2.14)
High grade IVH‡	1.63 (0.89 to 2.96)	1.67 (0.89 to 1.40)
In-hospital mortality	1.55 (0.75 to 3.18)	1.52 (0.68 to 3.40)
Composite morbidity§	1.30 (0.92 to 1.84)	1.28 (0.86 to 1.92)

*Binary logistic regression. OBU set as reference. ORs display risk of morbidity in SRU vs OBU.
†Models adjusted for gestational age, sex, antenatal steroid therapy and low 5 min Apgar score (<7).
‡Defined as IVH grade three or any grade IVH complicated by periventricular haemorrhagic infarction and/or posthaemorrhagic ventricular dilatation.
§Composite morbidity defined as the presence of one or more of the following: ROP≥2, high grade IVH, BPD>mild and death.
BPD, bronchopulmonary dysplasia; IVH, intraventricular haemorrhage; ROP, retinopathy of prematurity; sPDA, symptomatic patent ductus arteriosus.

It has been hypothesised by previous studies that sound abatement, sensory minimisation and increased privacy and parental involvement, all of which are hypothetically facilitated by the SRU-design, lead to lower risk of major neonatal morbidity. However, it remains unclear if and to what extent SRU move the needle towards enhanced physiological stability and developmental maturation in preterm neonates. Even though environmental factors are important in their own right, they may not necessarily be directly related to short-term medical outcomes. It is well known that healthy maturation and avoidance of adverse morbidity are unavoidably altered by fetal and postnatal disruptive events which may not be directly mitigated by any particular care strategy. Factors that have been associated with the occurrence of BPD, ROP and IVH include sex, low BW, postnatal resuscitation, sepsis, high fraction of inspired oxygen and metabolic acidosis.[22–24] As such, rather than the physical design of

the NICU, it seems that factors related to prematurity, including antenatal and postnatal events, are critical drivers of adverse short-term morbidity outcomes. Nonetheless, the potential modulating effect of non-medical interventions associated with the single-room model of care on neurobehavioral outcomes cannot be disregarded. Vohr *et al*[8] reported improved Bayley cognitive and language scores in preterm neonates at 18–24 months corrected age who had been hospitalised in an SRU NICU, and attributed these findings to the enhanced maternal involvement characterised by kangaroo care, breast feeding and parental speaking.[8] As such, determining which elements of care improve neurodevelopmental outcomes, while bearing in mind the biology of prematurity as a recurrent big player, warrants further investigation.

Despite widespread appreciation surrounding the theoretical benefits of the SRU design, the latter's influence on parental perceptions and maternal health factors remain unclear. Pineda *et al*[4] reported higher levels of stress among mothers with neonates in single-patient rooms, raising the question as to whether SRUs insidiously promote an increased feeling of isolation and accountability for the medically instable neonate.[4] Evidence regarding the hypothetically positive impact of SRUs for NICU staff has been equally mixed. Recent research found nursing staff to perceive daily tasks in the SRU to be more physically demanding, more stressful and less socially interactive.[25–27] Moreover, the altered work dynamic has brought along a simultaneous increased dependency on patient monitoring systems, adding another dimension of work-related stress in the form of alarm pressure.[28] As such, the stressful work environment may have nullified the potential positive impact of single-room care on neonatal outcomes. Research into befitting social interventions that alleviate the effects of stress for parents and enhance overall job satisfaction for staff is thus warranted.

Strengths and limitations

The main strengths of this study include its detailed data collection and inclusion of a wide range of clearly defined medical outcomes. Adjusting for well-established confounding factors in regression analyses enabled us to enhance the accuracy of our results. We also acknowledge a number of limitations to our study. First, despite the reduction in several of the morbidity outcomes (ie, transfusion need, pneumothorax, IVH, among others), the limited power of our study may have impeded the results of low prevalent outcomes from reaching statistical significance, as reflected in the relative imprecision (wide confidence intervals) of many of the investigated parameters. Second, we were unable to fully account for potential coexisting regional and/or national trends in major neonatal morbidities due to lack of available data. Likewise, no consideration was given to other clinical efforts to improve outcomes, such as changes in transfusion limits, which may have concurrently transpired with the transition to the new unit. Third, and unlike in many other open-ward NICUs, several elements of family-centred care such as the individualisation of care and limitation of environmental stressors (ie, noise and light) were already being implemented in our OBU NICU, which may have partially accounted for the lack of differences in neonatal outcomes between our two units. Fourth, our study did not measure factors related to parental involvement such as duration of visitation and holding practices, which may have mediated certain associations between single-room care and morbidity and mortality. Differences in certain developmental care-related factors such as skin-to-skin contact, breastfeeding rates and sedative use between the two unit types will be reported in a separate study by our group. Finally, the single-centre nature of our study may have reduced the external validity required to recommend the widespread implementation of the SRU design and hindered the acquisition of additional insights regarding the influence of important contextual factors such as heterogeneity in clinical practice.

CONCLUSION

Although it is assumed that the single-room design promotes optimal care, we were unable to confirm a significant impact of the physical setting of a SRU NICU on major neonatal morbidity and mortality outcomes in prematurely born neonates. Given that single-room care embodies not just a new physical design but a complex interplay of other elements including but not limited to staff workload, communication, safety, privacy and parental interaction, further assessment and analysis of these potential mediating and moderating factors is necessary to further evaluate the impact of single-room care on (adverse) neonatal outcomes.

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Contributors SJ collected and analysed the data, drafted the initial and final version of the manuscript and is responsible for the overall content as the guarantor. ABtP, NE and AvdH critically reviewed and revised the manuscript for important intellectual content. RJMB, SJ and LSdV collected a part of the data and critically reviewed and revised the manuscript for important intellectual content. EL and VB conceptualised the study, supervised data collection and critically reviewed and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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