

## REGULAR ARTICLE

# Single-family room design in the neonatal intensive care unit did not improve growth

Bente Silnes Tandberg (btandb@vestreviken.no)<sup>1,2</sup> , Kathrine Frey Frøslie<sup>3</sup>, Trond Markestad<sup>2</sup>, Renè Flacking<sup>4</sup>, Hege Grundt<sup>5</sup>, Atle Moen<sup>1,6</sup>

1.Department of Pediatric and Adolescent Medicine, Drammen Hospital, Vestre Viken Hospital Trust, Drammen, Norway

2.Department of Clinical Science, Faculty of Medicine and Dentistry, University of Bergen, Bergen, Norway

3.Norwegian Resource Centre for Women's Health, Oslo University Hospital, Rikshospitalet, Norway

4.School of Education, Health and Social Studies, Dalarna University, Falun, Sweden

5.Department of Pediatrics, Haukeland University Hospital, Bergen, Norway

6.Department of Neonatology, Oslo University Hospital, Oslo, Norway

## Keywords

Family-centred care, Growth, Single-family room, Skin-to-skin contact, Very premature infant

## Correspondence

BS Tandberg, Department of Pediatric and Adolescent Medicine, Drammen Hospital, Dronningt 28, 3004 Drammen, Norway.  
Tel.: +4793010666 |  
Fax: +4732862430 |  
Email: btandb@vestreviken.no

## Received

17 September 2018; revised 25 January 2019; accepted 4 February 2019.

DOI:10.1111/apa.14746

## INTRODUCTION

The physical environment in the neonatal intensive care unit (NICU) may influence short- and long-term outcomes in preterm infants (1–3). Involvement of parents (4), and family-centred care with parents as primary caregivers, has been associated with faster attainment of full enteral feeds (5) and weight gain (4). As opposed to open-bay (OB) units, single-family room (SFR) units protect the infant and parents from environmental stress and offer more privacy, which may facilitate long-term parent–infant closeness and skin-to-skin contact (SSC) (6,7). SFR design has been associated with more hours of maternal presence (8) improved weight gain (9), earlier feeding (10), reduced risk of infection and earlier discharge (11) and improved neurobehavioral and pulmonary outcomes (9,12,13). However, the results are conflicting and delayed language

development has been reported after SFR care with limited parental presence (14).

In 2012, the NICU at Vestre Viken Hospital Trust (VVHT), Norway, was established as a SFR unit where parents could stay with their infant day and night from birth to discharge and participate as primary caregivers. From 2005, when the unit had an OB design, we registered weight at the postmenstrual age (PMA) of 34 weeks, at discharge, and at term date for infants with birth weights less than 1500 g and noted a substantial improvement in weight gain after the introduction of SFR care. We therefore hypothesised that a SFR

## ABSTRACT

**Aim:** The aim was to compare growth in very premature infants cared for in a single-family room (SFR) and an open-bay (OB) unit. We recorded duration of parental presence and skin-to-skin contact as proxies for parental involvement in care of their infants.

**Methods:** We consecutively included infants with gestational ages 28 + 0 through 32 + 0 weeks at two hospitals in Norway, one SFR unit (n = 35) and one OB unit (n = 42). Weight, length, and head circumference were followed from birth to four months after term date. Both units adhered to the same nutritional protocol and methods of recording events.

**Results:** The SFR mothers spent a mean (standard deviation) of 111 (38) hours and the OB mothers 33 (13) hours with their infants during the first week and 21 (5) versus 7 (3) hours per day later. The respective duration of skin-to-skin care was 21 (10) versus 12 (8) hours during the first week and 4.2 (2) versus 3.0 (2) hours per day later. The differences were similar, but less pronounced for the fathers. The growth trajectories did not differ between the groups.

**Conclusion:** SFR care was associated with more parental involvement, but not with better growth.

## Abbreviations

CI, Confidence interval; HUH, Haukeland University Hospital; NICU, Neonatal intensive care unit; OB, Open bay; PMA, Postmenstrual age; SFR, Single-family room; SSC, Skin-to-skin contact; VVHT, Vestre Viken Hospital Trust.

## Key notes

- Single-family room (SFR) encourages parent involvement but it is uncertain whether it improves growth in very premature infants.
- The SFR parents spent more time in the unit and in providing skin-to-skin care than parents in the open-bay unit, but the infants' growth trajectories were similar.
- We cannot exclude that a minimum of parental participation affects growth since the parents in both units spent much time with their infants.

design may improve growth through close parent–infant interaction, including more SSC.

Our aim was to compare growth velocities for weight, length and head circumference during and after hospitalisation in infants born prematurely at gestational ages 28 + 0 through 32 + 0 weeks who were cared for in an SFR and an OB unit. We recorded duration of parental presence and provision of SSC as indicators of parental involvement and adhered to the same protocols for nutrition and assessments.

## PATIENTS AND METHODS

### The SFR and OB units

In Norway, hospital care is financed through a public health insurance system and is free of charge for all citizens irrespective of income. No private neonatal intensive care is available. Parents also have extensive publicly financed social security benefits during pregnancy and when giving birth, and both parents are generally entitled job leave with full economic compensation during the hospitalisation of their infant. More than 90% of Norwegian children are in a kindergarten at day time; therefore, most siblings in our families would be expected to attend kindergarten during day time. Inclusion to the study started on May 1, 2014 and had to end on July 31, 2016, because the OB unit was moved to another building because the old paediatric department with the OB unit was demolished.

The SFR unit was located in Drammen and the OB unit at Haukeland University Hospital (HUH) in Bergen, Norway. Both units were located in maternity hospitals. At VVHT the infants were delivered in the same building and close to the NICU. At HUH the obstetric department was located in a different building 500 m from the NICU, and all infants requiring NICU care were transferred by ambulance. Both units provided care from birth until discharge for all infants born from a gestational age of 28 weeks within their hospital referral area. Both units encouraged and guided mothers in providing breast milk from day one and provided donor breast milk.

The SFR unit was built in 2012 and admits approximately 450 infants in 17 beds annually. It provides bathroom facilities for parents within the patient room area. Both parents can stay with their infant as long as they want, but mothers have to stay in the obstetric unit during the night until 48 hours after giving birth. All meals are provided without cost to both parents. Parents were encouraged and guided to provide SSC for as many hours as they wanted, and high-quality adjustable hospital beds were present for parents beside the infant's incubator or cot. Parents were also present and participated actively during daily rounds.

The OB unit was built in 1979 and was only modestly upgraded until the end of this study. It had 21 beds and admitted approximately 500 infants per year. Except for one single bedroom, which was used for particularly intensive or end-of-life care, the unit had two rooms; one for intensive- and intermediate care patients and one for care in cots before discharge home. The rooms were crowded, but one

reclining armchair could be placed between incubators or cots, and screens could be placed around the family to provide some privacy. The parents had unlimited access at all hours, but they could not stay overnight in the unit. Mothers were accommodated in another building at the hospital after discharge from the maternity ward, and meals were only provided for the mothers. SSC was already established practice at both units for years before this study and was encouraged whenever parents were present.

### Participants

To assure comparable cohorts, we limited the study to infants born at gestational ages of 28 + 0 through 32 + 0 weeks of families living in the respective catchment areas. The units were the only NICUs in their respective area. We excluded infants with congenital malformations, infants who experienced major complications such as intraventricular haemorrhage grade III/ IV or necrotising enterocolitis or who had a birth weight <800 g, in order to avoid infants with severe intrauterine growth restrictions and complex morbidities. We also excluded infants of parents who had a major mental illness or did not understand Norwegian language, infants of mother who had used illicit drugs or were on methadone during pregnancy and infants who were in the custody of the Child Protection Services from birth.

In both hospitals, gestational age was based on ultrasound assessment at 17–18 weeks of pregnancy, or on the last menstrual period if ultrasound assessment was not performed. The infants were recruited consecutively at admission. The parents received the same oral and written information and were included if both of them gave written consent within the second day. The study was approved by the Norwegian Regional Committee for Medical Research Ethics and registered in ClinicalTrials.gov (NCT 02452580).

### Nutrition

The units agreed on a common feeding protocol (Table S1 and Table S2). The goal was to give 80 mL/kg during the first 24 hours and thereafter increase the volume by 20 mL/kg/day until 180 mL/kg/day. Infants with a birth weight above 1250 g received full enteral feeds from day one, while infants with birth weights less than 1250 g received partial and decreasing parenteral nutrition for the first five days. Enteral feeds were started as either donor breast milk or preterm formula if breast milk was not available. Donor milk or preterm formula was replaced with the mother's own milk as production increased. A breast milk fortifier (FM85 Nestle®, Copenhagen Nordic, Denmark) was added to breastmilk according to protocol and continued until the infant weighed 2000 g or was fully breastfed. Subsequently, nutrition continued as breastmilk or a regular infant formula. Daily nutritional intake was registered from birth to PMA of 34 weeks, and nutrient intake was calculated according to our nutritional standards for breast milk and formula (15). Breastmilk feeding was registered as exclusive, partial or none at discharge, at expected term date, and at four months corrected age.

## Assessments

Weight was registered daily, while crown to heel length and head circumference were measured at birth, after each completed week according to PMA until the PMA of 34 + 0 weeks, at discharge, at expected term date, and four months after expected term date. Weight was measured on electronic scales, which were routinely calibrated twice a year. Head circumference was measured with a nonstretch measuring tape and crown to heel length with the measuring tape at birth, at admission to the hospital, and when the infant was cared for in an incubator, but later with a stadiometer. The methods for measurements were standardised. All the infants were brought back for the measurements at term and all but one infant at each centre were brought back for the four months measurements. These measurements were performed by one person at each centre. The two remaining infants had their measurement at a public child healthcare clinic at four months. The infants were weighed naked. The number of skin-breaking procedures (heel lance, arterial and venous punctures) was also registered.

For each infant, both parents prospectively recorded the time present in the unit with their infant and the duration of SSC on the mother's or father's bare chest. Both periods were registered each day from birth to the PMA of 34 weeks in a closeness diary which was kept with the infant. In case of twins, each infant had a separate diary.

## Statistics

The study was powered to examine the difference in mean weight at discharge between the SFR and OB units. In the pilot study at VVHT, the mean weight at discharge was 300 g higher in the SFR than in the OB unit. Based on an expected difference of 300 g, a power calculation suggested that 10 infants were needed in each group to obtain a significant result with a  $p < 0.05$  and a power of 80%. However, the observed difference occurred in parallel with the reorganization of the unit within the hospital and was not necessarily representative when comparing the two units. We therefore chose to include up to total of 80 infants.

Data are presented as means with standard deviation (SD) and frequencies (percentages). We compared sample characteristics, nutritional intakes and measurements with two-sample *t*-tests and Pearson's chi-square tests. Mean differences in measures of growth velocities in weight, length and head circumference from birth to four months after expected term date were analysed with linear mixed models with random intercept and fixed effects for unit, PMA, and an interaction term between unit and PMA, that is, two-level models with weight, length or head circumference nested within each infant. The interaction term, interpreted as difference in growth slope (grams or mm per week) between the units was used to quantify velocities in weight, length and head circumference. In all models, a second-order polynomial term for PMA was added if significant. If such a term was added, we also checked for

a corresponding interaction with unit. All models were also run with adjustments for differences in mode of delivery. Detailed information about the notation of the mixed model is provided (Appendix S1). The potential confounding effect of the difference between the groups in parental education was also explored but did not alter results. Due to the restricted number of infants in each of the units held up against the total number of parameters in the model, we did not include a formal adjustment for small for gestational age, multiples or first borne/siblings in the models. These parameters also had a similar distribution between the groups.

Mean differences in duration of parental presence and SSC until PMA of 34 weeks between the SFR and OB units were analysed in linear regression analyses. The main exposure was the unit (SFR or OB), and PMA at birth, mode of delivery (vaginal or caesarean section), parents education (elementary/high school or college/university).

Analyses of parental presence were done separately for mothers' and fathers' with an additional analysis of the cumulative parental presence and SSC for each infant.

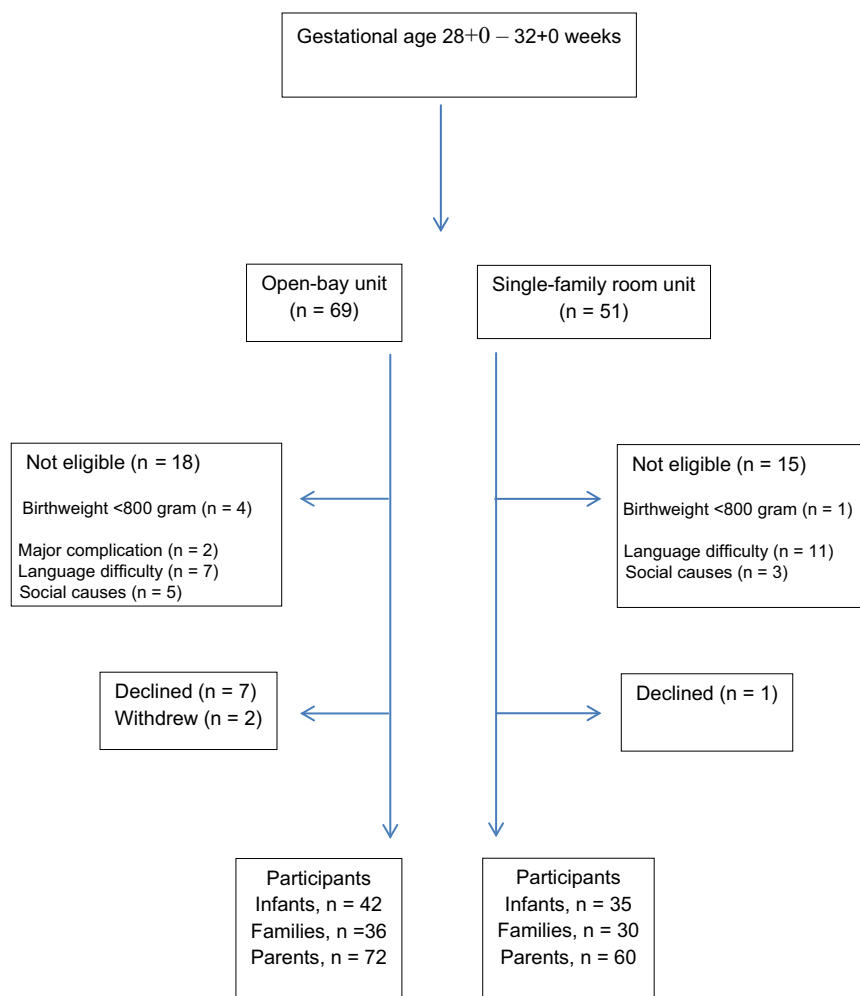
Descriptive statistics, bivariate tests and linear regression models were done in SPSS statistic version 25 (IBM Inc., Armonk, NY, USA). The mixed-model analysis was done in The R Foundation software, version 3.5.0, using the function *lme* in the *nlme* package. A  $p$  value  $\leq 0.05$  was considered statistically significant.

## RESULTS

Of 51 neonates admitted to the SFR unit, 15 did not fulfil the inclusion criteria, and the parents of one eligible neonate declined, leaving 35 neonates and 60 parents in the study. Of 69 neonates in the OB unit, 18 were not eligible, and the parents of nine eligible infants either declined (7) or withdrew (2), leaving 42 neonates and 72 parents in the study (Fig. 1). All the infants were cared for in their respective NICUs from birth until discharge.

The only significant differences between the infants in the OB and SFR units were that: both parents had higher education, the mean gestational age at birth was four days lower and the proportion of infants delivered by caesarean section was lower while the proportion treated with mechanical ventilation and the number of skin-breaking procedures were higher in the OB group. There were no significant differences between the units in the proportion of infants born small for gestational age, prevalence of bronchopulmonary dysplasia (Bancalari criteria), culture verified sepsis or length of stay (Table 1).

Due to an unexpected lack of banked breast milk, which was replaced with preterm formula during the first months of the study, the infants in the OB unit received significantly more protein and carbohydrates than the infants in the SFR unit during the first week of life (Table 2). The difference was moderate and did not result in different weight loss or time to regain birth weight (Table 3). There were no



**Figure 1** Flow diagram of participant recruitment.

differences in nutrient intake after the first week until the PMA of 34 weeks, or in the proportions of infants receiving breastmilk and regular formula at discharge, term date or four months after term date (Table 2).

On average, both the mothers and fathers in the SFR unit spent 80 more hours with their infant than the parents in the OB unit during the first week. After the first week, until the PMA of 34-week mothers spent 14 hours and fathers nine more hours in the SFR unit (Table 4). Adjustments for mode of delivery and gestational age or parental education did not alter these differences. The duration of SSC was also significantly higher for the mothers in the SFR unit. For fathers, the difference of duration of SSC was not significant after the first week (Table 4).

There were no significant differences in mean weight, length or head circumference at birth or at PMA of 34 weeks, discharge, term date or four months after term date (Table 2). Adjustments for gestational age and mode of delivery did not alter the differences significantly (data not shown). The individual variation in growth curves was much larger than the variation between units (Fig. 2). A linear model for

weight fitted the data well and the growth slope did not differ between the units (the adjusted estimate for difference in slope was 4.0 g/week [95% Confidence interval (CI): -5.0, 13.0,  $p = 0.38$ ]. For length and head circumference, a polynomial term for PMA was added (Fig. 2B,C), but there was no interaction with unit, and the slopes did not differ between the units; the adjusted estimate for difference between the slopes was 0.32 mm/week (95% CI: -0.02, 0.67,  $p = 0.06$ ) for length and 0.03 mm/week (95% CI: -0.19, 0.24,  $p = 0.79$ ) for head circumference.

## DISCUSSION

The two involved NICUs had the most modern and the most outdated design among NICUs in Norway. The parents in the SFR unit spent significantly more time with their infants and in provided more SSC than the parents in the OB unit, but despite these differences, the infants had similar developmental trajectories for weight, length and head circumference from birth until four months after expected term date.



**Table 1** Characteristics of the families and infants treated in the single-family room (SFR) and open-bay (OB) units

Variable	SFR unit (n = 35)	OB unit (n = 42)	p-value*
<b>Parents</b>			
Mothers' age, years, mean(SD)	31 (7)	32 (6)	0.38
Fathers' age, years, mean (SD)	36 (10)	34 (7)	0.45
Single mother, n (%)	0 (0)	1 (2)	0.66
<b>Norwegian first language, n (%)</b>			
Mothers	28 (80)	39 (93)	0.21
Fathers	30 (86)	39 (93)	0.30
<b>Education level, n (%)</b>			
<b>Mothers</b>			
Elementary	4 (13)	0 (0)	0.015
High school	10 (33)	10 (30)	
College/university	15 (50)	23 (70)	
<b>Fathers</b>			
Elementary	3 (10)	0 (0)	0.012
High school	15 (50)	12 (38)	
College/university	12 (40)	20 (63)	
<b>Infant</b>			
Delivered by caesarean section, n (%)	25 (71)	20 (48)	0.04
Primipara, n (%)	8 (23)	11 (34)	0.64
Male sex, n (%)	19 (54)	15 (36)	0.11
Twins, n (%)	10 (29)	18 (43)	0.30
Small for gestational age <sup>†</sup> , n (%)	7 (20)	10 (24)	0.69
Gestational age, Weeks + days; mean (min, max)	30.5 (28.2, 32.0)	30.1 (28.1, 31.6)	0.03
PMA <sup>‡</sup> at discharge, days, mean (SD)	252 (9)	255 (14)	0.34
Length of stay, days, mean (SD)	37 (11)	45 (18)	0.16
BPD, n (%)	0 (0)	2 (5)	0.20
Mechanical ventilation, n (%)	0 (0)	9 (22)	0.01
Ventilation, days, mean (SD)	0 (0)	0.3 (0.7)	0.01
Skin-breaking procedures <sup>§</sup> , mean (SD)	10 (3)	20 (9)	0.01
Septicaemia, n (%)	0 (0)	1 (2)	0.36
<b>Breastmilk feeding, n (%)</b>			
<b>At discharge</b>			
Exclusive	26 (77)	29 (69)	0.45
Partial	5 (15)	5 (12)	
None	3 (9)	8 (19)	
<b>At expected term date</b>			
Exclusive	20 (61)	18 (45)	0.61
Partial	6 (18)	11 (28)	
None	7 (21)	11 (28)	
<b>Four months after term date</b>			
Exclusive	5 (15)	4 (11)	0.42
Partial	14 (42)	13 (33)	
None	14 (42)	23 (58)	

\*Two-sample *t*-test or Pearson's chi-square tests.<sup>†</sup>Below the 10 th percentile.<sup>‡</sup>Postmenstrual age.<sup>§</sup>Heel lance/arterial/venous punctures.**Table 2** Macronutrients (means and SDs) per kg weight from birth to PMA of 34<sup>0</sup> weeks<sup>†</sup>

	SFR unit (n = 35)	OB unit (n = 42)	p-value*
<b>First eight days</b>			
Energy, kcal	703 (40.0)	735 (93.0)	0.06
Protein gram	15.5 (3.1)	17.7 (4.9)	0.03
Fat gram	37.8 (3.5)	37.7 (8.2)	0.94
Carbohydrates gram	73.4 (4.5)	80.0 (8.1)	0.01
<b>Per day from the 8th day</b>			
Calories, kcal	169 (27.0)	165 (21.0)	0.51
Protein gram	4.3 (0.8)	4.3 (0.7)	0.69
Fat gram	8.3 (1.4)	8.0 (1.2)	0.47
Carbohydrates gram	19.0 (3.0)	18.3 (2.7)	0.29

\*Two-sample *t*-tests.**Table 3** Weight (gram), length (cm) and head circumference (cm) from birth to four months after term date in infants cared for in single-family room (SFR) and open-bay (OB) units

	SFR unit (n = 35)	OB unit (n = 42)
<b>Birth</b>		
Weight	1452 (301)	1382 (274)
Length	39.6 (2.7)	39.0 (2.3)
Head circumference	28.5 (1.6)	27.9 (1.9)
Postnatal weight loss	131 (66)	126 (92)
Days to regain birth weight	9 (3)	10 (3)
<b>PMA 34 weeks</b>		
Weight	1999 (269)	1984 (249)
Length	43.1 (1.8)	42.8 (2.3)
Head circumference	31.2 (1.0)	30.9 (1.0)
<b>Discharge</b>		
Weight	2271 (299)	2317 (297)
Length	45.4 (1.8)	45.0 (1.8)
Head circumference	32.7 (1.7)	32.6 (1.4)
<b>Term date</b>		
Weight	3346 (496)	3323 (454)
Length	49.3 (2.3)	49.8 (2.2)
Head circumference	35.8 (1.2)	35.8 (0.9)
<b>Four months after term date</b>		
Weight	6643 (807)	6686 (992)
Length	62.7 (2.8)	63.3 (2.5)
Head circumference	42.7 (2.9)	42.1 (2.5)

Data presented as means (SDs).

The strengths of this study were the uniform rights of parents and infants to health care and social benefits, the strict inclusion of comparable infants, the same nutrition

protocol and uniform ways of registering nutritional practices, growth, parental presence and SSC. The method for recording presence and SSC through self-reports has been shown to be more reliable than registration recorded by nurses (16). Furthermore, we consider it important that the units were located in different parts of the country and without cooperation beyond this specific project. A randomized-controlled trial within one NICU would have introduced a great risk of bias since positive and negative expectations from staff and parents related to what was perceived as the superior treatment, could have

contaminated the study (17). The higher proportion of ventilated infants in the OB unit was probably due to the need for safe stabilisation before transportation since all the infants had to be transported in an ambulance from the maternity ward to the NICU. However, the time on mechanical ventilation was very short and does not indicate more severe airway disease. There was a difference in the number of skin-breaking procedures, which may be due to different routines or an effect of parents questioning the necessity of tests in the SFR unit. No other data indicated differences in disease severity between the two units. Further, there were no differences in infants receiving mothers' milk. The similar growth makes it unlikely that a study with a higher number of participants would have disclosed clinically significant differences. However, since the study did not include extremely preterm infants or infants with major morbidity, we cannot exclude a beneficial effect on growth when caring for more vulnerable infants.

We succeeded in providing macronutrients at or above recommendations for premature infants (18). Still, the infants in both groups did not attain a mean weight near the 50th percentile for intrauterine growth for Norwegian

infants at the PMA of 34 weeks or at expected term date (19,20). In a setting with suboptimal nutrition or severe growth restriction due to medical complications, we cannot exclude a potential benefit of stress reduction in the infant from extensive parental involvement in a SFR setting.

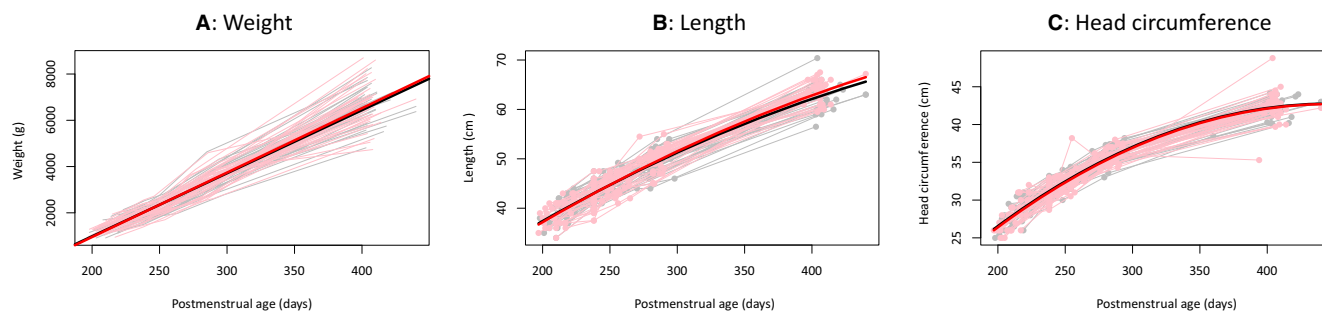
The lack of effect on growth in our study is contrary to the findings of Lester et al. (9). They found positive effects of SFR care on growth, morbidity, neurobehavioral outcome and parental health (9,12,13). However, their study design compared outcomes before and after reallocation from OB to SFR care. A design with an asynchrony in time between a control and a study group may be particularly sensitive to gradual and unrecognised changes in many practices, including nutrition, which was probably the reason why we observed an increase in weight at PMA of 34 weeks when moving from an OB to a SFR unit.

Our hypothesis of a positive effect of SFR care on growth was based on an assumption that less strain from environmental stressors and increased positive sensory stimulation from the parents and other effects of SFR care would leave more energy for growth. There is evidence of improved clinical stability during hospitalisation and of better short-

**Table 4** Hours (SD) of parental presence and skin-to-skin care (SSC) in single-family room (SFR) and open-bay (OB) units

	SFR unit Mean hours (SD)	OB unit Mean hours (SD)	Adjusted mean difference*	95% CI	p-value
Presence					
Mother first week	111 (38)	33 (13)	82	72, 91	0.000
Father first week	115 (39)	31 (13)	78	62, 95	0.000
Mothers' per day until 34 weeks' PMA	21 (5)	7 (3)	14	13, 15	0.000
Fathers' per day until 34 weeks' PMA	16 (6)	5 (2)	9	9, 13	0.000
Skin-to-skin contact					
Mother first week	21 (10)	12 (8)	11	7, 15	0.000
Father first week	13 (7)	8 (5)	4	0, 8	0.003
Parents' per day until 34 weeks' PMA	6.0 (2)	4.4 (2)	1.9	1, 3	0.000
Mothers' per day until 34 weeks' PMA	4.2 (2)	3.0 (2)	1.6	0.7, 2	0.000
Fathers' per day until 34 weeks' PMA	1.8 (1)	1.4 (1)	0.4	-0.1, 0.9	0.091

\*Adjusted for mode of delivery (vaginal vs caesarean section), gestational age, parents education (elementary/high school or college/university) in linear regression analysis.



**Figure 2** A–C. Individual growth trajectories from birth to PMA of four months'. Dots are measurements of the infants at birth, PMA of 34 weeks', discharge from the hospital, term date and four months after term date; the grey colour represents the single-family room (SFR) unit, and pink represents the open-bay (OB) unit. The grey and pink lines are the interpolation lines for individual growth trajectories. The black and red lines are the expected growth in the SFR and OB units, respectively, as estimated from a linear mixed model with random intercept and fixed effects for unit, PMA, and an interaction term between unit and PMA.

and long-term outcome if SSC and family-centred care are practiced on a daily basis (4,21). Both our and other studies (7) concluded that SFR care facilitate early and prolonged parental presence and involvement, and Lester et al. (12) suggested that these factors, together with developmental support, were the main mediators of the positive effects of SFR care. A possible explanation for the lack of difference on morbidity and growth between our two groups may be that family-centred care and SSC were practiced quite extensively in both units and that there may be a threshold for positive effects at less involvement than in our OB groups. Indeed, Cong et al. (22) reported that one hour of SSC per day was associated with improved cognitive and neurobehavioral outcome. In a meta-analysis, Boundy et al. (23) found that SSC had a long-term positive effect on head growth and weight, but there were major methodological issues such as a lack of detailed information about interventions and heterogeneity in the components of SSC and conventional care, and only a few studies were from high-income countries. SSC has also been associated with improved short-term clinical stability and decreased stress during procedures (21,24) as well as hormonal changes suggestive of reduced stress in parents and their infants (22). However, neither potential biological mechanism (25) nor dose-response relationship are known (21).

The relationship between the design of the unit and the culture of care are not independent of each other. We found care in SFR unit promotes parental involvement, including extensive presence and SSC. However, our study also documented that extensive presence and SSC can be accomplished in a traditional and crowded OB unit. Dedicated staff and extensive social security benefits for the families were probably important contributing factors. Our results should therefore be interpreted in the socio-economic context of a publicly financed healthcare system with extensive benefits for parents and children. Future research should also study the effect of social security systems and benefits for parents on infant outcomes and parents role in the NICU.

## CONCLUSION

For the infant to gain full advantage of the benefits of SFR care, it requires a social security system for parents allowing them to be present with their infant for longer periods every day. The families in the SFR unit spent substantially more time with their infants and in providing SSC than the families in the OB unit, but the growth trajectories of the infants did not differ.

## FUNDING

The study was supported by a research grant from and the Norwegian Extra Foundation for Health and Rehabilitation.

## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article:

**Table S1** Feeding protocol if infants  $\leq 1250$  g.

**Table S2** Feeding protocol  $> 1250$  g.

**Appendix S1** Detailed information about the notation of the mixed model.