



Impact of a nurse education program on oral feeding in a neonatal unit.

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ABSTRACT

Background

Premature neonates often experience feeding difficulties during their hospital stay, and evidence-based interventions have been shown to improve feeding outcomes.

Aim

This study investigated whether an infant-led educational bundle led by nurses accelerates the achievement of independent oral feeding in neonates in a neonatal intensive care unit.

Study Design

A quality improvement study with a pre, during and post intervention test design. All premature neonates admitted to the unit were eligible. The feeding program included a four-month nurse training module and nurse coaching.

Results

125 nurses or nurse assistants attended the program and 706 neonates were included. The median time to independent oral feeding (IOF) was 40, 36 and 37 days respectively for pre, during and post intervention. The reduction in time to IOF observed during the post-intervention period compared to the baseline period was significant (HR=1.32, CI 95%: 1.01-1.74). No difference was noted in the length of hospital stay between the three study periods.

Conclusions

An infant-led nurse educational bundle can promote earlier achievement of IOF in preterm neonates.

Relevance to Clinical Practice

This quality improvement study demonstrates the impact that a nurse-driven intervention in neonatal care can have on improving practice. Feeding interventions involve the early introduction of oral feeding, non-nutritive sucking (NNS) and oral motor stimulation, and should be individualised for each neonate. These individualised feeding interventions applied by all nurses and assistant nurses can facilitate the achievement of earlier independent oral

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3 feeding in preterm infants and should be included in neonatal critical care nurse education
4 programs.
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8 **What is known about this topic?**

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- 11 • Premature neonates often experience feeding difficulties during their hospital stay.
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- 13 • Different evidence-based interventions can improve feeding outcomes in neonates.
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- 15 • Individualised feeding approaches can improve feeding in preterm neonates.
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- 17 • Feeding strategies vary between individual healthcare providers, based on caregivers' beliefs
- 18 rather than scientific evidence.
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23 **What this paper adds?**

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26 The combination of a detailed nurse-training program, based on an individualised neonatal
27 cue-based and semi-demand feeding approach, with interventions to ensure successful
28 feeding transition and maintenance of neonatal feeding competencies, can promote the
29 earlier achievement of independent oral feeding in preterm neonates.
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34 **KEYWORDS**

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36 Nurse education, neonatal intensive care, nutrition, preterm infants, feeding bundle.
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46 **ABBREVIATIONS**

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49 BPD: bronchopulmonary dysplasia
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52 CI: Confidence Interval
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55 GA: Gestational Age
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58 HR: Hazard Ratio
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3 IOF: independent oral feeding
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6 IVH: intraventricular hemorrhage
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9 LOS: length of hospital stay
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13 NEC: necrotising enterocolitis
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16 NICU: Neonatal Intensive Care Unit
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19 NNS: nonnutritive sucking
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23 PMA: postmenstrual age
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26 PVL: periventricular leucomalacia
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29 SD: standard deviation
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For Review Only

INTRODUCTION

Premature neonates often experience feeding difficulties during their hospital stay (1). These feeding issues arise from transitioning from parenteral to tube feeding and then to independent oral feeding. These difficulties can prolong their hospital stay, increase costs and may lead to feeding dysfunction in childhood (2,3). Immature sucking, delayed swallow and/or inadequate coordination of sucking, swallowing and respiration are potential causes for oral feeding issues (4). Different evidence-based interventions have been proposed to improve feeding outcomes in neonates, such as the early introduction of oral feeding, non-nutritive sucking (NNS) or oral motor stimulation used separately and/or in combination (5-11). In addition, feeding approaches, which consider the individual infants' feeding patterns in order to develop cue-based feedings, can improve oral feeding achievement in neonates (12-15). Furthermore, without formal guidelines and protocols neonatal feeding strategies can vary between individual healthcare providers, based on their beliefs and intuitions rather than scientific evidence (15,16,17). Individualised feeding strategies based on simplified, approaches implemented after educational multidisciplinary rounds have been shown to improve infants, feeding pattern (15,18,19,20). For example, the introduction of premature infant feeding assessment flowsheets was associated with a significant reduction in time to full feeds and discharge (18). In addition, process optimisation and the implementation of a standardised feeding strategy minimizes practice variability, accelerates the attainment of enteral and oral feeding milestones and decreases length of hospital stay (15,17,20). We aimed to assess whether a focused nurse education program linked to an established individualised infant-driven feeding pathway could accelerate the achievement of independent oral feeding in premature neonates.

METHODS

Study design and population

This quality improvement study methodology has been described in more detail in our published protocol paper (21). The study had a pre, during and post interventional test design

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3 with (1) A six-month baseline period; (2) a 22-month intervention period; and (3) a six-month
4 post-intervention period and was conducted from April 2013 to January 2016 (22).

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7 The study is reported following the Standards for Quality Improvement Reporting Excellence
8 (SQUIRE) 2.0 guidelines (23).

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11 The study took place in a 44-bed, level IIIC open ward Neonatal Intensive Care Unit (NICU)
12 of a university hospital in Lyon, France. (A level IIIC NICU is a tertiary level neonatal
13 intensive care unit that provides medical and surgical care) (24). Eighteen neonatologists,
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120 registered nurses and 12 nurse assistants worked in this medical and surgical neonatal
unit at the time.

All nurses and nurse assistants were asked to participate. Fifty percent of the nurses were
paediatric nurses (additional year of specialisation in France). Nurse assistants were
licensed after a one-year training and work directly under the supervision of the registered
nurses.

All premature neonates of less than 34 weeks postmenstrual age (PMA) with a nasogastric
tube for feeding, admitted to the unit during the three study periods, were included. Below 34
weeks PMA a nasogastric tube was systematically placed in the NICU. After 34 weeks PMA
a nasogastric tube was only inserted if the child did not suck. Neonates were excluded if they
presented with major congenital malformations or underwent surgery and required
endotracheal intubation.

Once their condition was considered stable, premature neonates could be transferred if they
still needed support either to level II step down beds part of the unit or to another level II
hospital close to their homes or discharged home if ready. This corresponded to the usual
regional neonatal network functioning. Transfer criteria could change during the study period.
Neonates were followed-up until their discharge home.

Baseline period

For premature neonates included during the six-month baseline period, unit practice was that
oral feedings were initiated at 33 weeks PMA. No oral feeding protocol was in place at the

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3 time. There was no volume limit per oral feeding. Parents participated in feeding whenever
4 they were present. Once a neonate achieved 75% of the oral feedings per day and the
5 physician and bedside nurse were satisfied and the child was stable, the nasogastric tube
6 was removed. Neonates presenting with feeding issues were detected during the daily round
7 by the bedside nurse and the physician in charge. If detected they were then referred for an
8 oral-motor rehabilitation program conducted by a physiotherapist or a speech therapist
9 specialised in feeding disorders. Historically, in this NICU physiotherapists take care of
10 premature neonates presenting with feeding disorders. This is linked to the fact that speech
11 therapists are not dedicated to the NICU. This oral-motor rehabilitation program consisted of
12 twenty minutes daily oral motor stimulation sessions.
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26 **Intervention period**

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28 The intervention is described in depth in a previous publication (21) but consisted of an
29 educational program, for nurses and nurse assistants, on the feeding pattern in premature
30 neonates (21). This program included a four-month training module and continuous practice
31 nurse coaching throughout the intervention period. Fifteen to 30 nurses or nurse assistants
32 attended each training module. Six modules were scheduled over the 22-month period to
33 include the 120 nurses and 12 nurse assistants from the unit. All newly employed nurses
34 entered the training program after starting in NICU. The training module consisted of two
35 days of teaching followed by two, two-hour-multidisciplinary workshops (see previous
36 publication for details) (21). The individualised infant-driven feeding protocol, was developed
37 after a literature review, and was introduced during the two-day teaching (5-15). An Infant-
38 driven feeding regime is based on infant needs and responses, rather than on time periods.
39 Figure 1 shows the individualised feeding protocol.
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53 In addition to the training module, expert feeding rounds took place throughout the
54 intervention period on a regular basis by the physiotherapist (one-hour round per day) and
55 speech therapist (three-hours round per week) (21). The physiotherapist and the speech
56 therapist were specialists in feeding disorders. The practice nurse coaching was conducted
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3 in the NICU to (1) reinforce the key messages of the feeding protocol, (2) monitor staff
4 compliance (3) identify neonates for whom the feeding protocol was not applied correctly,
5 and (4) engage provider focused feeding discussions. Nurses and nurse assistants were
6 supported in their routine feeding practice and application of feeding protocols, and helped
7 with early detection of infants presenting with feeding issues. When necessary, the
8 physiotherapist or the speech therapist applied the oral motor rehabilitation protocol.
9 Parents also participated in the intervention. When they were present, they undertook oral
10 and perioral stimulation as well as nonnutritive sucking for their child. They also gave oral
11 feeds when their child was older than 32 weeks PMA.
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24 **Post-intervention period**

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26 During the post-intervention period, nurses and nurse assistants maintained nonnutritive
27 sucking, oral and perioral stimulation as well as early oral feedings according to the
28 individualised infant-driven feeding protocol. The physiotherapist specialised in feeding
29 disorders and speech therapist continued regular practice nurse coaching and assisted
30 caregivers with early detection of infants presenting with feeding issues. They applied the
31 oral-motor rehabilitation protocol if necessary.
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41 **Outcome measures**

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43 The primary outcome was the time to independent oral feeding, defined as the duration
44 between the date of birth and the date of withdrawal feeding tube expressed as the postnatal
45 age in days and as the gestational age in weeks. The transition time corresponded to the
46 duration between the date of feeding tube placement and the date of its withdrawal for alive
47 neonates at NICU discharge or for neonates transferred from NICU to another hospital.
48 Length of hospital stay (LOS) was defined as the duration from the date of a neonate's
49 NICU's admission to the date of home discharge for alive and not lost to follow up. Neonatal
50 pathologies, which occurred during NICU stay, for neonates who went home at NICU
51 discharge, were monitored and included bronchopulmonary dysplasia (BPD), necrotising
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3 enterocolitis (NEC), periventricular leucomalacia (PVL), intraventricular hemorrhage (IVH),
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5 culture proven bloodstream infections. Severe morbidity was defined if culture proven
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7 bloodstream infections or BPD or PVL or IVH >grade 2 or NEC \geq grade 2 occurred. Another
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9 secondary outcome was the percentage of neonates who died during the NICU stay. The
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11 percentage of neonates who were breastfed at the time of NICU discharge as well as weight
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13 gain per day for neonates who were not transferred to another hospital at NICU discharge
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15 were also collected.
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18 Nurses' participation in the training modules was evaluated through their presence at the
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20 training sessions. At the end of the training module, their theoretical knowledge was
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22 assessed with a score between 0 and 20 through a 12 item multiple-choice knowledge
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24 questionnaire, around physiology (4 items), feeding strategies (3 items), recognising and
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26 treating feeding disorders (5 items), and one question about the adequacy of provision of
27
28 sufficient information about feeding issues in the training.
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31 At the end of the intervention period, feeding protocol compliance was assessed through a
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33 self-administered questionnaire completed by nurses, consisting of questions concerning the
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35 application of the individualised infant-driven feeding protocol (time dedicated to daily feeding
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37 practice and application of feeding protocols rated on a Likert scale).
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41 **Statistical Analysis**

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43 Data were collected and entered into a Microsoft Excel file and then transferred to Statistical
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45 analysis software (SAS Institute, Cary, NC, version 9.3) for further inferential analysis. To
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47 account for censored neonates (censored neonates did not present the primary outcome
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49 measure), the time to independent oral feeding was compared between periods using
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51 survival analysis (Kaplan Meier and Cox proportional hazards regression model) adjusted for
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53 gestational age and severe morbidity. Infants were censored if they died prior to the tube
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55 removal, were discharged home with a feeding tube, or were lost to follow-up after their
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57 NICU discharge. Their data has been taken into account in the analysis.
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3 Results were expressed with Hazard Ratio (HR) and associated 95% confidence interval
4 (CIs) with HR <1 indicating a positive effect of the intervention. Sensitivity analyses that
5 excluded neonates who died with a feeding tube in place and those who were transferred to
6 another hospital with a feeding tube were performed. Among non-censored neonates, the
7 time to independent oral feeding was compared between periods using ANOVA (one-way
8 analysis of variance).

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18 Secondary outcomes were compared between periods using linear models and logistic
19 regression models or Fisher's test exact with Bonferroni adjustment to correct for multiple
20 comparisons when appropriate. The percentage of alive neonates who were breastfed by the
21 time of their NICU discharge, and the weight gain per day among neonates who were alive
22 and not transferred to another hospital at their NICU discharge were summarized in each
23 period. Analyses were performed using SAS software (SAS Institute, Cary, NC, version 9.3).
24 A p-value <0.05 was considered statistically significant.

25 26 27 28 29 30 31 32 33 34 **RESULTS**

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37 A total of 711 preterm infants were included in the study, after the exclusion of 5 neonates
38 with major congenital anomalies, the data of 706 neonates (104 in the baseline period, 439 in
39 the intervention period and 163 in the post-intervention period) were analyzed. Figure 2
40 shows the study flow chart.

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45 Eighty-nine (13%) neonates died before their NICU discharge 16 (15%) in the baseline
46 period, 56 (13%) in the intervention period and 17 (10%) in the post-intervention period). Out
47 of the 617 (87%) neonates alive (88 (85%) in the baseline period, 383 (87%) in the
48 intervention period and 146 (90%) in the post-intervention period), 221 (36%) were
49 discharged home (47 (53%) in the baseline period, 133 (35%) in the intervention period and
50 41 (28%) in the post-intervention period). 396 (56%) were transferred to another hospital (41
51 (47%) in the baseline period, 250 (65%) in the intervention period and 105 (72%) in the post-
52 intervention period). The proportion of neonates transferred to another hospital was
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3 significantly different between the three study periods ($p=0.0003$). Of the 396 transferred
4 neonates, 291 neonates (73%) still had their feeding tube at the time of their transfer (32
5 (78%) in the baseline period, 183 (73%) in the intervention period and 76 (72%) in the post-
6 intervention period). Infants were transferred on average $25.9 \pm \text{SD } 22.5$ days after their
7 NICU admission ($26.9 \pm \text{SD } 22.3$ days in baseline period, $25.8 \pm \text{SD } 23.0$ days in intervention
8 period and $26.0 \pm \text{SD } 21.6$ days in post-intervention period). When transferred, they were
9 aged on average $34.3 \pm \text{SD } 2.3$ gestational age (GA) ($34.8 \pm \text{SD } 2.0$ in the baseline period,
10 $34.3 \pm \text{SD } 2.4$ GA in the intervention period and $34.2 \pm \text{SD } 2.2$ GA in the post-intervention
11 period).

22 23 24 **Neonates' characteristics**

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26 The neonates' characteristics are presented in Table 1. There was no statistically significant
27 difference in PMA at birth, congenital anomalies, antenatal steroids, gender, delivery mode
28 and median 5 min Apgar scores between the three periods. However, neonates from the
29 baseline period were smaller compared to babies from the intervention and post-intervention
30 periods. More single births occurred during the intervention and post-intervention periods
31 compared to the baseline period.

32 33 34 35 36 37 38 39 40 41 **Time to independent oral feeding**

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43 Among the 706 neonates, 610 (86%) were feeding tube free (87 in the baseline period, 373
44 in the intervention period and 150 in the post-intervention period). For 597 (85 %) of them,
45 the nasogastric tube was removed before hospital discharge (87 in the baseline period, 373
46 in the intervention period and 150 in the post-intervention period), three after hospital
47 discharge (one in the baseline period, two in the intervention period) and 10 before their
48 death (1 in the baseline period, 4 in the intervention period and 5 in the post-intervention
49 period). 96 (14%) were censored for time to feeding tube withdrawal: 79 died (15 in the
50 baseline period, 52 in the intervention period and 12 in the post-intervention period) and 17
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3 were lost to follow up after hospital discharge (2 in the baseline period, 14 in the intervention
4 period and 1 in the post-intervention period).

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7 The median time to independent oral feeding was 40, 36 and 37 days respectively for the
8 baseline, intervention, and post-intervention period. The difference was not significant
9 between the three periods (trend logrank test, $p=0.5795$). After adjustment in the Cox
10 proportional hazards model (Table 2a), there was a significant reduction in the time to
11 independent oral feeding between the post-intervention period compared to the baseline
12 period (HR=1.32, 95% confidence interval (CI): 1.01-1.74, $p=0.0301$). Infants in the post-
13 intervention period were able to achieve independent oral feeding on average at 35.5 ± 2.1
14 PMA compared to 36.2 ± 2.2 PMA in the baseline period (mean difference: -0.7; 95% CI: -
15 1.2- -0.2, Table 2b).

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18 No change in results occurred after excluding the 79 deceased neonates who still had their
19 nasogastric tube in place and the 291 neonates who were transferred to another hospital
20 with their tube in place after their NICU discharge.

21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 **Secondary outcomes**

36 The transition times were significantly longer for the post-intervention period compared to the
37 baseline and intervention period ($p=0.0031$). No difference was shown between the three
38 study periods in terms of LOS, the percentage of neonates who died during the NICU stay;
39 and those who developed neonatal pathologies. Weight gain and breastfeeding rates
40 remained stable throughout the study periods (Table 3).

41 42 43 44 45 46 47 48 49 **Improvement in nurses' knowledge after implementation of the educational program**

50 A hundred and twenty-five registered nurses and assistant nurses out of 132 (95 %)
51 undertook the training module during the intervention period. Eighty-eight nurses and nurse
52 assistants (70.4%) were able to complete the entire training consisting of the theoretical two-
53 day session and the two workshops. Fifteen nurses and nurse assistants (12 %) did not
54 participate in any workshop.

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3 The median score of the nurses' knowledge questionnaire, completed at the end of the
4 training session by 125 nurses and nurse assistants, was 14.1 out of 20 [IQR13.0-14.5]. At
5 the end of the intervention period, 81 nurses and assistant nurses responded to the self-
6 report questionnaire to assess compliance with the feeding protocol. More than half (62 %) of
7 the nurses and nurse assistants spent five minutes or more per feeding when using the
8 feeding protocol. Almost all, 98 % of the nurses administered the feeding protocol frequently
9 or for each neonate, and 89 % of the nurses initiated feedings at 29 weeks PMA.
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22 **DISCUSSION**

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24 This study showed that implementation of an infant led educational feeding bundle and nurse
25 education program was associated with an earlier attainment of independent oral feeding in
26 neonates of less than 34 weeks PMA. To our knowledge, this is the first study evaluating the
27 combination of an educational nurse-training program, combined with an individualized cue-
28 based and semi-demand feeding approach and interventions to ensure successful feeding
29 transition and maintenance of neonatal feeding achievement. McCain *et al* and Kirk *et al*
30 found that cue-based and semi-demand fed infants reached independent oral feedings 6 and
31 5 days earlier, respectively, compared to infants transitioning to independent oral feeds
32 based on physicians' orders (12,13). However, Kirk *et al* did not note any difference in LOS
33 between the study periods (13). Other researchers found that educational training programs
34 associated with the development of neonatal feeding management guidelines accelerated
35 the attainment of independent oral feedings and decreased LOS in premature healthy
36 neonates (15,18,19, 25).
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51 The early introduction of oral feeding, before 30 weeks PMA, appears to be effective to
52 accelerate oral feedings in neonates (5,26). A meta-analysis showed that NNS accelerated
53 the transition time from tube to independent oral feeding, shortened the transition time from
54 start to full oral feeding, and reduced LOS (6). An oral motor stimulation intervention also
55 improves feeding progression and reduces LOS (7,8). A combination of NNS and oral
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3 stimulation improved the feeding ability of premature infants and shortened transition time
4 from tube assisted to independent oral feeding. Unfortunately, no earlier discharge was
5 obtained (27).
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9 Our findings suggested identical weight gain for both study periods, the baseline and post-
10 intervention period. These results are consistent with previous studies (13,15).
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13 However, even though we found an earlier gestational age at independent oral feeding for
14 neonates who had the intervention, no difference in LOS was observed. Several factors may
15 have contributed to this result. Firstly, home discharge conditions were not monitored as part
16 of the study, and may have changed over the duration of the study. For example, the
17 criterion "no bradycardia for 5 days" was replaced by a new discharge criterion "the mature
18 heart rate variability" which may have influenced LOS (28).
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21 Secondly, the continuous monitoring of apnoea and bradycardia until NICU discharge may
22 have influenced LOS, even if neonates achieved independent oral feeding earlier. Our
23 findings are consistent with earlier studies who showed similar results with improved feeding
24 achievement without shortening the LOS (13,29). Almost all nurses and nurse assistants (95
25 %) started the training session during the implementation period. Their knowledge acquisition
26 was good at the end of the training session and most nurses considered the content of the
27 training session as adequate. Nurses reported compliance with the feeding protocol was also
28 very good, with almost all stating they used the feeding protocol for each feeding.
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43 **Limitations**

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45 This study has several limitations: Firstly, feeding protocol compliance was not objectively
46 measured during the study period. Initially it was planned in the study protocol to measure
47 this for each child. Unfortunately, this was not feasible. Secondly, the self-report
48 questionnaire has a risk of bias, and may reveal an acceptance of the feeding pathway rather
49 than compliance with the feeding protocol in clinical practice. Thirdly, discharge criteria were
50 not monitored during the study, which made it difficult to distinguish between the evolution of
51 feeding and apnoea/bradycardia discharge criteria over time. Fourthly, the effect of the
52 educational program on the time to independent oral feeding could be underestimated
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3 because of the transfer out of the NICU to another hospital and the neonates not being
4 feeding tube free although it was not assessed through the sensitivity analysis. In addition,
5 neonates from the baseline period were smaller compared to babies from the intervention
6 and post-intervention period which could have impacted on LOS. Finally, parental
7 involvement and satisfaction were not monitored during the study. It would have been
8 interesting to compare parents' involvement and satisfaction before and after the feeding
9 protocol implementation. Despite these limitations, our study is based on a broad population
10 and lost very few patients to follow up which suggests that this is feasible.
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22 **Implications and recommendations for practice**

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24 Feeding difficulties in neonates are common and important. Feeding interventions such as
25 the early introduction of oral feeding, non-nutritive sucking (NNS) and oral motor stimulation
26 should be implemented for all preterm neonates because they have been shown to promote
27 earlier achievement of oral feeding and earlier discharge. They can also prevent feeding
28 dysfunction in childhood. In addition, these feeding strategies should be individualised for
29 each neonate. Nurse driven protocols like this, based on infant cues, used consistently by all
30 nurses and assistant nurses in a unit can positively impact on neonatal outcomes and should
31 be included in neonatal nursing education programs and be implemented in clinical practice.
32 Future studies should analyse parents' satisfaction and participation in these feeding
33 pathways and the impact of these in the longer term.
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47 **Conclusions**

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49 In conclusion, an infant-driven feeding protocol combined with a nurse-training program may
50 be associated with a significant earlier achievement of independent oral feeding in premature
51 infants. This type of program is feasible and well-accepted. Future research should explore
52 the long-term impact of such programs on both parental satisfaction and longer term feeding
53 disorders in ex-preterm children.
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REFERENCES

1. Wang ML Dorer DJ, Fleming MP, Catlin EA. Clinical outcomes of near-term infants. *Pediatrics* 2004;114(2):372-376.
2. Barlow SM. Oral and respiratory control for preterm feeding. *Curr Opin Otolaryngol Head Neck Surg* 2009;17(3):179-186.
3. Rommel N, De Meyer AM, Feenstra L, Veereman-Wauters G. The complexity of feeding problems in 700 infants and young children presenting to a tertiary care institution. *J Pediatr Gastroenterol Nutr* 2003;37(1):75-84.
4. Lau C, Schanler RJ. Oral feeding in premature infants: advantage of a self-paced milk flow. *Acta Paediatr* 2000;89(4):453-459.
5. Simpson C, Schanler RJ, Lau C. Early introduction of oral feeding in preterm infants. *Pediatrics* 2002;110(3):517-522.
6. Foster JP, Psaila K, Patterson T. Non-nutritive sucking for increasing physiologic stability and nutrition in preterm infants. *Cochrane Database Syst Rev* 2016;10(10):CD001071.
7. Lessen BS. Effect of the premature infant oral motor intervention on feeding progression and length of stay in preterm infants. *Adv Neonatal Care* 2011;11(2):129-139.
8. Ghomi H, Yadegari F, Soleimani F, Lessen Knoll B, Noroozi M, Mazouri A. The effects of premature infant oral motor intervention (PIOMI) on oral feeding of preterm infants: A randomized clinical trial. *Int J Pediatr Otorhinolaryngol* 2019;120:202-209.
9. Greene Z, O'Donnell CP, Walshe M. Oral stimulation for promoting oral feeding in preterm infants. *Cochrane Database Syst Rev* 2016;(9): CD009720.
10. Thabet AM, Sayed ZA. Effectiveness of the Premature Infant Oral Motor Intervention on Feeding Performance, Duration of Hospital Stay, and Weight of Preterm Neonates in Neonatal Intensive Care Unit: Results From a Randomized Controlled Trial. *Dimens Crit Care Nurs* 2021 Jul-Aug 01;40(4):257-265.

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3 11. Ghomi H, Yadegari F, Soleimani F, Knoll BL, Noroozi M, Mazouri A. The effects of
4 premature infant oral motor intervention (PIOMI) on oral feeding of preterm infants: A
5 randomized clinical trial. *Int J Pediatr Otorhinolaryngol* 2019 May;120:202-209.
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9 12. McCain GC, Gartside PS, Greenberg JM, Wright Lott J. A feeding protocol for healthy
10 preterm infants that shortens time to oral feeding. *J Pediatr* 2001;139(3):374–379.
11
12
- 13 13. Kirk AT, Alder SC, King JD. Cue-based oral feeding clinical pathway results in earlier
14 attainment of full oral feeding in premature infants. *J Perinatol* 2007;27(9):572-578.
15
16
- 17 14. Pickler RH, Reyna BA, Wetzel PA, Lewis M. Effect of four approaches to oral feeding
18 progression on clinical outcomes in preterm infants. *Nurs Res Pract*
19 2015;2015:716828.
20
21
22
- 23 15. Jadcherla SR; Dail J, Malkar MB, McClead R, Kelleher K, Nelin L. Impact of Process
24 Optimization and Quality Improvement Measures on Neonatal Feeding Outcomes at
25 an All-Referral Neonatal Intensive Care Unit. *JPEN J Parenter Enteral Nutr* 2016
26 Jul;40(5):646-655.
27
28
29
- 30 16. Klingenberg C, Embleton ND, Jacobs SE, O'Connell LA, Kuschel CA. Enteral feeding
31 practices in very preterm infants: an international survey. *Arch Dis Child Fetal Neonatal*
32 *Ed* 2012;97(1):F56-F61.
33
34
35
36
37
- 38 17. Lyu T, Zhang Y, Hu X, Gu Y, Li L, Lau C. Management of Oral Feeding Challenges in
39 Neonatal Intensive Care Units (NICUs): A National Survey in China. *Front Pediatr* 2020
40 Jun 24;8:336.
41
42
43
44
- 45 18. Wellington A, Perlman JM. Infant-driven feeding in premature infants: a quality
46 improvement project. *Arch Dis Child Fetal Neonatal Ed* 2015;100(6):F495–F500.
47
48
- 49 19. Osman A, Ibrahim M, Saunders J, Merheb R, Moscorelli M, Caretto V, Groh-Wargo S.
50 Effects of Implementation of Infant-Driven Oral Feeding Guideline on Preterm Infants'
51 Abilities to Achieve Oral Feeding Milestones, in a Tertiary Neonatal Intensive Care Unit.
52 *Nutr Clin Pract* 2021 Dec;36(6):1262-1269.
53
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55
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2
3 20. Bapat R, Gulati IK, Jadcherla S. Impact of SIMPLE Feeding Quality Improvement
4 Strategies on Aerodigestive Milestones and Feeding Outcomes in BPD Infants. *Hosp*
5 *Pediatr* 2019 Nov;9(11):859-866.
6
7
8
9 21. Touzet S, Beissel A, Denis A, Pillet F, Gauthier-Moulinier H, Hommey S, Claris O.
10 TOP Study Group. Effectiveness of a nurse educational oral feeding programme on
11 feeding outcomes in neonates: protocol for an interrupted time series design. *BMJ*
12 *Open* 2016 Apr 15;6(4):e010699.
13
14
15
16
17 22. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series
18 designs in health technology assessment: lessons from two systematic reviews of
19 behavior change strategies. *Int J Technol Assess Health Care* 2003;19(4):613–623.
20
21
22
23 23. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. Squire 2.0
24 (Standards for Quality Improvement Reporting Excellence): revised publication
25 guidelines from a detailed consensus process. *Am J Crit Care* 2015 Nov;24(6):466-
26 73.
27
28
29
30
31
32 24. Stark AR; American Academy of Pediatrics Committee on Fetus and Newborn. Levels
33 of neonatal care. [published correction appears in *Pediatrics*. 2005 Apr;115(4):1118].
34 *Pediatrics* 2004;114(5):1341-1347.
35
36
37
38 25. Chrupcala KA, Edwards TM, Spatz DL. A Continuous Quality Improvement Project to
39 Implement Infant-Driven Feeding as a Standard of Practice in the Newborn/Infant
40 Intensive Care Unit. *J Obstet Gynecol Neonatal Nurs* 2015;44(5):654-664.
41
42
43
44 26. Lau C, Sheena HR, Shulman RJ, Schanler RJ. Oral Feeding in Low Birth Weight
45 Infants. *J Pediatr* 1997; Apr;130(4):561-569.
46
47
48
49 27. Li XL, Liu Y, Liu M, Yang CY, Yang QZ. Early Premature Infant Oral Motor
50 Intervention Improved Oral Feeding and Prognosis by Promoting Neurodevelopment.
51 *Am J Perinatol* 2020;37(6):626-632.
52
53
54
55 28. Javorka K, Lehotska Z, Kozar M, Uhríkova Z, Kolarovszki B, Javorka M, Zibolen M.
56 Heart rate variability in newborns. *Physiol Res* 2017;66(Suppl 2):S203-S214.
57
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59
60

- 1
2
3 29. Eichenwald EC, Blackwell M, Lloyd JS, Tran T, Wilker RE, Richardson DK. Inter-
4 neonatal intensive care unit variation in discharge timing; influence of apnea and
5 feeding management. *Pediatrics* 2001;108(4):928–933.
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For Review Only

Table 1 Neonates' characteristics at NICU admission

	Baseline N=104	Intervention N=439	Post- intervention N=163	p-value
Male, n (%)	58 (55.8)	233 (53.1)	82 (50.3)	0.6745
Gestational age (weeks), mean (SD)	29.9 (2.7)	29.8 (2.6)	29.8 (2.7)	0.9713
Birth weight (z-score), n (%)				0.0174
<10%	25 (24)	57 (13)	15 (9)	
10-90%	76 (73)	369 (84)	144 (88)	
>90%	3 (3)	13 (3)	4 (3)	
Apgar at 5', mean (SD)	8 (2.4)	8.4 (2)	8.3 (2.1)	0.5202
Multiple labor, n(%)	35 (33.7)	205 (46.7)	78 (47.9)	0.0397
Antenatal steroids, n (%)	93 (89.4)	387 (88.2)	147 (90.2)	0.9464
Outborn status, n(%)	10 (9.6)	71 (16.2)	22 (13.5)	0.2118
SD: standard deviation				

Table 2a. Impact of the nurse educational program feeding on time to independent oral feeding for all neonates

	N	HR [CI 95 %]*	p-value*
Days of life to IOF (days)			0.0301
Baseline	104	-	-
Intervention	439	1.03 [0.81 ; 1.31]	0.7993
Post-intervention	163	1.32 [1.01 ; 1.74]	0.0430
PMA to IOF (weeks)			0.0368
Baseline	104	-	-
Intervention	439	1.20 [0.94 ; 1.52]	0.1368
Post-intervention	163	1.41 [1.08 ; 1.85]	0.0115

IOF: Independent Oral Feeding, PMA: postmenstrual age, CI: Confidence Interval, HR: Hazard Ratio* p-values were obtained from Cox proportional hazard model adjusted for gestational age and severe morbidity (sepsis with positive blood culture or BPD or PVL or IVH grade III/IV or NEC \geq stage 2). HR <1 indicates a positive intervention effect.

Table 2b. Impact of the nurse educational program feeding on time to independent oral feeding for not censored neonates

	N*	Mean (SD)	Difference with baseline group, mean [CI 95%]	p-value**
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Days of life to IOF (days)				0.717
Baseline	87	40.8 (24.9)	-	
Intervention	373	39.2 (22.5)	-0.9 [-5.3 ; 3.4]	
Post-intervention	150	38.3 (22.3)	-2.5 [-8.5 ; 3.5]	
<hr/>				
PMA to IOF (weeks)				0.0302
Baseline	87	36.2 (2.2)		
Intervention	373	35.8 (1.9)	-0.3 [-0.7 ; 0.1]	
Post-intervention	150	35.5 (2.1)	-0.7 [-1.2 ; -0.2]	

IOF: Independent Oral Feeding, PMA: postmenstrual age, SD: Standard Deviation, CI: Confidence Interval

* number after excluding censored neonates (died prior to the tube removal, discharged home with a feeding tube or lost to follow-up after their NICU discharge)

** ANOVA-F-test

Table 3. Secondary outcomes

	Baseline	Intervention	Post-intervention	p-value
Transition time (weeks)*, ^a	N=56	N=200	N=70	
mean (SD)	3.4 (1.7)	4.5 (2.2)	4.6 (2.5)	<0,001
Neonatal pathology ^b	N=47	N=133	N=41	
BPD, n (%)	10 (21)	35 (26)	9 (22)	1.0000
NEC≥ stage 2, n (%)	1 (2)	1 (1)	3 (7)	1.0000
Grade III/IV IVH, n (%)	0 (0)	1 (1)	1 (2)	1.0000
Sepsis, positive blood culture, n (%)	5 (11)	35 (26)	6 (15)	0.2454
PVL, n (%)	2 (4)	5 (4)	4 (10)	1.0000
Death during the NICU stay ^c	N=104	N=439	N=163	
N (%)	16 (15)	56 (13)	17 (10)	0.1940
LOS (weeks) ^a	N=87	N=380	N=145	
mean (SD)	51.8 (32.8)	51.8 (28.7)	50.1 (24.6)	0.9237
Weight gain (g/day) ^d	N=47	N=133	N=41	-
mean (SD)	26.6 (5.4)	26.0 (5.1)	25.6 (5.1)	
Breastfeeding, n (%) ^d	N=88	N=383	N=146	-
	59 (67)	218 (57)	101 (69)	

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3 SD: standard deviation, BPD: bronchopulmonary dysplasia, NEC: necrotizing enterocolitis, IVH: intraventricular hemorrhage, PVL: periventricular
4 leucomalacia, Severe morbidity: Sepsis, positive blood culture or BPD or PVL or IVH grade III/IV or NEC \geq stage 2, LOS : length of hospital stay
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7 *Transition time corresponded to the duration between the date of tube feeding placement and the date of withdrawal feeding tube for alive neonates at NICU discharge
8 or for neonates transferred from NICU to another hospital without a feeding tube.
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11 ^a p-values were obtained from linear model adjusted for gestational age and severe morbidity.
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13 ^b p-values were obtained from logistic regression model adjusted for gestational age or fisher's test exact and Bonferroni correction.
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15 ^c p-values were obtained from logistic regression model adjusted for gestational age, Apgar score at 5', severe morbidity and LOS in NICU.
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17 ^d not tested given that these 2 variables are additional in the protocol.
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3 **FIGURE LEGENDS**
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6 **Figure 1:** ~~Standardised~~ individualised feeding protocol
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9 **Figure 2:** Study flow chart
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ABSTRACT

Background

Premature neonates often experience feeding difficulties during their hospital stay, and evidence-based interventions have been shown to improve feeding outcomes.

Aim

This study investigated whether an  educational bundle led by nurses accelerates the achievement of independent oral feeding in neonates in a neonatal intensive care unit.

Study Design

A quality improvement study with a pre, during and post intervention test design. All premature neonates admitted to the unit were eligible. The feeding program included a four-month nurse training module and nurse coaching.

Results

125 nurses or nurse assistants attended the program and 706 neonates were included. The median time to independent oral feeding (IOF) was 40, 36 and 37 days respectively for pre, during and post intervention. The reduction in time to IOF observed during the post-intervention period compared to the baseline period was significant (HR=1.32, CI 95%: 1.01-1.74). No difference was noted in the length of hospital stay between the three study periods.

Conclusions

An infant-led nurse educational bundle can promote earlier achievement of IOF in preterm neonates.

Relevance to Clinical Practice

This quality improvement study demonstrates the impact that a nurse-driven intervention in neonatal care can have on improving practice. Feeding interventions involve the early introduction of oral feeding, non-nutritive sucking (NNS) and oral motor stimulation, and should be individualised for each neonate. These individualised feeding interventions applied by all nurses and assistant nurses can facilitate the achievement of earlier **independent oral**

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3 **feeding** in preterm infants and should be included in neonatal critical care nurse education
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5 programs.
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8 **What is known about this topic?**

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- 11 • Premature neonates often experience feeding difficulties during their hospital stay.
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- 13 • Different evidence-based interventions can improve feeding outcomes in neonates.
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- 15 • Individualised feeding approaches can improve feeding in preterm neonates.
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- 17 • Feeding strategies vary between individual healthcare providers, based on caregivers' beliefs
- 18 rather than scientific evidence.
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23 **What this paper adds?**

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26 The combination of a detailed nurse-training program, based on an individualised neonatal
27 cue-based and semi-demand feeding approach, with interventions to ensure successful
28 feeding transition and maintenance of neonatal feeding competencies, can promote the
29 feeding transition and maintenance of neonatal feeding competencies, can promote the
30 earlier achievement of **independent oral feeding** in preterm neonates.
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34 **KEYWORDS**

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36 **Nurse education, neonatal intensive care, nutrition, preterm infants, feeding bundle.**
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46 **ABBREVIATIONS**

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49 BPD: bronchopulmonary dysplasia
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52 CI: Confidence Interval
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55 **GA: Gestational Age**
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59 HR: Hazard Ratio
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3 IOF: independent oral feeding
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6 IVH: intraventricular hemorrhage
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9 LOS: length of hospital stay
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13 NEC: necrotising enterocolitis
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16 NICU: Neonatal Intensive Care Unit
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19 NNS: nonnutritive sucking
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23 PMA: postmenstrual age
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26 PVL: periventricular leucomalacia
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29 SD: standard deviation
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INTRODUCTION

Premature neonates often experience feeding difficulties during their hospital stay (1). These feeding issues arise from transitioning from parenteral to tube feeding and then to independent oral feeding. These difficulties can prolong their hospital stay, increase costs and may lead to feeding dysfunction in childhood (2,3). Immature sucking, delayed swallow and/or inadequate coordination of sucking, swallowing and respiration are potential causes for oral feeding issues (4). Different evidence-based interventions have been proposed to improve feeding outcomes in neonates, such as the early introduction of oral feeding, non-nutritive sucking (NNS) or oral motor stimulation used separately and/or in combination (5-11). In addition, feeding approaches, which consider the individual infants' feeding patterns in order to develop cue-based feedings, can improve oral feeding achievement in neonates (12-15). Furthermore, without formal guidelines and protocols neonatal feeding strategies can vary between individual healthcare providers, based on their beliefs and intuitions rather than scientific evidence (15,16,17). Individualised feeding strategies based on simplified, approaches implemented after educational multidisciplinary rounds have been shown to improve infants' feeding pattern (15,18,19,20). For example, the introduction of premature infant feeding assessment flowsheets was associated with a significant reduction in time to full feeds and discharge (18). In addition, process optimisation and the implementation of a standardised feeding strategy minimizes practice variability, accelerates the attainment of enteral and oral feeding milestones and decreases length of hospital stay (15,17,20). We aimed to assess whether a focused nurse education program linked to an established individualised infant-driven feeding pathway could accelerate the achievement of independent oral feeding in premature neonates.

METHODS

Study design and population

This quality improvement study methodology has been described in more detail in our published protocol paper (21). The study had a pre, during and post interventional test design

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3 with (1) A six-month baseline period; (2) a 22-month intervention period; and (3) a six-month
4 post-intervention period and was conducted from April 2013 to January 2016 (22).

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7 The study is reported following the Standards for Quality Improvement Reporting Excellence
8 (SQUIRE) 2.0 guidelines (23).

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11 The study took place in a 44-bed, level IIIC open ward Neonatal Intensive Care Unit (NICU)
12 of a university hospital in Lyon, France. (A level IIIC NICU is a tertiary level neonatal
13 intensive care unit that provides medical and surgical care) (24). Eighteen neonatologists,
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The study took place in a 44-bed, level IIIC open ward Neonatal Intensive Care Unit (NICU)
of a university hospital in Lyon, France. (A level IIIC NICU is a tertiary level neonatal
intensive care unit that provides medical and surgical care) (24). Eighteen neonatologists,
120 registered nurses and 12 nurse assistants worked in this medical and surgical neonatal
unit at the time.

All nurses and nurse assistants were asked to participate. Fifty percent of the nurses were
paediatric nurses (additional year of specialisation in France). Nurse assistants were
licensed after a one-year training and work directly under the supervision of the registered
nurses.

All premature neonates of less than 34 weeks postmenstrual age (PMA) with a nasogastric
tube for feeding, admitted to the unit during the three study periods, were included. Below 34
weeks PMA a nasogastric tube was systematically placed in the NICU. After 34 weeks PMA
a nasogastric tube was only inserted if the child did not suck. Neonates were excluded if they
presented with major congenital malformations or underwent surgery and required
endotracheal intubation.

Once their condition was considered stable, premature neonates could be transferred if they
still needed support either to level II step down beds part of the unit or to another level II
hospital close to their homes or discharged home if ready. This corresponded to the usual
regional neonatal network functioning. Transfer criteria could change during the study period.
Neonates were followed-up until their discharge home.

Baseline period

For premature neonates included during the six-month baseline period, unit practice was that
oral feedings were initiated at 33 weeks PMA. No oral feeding protocol was in place at the

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3 time. There was no volume limit per oral feeding. Parents participated in feeding whenever
4 they were present. Once a neonate achieved 75% of the oral feedings per day and the
5 physician and bedside nurse were satisfied and the child was stable, the nasogastric tube
6 was removed. Neonates presenting with feeding issues were detected during the daily round
7 by the bedside nurse and the physician in charge. If detected they were then referred for an
8 oral-motor rehabilitation program conducted by a physiotherapist or a speech therapist
9 specialised in feeding disorders. Historically, in this NICU physiotherapists take care of
10 premature neonates presenting with feeding disorders. This is linked to the fact that speech
11 therapists are not dedicated to the NICU. This oral-motor rehabilitation program consisted of
12 twenty minutes daily oral motor stimulation sessions.
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26 **Intervention period**

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28 The intervention is described in depth in a previous publication (21) but consisted of an
29 educational program, for nurses and nurse assistants, on the feeding pattern in premature
30 neonates (21). This program included a four-month training module and continuous practice
31 nurse coaching throughout the intervention period. Fifteen to 30 nurses or nurse assistants
32 attended each training module. Six modules were scheduled over the 22-month period to
33 include the 120 nurses and 12 nurse assistants from the unit. All newly employed nurses
34 entered the training program after starting in NICU. The training module consisted of two
35 days of teaching followed by two, two-hour-multidisciplinary workshops (see previous
36 publication for details) (21). The individualised infant-driven feeding protocol, was developed
37 after a literature review, and was introduced during the two-day teaching (5-15). **An Infant-**
38 **driven feeding regime is based on infant needs and responses, rather than on time periods.**
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51 Figure 1 shows the individualised feeding protocol.

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53 In addition to the training module, expert feeding rounds took place throughout the
54 intervention period on a regular basis by the physiotherapist (one-hour round per day) and
55 speech therapist (three-hours round per week) (21). The physiotherapist and the speech
56 therapist were specialists in feeding disorders. The practice nurse coaching was conducted
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3 in the NICU to (1) reinforce the key messages of the feeding protocol, (2) monitor staff
4 compliance (3) identify neonates for whom the feeding protocol was not applied correctly,
5 and (4) engage provider focused feeding discussions. Nurses and nurse assistants were
6 supported in their routine feeding practice and application of feeding protocols, and helped
7 with early detection of infants presenting with feeding issues. When necessary, the
8 physiotherapist or the speech therapist applied the oral motor rehabilitation protocol.
9 Parents also participated in the intervention. When they were present, they undertook oral
10 and perioral stimulation as well as nonnutritive sucking for their child. They also gave oral
11 feeds when their child was older than 32 weeks PMA.
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24 **Post-intervention period**

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26 During the post-intervention period, nurses and nurse assistants maintained nonnutritive
27 sucking, oral and perioral stimulation as well as early oral feedings according to the
28 individualised infant-driven feeding protocol. The physiotherapist specialised in feeding
29 disorders and speech therapist continued regular practice nurse coaching and assisted
30 caregivers with early detection of infants presenting with feeding issues. They applied the
31 oral-motor rehabilitation protocol if necessary.
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41 **Outcome measures**

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43 The primary outcome was the time to independent oral feeding, defined as the duration
44 between the date of birth and the date of withdrawal feeding tube expressed as the postnatal
45 age in days and as the gestational age in weeks. The transition time corresponded to the
46 duration between the date of feeding tube placement and the date of its withdrawal for alive
47 neonates at NICU discharge or for neonates transferred from NICU to another hospital.
48 Length of hospital stay (LOS) was defined as the duration from the date of a **neonate's**
49 NICU's admission to the date of home discharge for alive and not lost to follow up. Neonatal
50 pathologies, which occurred during NICU stay, for neonates who went home at NICU
51 discharge, were monitored and included bronchopulmonary dysplasia (BPD), necrotising
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3 enterocolitis (NEC), periventricular leucomalacia (PVL), intraventricular hemorrhage (IVH),
4 culture proven bloodstream infections. Severe morbidity was defined if culture proven
5 bloodstream infections or BPD or PVL or IVH >grade 2 or NEC \geq grade 2 occurred. Another
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7 secondary outcome was the percentage of neonates who died during the NICU stay. The
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9 percentage of neonates who were breastfed at the time of NICU discharge as well as weight
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11 gain per day for neonates who were not transferred to another hospital at NICU discharge
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13 were also collected.
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17 Nurses' participation in the training modules was evaluated through their presence at the
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19 training sessions. At the end of the training module, their theoretical knowledge was
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21 assessed with a score between 0 and 20 through a 12 item multiple-choice knowledge
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23 questionnaire, around physiology (4 items), feeding strategies (3 items), recognising and
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25 treating feeding disorders (5 items), and one question about the adequacy of provision of
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27 sufficient information about feeding issues in the training.
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31 At the end of the intervention period, feeding protocol compliance was assessed through a
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33 self-administered questionnaire completed by nurses, consisting of questions concerning the
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35 application of the individualised infant-driven feeding protocol (time dedicated to daily feeding
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37 practice and application of feeding protocols rated on a Likert scale).
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41 **Statistical Analysis**

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43 Data were collected and entered into a Microsoft Excel file and then transferred to **Statistical**
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45 **analysis software (SAS Institute, Cary, NC, version 9.3)** for further inferential analysis. ~~To~~

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47 ~~account for censored neonates (censored neonates did not present the primary outcome~~
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49 ~~measure),~~ the time to independent oral feeding was compared between periods using
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51 survival analysis (Kaplan Meier and Cox proportional hazards regression model) adjusted for
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53 gestational age and severe morbidity. Infants were ~~censored~~ if they
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55 removal, were discharged home with a feeding tube, or were lost to follow-up after their
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57 NICU discharge. ~~Their data has been taken into account in the analysis.~~
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3 Results were expressed with Hazard Ratio (HR) and associated 95% confidence interval
4 (CIs) with HR <1 indicating a positive effect of the intervention. Sensitivity analyses that
5 excluded neonates who died with a feeding tube in place and those who were transferred to
6 another hospital with a feeding tube were performed. Among non-censored neonates, the
7 time to independent oral feeding was compared between periods using ANOVA (one-way
8 analysis of variance).

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18 Secondary outcomes were compared between periods using linear models and logistic
19 regression models or Fisher's test exact with Bonferroni adjustment to correct for multiple
20 comparisons when appropriate. The percentage of alive neonates who were breastfed by the
21 time of their NICU discharge, and the weight gain per day among neonates who were alive
22 and not transferred to another hospital at their NICU discharge were summarized in each
23 period. Analyses were performed using SAS software (SAS Institute, Cary, NC, version 9.3).
24 A p-value <0.05 was considered statistically significant.

25 26 27 28 29 30 31 32 33 34 35 **RESULTS**

36
37 A total of 711 preterm infants were included in the study, after the exclusion of 5 neonates
38 with major congenital anomalies, the data of 706 neonates (104 in the baseline period, 439 in
39 the intervention period and 163 in the post-intervention period) were analyzed. Figure 2
40 shows the study flow chart.

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45 Eighty-nine (13%) neonates died before their NICU discharge 16 (15%) in the baseline
46 period, 56 (13%) in the intervention period and 17 (10%) in the post-intervention period). Out
47 of the 617 (87%) neonates alive (88 (85%) in the baseline period, 383 (87%) in the
48 intervention period and 146 (90%) in the post-intervention period), 221 (36%) were
49 discharged home (47 (53%) in the baseline period, 133 (35%) in the intervention period and
50 41 (28%) in the post-intervention period). 396 (56%) were transferred to another hospital (41
51 (47%) in the baseline period, 250 (65%) in the intervention period and 105 (72%) in the post-
52 intervention period). The proportion of neonates transferred to another hospital was

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3 significantly different between the three study periods ($p=0.0003$). Of the 396 transferred
4 neonates, 291 neonates (73%) still had their feeding tube at the time of their transfer (32
5 (78%) in the baseline period, 183 (73%) in the intervention period and 76 (72%) in the post-
6 intervention period). Infants were transferred on average $25.9 \pm \text{SD } 22.5$ days after their
7 NICU admission ($26.9 \pm \text{SD } 22.3$ days in baseline period, $25.8 \pm \text{SD } 23.0$ days in intervention
8 period and $26.0 \pm \text{SD } 21.6$ days in post-intervention period). When transferred, they were
9 aged on average $34.3 \pm \text{SD } 2.3$ gestational age (GA) ($34.8 \pm \text{SD } 2.0$ in the baseline period,
10 $34.3 \pm \text{SD } 2.4$ GA in the intervention period and $34.2 \pm \text{SD } 2.2$ GA in the post-intervention
11 period).

22 23 24 **Neonates' characteristics**

25
26 The neonates' characteristics are presented in Table 1. There was no statistically significant
27 difference in PMA at birth, congenital anomalies, antenatal steroids, gender, delivery mode
28 and median 5 min Apgar scores between the three periods. However, neonates from the
29 baseline period were smaller compared to babies from the intervention and post-intervention
30 periods. More single births occurred during the intervention and post-intervention periods
31 compared to the baseline period.

32 33 34 35 36 37 38 39 40 41 **Time to independent oral feeding**

42
43 Among the 706 neonates, 610 (86%) were feeding tube free (87 in the baseline period, 373
44 in the intervention period and 150 in the post-intervention period). For 597 (85 %) of them,
45 the nasogastric tube was removed before hospital discharge (87 in the baseline period, 373
46 in the intervention period and 150 in the post-intervention period), three after hospital
47 discharge (one in the baseline period, two in the intervention period) and 10 before their
48 death (1 in the baseline period, 4 in the intervention period and 5 in the post-intervention
49 period). 96 (14%) were censored for time to feeding tube withdrawal: 79 died (15 in the
50 baseline period, 52 in the intervention period and 12 in the post-intervention period) and 17
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3 were lost to follow up after hospital discharge (2 in the baseline period, 14 in the intervention
4 period and 1 in the post-intervention period).

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7 The median time to independent oral feeding was 40, 36 and 37 days respectively for the
8 baseline, intervention, and post-intervention period. The difference was not significant
9 between the three periods (trend logrank test, $p=0.5795$). After adjustment in the Cox
10 proportional hazards model (Table 2a), there was a significant reduction in the time to
11 independent oral feeding between the post-intervention period compared to the baseline
12 period (HR=1.32, 95% confidence interval (CI): 1.01-1.74, $p=0.0301$). Infants in the post-
13 intervention period were able to achieve independent oral feeding on average at 35.5 ± 2.1
14 PMA compared to 36.2 ± 2.2 PMA in the baseline period (mean difference: -0.7; 95% CI: -
15 1.2- -0.2, Table 2b).

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18 No change in results occurred after excluding the 79 deceased neonates who still had their
19 nasogastric tube in place and the 291 neonates who were transferred to another hospital
20 with their tube in place after their NICU discharge.

21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 **Secondary outcomes**

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37 The transition times were significantly longer for the post-intervention period compared to the
38 baseline and intervention period ($p=0.0031$). No difference was shown between the three
39 study periods in terms of LOS, the percentage of neonates who died during the NICU stay;
40 and those who developed neonatal pathologies. Weight gain and breastfeeding rates
41 remained stable throughout the study periods (Table 3).

42 43 44 45 46 47 48 49 **Improvement in nurses' knowledge after implementation of the educational program**

50
51 A hundred and twenty-five registered nurses and assistant nurses out of 132 (95 %)
52 undertook the training module during the intervention period. Eighty-eight nurses and nurse
53 assistants (70.4%) were able to complete the entire training consisting of the theoretical two-
54 day session and the two workshops. Fifteen nurses and nurse assistants (12 %) did not
55 participate in any workshop.

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3 The median score of the nurses' knowledge questionnaire, completed at the end of the
4 training session by 125 nurses and nurse assistants, was 14.1 out of 20 [IQR13.0-14.5]. At
5 the end of the intervention period, 81 nurses and assistant nurses responded to the self-
6 report questionnaire to assess compliance with the feeding protocol. More than half (62 %) of
7 the nurses and nurse assistants spent five minutes or more per feeding when using the
8 feeding protocol. Almost all, 98 % of the nurses administered the feeding protocol frequently
9 or for each neonate, and 89 % of the nurses initiated feedings at 29 weeks PMA.
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22 DISCUSSION

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24 This study showed that implementation of an infant led educational feeding bundle and nurse
25 education program was associated with an earlier attainment of independent oral feeding in
26 neonates of less than 34 weeks PMA. To our knowledge, this is the first study evaluating the
27 combination of an educational nurse-training program, combined with an individualized cue-
28 based and semi-demand feeding approach and interventions to ensure successful feeding
29 transition and maintenance of neonatal feeding achievement. McCain *et al* and Kirk *et al*
30 found that cue-based and semi-demand fed infants reached independent oral feedings 6 and
31 5 days earlier, respectively, compared to infants transitioning to independent oral feeds
32 based on physicians' orders (12,13). However, Kirk *et al* did not note any difference in LOS
33 between the study periods (13). Other researchers found that educational training programs
34 associated with the development of neonatal feeding management guidelines accelerated
35 the attainment of independent oral feedings and decreased LOS in premature healthy
36 neonates (15,18,19, 25).
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51 The early introduction of oral feeding, before 30 weeks PMA, appears to be effective to
52 accelerate oral feedings in neonates (5,26). A meta-analysis showed that NNS accelerated
53 the transition time from tube to independent oral feeding, shortened the transition time from
54 start to full oral feeding, and reduced LOS (6). An oral motor stimulation intervention also
55 improves feeding progression and reduces LOS (7,8). A combination of NNS and oral
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3 stimulation improved the feeding ability of premature infants and shortened transition time
4 from tube assisted to independent oral feeding. Unfortunately, no earlier discharge was
5 obtained (27).
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9 Our findings suggested identical weight gain for both study periods, the baseline and post-
10 intervention period. These results are consistent with previous studies (13,15).
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13 However, even though we found an earlier gestational age at independent oral feeding for
14 neonates who had the intervention, no difference in LOS was observed. Several factors may
15 have contributed to this result. Firstly, home discharge conditions were not monitored as part
16 of the study, and may have changed over the duration of the study. For example, the
17 criterion "no bradycardia for 5 days" was replaced by a new discharge criterion "the mature
18 heart rate variability" which may have influenced LOS (28).
19

20
21 Secondly, the continuous monitoring of apnoea and bradycardia until NICU discharge may
22 have influenced LOS, even if neonates achieved independent oral feeding earlier. Our
23 findings are consistent with earlier studies who showed similar results with improved feeding
24 achievement without shortening the LOS (13,29). Almost all nurses and nurse assistants (95
25 %) started the training session during the implementation period. Their knowledge acquisition
26 was good at the end of the training session and most nurses considered the content of the
27 training session as adequate. Nurses reported compliance with the feeding protocol was also
28 very good, with almost all stating they used the feeding protocol for each feeding.
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43 **Limitations**

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45 This study has several limitations: Firstly, feeding protocol compliance was not objectively
46 measured during the study period. Initially it was planned in the study protocol to measure
47 this for each child. Unfortunately, this was not feasible. Secondly, the self-report
48 questionnaire has a risk of bias, and may reveal an acceptance of the feeding pathway rather
49 than compliance with the feeding protocol in clinical practice. Thirdly, discharge criteria were
50 not monitored during the study, which made it difficult to distinguish between the evolution of
51 feeding and apnoea/bradycardia discharge criteria over time. Fourthly, the effect of the
52 educational program on the time to independent oral feeding could be underestimated
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3 because of the transfer out of the NICU to another hospital and the neonates not being
4 feeding tube free although it was not assessed through the sensitivity analysis. In addition,
5 neonates from the baseline period were smaller compared to babies from the intervention
6 and post-intervention period which could have impacted on LOS. Finally, parental
7 involvement and satisfaction were not monitored during the study. It would have been
8 interesting to compare parents' involvement and satisfaction before and after the feeding
9 protocol implementation. Despite these limitations, our study is based on a broad population
10 and lost very few patients to follow up **which suggests** that this is feasible.
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22 **Implications and recommendations for practice**

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24 Feeding difficulties in neonates are common and important. Feeding interventions such as
25 the early introduction of oral feeding, non-nutritive sucking (NNS) and oral motor stimulation
26 should be implemented for all preterm neonates because they have been shown to promote
27 earlier achievement of oral feeding and earlier discharge. They can also prevent feeding
28 dysfunction in childhood. In addition, these feeding strategies should be individualised for
29 each neonate. Nurse driven protocols like this, based on infant cues, used consistently by all
30 nurses and assistant nurses in a unit can positively impact on neonatal outcomes and should
31 be included in neonatal nursing education programs and be implemented in clinical practice.
32 Future studies should analyse parents' satisfaction and participation in these feeding
33 pathways and the impact of these in the longer term.
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47 **Conclusions**

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49 In conclusion, an infant-driven feeding protocol combined with a nurse-training program may
50 be associated with a significant earlier achievement of independent oral feeding in premature
51 infants. This type of program is feasible and well-accepted. Future research should explore
52 the long-term impact of such programs on both parental satisfaction and longer term feeding
53 disorders in ex-preterm children.
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REFERENCES

1. Wang ML Dorer DJ, Fleming MP, Catlin EA. Clinical outcomes of near-term infants. *Pediatrics* 2004;114(2):372-376.
2. Barlow SM. Oral and respiratory control for preterm feeding. *Curr Opin Otolaryngol Head Neck Surg* 2009;17(3):179-186.
3. Rommel N, De Meyer AM, Feenstra L, Veereman-Wauters G. The complexity of feeding problems in 700 infants and young children presenting to a tertiary care institution. *J Pediatr Gastroenterol Nutr* 2003;37(1):75-84.
4. Lau C, Schanler RJ. Oral feeding in premature infants: advantage of a self-paced milk flow. *Acta Paediatr* 2000;89(4):453-459.
5. Simpson C, Schanler RJ, Lau C. Early introduction of oral feeding in preterm infants. *Pediatrics* 2002;110(3):517-522.
6. Foster JP, Psaila K, Patterson T. Non-nutritive sucking for increasing physiologic stability and nutrition in preterm infants. *Cochrane Database Syst Rev* 2016;10(10):CD001071.
7. Lessen BS. Effect of the premature infant oral motor intervention on feeding progression and length of stay in preterm infants. *Adv Neonatal Care* 2011;11(2):129-139.
8. Ghomi H, Yadegari F, Soleimani F, Lessen Knoll B, Noroozi M, Mazouri A. The effects of premature infant oral motor intervention (PIOMI) on oral feeding of preterm infants: A randomized clinical trial. *Int J Pediatr Otorhinolaryngol* 2019;120:202-209.
9. Greene Z, O'Donnell CP, Walshe M. Oral stimulation for promoting oral feeding in preterm infants. *Cochrane Database Syst Rev* 2016;(9): CD009720.
10. Thabet AM, Sayed ZA. Effectiveness of the Premature Infant Oral Motor Intervention on Feeding Performance, Duration of Hospital Stay, and Weight of Preterm Neonates in Neonatal Intensive Care Unit: Results From a Randomized Controlled Trial. *Dimens Crit Care Nurs* 2021 Jul-Aug 01;40(4):257-265.

- 1
2
3 11. Ghomi H, Yadegari F, Soleimani F, Knoll BL, Noroozi M, Mazouri A. The effects of
4 premature infant oral motor intervention (PIOMI) on oral feeding of preterm infants: A
5 randomized clinical trial. *Int J Pediatr Otorhinolaryngol* 2019 May;120:202-209.
6
7
- 8
9 12. McCain GC, Gartside PS, Greenberg JM, Wright Lott J. A feeding protocol for healthy
10 preterm infants that shortens time to oral feeding. *J Pediatr* 2001;139(3):374–379.
11
12
- 13 13. Kirk AT, Alder SC, King JD. Cue-based oral feeding clinical pathway results in earlier
14 attainment of full oral feeding in premature infants. *J Perinatol* 2007;27(9):572-578.
15
16
- 17 14. Pickler RH, Reyna BA, Wetzel PA, Lewis M. Effect of four approaches to oral feeding
18 progression on clinical outcomes in preterm infants. *Nurs Res Pract*
19 2015;2015:716828.
20
21
- 22 15. Jadcherla SR; Dail J, Malkar MB, McClead R, Kelleher K, Nelin L. Impact of Process
23 Optimization and Quality Improvement Measures on Neonatal Feeding Outcomes at
24 an All-Referral Neonatal Intensive Care Unit. *JPEN J Parenter Enteral Nutr* 2016
25 Jul;40(5):646-655.
26
27
- 28 16. Klingenberg C, Embleton ND, Jacobs SE, O'Connell LA, Kuschel CA. Enteral feeding
29 practices in very preterm infants: an international survey. *Arch Dis Child Fetal Neonatal*
30 *Ed* 2012;97(1):F56-F61.
31
32
- 33 17. Lyu T, Zhang Y, Hu X, Gu Y, Li L, Lau C. Management of Oral Feeding Challenges in
34 Neonatal Intensive Care Units (NICUs): A National Survey in China. *Front Pediatr* 2020
35 Jun 24;8:336.
36
37
- 38 18. Wellington A, Perlman JM. Infant-driven feeding in premature infants: a quality
39 improvement project. *Arch Dis Child Fetal Neonatal Ed* 2015;100(6):F495–F500.
40
41
- 42 19. Osman A, Ibrahim M, Saunders J, Merheb R, Moscorelli M, Caretto V, Groh-Wargo S.
43 Effects of Implementation of Infant-Driven Oral Feeding Guideline on Preterm Infants'
44 Abilities to Achieve Oral Feeding Milestones, in a Tertiary Neonatal Intensive Care Unit.
45 *Nutr Clin Pract* 2021 Dec;36(6):1262-1269.
46
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3 20. Bapat R, Gulati IK, Jadcherla S. Impact of SIMPLE Feeding Quality Improvement
4 Strategies on Aerodigestive Milestones and Feeding Outcomes in BPD Infants. *Hosp*
5 *Pediatr* 2019 Nov;9(11):859-866.
6
7
8
9 21. Touzet S, Beissel A, Denis A, Pillet F, Gauthier-Moulinier H, Hommey S, Claris O.
10 TOP Study Group. Effectiveness of a nurse educational oral feeding programme on
11 feeding outcomes in neonates: protocol for an interrupted time series design. *BMJ*
12 *Open* 2016 Apr 15;6(4):e010699.
13
14
15
16
17 22. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE. Interrupted time series
18 designs in health technology assessment: lessons from two systematic reviews of
19 behavior change strategies. *Int J Technol Assess Health Care* 2003;19(4):613–623.
20
21
22
23 23. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. Squire 2.0
24 (Standards for Quality Improvement Reporting Excellence): revised publication
25 guidelines from a detailed consensus process. *Am J Crit Care* 2015 Nov;24(6):466-
26 73.
27
28
29
30
31
32 24. Stark AR; American Academy of Pediatrics Committee on Fetus and Newborn. Levels
33 of neonatal care. [published correction appears in *Pediatrics*. 2005 Apr;115(4):1118].
34 *Pediatrics* 2004;114(5):1341-1347.
35
36
37
38 25. Chrupcala KA, Edwards TM, Spatz DL. A Continuous Quality Improvement Project to
39 Implement Infant-Driven Feeding as a Standard of Practice in the Newborn/Infant
40 Intensive Care Unit. *J Obstet Gynecol Neonatal Nurs* 2015;44(5):654-664.
41
42
43
44 26. Lau C, Sheena HR, Shulman RJ, Schanler RJ. Oral Feeding in Low Birth Weight
45 Infants. *J Pediatr* 1997; Apr;130(4):561-569.
46
47
48
49 27. Li XL, Liu Y, Liu M, Yang CY, Yang QZ. Early Premature Infant Oral Motor
50 Intervention Improved Oral Feeding and Prognosis by Promoting Neurodevelopment.
51 *Am J Perinatol* 2020;37(6):626-632.
52
53
54
55 28. Javorka K, Lehotska Z, Kozar M, Uhríkova Z, Kolarovszki B, Javorka M, Zibolen M.
56 Heart rate variability in newborns. *Physiol Res* 2017;66(Suppl 2):S203-S214.
57
58
59
60

- 1
2
3 29. Eichenwald EC, Blackwell M, Lloyd JS, Tran T, Wilker RE, Richardson DK. Inter-
4 neonatal intensive care unit variation in discharge timing; influence of apnea and
5 feeding management. *Pediatrics* 2001;108(4):928–933.
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For Review Only

Table 1 Neonates' characteristics at NICU admission

	Baseline N=104	Intervention N=439	Post- intervention N=163	p-value
Male, n (%)	58 (55.8)	233 (53.1)	82 (50.3)	0.6745
Gestational age (weeks), mean (SD)	29.9 (2.7)	29.8 (2.6)	29.8 (2.7)	0.9713
Birth weight (z-score), n (%)				0.0174
<10%	25 (24)	57 (13)	15 (9)	
10-90%	76 (73)	369 (84)	144 (88)	
>90%	3 (3)	13 (3)	4 (3)	
Apgar at 5', mean (SD)	8 (2.4)	8.4 (2)	8.3 (2.1)	0.5202
Multiple labor, n(%)	35 (33.7)	205 (46.7)	78 (47.9)	0.0397
Antenatal steroids, n (%)	93 (89.4)	387 (88.2)	147 (90.2)	0.9464
Outborn status, n(%)	10 (9.6)	71 (16.2)	22 (13.5)	0.2118

SD: standard deviation

Table 2a. Impact of the nurse educational program feeding on time to independent oral feeding for all neonates

	N	HR [CI 95 %]*	p-value*
Days of life to IOF (days)			0.0301
Baseline	104	-	-
Intervention	439	1.03 [0.81 ; 1.31]	0.7993
Post-intervention	163	1.32 [1.01 ; 1.74]	0.0430
PMA to IOF (weeks)			0.0368
Baseline	104	-	-
Intervention	439	1.20 [0.94 ; 1.52]	0.1368
Post-intervention	163	1.41 [1.08 ; 1.85]	0.0115

IOF: Independent Oral Feeding, PMA: postmenstrual age, CI: Confidence Interval, HR: Hazard Ratio* p-values were obtained from Cox proportional hazard model adjusted for gestational age and severe morbidity (sepsis with positive blood culture or BPD or PVL or IVH grade III/IV or NEC \geq stage 2). HR <1 indicates a positive intervention effect.

Table 2b. Impact of the nurse educational program feeding on time to independent oral feeding for not censored neonates

	N*	Mean (SD)	Difference with baseline group, mean [CI 95%]	p-value**
Days of life to IOF (days)				0.717
Baseline	87	40.8 (24.9)	-	
Intervention	373	39.2 (22.5)	-0.9 [-5.3 ; 3.4]	
Post-intervention	150	38.3 (22.3)	-2.5 [-8.5 ; 3.5]	
PMA to IOF (weeks)				0.0302
Baseline	87	36.2 (2.2)		
Intervention	373	35.8 (1.9)	-0.3 [-0.7 ; 0.1]	
Post-intervention	150	35.5 (2.1)	-0.7 [-1.2 ; -0.2]	

IOF: Independent Oral Feeding, PMA: postmenstrual age, SD: Standard Deviation, CI: Confidence Interval

* number after excluding censored neonates (died prior to the tube removal, discharged home with a feeding tube or lost to follow-up after their NICU discharge)

** ANOVA-F-test

Table 3. Secondary outcomes

	Baseline	Intervention	Post-intervention	p-value
Transition time (weeks)*, ^a	N=56	N=200	N=70	
mean (SD)	3.4 (1.7)	4.5 (2.2)	4.6 (2.5)	<0.001
Neonatal pathology ^b	N=47	N=133	N=41	
BPD, n (%)	10 (21)	35 (26)	9 (22)	1.0000
NEC≥ stage 2, n (%)	1 (2)	1 (1)	3 (7)	1.0000
Grade III/IV IVH, n (%)	0 (0)	1 (1)	1 (2)	1.0000
Sepsis, positive blood culture, n (%)	5 (11)	35 (26)	6 (15)	0.2454
PVL, n (%)	2 (4)	5 (4)	4 (10)	1.0000
Death during the NICU stay ^c	N=104	N=439	N=163	
N (%)	16 (15)	56 (13)	17 (10)	0.1940
LOS (weeks) ^a	N=87	N=380	N=145	
mean (SD)	51.8 (32.8)	51.8 (28.7)	50.1 (24.6)	0.9237
Weight gain (g/day) ^d	N=47	N=133	N=41	-
mean (SD)	26.6 (5.4)	26.0 (5.1)	25.6 (5.1)	
Breastfeeding, n (%) ^d	N=88	N=383	N=146	-
	59 (67)	218 (57)	101 (69)	

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3 SD: standard deviation, BPD: bronchopulmonary dysplasia, NEC: necrotizing enterocolitis, IVH: intraventricular hemorrhage, PVL: periventricular
4 leucomalacia, Severe morbidity: Sepsis, positive blood culture or BPD or PVL or IVH grade III/IV or NEC \geq stage 2, LOS : length of hospital stay

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7 *Transition time corresponded to the duration between the date of tube feeding placement and the date of withdrawal feeding tube for alive neonates at NICU discharge
8 or for neonates transferred from NICU to another hospital without a feeding tube.

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11 ^a p-values were obtained from linear model adjusted for gestational age and severe morbidity.

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13 ^b p-values were obtained from logistic regression model adjusted for gestational age or fisher's test exact and Bonferroni correction.

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15 ^c p-values were obtained from logistic regression model adjusted for gestational age, Apgar score at 5', severe morbidity and LOS in NICU.

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17 ^d not tested given that these 2 variables are additional in the protocol.
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FIGURE LEGENDS

Figure 1: Standardised individualised feeding protocol

Figure 2: Study flow chart

For Review Only

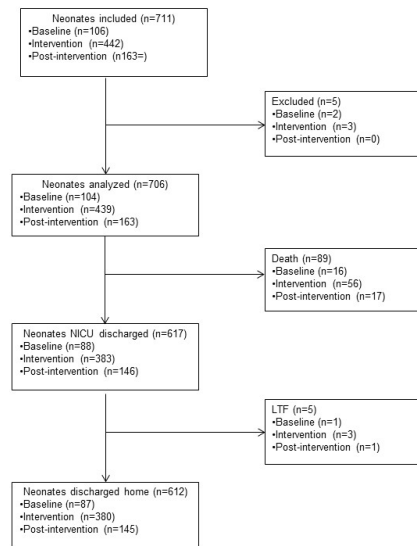
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	Nonnutritive sucking	Oral/Perioral stimulation	Early Oral Feeding	Oral Motor Rehabilitation
Infant characteristics	<ul style="list-style-type: none"> • ≥24 weeks PMA • from day one of life 	<ul style="list-style-type: none"> • ≥24 weeks PMA • from day one of life 	<ul style="list-style-type: none"> • ≥29 weeks PMA • from day one of life 	feeding difficulty symptoms
Intervention	<ul style="list-style-type: none"> • pacifier • during tube feeding or outside feeding times 	<ul style="list-style-type: none"> • oral and perioral stimulation provide sensorimotor input to oral and perioral structures 	<ul style="list-style-type: none"> • start at one ml • Advancement every 24 hours according to age and feeding ability 	<ul style="list-style-type: none"> • procedure diagram placed at the infants' bedside
Time Frame	5 to 10 minutes prior to feedings	5 to 10 minutes prior to feedings		5 to 10 minutes prior to feedings

Standardised individualised feeding protocol



338x190mm (96 x 96 DPI)



Study flow chart

338x190mm (96 x 96 DPI)

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