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# Protocols for early discharging of premature infants: an empirical assessment on safety and savings

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**Abstract**

**Background:** Preterm newborns may be discharged when clinical conditions are stable. Several criteria for early discharge have been proposed in the literature. This study carried out the first quantitative comparison of their impact in terms of hospitalization savings, safety and costs.

**Methods:** This study was based on the clinical histories of 213 premature infants born in the Neonatal Intensive Care Unit of Padova University Hospital between 2013 and 2014. Seventeen early discharge criteria were drawn from the literature and retrospectively applied to these data, and computation of hospitalization savings, safety and costs implied by each criterion was carried out.

**Results:** Among the criteria considered, average gains ranged from 1.1 to 10.3 hospital days and between 0.3 and 1.1 fewer infections per discharged infant. Criteria that led to saving more hospital days had higher cost-effectiveness in terms of crisis and infection, and they spared infants from more infections. However, episodes of apnea and bradycardia were detected after the potential early discharge date for all criteria, with a mean number of episodes numbering between 0.3 and 1.4.

**Conclusion:** The results highlight a clear trade-off between days saved and health risks for infants, with potential consequences for health care costs.

**Keywords:** cost-effectiveness; criteria for discharge; early discharge infants; safety.

## Introduction

Early discharge programs were introduced in most neonatal intensive care units (NICUs) worldwide to reduce the hospital length of stay for preterm infants [1]. Leaving economic considerations aside, discharging patients as soon as possible or transferring them to lower levels of care while still hospitalized could decrease risks related to hospitalization and hospital-acquired infections, and could be beneficial for infants' development and for the family's psychological and emotional condition.

Preterm newborns may be discharged when stabilization of clinical conditions and maturity of physiological functions have been gained. Specifically, an early discharge is aimed at reducing the negative effects of hospitalization. As NICU stays often represent a stressful – almost traumatic – period, reducing them may improve outcomes for both the baby and the parents. However, the definition of common criteria for early discharge that would not result in increased risk for neonates' health is far from settled. Indeed, no consensus on parameters such as weight and gestational age at discharge has yet been reached [2], and many criteria coexist in the literature.

One reason for such an ambiguity is the lack of a quantitative comparison for each criterion outcome in terms of cost savings, on the one hand, and risks for infants' health, on the other hand.

This work aims at filling this gap in the literature by providing an empirical assessment of the impact of the application of several early discharge criteria proposed in the literature in terms of hospitalization savings, safety and costs, via a retrospective analysis of patients admitted to the NICU of the Padova University Hospital and a simulation on the potential incidence of adverse events and costs.

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# Materials and methods

## Study design

All patients admitted into the NICU of Padova University Hospital between 1st January 2013 and 30th June 2014 were included in the analysis. Criteria for inclusion and exclusion from the study, as well as resulting sample size, are reported in Figure 1. Hospitalization history has been reconstructed on a day-by-day basis using medical records for each patient. Patients could be discharged from Padova's NICU if their weight was above 1800 g, they had a gestational age of at least 36 gestational weeks (GWs), they did not experience apnea or bradycardia for at least 5 days and they were fully fed with a baby bottle. Selected discharge criteria taken from the literature and discussed below have been retrospectively applied to each patient's history, creating a simulated *what-if* scenario in correspondence to each discharge criterion.

## Discharge criteria

Seventeen criteria [2–18] for early discharge of premature infants proposed in the literature have been considered in this paper. All criteria were based on the following parameters: weight, gestational age, feeding, temperature and clinical conditions. No considered criterion included "parental involvement" as a parameter to determine early discharge, as this information was not available in the medical records of the Padova University Hospital's NICU. Criteria and parameters are listed in Table 1.

Among the 17 criteria, 2 were considered only for an initial analysis and excluded from the subsequent analyses, as they involve full feeding at the breast as a condition for early discharge. Breastfeeding was uncommon in Padova University Hospital's NICU, and discharge was usually allowed even at the earlier development stage of feeding via a baby bottle. In this NICU, parents' visits were permitted for only a few hours a day due to space constraints. Hence, although mothers could occasionally feed their child at the breast, breastfeeding was not a regular practice and it was not considered among the discharge criteria. At discharge, 100% of babies were fed by a baby bottle.

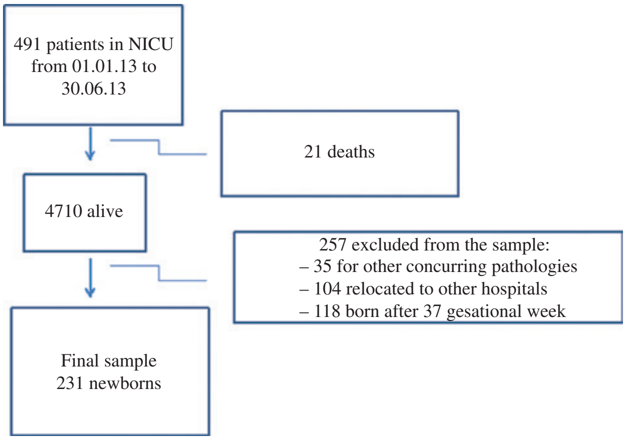

**Figure 1:** Sample selection criteria. NICU, neonatal intensive care unit.

## Variables definition and data collection

Following the definition provided by the World Health Organization (WHO) [19], in this study babies were considered premature if they were born before the 37th GW; in particular, they were considered extremely preterm if they were born before 28 GWs, very preterm between 28 and 32 GWs, and moderate and late preterm above 32 GWs.

An infant was defined as normo-thermic if her/his temperature was between 36.5°C and 37.4°C for more than 24 h [20]. An episode of infection was defined in correspondence with the beginning of any antibiotic therapy. On any given day, babies were considered to experience bradycardia if at least one episode of less than 100 beats per minute was recorded. Similarly, apnea was defined as the presence of either a respiratory break of at least 20 s or an episode of desaturation (oxygen saturation below 85%). However, no information about the severity or duration of the episodes of apnea or bradycardia were available in the data, neither was information about whether apneas resolved spontaneously or required stimulation by nurses. Therefore, we considered this information only a categorical variable. Consequently, a crisis on any given day was defined as the experience of apnea, bradycardia or both.

Basic demographic information (sex, gestational age at birth, cause of birth, maternal disease, twin, relocated, follow-up days) were collected, together with a daily diary with data on health status (presence/absence of bradycardia, apnea, desaturation, temperature, blood pressure, ventilation type, drugs, infusion, weight, nutrition type). Data were collected via REDCap [21]. Permission to collect the data was granted by the central administration of Padova University Hospital. Informed consent was not applicable because it was granted under the general agreement of the health care system.

## Statistical methods

Basic exploratory data analysis was performed on the sample and reported using median and I, III quartiles for continuous variables, and percentages (absolute numbers) for categorical variables. Chi-square ($\chi^2$) tests or Wilcoxon signed rank tests were used to evaluate the significance of differences in factor distributions across prematurity classes.

For each criterion, the number of hospital days saved was computed as the difference between the date at which babies would have been eligible for early discharge and their actual discharge date. The average number of days saved, the number and the percentage of babies that would have been eligible for early discharge were estimated, together with their 95% confidence intervals (CIs).

For each criterion, the probability of observing an infection, apnea, bradycardia or both were computed as the percentage of discharged children that presented at least one event in the period between the hypothetical early discharge date and the observed one. The mean number of apnea, bradycardia and crisis events per child were estimated using zero-inflated Poisson models [22], and their 95% CIs were estimated by 1000 bootstrap samples.

Finally, a cost-effectiveness analysis was carried out using American [23] and European [24] data to compute for each criterion the cost needed to reduce the observed number of crises by one unit. Cost distribution was estimated using micro simulations, and corresponding credibility intervals at the 95% level are presented. Analyses were conducted using the R system [25] with root mean squares (RMS) [26], bootstrap [27] and pscl [28] libraries.

**Table 1:** Criteria evaluated in the paper with main discharge indicators.

| Author | Weight or GW | Feeding | Temperature | Clinical conditions |
|---|---|---|---|---|
| Dillard and Korones (1973) [9] | Study group >2000 g<br>Control group >2200 g | >15 g/day from 2 days | Not a criterion | No acute illness |
| Lefebvre, Villeux and Bard (1982) [12] | Outgrown birth weight and established satisfactory weight gain | All feeding by breast | Stable temperature control in room air | Good clinical conditions, all medical problems under control |
| Derbyshire, Davies and Bacco (1982) [8] | Gets back to weight at birth | Baby bottle/breastfeeding | Not considered | Good clinical conditions |
| Brooten et al. (1986) [5] | No weight criteria | Feed by nipple every 4 h | Stable temperature control in room air | Good clinical conditions, no apnea or bradycardia in 12 h |
| Schmidt and Levine (1990) [16] | ≥1800 g and satisfactorily weight gain | Feed well by nipple | Stable temperature control in room air | Medically stable |
| Casiro et al. (1993) [6] | Not a criterion | Feed satisfactorily by breast or bottle (not gavage feedings) | Thermo-stable in open crib | Good clinical conditions, no respiratory failure, no apnea for at least 3 days whitout apnea medication |
| Kotagal et al. (1995) [11] | Gains weight by breastfeeding | Breastfeeding | Thermo-stable in open crib | Clinical stabilty, no apnea or bradycardia |
| Rawlings and Scott (1996) [15] | 1800–2000 g, the baby is gaining weight. | Standard enteral feeding | Thermo-stable in open crib | Not criteria |
| Evanochko et al. (1996) [10] | >35 GW | Breastfeeding or baby bottle in 2/3 of lunches in 24 h | Thermo-stable | No apnea or bradycardia, not receiving theophylline |
| Merrit (2003) [13] | Gains weight on all feeds | Baby bottle or breastfeeding | Thermo-stable in open crib | Not considered |
| Vecchi (1996) [18] | >1800 g | Baby bottle or breastfeeding or gavage until baby bottle feeding is not reached | Thermo-stable in cradle | Respiratory stability, oral pharmacological regime established |
| Cruz (1996) [7] | Consistent weight gains for 3 consecutive days before discharge | Ability to suck nipplet at least 5 days (120 cal/kg/day) | Thermo-stable in open crib | Asymtomatic, no medicine for 3 days |
| Ortenstrand et al. (1999) [14] | Not considered | NGT | Thermo-stable in cradle | No apnea or bradycardia, stable parameters |
| Sellers and Davidson (2000) [17] | Consistent weight gain | Gavage, breastfeeding, baby bottle | Thermo-stable in open crib | No apnea or bradycardia |
| Lian et al. (2008) [2] | ≥1800 g and stable weight gains in the 5–7 days before discharge | Enteral feeding. No apnea, vomit or cyanosis during feeding | Thermo-stable in open crib | No apnea for 1 week |
| Ahamadpour-Kacho et al. (2012) [3] | >1500 g, consistent weight gains for 3 consecutive days before discharge | Full oral sucking feeds, at least 120 cal/kg/day | Thermo-stable in open crib | Vital signs stable, no symptoms and no medicine for 3 days |
| Bathie and Shaw (2013) [4] | >1500 g, gaining weight adequately | NGT or a mix between gavage and oral feeding | Thermo-stable in open crib | Stable. Only reason for staying in NICU is feeding |

NGT, nasogastric tube.

## Results

Overall, 234 children were enrolled in the study. Twenty subjects died within the first week after birth from pathologies that had compromised survival since birth. In one case, death occurred 2 months after birth, when the neonate reached the 37th GW; the death was due to a respiratory virus. For none of the criteria considered was this child dismissible before contracting the virus. The final sample was composed of 213 subjects. Characteristics of the sample are reported in Table 2.

Fifteen percent of the sample was born before the 28th GW, 31.5% between the 28th and the 32nd GW and the remaining 53.5% after the 32nd GW. The average gestational age at birth was 32 weeks, and the average birth weight was 1605 g. More than half of the subjects were allowed to quit the NICU; such relocation can take place in Padova University Hospital only if the baby reached the 34th GW and 1500 g.

## Days saved and infections

Table 3 and Figure 2 show that all but two criteria [3, 12] would have led to a significant and positive decrease in hospitalization days, with average gains ranging from

**Table 2:** Main characteristics of the sample. Data are presented as percentages (absolute numbers) or I quartile/median/III quartile respectively for categorical or continuous variables. P-value refers to overall differences test according to gestational age at delivery.

| Characteristics | Combined (n=213) | Extremely preterm (n=33) | Very preterm (n=67) | Moderate and late preterm (n=113) | P-value |
|---|---:|---:|---:|---:|---:|
| Male (n) | 57% (122) | 52% (17) | 51% (34) | 63% (71) | 0.219 |
| Twins (n) | 36% (77) | 36% (12) | 37% (25) | 35% (40) | 0.967 |
| Gestational age, weeks | 29/32/33 | 24/26/27 | 29/30/31 | 32/33/34 | <0.001 |
| Follow-up days | 11/28/53 | 63/92/123 | 34/42/59 | 6/11/18 | <0.001 |
| Weight, g | 1135/1605/2041 | 545/720/890 | 1092/1290/1505 | 1767/2010/2351 | <0.001 |
| Weight at discharge, g | 2015/2205/2466 | 2165/2400/2822 | 2010/2300/2470 | 2015/2150/2440 | 0.317 |
| Relocated at neonatal unit (n) | 59% (125) | 24% (8) | 49% (33) | 74% (84) | <0.001 |
| Mean number of infections per infant | 0/0/1 | 1/3/4 | 0/1/1 | 0/0/0 | <0.001 |
| Mean number of apneas per infant | 0/1.0/5.0 | 9.0/10.0/12.0 | 2.0/4.0/6.5 | 0.0/0.0/1.0 | <0.001 |
| Mean bradycardia per infant | 0/2/5 | 6/9/10 | 2/4/6 | 0/0/1 | <0.001 |
| Mean crisis per infant | 1/2/6 | 9/10/12 | 3/5/6 | 0/1/1 | <0.001 |
| Number of days of infection | 0/0/1 | 11/17/32 | 0/1/14 | 0/0/0 | <0.001 |

**Table 3:** Potential saving in terms of hospitalizations and burden of infections as simulated by the retrospective application of each criterion.

| Discharge criterion | No. of discharged infant | % discharged infant (95% CI) | Mean days saved per early-discharged infant (95% CI) | Probability of infection (95% CI) | Overall number of infections days (95% CI) | Mean number of infections per children (95% CI) |
|---|---:|---:|---:|---:|---:|---:|
| Dillard and Korones (1973) [9] | 90 | 42.2 (35.6; 48.8) | 3.8 (2.8; 4.8) | 2.2 (0; 5.2) | 31 (0; 78) | 0.3 (0; 0.8) |
| Derbyshire et al. (1982) [8] | 100 | 46.9 (40.2; 53.6) | 4.5 (3.3; 5.7) | 11.0 (4.8; 17.1) | 66 (26; 118) | 0.6 (0.2; 1.2) |
| Brooten et al. (1986) [5] | 88 | 41.3 (34.7; 47.9) | 3.9 (2.7; 5.0) | 9.1 (3.2; 15.1) | 46 (13; 95) | 0.5 (0.1; 1.0) |
| Schmidt and Levine (1990) [16] | 51 | 23.9 (18.2; 29.7) | 1.6 (0.3; 2.2) | 9.8 (1.6; 18.0) | 34 (5, 78) | 0.7 (0.1; 1.5) |
| Casiro et al. (1993) [6] | 82 | 38.5 (31.9; 45.0) | 3.2 (2.3; 4.1) | 6.1 (0.9; 11.2) | 36 (6; 79) | 0.4 (0.1; 0.9) |
| Kotagal et al. (1995) [11] | 77 | 36.1 (29.7; 42.6) | 3.0 (2.1; 4.0) | 9.1 (2.7; 15.5) | 41 (11; 83) | 0.5 (0.1; 1.1) |
| Rawlings and Scott (1996) [15] | 49 | 23.0 (17.3; 28.6) | 2.2 (1.4; 3.0) | 6.1 (0; 12.8) | 22 (0; 58) | 0.4 (0; 1.7) |
| Evanochko et al. (1996) [10] | 100 | 46.9 (40.2; 53.6) | 8.3 (6.5; 10.2) | 16.0 (8.8; 23.1) | 105 (56; 175) | 1.0 (0.5; 1.7) |
| Merrit (2003) [13] | 85 | 39.9 (33.3; 46.4) | 3.4 (2.4; 4.4) | 9.4 (3.2; 15.6) | 44 (13; 9) | 0.5 (0.1; 1.0) |
| Vecchi (1996) [18] | 108 | 50.7 (43.9; 57.4) | 5.8 (4.6; 6.9) | 12.0 (5.9; 18.1) | 88 (39; 153) | 0.8 (0.3; 1.4) |
| Cruz et al. (1996) [7] | 28 | 13.1 (8.6; 17.7) | 1.1 (0.4; 1.7) | 3.6 (0; 10.4) | 15 (0; 45) | 0.5 (0.0; 1.6) |
| Ortenstrand et al. (1999) [14] | 128 | 60.0 (53.5; 66.6) | 10.3 (8.3; 12.3) | 11.7 (6.1; 17.2) | 122 (59; 206) | 0.9 (0.4; 1.6) |
| Sellers and Davidson (2000) [17] | 89 | 41.7 (35.1; 48.4) | 7.1 (5.5; 8.0) | 16.8 (9.0; 24.6) | 101.0 (48.0; 169.0) | 1.1 (0.5; 1.8) |
| Lian et al. (2008) [2] | 54 | 25.3 (19.5; 31.1) | 2.4 (1.6; 3.2) | 1.9 (0; 5.4) | 15.0 (0; 60) | 0.2 (0; 1.1) |
| Bathie and Shaw (2013) [4] | 88 | 41.3 (34.7; 47.9) | 7.0 (5.4; 8.6) | 12.5 (5.6; 19.4) | 84.0 (35.9; 146.0) | 0.9 (0.4; 1.6) |

CI, confidence interval.

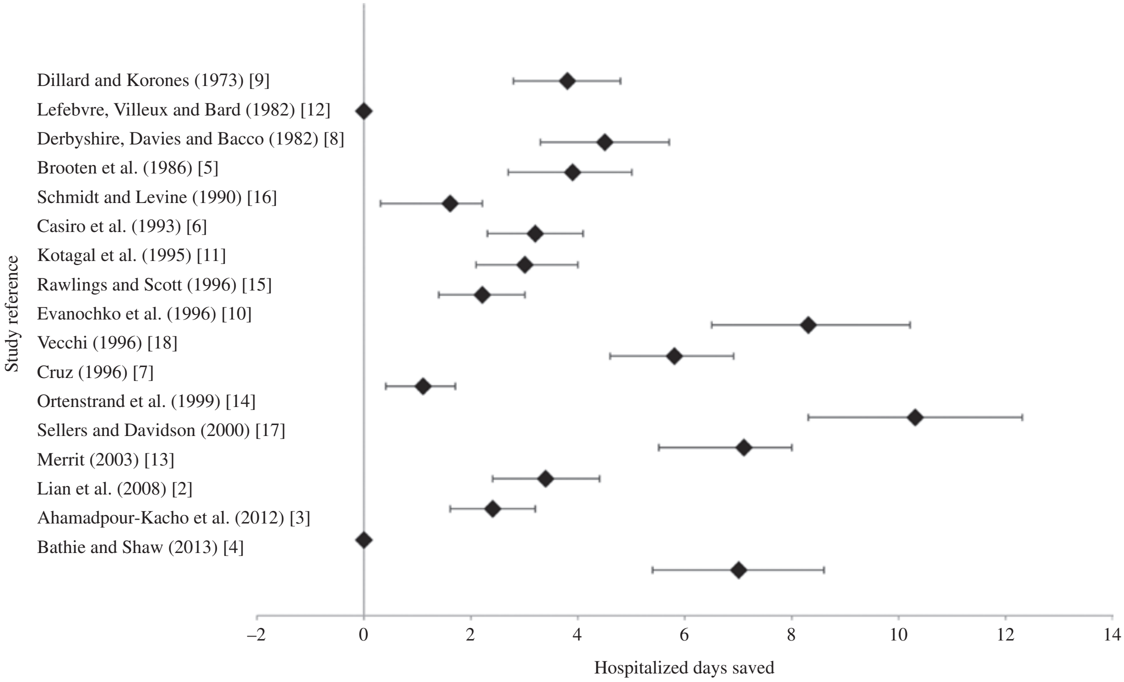

**Figure 2:** Box plot representing hospitalization days saved, by criterion.

1.1 to 10.3 days saved. Depending on the criterion considered, from 13.1% to 60.0% of infants would have been eligible for early discharge.

Assuming that hospital-acquired infections are the only ones that infants would develop in the absence of infusion or central access and mechanical ventilation, we examined whether early discharge can spare children from infectious episodes. Table 3 also presents the percentage, for each criterion, of early-discharged infants that would have experienced an infection after the early discharge threshold. Four criteria would lead to a positive but no significant increase in the percentage of babies getting an infection, while for the others the probability of getting an infection was between 6.1% and 16.8%. The total number of infection days recorded ranged from 36 to 122, implying a mean number of infection days per child between 0.4 and 1.1.

## Apnea, bradycardia and crisis

Table 4 reports the percentage of early discharged infants that experienced an apnea (or an episode of desaturation), episodes of bradycardia and crisis after the early discharge day.

For all criteria, infants experienced at last one apnea episode between the hypothetical and actual discharge. The percentage of infants with apnea varied from 9.8% to 33.0%, and the number of apneas from eight to 129. The mean number of apneas per discharged child ranged between 0.3 and 1.2.

The percentage of children with bradycardia varied from 7.4% to 34.0%, and the number of bradycardia episodes between eight and 113. Hence, we computed a mean number of bradycardia episodes per child between 0.3 and 1.0.

Overall, children experiencing a crisis ranged from 11.8% to 37.1%, depending on the criteria considered, and the number of crisis varied between 17 and 156. Hence, the mean number of crisis episodes per child ranged between 0.3 and 1.4.

## Economic impact analysis

The choice of the criteria used for early discharge of the child is not irrelevant from the point of view of its economic implications. As a proof-of-concept, a simple cost analysis exercise showed that the costs necessary to avoid one crisis (thus not discharging the child) were estimated to range between €23,790 and €52,953 ($36,733 and $81,271 with respect to US standards), depending on the chosen criterion (Table 5). On the other hand, the savings associated with one avoided infection were estimated to vary between €26,565 and €51,719 ($40,428 and $79,057).

**Table 4:** Potential risks of adverse events in terms of apnea, bradycardia and overall crisis as simulated by the retrospective application of each criterion.

| Discharge criterion | Apneas | | | Bradycardias | | | Crisis | | |
|---|---|---|---|---|---|---|---|---|---|
| | Probability of an event (95% CI) | Overall number of events (95% CI) | Mean number of events per children (95% CI) | Probability of an event (95% CI) | Overall number of events (95% CI) | Mean number of events per children (95% CI) | Probability of an event (95% CI) | Overall number of events (95% CI) | Mean number of events per children (95% CI) |
| Dillard and Korones (1973) [9] | 15.6 (8.1–23.1) | 39 (17–66) | 0.4 (0.2–0.7) | 15.6 (8.1–23.1) | 35 (15–62) | 0.4 (0.2–0.7) | 18.9 (11.6–26.2) | 46 (22–75) | 0.5 (0.2–0.8) |
| Derbyshire et al. (1982) [8] | 16. 0 (8.8–23.2) | 50 (21–87) | 0.5 (0.2–0.9) | 16.0 (8.8–23.2) | 49 (21–89) | 0.5 (0.2–0.9) | 19.0 (11.9–26.1) | 64 (30–106) | 0.6 (0.3–1.1) |
| Brooten et al. (1986) [5] | 14.8 (7.4–22.2) | 45 (17–81) | 0.5 (0.2 –0.9) | 15.9 (8.3–23.6) | 47 (19–83) | 0.5 (0.2–0.9) | 17.1 (9.5–24.6) | 57 (24–99) | 0.7 (0.3–1.1) |
| Schmidt and Levine (1990) [16] | 9.8 (1.6–18.0) | 15 (3–33) | 0.3 (0.1– 0.7) | 9.8 (1.6–18.0) | 13 (2–31) | 0.3 (0–0.6) | 11.8 (3.7–19.8) | 17 (4–37) | 0.3 (0.1–0.7) |
| Casiro et al. (1993) [6] | 12.2 (5.1–19.3) | 26 (9–49) | 0.3 (0.1–0.6) | 13.4 (6.0–20.8) | 23 (8–45) | 0.3 (0.1–0.6) | 14.6 (7.3–22.0) | 31 (12–56) | 0.4 (0.1–0.7) |
| Kotagal et al. (1995) [11] | 14.3 (6.5–22.1) | 30 (11–56) | 0.4 (0.1– 0.7) | 15.6 (7.5–23.7) | 31 (14–54) | 0.4 (0.2–0.7) | 16.9 (8.8–24.9) | 40 (17–68) | 0.5 (0.2–0.9) |
| Rawlings and Scott (1996) [15] | 16.3 (6.0–26.7) | 28 (6–64) | 0.6 (0.1–1.3) | 18.4 (7.5–29.2) | 34 (10–75) | 0.7 (0.2–1.5) | 20.4 (9.7–31.1) | 38 (12–80) | 0.8 (0.2–1.6) |
| Evanochko et al. (1996) [10] | 30.0 (21.0–39.0) | 108 (63–163) | 1.1 (0.6–1.6) | 34.0 (24.7–43.3) | 101 (63–143) | 1.0 (0.6–1.4) | 37.0 (27.9–46.1) | 135 (84–195) | 1.3 (0.8–2.0) |
| Merrit (2003) [13] | 12.9 (5.8–20.1) | 32 (11–64) | 0.4 (0.1–0.8) | 15.3 (7.6–22.9) | 34 (15–60) | 0.4 (0.2–0.7) | 16.5 (8.9–24.1) | 42 (18–78) | 0.5 (0.2–0.9) |
| Vecchi (1996) [18] | 18.5 (11.2–25.9) | 59 (33–91) | 0.5 (0.3–0.8) | 19.4 (12.0–26.9) | 59 (32–94) | 0.6 (0.3–0.9) | 25.0 (17.8–32.2) | 75 (45–112) | 0.7 (0.4–1.0) |
| Cruz et al. (1996) [7] | 14.3 (1.3–27.3) | 8 (1–19) | 0.3 (0–0.7) | 14.3 (1.3–27.3) | 8 (1–16) | 0.3 (0–0.6) | 17.9 (5.2–30.6) | 10 (3–22) | 0.4 (0.1–0.8) |
| Ortenstrand et al. (1999) [14] | 28.1 (20.3–35.9) | 129 (80–186) | 1.0 (0.6–1.5) | 30.5 (22.5–38.4) | 113 (73–161) | 0.9 (0.6–1.3) | 33.6 (25.8–41.4) | 156 (101–210) | 1.2 (0.8–1.7) |
| Sellers and Davidson (2000) [17] | 32.6 (22.8–42.3) | 108 (64–166) | 1.2 (0.7–1.9) | 33.7 (23.9–43.5) | 90 (54–136) | 1.0 (0.6–1.5) | 37.1 (27.5–46.7) | 124 (76–186) | 1.4 (0.9–2.1) |
| Lian et al. (2008) [2] | 11.1 (2.7–19.5) | 16 (4–36) | 0.3 (0.1–0.7) | 7.4 (0.4–14.4) | 17 (1–44) | 0.3 (0–0.8) | 13.0 (6.2–19.7) | 22 (4–51) | 0.4 (0.1–0.9) |
| Bathie and Shaw (2013) [4] | 33.0 (23.1–42.8) | 109 (67–171) | 1.2 (0.8–1.9) | 32.9 (23.1–42.8) | 88 (54–138) | 1.0 (0.6–1.6) | 36.4 (26.8–45.9) | 123 (77–194) | 1.4 (0.9–2.2) |

CI, confidence interval.

**Table 5:** Potential economic impact of the application of each criterion, evaluated in terms of adverse events. Evaluation is based on You et al. for USA [23] and Vijgen et al. for Europe [24].

| Discharge criterion | Europe (€) | | USA ($) | |
|---|---|---|---|---|
| | Cost per avoiding a crisis (95% CI) | Savings associated to an infection (95% CI) | Cost per avoiding a crisis (95% CI) | Savings associated to an infection (95% CI) |
| Dillard and Korones (1973) [9] | 42,239 (36,148–47,152) | 44,393 (33,296–53,063) | 64,946 (54,430–74,972) | 69,523 (55,237–81,186) |
| Derbyshire et al. (1982) [8] | 38,493 (32,120–45,371) | 39,208 (31,596–47,506) | 59,132 (48,830–68,417) | 59,797 (47,728–70,330) |
| Brooten et al. (1986) [5] | 40,726 (32,473–47,764) | 42,251 (35,645–52,129) | 62,230 (51,468–71,738) | 64,202 (52,525–73,938) |
| Schmidt and Levine (1990) [16] | 50,537 (45,300–56,453) | 46,927 (38,315–55,564) | 77,480 (68,641–89,284) | 71,571 (59,312–84,305) |
| Casiro et al. (1993) [6] | 45,685 (39,955–52,786) | 43,863 (5,772–52,617) | 70,276 (61,673–79,603) | 68,519 (54,679–80,527) |
| Kotagal et al. (1995) [11] | 44,474 (37,806–50,956) | 44,088 (35,540–51,337) | 67,795 (56,308–77,644) | 67,289 (54,463–79,310) |
| Rawlings and Scott (1996) [15] | 45,187 (37,937–53,158) | 47,875 (38,704–56,071) | 69,231 (55,440–84,656) | 74,560 (61,502–89,446) |
| Evanochko et al. (1996) [10] | 27,283 (22,063–31,520) | 29,520 (24,356–35,105) | 41,925 (34,102–48,228) | 45,347 (36,257–54,982) |
| Merrit (2003) [13] | 43,112 (36,354–49,879) | 42,485 (35,142–50,543) | 66,539 (55,531–75,626) | 65,421 (54,731–77,942) |
| Vecchi (1996) [18] | 35,536 (30,826–41,365) | 34,036 (26,734–42,548) | 55,455 (46,558–62,317) | 51,767 (42,746–63,553) |
| Cruz et al. (1996) [7] | 52,953 (47,251–59,502) | 51,719 (43,277–59,147) | 81,271 (71,841–91,852) | 79,057 (66,708–92,200) |
| Ortenstrand et al. (1999) [14] | 23,790 (20,244–28,415) | 26,565 (19,919–31,595) | 36,733 (31,080–42,914) | 40,428 (31,795–50,719) |
| Sellers and Davidson (2000) [17] | 29,510 (23,383–34,007) | 31,573 (25,961–37,429) | 44,098 (36,460–52,139) | 47,226 (39,034–56,573) |
| Lian et al. (2008) [2] | 48,419 (42,228–55,967) | 50,101 (40,457–57,888) | 74,300 (62,479–85,478) | 76,947 (61,579–87,931) |
| Bathie and Shaw (2013) [4] | 29,525 (22,591–34,200) | 33,308 (26,784–39,206) | 45,503 (38,028–52,396) | 50,361 (43,534–59,801) |

CI, confidence interval.

# Discussion

## Days saved

According to the considered criteria, at least one infant could have been discharged earlier or could have avoided relocation, except for criteria that included breastfeeding as a parameter for early discharge.

Parameters established by four criteria [8, 10, 14, 18] would have granted early discharge to more than 100 infants. According to four studies, more than a week of hospital days could have been saved [4]. All these studies had a common feature: the discharge with nasogastric tube (NGT) feeding was allowed, as full feeding via a baby bottle or at the breast was not required as a condition for early discharge. Successful home NGT feeding is, however, possible only if parents are competent, confident, committed and supported enough. For this to be possible, parents should be involved with NGT feeding early on, during their child's hospital stay. Nevertheless, NGT feeding at home is perceived as a heavy burden for some families, especially because of the possibility of complications related to tube feeding [29]. Support in the community once discharged would also be required in this case [10, 30, 31], with potential increments in cost.

In our study, the criteria that would save the least number of days and to discharge the smallest fraction of children were those proposed by Cruz et al. [7], Schmidt and Levine [16] and by Lian et al. [2]. This happened because both criteria required weight limits similar to the ones adopted in Padova University Hospital (1800 g).

## Safety

As our study showed, at least one baby developed an infection within the early and actual discharge dates for all but three of the criteria considered. A strong association between days saved and infections saved has been found: the earlier the discharge (i.e. the higher the number of days saved), the higher the likelihood of not developing a hospital-acquired infection [4].

Results of this study showed that at least one baby developed a crisis between hypothetical and actual discharge dates and that the likelihood of a crisis was higher the earlier the baby was discharged, for each criterion considered. Hence, early discharge could have potential negative consequences for infants' health in terms of death or rehospitalization. Therefore, these results highlighted a clear trade-off between saving hospital days and protecting infants from hospital-acquired infections on the one hand, and the risk of developing crises at home on the other hand. Nevertheless, these aspects have not been stressed in the studies that proposed the criteria we have analyzed.

### Economic evaluation

The analysis of the costs to be sustained to avoid one crisis suggested a wide heterogeneity across criteria using both European and US standards. The ordering of criteria in terms of cost-efficacy was qualitatively similar to the one in terms of days saved and number of infections. Criteria that saved more hospitalization days were also the ones according to which it would be less costly to avoid one more crisis. Similarly, these criteria were also the ones according to which hospitalization costs to reduce infections were lower. The overall message, however, remains that the adoption of one instead of another criterion has potential economic implications. This perspective could also be considered in planning future studies on the topic.

### Study limitations

This study has several limitations. First, because only a yes/no indicator for the incidence of crisis is available in our data, this study cannot assess the severity of the health crisis detected in the period after the hypothetical early discharge date. On the one hand, no new pharmacological therapy is recorded after these crises. On the other hand, the data collected do not allow discerning if the crisis resolved spontaneously or if stimulation of infants by nurses was needed. In this latter case, the study would suggest a reconsideration of the health risks connected with early discharge. Another potential explanation for this new finding is that parents involved in other studies could not detect a crisis because they did not have the instruments to measure it.

The second limitation is related to the bias derived from the important presence of moderate and late preterm infants in the study population (53%). These neonates were also the larger ones. Therefore, some of the large effects reported could be related to an excessive delay in discharging ‘larger’ preterm infants (moderate and late preterm ones). Performing a subgroup analyses by gestational age would be helpful in addressing this topic, but the sample size of the study does not allow this type of analysis. To overcome these issues, a more contemporary prospective study would be the best next step, in order to increase the clinical evidence related to such an approach.

Furthermore, as a future perspective, a follow-up randomized control-trial study assigning infants to different criteria and carefully monitoring health outcomes at home after early discharge would provide clear answers in this sense.

## Conclusion

Early discharge of premature infants is a complex decision in pediatric medicine and nursing, and no consensus about common criteria in this sense has been reached. One reason for this uncertainty is surely the lack of information about the potential health-related benefits and cost savings related to different criteria. Indeed, prior to this study, no other quantitative benchmarking exercise was carried out to provide guidelines in this sense.

Results of this study allow the identification of more permissive and more conservative criteria, and highlight a clear trade-off between days saved and health risks for infants. Moreover, this study shows that more permissive criteria are also the more cost-effective ones in terms of costs to be sustained to decrease crisis and infection risks.

The first finding is particularly interesting and calls for further investigation, as no previous study detected health risks connected with early discharge. Overall, this quantitative evaluation provides a first step to develop new criteria for early discharge that will aim at balancing the trade-off discussed, with potential benefits in terms of both healthcare spending and infants’ health.

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