Early Weight Loss Nomograms for Exclusively Breastfed Newborns

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abstract BACKGROUND: The majority of newborns are exclusively breastfed during the birth hospitalization, and weight loss is nearly universal for these neonates. The amount of weight lost varies substantially among newborns with higher amounts of weight loss increasing risk for morbidity. No hour-by-hour newborn weight loss nomogram exists to assist in early identification of those on a trajectory for adverse outcomes.

METHODS: For 161 471 term, singleton neonates born at \geq 36 weeks' gestation at Northern California Kaiser Permanente hospitals in 2009–2013, data were extracted from the birth hospitalization regarding delivery mode, race/ethnicity, feeding type, and weights from electronic records. Quantile regression was used to create nomograms stratified by delivery mode that estimated percentiles of weight loss as a function of time among exclusively breastfed neonates. Weights measured subsequent to any nonbreastmilk feeding were excluded.

RESULTS: Among this sample, 108 907 newborns had weights recorded while exclusively breastfeeding with 83 433 delivered vaginally and 25 474 delivered by cesarean. Differential weight loss by delivery mode was evident 6 hours after delivery and persisted over time. Almost 5% of vaginally delivered newborns and >10% of those delivered by cesarean had lost \geq 10% of their birth weight 48 hours after delivery. By 72 hours, >25% of newborns delivered by cesarean had lost \geq 10% of their birth weight.

CONCLUSIONS: These newborn weight loss nomograms demonstrate percentiles for weight loss by delivery mode for those who are exclusively breastfed. The nomograms can be used for early identification of neonates on a trajectory for greater weight loss and related morbidities.

WHAT'S KNOWN ON THIS SUBJECT: Exclusively breastfed newborns lose weight daily in the first few days after birth. The amount of weight lost varies substantially between newborns, with higher amounts of weight loss increasing risk for morbidity.

WHAT THIS STUDY ADDS: This study presents nomograms demonstrating percentiles for weight loss by delivery mode for those who are exclusively breastfed. The nomograms have potential to be used for early identification of neonates on a trajectory for greater weight loss and related morbidities. Departments of ^aPediatrics, and ^bEpidemiology and Biostatistics, School of Medicine, University of California, San Francisco, California; Departments of ^ePublic Health Sciences, and ^ePediatrics, Penn State College of Medicine, Hershey, Pennsylvania; and ^dDivision of Research, Kaiser Permanente, Oakland, California

Dr Flaherman conceptualized and designed this study, oversaw all aspects of the data collection and analysis, and drafted the initial manuscript; Mr Schaefer contributed to the study design, analyzed the data, and critically revised the manuscript for important scientific content; Dr Kuzniewicz contributed to the study design, participated in data analysis, and critically revised the manuscript for important scientific content; Ms Li contributed to the study design, coordinated data collection, carried out preliminary analyses, and critically revised the manuscript for important scientific content; Ms Walsh participated in study design and data analysis and critically revised the manuscript for important scientific content; Dr Paul conceptualized and designed this study, obtained funding, and critically revised the manuscript for important scientific content; and all authors approved this manuscript as submitted.

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The World Health Organization, the Centers for Disease Control and Prevention, and the American Academy of Pediatrics all recommend breastfeeding exclusively during the birth hospitalization without any supplementary formula or water,¹⁻³ and in the United States, 60% of newborns are breastfed exclusively for at least the first 2 days.⁴ Among such exclusively breastfed neonates, enteral intake is low during the time of colostrum production,^{5–7} and initial postnatal weight loss is nearly universal.^{8–10} Although the brief period of low enteral intake and weight loss is well tolerated by most newborns, some develop complications of weight loss such as hyperbilirubinemia and dehydration, the 2 most common causes of neonatal morbidity.¹¹⁻¹⁷

To monitor for potential morbidity, weight and jaundice are evaluated daily during the birth hospitalization, with weight generally decreasing and bilirubin levels generally increasing. A nomogram published in 1999 depicting bilirubin levels by hour of age¹⁸ is widely used to evaluate trajectories of neonatal hyperbilirubinemia¹⁹ and has been incorporated into the American Academy of Pediatrics guideline on hyperbilirubinemia management.²⁰ However, similarly detailed hourspecific values and trajectories for newborn weight loss have not been previously reported. Therefore, we sought to develop a detailed graphical depiction of early trajectories of weight loss for exclusively breastfed newborns. Such a weight loss nomogram would be of great clinical utility because newborn weight is measured daily at varying hours of age, and these measurements become the basis for multiple clinical decisions including timing of discharge, need for lactation support or supplementation, and timing and type of newborn followup.^{21,22}

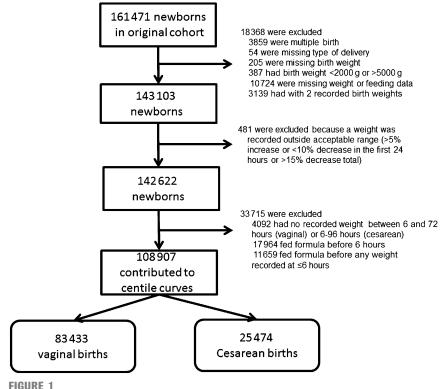
METHODS

Participants and Outcomes

The analysis included 161 471 newborns who were born at \geq 36 weeks' gestation at 1 of 14 Kaiser Permanente Northern California hospitals between January 1, 2009, and December 31, 2013, who survived to discharge home and who did not receive Level II or Level III care. For this reason, newborns with infectious disease or congenital abnormalities requiring Level II or Level III care were not included in this cohort. For included newborns, data were extracted on all weights obtained during the birth hospitalization as well as on gestational age, method of delivery, length of stay, hospital of birth, maternal race/ethnicity, and timing (hour of age) and type (breast milk or formula) of all inpatient feedings. From this cohort, newborns were excluded if they had missing data on type of delivery, weight or feeding, birth weight <2000 g or >5000 g, multiple birth, discrepantly reported birth weights between data sources, or no weight

documented after 6 hours of age and before initiation of formula feeding.

Weight change was defined as the difference between birth weight and each weight recorded subsequently, calculated as a percentage of birth weight as is typically done daily in clinical practice. Excess weight loss was defined as the loss of $\geq 10\%$ of birth weight.^{9,23} Newborns with implausible weight loss or weight gain values (>10% loss in the first 24 hours, >15% loss at any time thereafter, gain >5%) were excluded. Because length of stay varies by method of delivery and because neonates are usually weighed once daily during the birth hospitalization but not usually within 6 hours of birth, weight loss percentiles were determined from 6 to 72 hours for vaginal births and from 6 to 96 hours for cesarean births, reflecting the difference in length of stay by delivery mode and the corresponding variation in availability of weight measurements between vaginally delivered newborns and those delivered by cesarean.24



Derivation of the final analytic cohort.

 TABLE 1
 Demographic and Clinical Characteristics of Included Newborns, by Type of Delivery

	Vaginal $(n = 83433)$	Cesarean ($n = 25474$)	
Birth wt (g)			
Mean (SD)	3416.9 (426.2)	3487.7 (462.6)	
Median	3402	3470	
Interquartile range	(3120-3700)	(3170–3790)	
Range	(2000–5000)	(2010-5000)	
Gestational age (wk), n (%)			
36	1429 (1.7)	458 (1.8)	
37	5817 (7.0)	1707 (6.7)	
38	15114 (18.1)	3830 (15.0)	
39	27335 (32.8)	11515 (45.2)	
40	24011 (28.8)	4743 (18.6)	
41	9375 (11.2)	3041 (11.9)	
42	352 (0.4)	175 (0.7)	
43	0 (0.0)	5 (<0.1)	
Gestational age (wk)			
Mean (SD)	39.2 (1.2)	39.1 (1.1)	
Median	39	39	
Interquartile range	(38–40)	(39–40)	
Range	(36–42)	(36–43)	
Maternal race/ethnicity, n (%)			
Hispanic	20234 (24.5)	5897 (23.1)	
American Indian/Eskimo	335 (0.4)	104 (0.4)	
Asian	19765 (23.7)	6079 (23.9)	
Black, non-Hispanic	5165 (6.2)	1898 (7.5)	
White, non-Hispanic	35704 (42.8)	10772 (42.3)	
Unknown	2230 (2.7)	724 (2.8)	
Newborn hospital length of stay (d) ^a			
Mean (SD)	1.7 (0.8)	2.8 (0.9)	
Median	1.6	2.6	
Interguartile range	(1.2–2.0)	(2.1–3.2)	

^a There were missing length of stay data for 210 vaginally delivered and 87 Cesarean-delivered newborns.

A newborn was included in the final analysis if any weight measurement was obtained during the birth hospitalization after 6 hours of age and before exclusive breastfeeding was discontinued. Between 6 and 72 hours for vaginal births and 6 and 96 hours for cesarean births, all weights obtained during the birth hospitalization were used if at the time the weight was obtained the newborn remained exclusively breastfed as defined by the World Health Organization (nothing other than breast milk, vitamins, minerals, and oral medications).^{25,26} Newborns were censored at the time of the first supplementary feeding. No weights obtained subsequent to censoring or after discharge from the birth hospitalization were used in this analysis. This study was approved by the University of California San Francisco Committee on Human Research and by the Institutional

Review Boards of Penn State Medical College and Kaiser Permanente Northern California.

Analyses

Quantile regression methods appropriate for data with repeated measures were used to estimate 50th (median), 75th, 90th, and 95th percentiles of weight loss as a function of time after birth. The penalized fixed-effects model in the R package "Regression Quantiles for Panel Data" was used to estimate the percentile curves.²⁷ The model is an extension of ordinary quantile regression²⁸ to longitudinal settings in which newborns may be weighed at multiple time points. The model accounts for multiple (or repeated) weights from a newborn by including a separate intercept parameter for each newborn, with regularization used to estimate these intercepts by shrinking them toward a common value. The amount of regularization is controlled by a tuning parameter, which was set equal to 5 so that most intercepts were shrunk to zero, a prudent choice for sparse longitudinal data that includes many newborns contributing only a single data point (62% of newborns in the sample had only 1 weight included in the analysis). A B-spline basis with 4 degrees of freedom was used to generate nonlinear percentile curves.²⁹ Nonparametric bootstrapping with 500 resamples and the percentile method were used to obtain confidence intervals for each percentile curve.³⁰ To examine the reliability and robustness of the final estimated percentile curves, we generated separate curves for the cohort born 2009-2010 and the cohort born 2011-2013.

We examined whether our nomograms were affected by the inclusion of late preterm, postterm, and small or large-for-gestational-age infants by removing all newborns born at <37 weeks and ≥42 weeks from the cohort, and those with birth weights below the 10th percentile and above the 90th percentile for gestational age. The quantile regression model was refit on the basis of these exclusions, and we examined how the estimated percentile curves changed.

To determine whether censoring newborns after formula use may have caused bias to the estimated percentile curves, we undertook

	TABLE 2	Number of	Weights	Used in	the Final	Analysis, <i>i</i>	ı (%)
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Weights Recorded After Birth Weight	Vaginal (<i>n</i> = 83 433), <i>n</i> (%)	Cesarean (n = 25 474), n (%)
1	59 953 (71.9)	6402 (25.1)
2	21 440 (25.7)	12 423 (48.8)
3	1825 (2.2)	5555 (21.8)
4	215 (0.3)	1094 (4.3)

TABLE 3 Number of Weights Included for Each 12-Hour Interval

Time, h	Vaginal (n = 109 190), n (%)	Cesarean (<i>n</i> = 52 443), <i>n</i> (%)
6–12	23 914 (21.9)	7221 (13.8)
13–24	45 394 (41.6)	14 377 (27.4)
25-36	26 185 (24)	9866 (18.8)
37–48	10 833 (9.9)	11 192 (21.3)
49–60	2168 (2.0)	5040 (9.6)
61-72	696 (0.6)	3535 (6.7)
73–84	—	780 (1.5)
85–96	_	432 (0.8)

—, not included.

a sensitivity analysis. If previously exclusively breastfed newborns began using formula supplementation primarily because of high levels of weight loss, then the estimated curves may have underestimated the actual weight loss in the population. To examine this possibility, the sensitivity analysis recreated the nomograms after using matching to impute subsequent weights for newborns who had 1 included weight recorded during the birth hospitalization and then were censored. First, each newborn censored due to formula use was matched to 1 uncensored newborn using a greedy matching algorithm.³¹ Matches were conditional on 3 variables: time of most recent weight measurement in which the censored newborn had been exclusively breastfed (± 2 hours), percent weight loss at that time (± 3 percentage points), and gestational age $(\pm 3 \text{ weeks})$. The weight loss data from the uncensored newborn that occurred after formula use began for the censored newborn was then imputed as the actual weight loss data for the censored newborn. Last, the quantile regression model was refit using the original data plus the imputed data for censored newborns to examine how the estimated percentile curves changed. The main assumption of this sensitivity analysis is that the weight loss history of the matched uncensored newborn reasonably approximates the weight loss history that would have been observed for the censored newborn had formula never been introduced.

RESULTS

From 161 471 newborns in the cohort, 108 907 were included in the final analysis, of whom 83 433 (76.6%) were delivered vaginally and 25 474 (23.4%) were delivered by cesarean. Among 52 564 excluded newborns, 33 715 (64%) were excluded because no weight was obtained in the eligible period and before formula feeding, 18 368 (35%) were excluded due to either multiple birth or missing or discrepant birth data, and 481 (0.9%) were excluded because weight loss exceeded 10% in 24 hours or 15% at any time or because weight gain exceeded 5% (Fig 1). Data were available on race/ ethnicity for 97.3% of mothers, and the cohort was racially diverse; 24% of mothers were Hispanic, 24% were Asian, 7% were black non-Hispanic, and 43% were white non-Hispanic. Other demographic and clinical characteristics are summarized in Table 1.

For neonates delivered vaginally, 109 190 weights subsequent to birth weight were recorded (1.3 per newborn), and for those delivered by cesarean, 52 443 were recorded (2.1 per newborn). A majority delivered vaginally (71.9%) had only 1 weight recorded during the followup, whereas a majority delivered via cesarean (74.9%) had \geq 2 weights recorded (Table 2). The difference reflects the longer length of stay for cesarean newborns. See Table 3 for details on the distribution of age in hours for included weights.

Differences in weight loss by delivery type appeared early and were clearly

evident within 24 hours of birth. Figure 2A presents percentile curves for vaginally delivered newborns. Median percent weight loss for these neonates was 4.2%, 7.1%, and 6.4% at 24, 48, and 72 hours of age, respectively. By 48 hours, almost 5% of vaginally delivered newborns had lost at least 10% of their birth weight, and by shortly after 48 hours, the percentile curves for median weight loss had begun to rise. Figure 2B presents percentile curves for newborns delivered by cesarean. Median percent weight loss among these neonates was 4.9%, 8.0%, 8.6% and 5.8% at 24, 48, 72, and 96 hours after delivery. By 48 hours of age, almost 10% of newborns delivered by cesarean had lost at least 10% of their birth weight, and by 72 hours of age, the percentile curves for median weight loss had begun to rise, but >25% were at least 10% below their birth weight.

Percentile curves with 95% confidence intervals overlaid are shown in Supplementary Figure 3 A and B. Percentile curves estimated from the cohort of 34 809 newborns born 2009–2010 were similar to the percentile curves estimated from the cohort of 74 098 newborns born 2011– 2013 (Supplemental Figure 4 A and B). Percentile curves generated after removing late preterm, postterm, and small- and large-for-gestational-age newborns were not visually distinguishable from the main results (Supplemental Fig 5 A and B).

In our main analysis depicted in Fig 2 A and B, 8457 newborns delivered vaginally (10.1%) and 8414 newborns delivered by cesarean (33.0%) had at least 1 weight included in the analysis and at least 1 weight censored from the analysis because it was obtained subsequent to a supplementary feeding. In sensitivity analysis, weights were imputed for censored newborns based on matching to uncensored newborns. More than 98% of censored newborns had exact

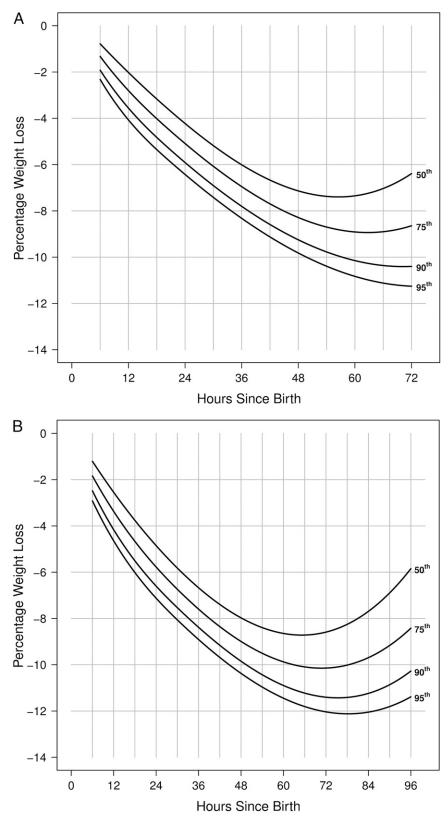
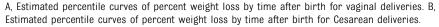


FIGURE 2



matches for time and gestational age, and >90% had a match of percent weight loss within 0.20 percentage points (Table 4). Percentile curves estimated from the original data plus the imputed data for censored weights were similar to the curves of the original data for newborns delivered vaginally and by cesarean. See the online supplement for this comparison (Supplemental Figure 6 A and B).

DISCUSSION

These results provide the first graphical depiction of hourly weight loss for exclusively breastfed newborns from a large, diverse population. Because weight changes steadily throughout the birth hospitalization and is measured at varied intervals from the hour of birth, these new nomograms should substantially aid medical management by allowing clinicians and lactation support providers to categorize newborn weight loss and calibrate decision-making to reflect hour of age. The use of these nomograms may allow a more nuanced clinical approach to weight loss in a manner similar to that of the widely used nomogram for hyperbilirubinemia. Similar to the bilitool.org Web site, a new Web site, http://www.newbornweight.org, has been developed by the study team to allow clinicians to compare individual newborns and their weight loss against our large sample.

With nomograms presented separately for newborns delivered vaginally and by cesarean, it is clear that differential weight loss by delivery method materialized early and persisted over time. Factors contributing to lactation difficulty have been well documented among those undergoing cesarean delivery.^{32,33} In addition, the administration of large volumes of intravenous fluid before cesarean may be an independent risk factor for newborn weight loss.^{34,35} Excess weight loss \geq 10%, which has been

 TABLE 4
 Summary of Matched Variables for Censored Newborns

	Vaginal (<i>n</i> =	= 8457), <i>n</i> (%)	Cesarean (<i>n</i>	= 8414), n (%)
Time (h)				
Exact match	8420	(99.6)	8325	(98.9)
1 h difference	36	(0.4)	83	(1.0)
2 h difference	1	(<0.1)	6	(0.1)
Weight loss, percentage points				
<0.05	7373	(87.2)	5998	(71.3)
0.05-0.20	651	(7.7)	1445	(17.2)
0.20-0.50	253	(3)	566	(6.7)
0.50–1	146	(1.7)	295	(3.5)
1–2	34	(0.4)	101	(1.2)
>2		0	9	(0.1)
Gestational age				
Exact match	8389	(99.2)	8241	(97.9)
1 wk difference	67	(0.8)	163	(1.9)
2 wk difference	1	(<0.1)	8	(0.1)
3 wk difference		0	2	(<0.1)

associated with increased risk of both hyperbilirubinemia and hypernatremic dehydration, 10,14,16,32 was common among both groups. Almost 5% of vaginally delivered newborns and almost 10% of those delivered by cesarean had lost $\geq 10\%$ of their birth weight by 48 hours. By 72 hours of age, >25% of newborns delivered by cesarean had lost $\geq 10\%$ of their birth weight. Weight gain typically began at 48 to 72 hours of age. Newborns with greater weight loss tended to have weight nadir at an older age.

Results from this study are unique because they contain detailed data by hour of life in a large, diverse population for which data were available on type and timing of all feedings. Therefore, our analysis included all weights obtained during the duration of exclusive breastfeeding and excluded any weight obtained after an infant received a supplementary feeding. Reliability of these nomograms is supported by the similarity between curves generated by the cohort born 2009-2010 and those born 2011-2013. Moreover, the similarity between the results presented in the main analysis and the results of sensitivity analysis in which weights were imputed for censoring due to formula use offers further evidence of the robust nature of the findings.

These analyses have several limitations. First, weights for this study were obtained in the course of routine care with various scales calibrated according to the guidelines of individual institutions. However, the results therefore reflect weight loss in a setting of routine clinical practice. Second, feeding reports in our study were obtained from the electronic medical record maintained by the nursing staff, and nursing staff may not have been aware of or documented all feedings. If some mothers fed formula without documentation in the medical record, our results might underestimate weight loss for exclusively breastfed newborns. Third, our study did not have access to accurate reports of reasons given for initiating formula feeding. If caregivers initiated formula because of weight loss, our results might underestimate weight loss for exclusively breastfed newborns. However, the similarity between our main model and our model obtained by imputing weights for censored newborns suggests that this was not a substantial source of bias. Fourth, our curves extend only to 72 hours for vaginal births and 96 hours for births by cesarean and therefore do not represent weight nadir for all newborns, although the majority of measured infants did begin weight

gain during this period. Fifth, the Northern California population studied was racially diverse with 43% being white non-Hispanic. Results could be different for populations with other racial and ethnic compositions. Additionally, we had no data on parity or previous maternal breastfeeding experience; weight loss may have been ameliorated for newborns of mothers multiparous or with previous breastfeeding experience.23 Sixth, our cohort excluded newborns who received Level II or Level III care but may have included some newborns with congenital anomalies such as trisomy 21. It is possible that such well newborns with congenital anomalies not requiring Level II or Level III care had different weight loss patterns than newborns without congenital anomalies, but the small proportion of well newborns with congenital anomalies makes this group unlikely to affect the nomogram results. These limitations illustrate the potential importance of a future large, prospective cohort study that could rigorously measure feeding practices and weights at prespecified intervals while simultaneously assessing the effect of various weight trajectories on clinical outcomes.

CONCLUSIONS

The availability of detailed data on weight and feeding for a large cohort allows this study to present the first graphical depiction of hourly weight loss for exclusively breastfed newborns from a large, diverse population. Similar to the widely used bilirubin nomogram by Bhutani et al. our findings, available at http://www. newbornweight.org, have the potential for wide clinical applicability and may have strong generalizability because data are included from a large, racially diverse cohort delivered at multiple hospitals.¹⁸ Our curves demonstrate that expected weight loss differs

substantially by method of delivery and that this difference persists over time. Our results also show that weight loss $\geq 10\%$ of birth weight is common and often occurs earlier in the postnatal course than previously documented. These nomograms provide normative data that may inform clinical care.

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