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Factors influencing the determination of dosing weight in the neonatal intensive care unit (NICU)

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The objective of this study is to describe the properties of dosing weight in the neonatal intensive care unit (NICU). Infants were identified from a database of very low birth weight infants. Before regaining birth weight (BW), dosing and birth weight% difference was described. After regaining BW, dosing and measured weight% difference and frequency of dosing weight updates were described. Associations with infant characteristics including comorbid conditions, serum biochemistries, fluid intake, and urine output were evaluated. There were 115 infants over 4,643 infant-days with a median BW of 1060 g (interquartile range [IQR]: 750, 1300) and median time to regain BW of 10 days (IQR: 8, 13). After regaining BW, dosing weight was 4.2% less than measured weight. The gap widened with increasing creatinine and narrowed with increasing urine output. The only factor associated with the frequency of dosing weight updates was day of the week. Dosing weights in the NICU appear to fall into one of three categories: BW prior to regaining BW, practical weight to facilitate medication and nutrition ordering, and "dry" weight, adjusting for fluid overloaded states. We recommend using measured weight to avoid a 4% daily loss in nutrition intake once BW is regained.

Dosing weight (DW) is an assigned weight that differs from the most recent measured weight (MW), which is typically obtained daily. In the neonatal intensive care unit (NICU), the DW facilitates medication and nutrition ordering by accounting for changes in fluid status, rapid growth, or measurement error[1,2]. Clinicians may also continue to use the birth weight (BW) as opposed to the MW for variable periods of time[3,4], as there are considerable shifts in fluid between intracellular and extracellular compartments after birth[5].

The chosen DW has important implications for nutrition management, fluid management, and medication dosing for infants in the NICU. Basing nutrition calculations on BW rather than MW until BW is regained has been associated with higher protein delivery and increased weight and head circumference percentiles at discharge[4]. DW may also represent a "dry" weight that reflects an assessment of fluid overload or state of edema secondary to acute kidney injury[6]. Determining the degree of fluid overload is important and has been previously shown to have significant implications in morbidity and mortality, as well as potential need for therapeutic interventions[6–8].

Assigning an appropriate DW for infants can be challenging for clinicians. There is minimal guidance on how to do so because the factors associated with DW assignment have not been fully explored. As a result, variation in the use of DW exists. A survey of NICUs in the Children's Hospital Neonatal Consortium demonstrated that 40% of electronic health records used the DW to automatically calculate fluid intake in mL/kg while 60% used the MW[9]. We aim to describe the DW of infants in the NICU, including how it compares to BW and MW, and whether the frequency and magnitude of DW changes are associated with infant characteristics or nonclinical factors.

Methods

The Institutional Review Board (IRB) of the Ann & Robert H. Lurie Children's Hospital reviewed the study and determined that it is exempt from IRB review (IRB #2015 – 522). The IRB committee waived the requirement for informed consent due to the retrospective nature of this study. All methods were performed in accordance with the relevant guidelines and regulations. The original dataset was created from three sources (manually

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abstracted data from Epic electronic health record, data from the Children's Hospital Neonatal Consortium (CHNC) Database, and data obtained through Lurie Children's Hospital Data Analytics and Reporting (DAR)) between the spring of 2015 and the fall of 2016. Additional data was obtained through all three sources (Epic, CHNC, DAR) in the spring and summer of 2021. Final analysis for the paper was performed on July 26, 2022 and August 1, 2022. The senior author (GF) had access to information that could identify individual participants during data collection from the electronic health record.

Setting

The Lurie Children's Hospital NICU is a 64-bed regional, referral level IV NICU in Chicago, IL that cares for critically ill preterm and term infants[10]. A multidisciplinary team including neonatologists, neonatal fellows, nurse practitioners, pediatric residents, bedside nurses, pharmacists, and dietitians reviews each patient during morning rounds at bedside. Discussions include but are not limited to intake, output, and growth. It is common practice to continue to use BW as the DW for the first two weeks of life or until BW is regained. After BW is regained, the team will review the DW with some regularity and modify the DW as the MW changes with infant growth. Unlike the MW or BW, which are measured values, the DW is an assigned value. Clinicians typically initiate parenteral nutrition at 80–100 mL/kg per day for preterm infants shortly after birth. Subsequently, they advance volume by 20mL/kg per day and introduce enteral feeds according to infant's clinical status until achieving a goal of 150-160mL/kg of full enteral feeds. After birth, infants remain in a humidified incubator until the infant can maintain euthermia without assistance.

Cohort and data abstraction

The cohort included infants from an existing nutrition and growth dataset of very low birth weight (< 1500 g) infants admitted to the NICU in the first week of life[11,12]. Infants with congenital anomalies, chromosomal abnormalities, or discharge prior to 28 days of life were excluded.

The dataset included data on infant characteristics, non-clinical factors, growth parameters, and fluid and nutrition intake during the first six weeks of life. Infant characteristics included gestational age, BW, small for gestational age (SGA), patent ductus arteriosus (PDA), necrotizing enterocolitis or spontaneous intestinal perforation (NEC/SIP), intubation on day 28, and blood stream infection (BSI). Non-clinical factors included whether the infant was managed by neonatal nurse practitioners or resident physicians and the day of the week, which is associated with changes in clinical care[13]. Growth parameters included daily MW, length, and head circumference. Daily fluid and nutrition intake were normalized using daily MW.

Additional data were obtained through the Children's Hospital Neonatal Consortium database and Data, Analytics, and Reporting of Lurie Children's Hospital[14]. These data included all DWs and the day of DW changes, the lowest serum sodium and highest creatinine values, daily urine output reported in mL/kg/hour using MW, and medications that may affect urine output (caffeine, indomethacin or ibuprofen, and maternal antenatal steroids).

Exploratory analyses

To facilitate interpretation of statistical analyses, these variables were centered to the following values: highest creatinine, 1 mg/dL (hospital reference range: 0.25-0.54 mg/dL); lowest sodium, 130 mEq/L (range: 136-149mEq/L); daily fluid intake, 140 mL/kg/day; hourly urine output, 2 mL/kg/hour. Statistical analyses with fluid intake were performed in 10 mL/kg/day units.

The DW-BW and DW-MW percent differences were calculated using the following formula:

$$\text{DW} - \text{BW Percent Difference} = 100^{*}\frac{(\text{DW} - \text{BW})}{\text{BW}}$$

$$\text{DW} - \text{MW Percent Difference} = 100^{*}\frac{(\text{DW} - \text{MW})}{\text{MW}}$$

The 5th, 25th, 50th, 75th, 95th percentiles for DW-BW and DW-MW differences were graphed daily for the first six weeks of life. Based on the unit practice to use the BW as the DW until BW was regained, subsequent analyses evaluated the DW-BW difference before the infant regained BW and the DW-MW difference on or after the infant regained BW. The time to regain BW was defined as the first of three consecutive days with the MW at or above BW following diuresis.

Analyses of dosing weight before infant regained birth weight

The median number of DW changes was calculated for each infant. Since most infants had only one DW assigned during this period, the average DW-BW difference was described using a histogram and evaluated for associations with infant characteristics and non-clinical factors. Analyses were limited to the highest creatinine, lowest sodium, and average fluid intake and urine output in the first week. Wilcoxon rank sum test and ordinary least square regression were used when appropriate. All statistical significance assumed a two-tailed test with an α of 0.05.

Analyses of dosing weight on or after infant regained birth weight

After the infant regained BW, we evaluated the DW-MW difference. Bivariable analyses determined the association between the daily DW-MW difference with each infant characteristic and non-clinical factor using mixed effects linear regression given data clustering (i.e., repeated measurements per infant)[15]. Analyses included the highest creatinine and lowest sodium over the entire six weeks. Because DW was typically assigned

in the morning during rounds before the total intake and output were determined for each day, 3-day moving averages (3DMA) of daily fluid intake and urine output were calculated to reflect the most recent fluid status of the infant and used in the analyses (e.g., the association between the DW-MW difference and fluid intake on day 21 corresponded to the 3DMA of fluid intake on days 18–20)[11,16]. Multivariable analyses employed models using backward stepwise reduction with a criterion of p-value less than 0.20. Beta coefficients, along with 95th percent confidence intervals [CI] and p-values were reported.

The DW-MW difference over time is logically the result of the frequency of DW changes and the magnitude of DW assignment on the day of change as the MW increases with infant growth. For example, a large DW-MW difference may accrue because of infrequent DW changes, a large magnitude in the DW-MW difference on the day the DW changes, or both. To distinguish between both effects, we subsequently evaluated the frequency and magnitude of DW-MW difference only on days when DW was changed. Bivariable analyses determined the association with each infant characteristics and non-clinical factors using mixed effects logistic and linear regression when appropriate, followed by multivariable analyses[15].

Results

Cohort

The cohort included 115 very low birth weight infants over a total of 4,643 infant-days with DW and MW recorded on 100% and 97.5% infant-days, respectively. Median day of admission was 0 (interquartile range [IQR]: 0, 1) and median day of discharge was 87 (IQR: 55, 128). Median birth weight was 1060 g (IQR: 750, 1300) and median gestational age was 28 and 0/7 weeks (IQR: 25 and 4/7, 30 and 1/7). SGA was present in 13 (11%), NEC/SIP in 21 (18%), day 28 intubation in 40 (35%), and BSI in 19 (17%) infants. PDA was present in 55 (48%) infants – 17 (15%) were untreated, 28 (24%) were only treated medically and 10 (9%) were treated surgically. Mothers of 80 (70%) infants received any steroids; 46 (40%) infants received indomethacin or ibuprofen as treatment or prophylaxis, and 67 (72%) infants received caffeine. Nurse practitioners cared for 46 (40%) infants, while resident physicians cared for 69 (60%) infants.

The median highest creatinine level was 0.92 mg/dL (IQR: 0.81, 1.05) and lowest sodium level was 130 mEq/L (IQR: 126, 134) over the six weeks. Of the 115 infants, 88 (77%) had hyponatremia with a sodium < 135 mEq/L, 55 (48%) had a sodium < 130 mEq/L, and 4 (3%) had a sodium < 120 mEq/L.(17,18) Values limited to the first week of life were similar for creatinine (median: 0.88; IQR: 0.79, 0.99) though less hyponatremic (median: 135; IQR: 132, 137). The median fluid intake was 145 mL/kg/day (IQR: 133, 154); however, intake rapidly increased over the first week before plateauing to just under 150 mL/kg/day (Fig. 1). The median urine output was 2.2 mL/kg/hour (IQR: 1.6, 3.9) and appeared stable over the six weeks (Fig. 2).

Exploratory analyses

The median time to regain BW in our cohort was 10 days (IQR: 8, 13). There were four infants who never diuresed, and two infants who regained BW prior to admission. Time to regain BW was set to day 1 for the former and day of admission for the latter.

Visual analysis of the DW-BW and DW-MW differences demonstrated that DW tracked BW in the early postnatal period before tracking MW (Figs. 3, 4). In both graphs, there is an inflection point at day 10, the median time to regain BW. The median DW-BW difference prior to day 10 is zero before increasing. The median DW-MW difference stabilizes around − 3 to -4% after day 10. This appeared consistent with the unit practice of using the BW as the DW until BW is regained.

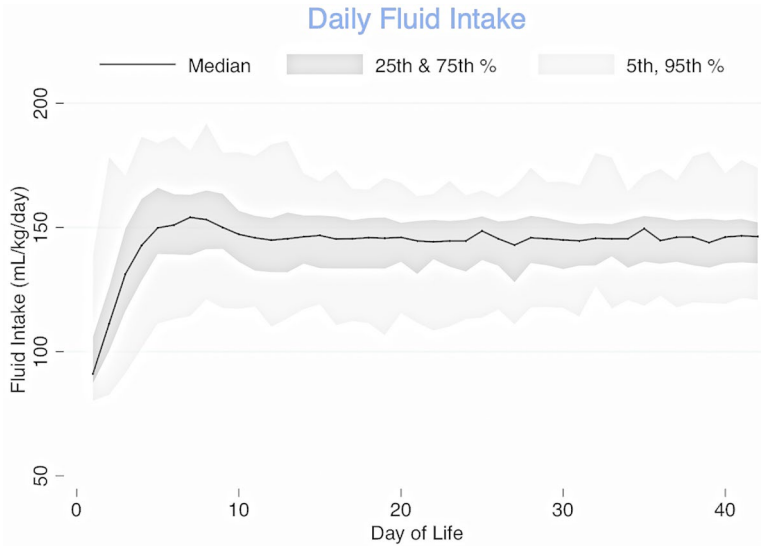

Fig. 1. Daily fluid intake in mL/kg/day over the first six weeks.

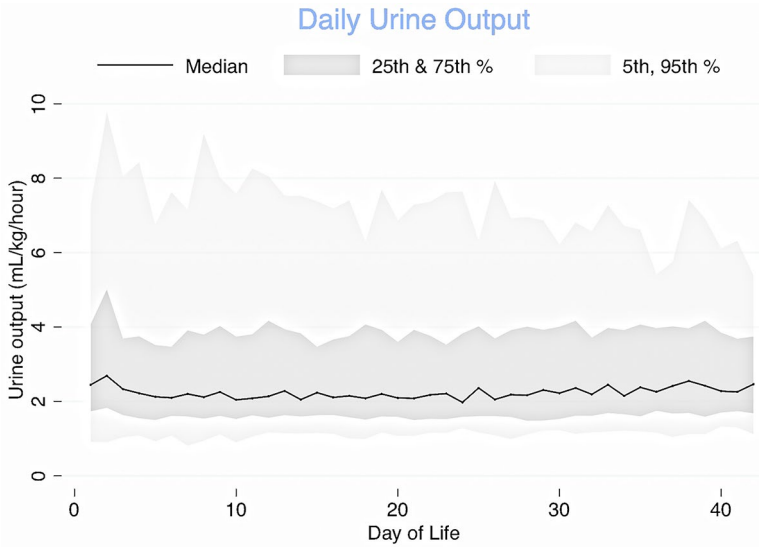

Fig. 2. Daily urine output in mL/kg/hour over the first six weeks.

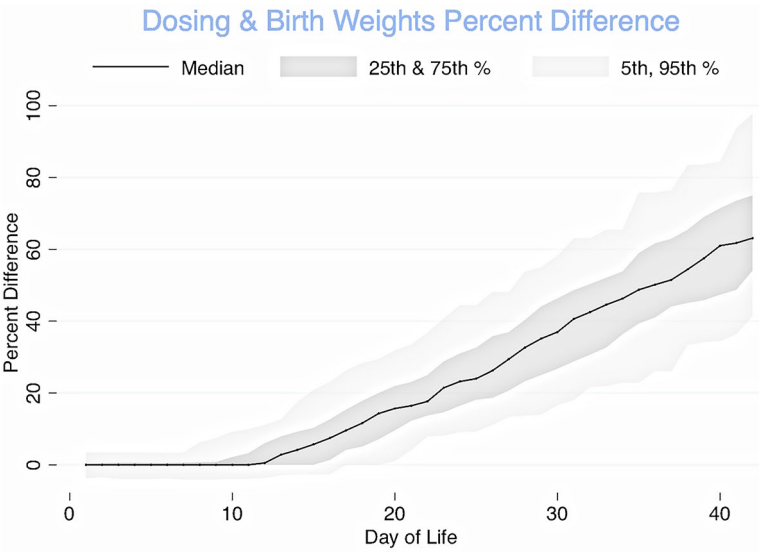

Fig. 3. Dosing & birth weights percent difference.

Analyses of dosing weight before infant regained birth weight

About 90% of infants had only one DW assigned (i.e., the initial DW) prior to regaining BW (median 1; IQR: 1, 1). The distribution of the average DW-BW difference is presented in Fig. 5. Though the median DW-BW difference was zero, the difference ranged −8.2 to 13.5%. This difference was not associated with any infant characteristics or non-clinical factor (Table 1).

Analyses of Dosing Weight on or after infant regained Birth Weight

The DW-MW difference on or after the infant regained BW is similar to Fig. 4 after day 10, the median time to regain birth weight (data not shown). Bivariable analyses demonstrated independent associations between DW-MW and BW, intubation, highest creatinine, and 3DMA of daily fluid intake and hourly urine output (Table 2); however, only highest creatinine and the 3DMA of urine output remained significantly associated with DW-MW percent difference in the multivariable model (Table 3). The referent DW-MW percent difference (i.e., intercept) in an infant whose peak creatinine was 1 mg/dL with urine output of 2 mL/kg/hour was −4.2%. This difference would change by -5.4% for every 1 mg/dL increase in peak creatinine and 0.8% for every 1 mL/kg/hour increase in the 3DMA of urine output. Therefore, an infant with peak creatinine of 2.0 mg/dL and a urine output of 1 mL/kg/hour in the past three days would have an average DW-MW percent difference of -10.4% ([-4.2] + [-5.4] + [0.8*-1]).

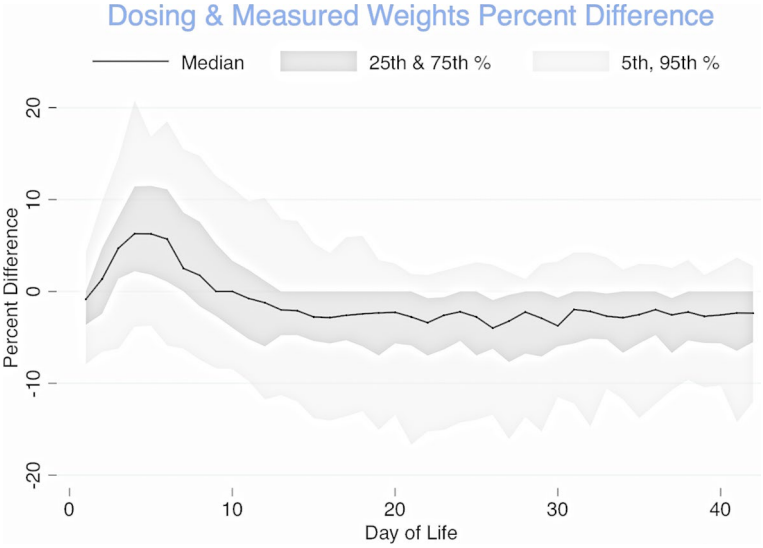

Fig. 4. Dosing & measured weights percent difference.

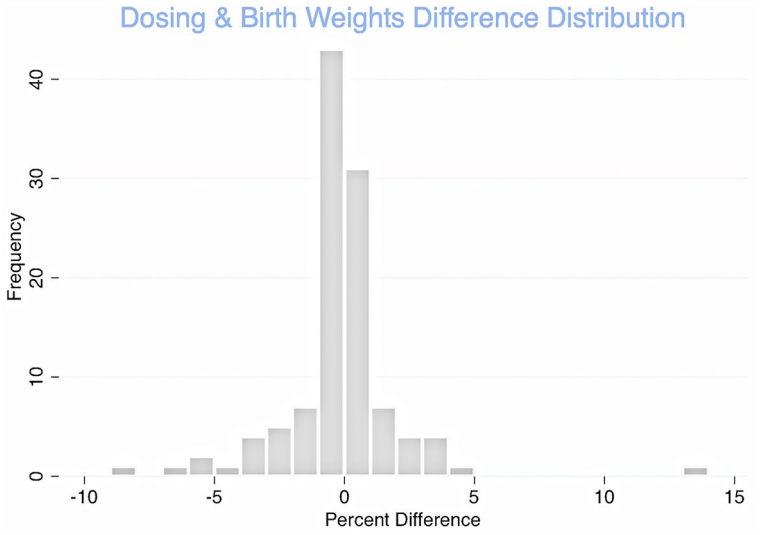

Fig. 5. Distribution of average dosing-birth weights percent difference.

The median number of DW changes after the infant regained BW was 6 (IQR: 5, 7). Figure 6 describes the frequency of changes and median DW-MW percent difference by day of the week. DW changes for all 115 infants most frequently occurred on Monday and Friday. As a result, the DW-MW difference narrowed on these days but gradually widened during the remaining days. Bivariable analyses only demonstrated an independent association with day of week (Table 4). Infant characteristics including comorbid conditions and renal function were not associated with a DW change. Multivariable logistic regression demonstrated that the odds of a DW change was increased on Mondays and Fridays (odds ratio [OR]: 8.5; CI: 6.9, 10.5; $p < 0.001$) and decreased on Saturdays and Sundays (OR: 0.7; CI: 0.5, 0.9; $p = 0.01$) referent to Tuesday, Wednesday, and Thursday.

Limited to days with DW changes, bivariable analyses demonstrated an independent association between DW-MW and BW, NEC/IP, intubation, highest creatinine, lowest sodium, indomethacin or ibuprofen, and day of the week (Table 5); however, only highest creatinine and the 3DMA of fluid intake remained significantly associated with DW-MW difference on days that DW were changed (Table 6). The referent DW-MW percent difference in an infant whose peak creatinine was 1 mg/dL and fluid intake over the past three days was 140 mL/kg/day was − 1.3%. This difference would change by -3.5% for every 1 mg/dL increase in peak creatinine and 0.4% for every 10 mL/kg/day increase in the 3DMA of fluid intake. Therefore, on days that DW was changed an infant with peak creatinine of 0.9 mg/dL and a total fluid intake of 160 mL/kg/day over the past three days would have an average assigned DW-MW difference of -0.2% ([-1.3] + [-3.5*-0.1] + [0.4*2]).

Infant or Unit Characteristic	Percent difference* (*p*-value)
Birth weight (kg)	-0.4 (0.607)
Small for gestational age	0 vs. 0 (0.5042)
Patent ductus arteriosus	0 vs. 0 (0.5903)
Necrotizing enterocolitis or spontaneous intestinal perforation	0 vs. 0 (1.000)
Intubated on day 28	0 vs. 0 (0.6271)
Blood stream infection	0 vs. 0 (0.7535)
Highest creatinine in mg/dL	0.18 (0.846)
Lowest sodium in mEq/L	-0.00 (0.917)
Daily fluid intake in 10mL/kg/day	-0.03 (0.654)
Daily urine output in mL/kg/hour	0.1 (0.489)
Maternal steroids	0 vs. 0 (0.3906)
NSAIDs	0 vs. 0 (0.6822)
Caffeine	0 vs. 0 (0.3715)
Clinician team (nurse practitioner vs. resident)	0 vs. 0 (0.9082)

Table 1. The bivariable associations between infant or unit characteristic and the dosing-birth weights percent difference. *Ordinary Least Square regression reported as beta coefficient (percent difference) and p-value; Wilcoxon Rank Sum test reported as median without versus with characteristic and p-value.

Infant or Unit Characteristic	Percent difference (95% Confidence Interval)*	*p*-value
Birth weight (kg)	2.0 (0.1, 3.8)	0.035
Small for gestational age	0.1 (-1.6, 1.8)	0.916
Patent ductus arteriosus	-0.9 (-2.0, 0.2)	0.115
Necrotizing enterocolitis or spontaneous intestinal perforation	-0.4 (-1.8, 1.1)	0.612
Intubated on day 28	-1.2 (-2.3, -0.1)	0.038
Blood stream infection	0.2 (-1.3, 1.7)	0.794
Highest creatinine in mg/dL	-5.6 (-7.1, -4.0)	< 0.001
Lowest sodium in mEq/L	0.1 (-0.03, 0.2)	0.179
3DMA of daily fluid intake, 10mL/kg/day	0.3 (0.2, 0.4)	< 0.001
3DMA of daily urine output, mL/kg/hour	0.8 (0.6, 1.0)	< 0.001
Maternal steroids	-0.2 (-1.2, 0.9)	0.780
NSAIDs	-0.9 (-2.0, 0.2)	0.104
Caffeine	-0.1 (-1.6, 1.3)	0.872
Resident team (referent to nurse practitioner team)	0.1 (-1.0, 1.3)	0.797

Table 2. The bivariable associations between infant or unit characteristic and the dosing-measured weights percent difference. 3DMA, 3-day moving average *Mixed effects linear regression reported as beta coefficient (percent difference) and p-value

Infant characteristics	Dosing - Measured Weight% difference (95% Confidence Interval) **	*p*-value
Intubation	-1.0 (-2.1, 0.1)	0.076
Highest creatinine, mg/dL	-5.4 (-7.2, -3.7)	< 0.001
3DMA of daily fluid intake, 10mL/kg/day	0.1 (-0.03, 0.2)	0.138
3DMA of daily urine output, mL/kg/hour	0.8 (0.6, 0.9)	< 0.001
Intercept**	-4.2 (-4.8, -3.5)	< 0.001

Table 3. The multivariable associations between infant characteristics and the dosing-measured weights percent difference*. 3DMA, 3-day moving average *Mixed effects linear regression reported as beta coefficient (percent difference), 95th % confidence interval, and p-value ** Final model predicting Dosing-Measured Weights Difference = [-4.2] + [-5.4*X_1] + [0.8*X_2]) where $X_1$is the highest creatinine referent to an infant to 1 mg/dL and $X_2$is the 3DMA of urine output referent to 2mL/kg/hr.

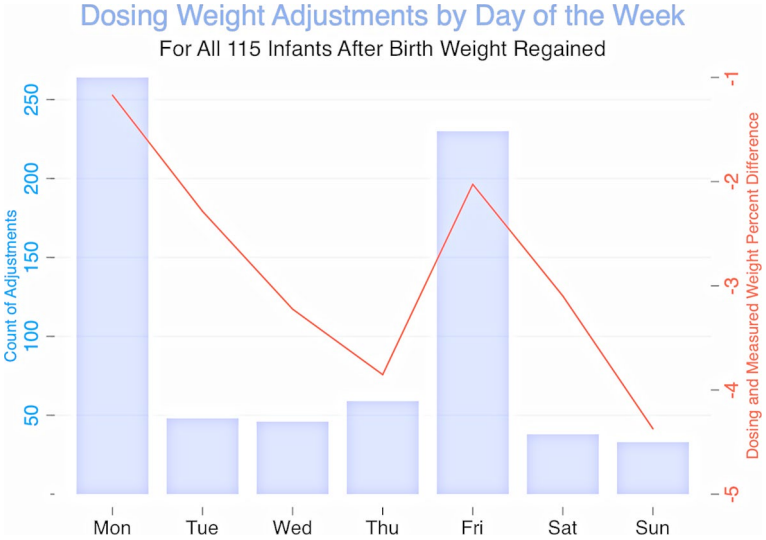

Fig. 6. Dosing weight changes & dosing-measured weights difference by day of the week.

Infant or Unit characteristics	Odds Ratio (95% Confidence Interval)*	*p*-value
Birth weight (kg)	0.9 (0.7, 1.2)	0.433
Small for gestational age	1.0 (0.8, 1.3)	0.901
Patent ductus arteriosus	1.0 (0.8, 1.1)	0.720
Necrotizing enterocolitis or spontaneous intestinal perforation	1.0 (0.8, 1.3)	0.823
Intubated on day 28	1.1 (0.9, 1.3)	0.468
Blood stream infection	1.1 (0.9, 1.4)	0.445
Highest creatinine in mg/dL	0.9 (0.7, 1.2)	0.494
Lowest sodium in mEq/L	1.0 (1.0, 1.0)	0.593
3DMA of daily fluid intake in 10mL/kg/day	1.0 (0.9, 1.0)	0.154
3DMA of daily urine output in mL/kg/hour	1.0 (1.0, 1.1)	0.466
Maternal steroids	1.1 (0.9, 1.3)	0.339
Ibuprofen or indomethacin	1.0 (0.9, 1.2)	0.881
Caffeine	1.1 (0.9, 1.3)	0.472
Monday or Friday	9.6 (8.0, 11.5)	< 0.001
Saturday or Sunday	0.2 (0.2, 0.3)	< 0.001
Resident team (referent to nurse practitioner team)	1.1 (0.9, 1.3)	0.304

Table 4. The bivariable associations between infant or unit characteristic and the dosing weight updates. 3DMA, 3-day moving average *Mixed effects logistic regression reported as an odds ratio and p-value

Discussion

Prior to regaining BW, the median DW-BW difference is zero and consistent with our practice of setting the DW to BW; however, there is significant variation without apparent rationale. After the infant has regained BW, the DW changes regularly. The frequency of changes is consistent with our unit's practice of updating DWs on Mondays and Fridays but independent of any infant characteristic. These periodic changes to the DW made during bedside rounds at the clinicians' discretion are practical adjustments. They facilitate medication and nutrition ordering by avoiding the need to update dosages each day due to small changes in the MW. The decrease in DW adjustments during the weekend may be secondary to decreased pharmacy coverage on the weekend or inconsistent physician coverage (neonatologists and neonatal fellows worked only one weekend of a three and four-week rotation, respectively).

On days that the DW is assigned, the DW-MW difference is inversely associated with peak creatinine and directly associated with recent fluid intake. Though we cannot determine the intent of clinicians, we suspect that clinicians may be accounting for states of fluid overload and edema associated with renal dysfunction by assigning a "dry" weight. In such edematous infants the DW-MW difference is more negative and widened. We would expect clinicians to manage renal dysfunction (i.e., increased creatinine) with fluid restriction (i.e., decreased fluid), and this is what we see. On days that DW is not updated, the DW-MW difference becomes more negative and widens as MW increases (i.e., infant growth) until the DW is updated again. This difference

Variables	Percent difference (95% Confidence Interval)*	*p*-value
Birth weight	2.1 (0.9, 3.4)	0.001
Small for gestational age	-0.007 (-1.2, 1.2)	0.990
Patent ductus arteriosus	-0.7 (-1.4, 0.1)	0.083
Necrotizing enterocolitis or spontaneous intestinal perforation	-1.0 (-1.9, 0.001)	0.050
Intubated Day 28	-1.2 (-2.0, -0.5)	0.002
Blood stream infection	-0.4 (-1.4, 0.6)	0.449
Highest creatinine in mg/dL	-4.1 (-5.2, -2.9)	< 0.001
Lowest sodium in mEq/L	0.1 (0.04, 0.2)	0.002
3DMA of daily fluid intake in 10mL/kg/day	0.4 (0.3, 0.6)	< 0.001
3DMA of daily urine output in mL/kg/hour	0.1 (-0.1, 0.3)	0.278
Maternal steroids	-0.2 (-0.9, 0.6)	0.660
NSAIDs (prophylactic or therapeutic)	-0.9 (-1.7, -0.2)	0.018
Caffeine	-0.0 (-1.0, 1.0)	0.973
Monday or Friday	0.5 (0.1, 1.0)	0.022
Weekend (Saturday or Sunday)	-0.8 (-1.5, -0.05)	0.036
Resident team (referent to nurse practitioner team)	0.2 (-0.6, 1.0)	0.666

Table 5. The bivariable associations between infant or unit characteristic and the dosing-measured weights percent difference limited to dosing weight changes. 3DMA, 3-day moving average *Mixed effects linear regression reported as beta coefficient (percent difference) and p-value

Infant characteristics	Dosing - Measured Weight% difference (95% Confidence Interval) **	*p*-value
Patent ductus arteriosus	0.7 (-0.1, 1.4)	0.080
Necrotizing enterocolitis or spontaneous intestinal perforation	-0.6 (-1.4, 0.2)	0.120
Highest creatinine in mg/dL	-3.5 (-4.6, -2.4)	< 0.001
Lowest sodium in mEq/L	0.1 (-0.01, 0.1)	0.070
3DMA of daily fluid intake in 10mL/kg/day	0.4 (0.2, 0.5)	< 0.001
Intercept**	-1.3 (-1.8, -0.9)	< 0.001

Table 6. The multivariable association between infant characteristic and the dosing-measured weights percent difference limited to dosing weight changes*. 3DMA, 3-day moving average *Mixed effects linear regression reported as beta coefficient (percent difference), 95th % confidence interval, and p-value ** Final model predicting Dosing-Measured Weights Difference = [-1.3] + [-3.5*X_1] + [0.4*X_2]) where $X_1$is the highest creatinine referent to an infant to 1 mg/dL and $X_2$is the 3DMA of fluid intake referent to 140mL/kg

similarly varies inversely with peak creatinine and directly with urine output. Infants who void appropriately will have a DW-MW difference that is more positive and narrowed as the DW more closely approximates MW.

Therefore, our analysis demonstrates that the DW falls into three broad categories: a BW prior to the infant regaining BW, a practical weight used to facilitate medication and nutrition ordering, and a "dry" weight that adjusts for infants with suspected renal dysfunction and fluid overload. This is not surprising. What is surprising is how little evidence guides the use of DW, including how frequently to update DW, how to appropriately assign a DW for critically ill infants, and whether to use a DW or MW for nutrition orders. A search on PubMed for "('dosing weight') AND (neonatal OR infant)" in August, 2024 yields thirteen publications[19]. This area requires further research, especially since the DW is used to identify fluid overload, which is associated with morbidity and mortality in critically ill infants[20]. A clinical decision support system may be able to assist clinicians in assigning a dosing wight and determining a dosing weight since they have already been used to estimate the discharge weight in preterm infants[21].

For infants without evidence of renal dysfunction, we recommend that clinicians utilize the MW rather than DW in fluid and nutrition calculations. The average DW-MW difference was −4%. Clinicians using the DW to calculate fluid and nutrition orders may deliver 4% less calories and 4% less nutrients than if they had used the MW. Though 4% seems small, cumulatively, this will contribute to the nutrient deficit that often accrues in preterm infants[22]. Early optimization of nutrition delivery is associated with improved outcomes such as improved postnatal growth measurements and higher intellectual functioning in childhood[23–25].

Another notable finding was that there was a significant rate of hyponatremia, which has been described previously in preterm infants[26]. At least three-quarters of our infants had hyponatremia with a sodium less than 135 mEq/L and around half had a sodium less than 130 mEq/L; sodium values appeared lower after the first week. Sodium delivery is justifiably kept lower in the early postnatal period to facilitate contraction of the

extracellular fluid compartment. After the infant has diuresed in the later postnatal period, these data suggest that further attention to fluid and sodium management is warranted.

As a retrospective review, this study has several limitations. First, we were unable to evaluate all the factors that influence DW assignment. We can only speculate how clinicians decided to assign DW. It is likely that DW assignment is associated with clinician experience, which may affect the objective and subjective assessments of renal injury and fluid overload[27], and nursing and parental input of edema. Additional factors not evaluated, such as the dosing and duration of medications (including caffeine, inotropes, vasopressors, diuretics or nephrotoxic antibiotics), and the use of phototherapy and humidified incubators[28], may also affect DW assignment. Further prospective studies, including direct observation of clinical rounds, are needed to more accurately determine how clinicians assess the multitude of factors and assign the DW during rounds. A second limitation is that we only evaluated DW in preterm infants. The results may not be generalizable to critically ill term infants undergoing surgery for congenital anomalies, therapeutic hypothermia for hypoxic ischemic encephalopathy or those infants receiving extracorporeal membrane oxygenation, where the increased volume of distribution can affect the pharmacokinetics of hydrophilic medications[29].

Clinicians use the DW every day in every NICU for every patient. Such a ubiquitous value requires more evidence guiding its use.

Data availability

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions

Dr. Falciglia was responsible for data acquisition and analysis. Dr. Montoya was responsible for drafting of the manuscript. All authors contributed to study concept and design, as well as critical revision of the manuscript.

Declarations

Competing interests

Dr. Gustave Falciglia has received a phase 1 small business technology transfer grant (STTR) with Medical Predictive Science Corporation (MPSC) through the National Institute of Health (NIH) to create a clinical decision support system to optimize nutrition delivery in the neonatal intensive care unit. He does not have a financial relationship with MPSC outside the grant. All remaining authors declare no conflict of interest.

Additional information

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