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Beyond Weight: Growth Faltering Across Anthropometric Measurements in Very Low Birth Weight Infants

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Abstract

Objective:

To characterize growth faltering (GF) in Very Low Birth Weight Infants (VLBW) and to identify associated clinical factors.

Study design:

Retrospective cohort of infants with birth weight ≤ 1500 g and gestational age ≤ 32 + 6 weeks. Declines of ≥ 0.8–<1.2, ≥ 1.2–<2.0, and ≥ 2.0 z-score units from birth to discharge/death or 50 weeks PMA defined mild, moderate, and severe GF, respectively. Proportional-odds logistic regression assessed associated clinical factors.

Result:

Among 110 infants, 76 (69.1%) met GF criteria using any anthropometric parameter versus 55 (50.0%) using weight alone. Multivariable analysis showed lower odds of greater GF severity with increasing gestational age (OR 0.71/week, 95% CI 0.56–0.89) and higher odds with delayed full enteral feeds (OR 1.27/10 days, 95% CI 1.06–1.52).

Conclusion:

Assessment based on weight alone identified substantially fewer infants with growth faltering. Multidimensional growth monitoring can provide a more comprehensive assessment of postnatal growth, provided measurements are accurate.

Introduction

Preterm infants, particularly very low birth weight infants (birth weight less than 1500 grams) have increased metabolic demands, and early adequate nutritional management is critical to improve outcomes (1). Advances in neonatal care have resulted in infants surviving at much younger ages than before (2), resulting in an increasing number of infants with complex nutritional needs. It is important to properly define growth faltering to identify infants who need additional support. Growth faltering has been shown to be highly prevalent in very low birth weight infants (3–5), with reported prevalence rates ranging from 41% to 64%, and associated with adverse neurodevelopmental and behavioral outcomes (6–9).

Over time, multiple definitions have been used to define growth faltering in this population. Initial studies focused on dietary intake for infants and their corresponding weight gain (10), with most defining growth faltering as a discharge percentile less than 10th (3, 11). As a discharge percentile cutoff appeared to be insufficient for analyzing the growth trajectory of infants, studies gradually shifted toward a longitudinal assessment with Z score differences from birth to discharge (4, 12, 13). To further characterize the

degree of faltering, some have proposed graded definitions to determine mild, moderate and severe thresholds (14). Overall, growth faltering definitions are heterogeneous throughout the literature (15, 16). Important concerns include the limited utility of discharge-based data for informing care during hospitalization, as well as the lack of validation of the proposed thresholds (17).

Most studies concerning growth faltering have used weight as the main variable to monitor. However, weight gain disproportionate to length may be detrimental to infants, and assessing all anthropometric measures is recommended (18, 19). Weight can be affected by fluid shifting, and is not an accurate marker of linear growth, as it does not provide any information on body composition. Length is a surrogate for linear growth, which has been shown to be linked to neurodevelopmental outcomes (20–22). A recent study (7) using a Z score decline > 0.8 in any of the three measures found that more infants were classified as growth faltering using length than using weight.

Despite increasing recognition of the value of multidimensional assessment, few studies have applied a graded definition across weight, length, and head circumference. In this study, our aim was to describe growth faltering among VLBW infants using a graded definition, incorporating weight, length and head circumference from birth to discharge or end of follow up. This approach supports a broader focus on growth monitoring beyond weight alone.

Methods

A. Study Design, setting and population.

This study was a retrospective cohort study conducted in a level III Neonatal Intensive Care Unit (NICU).

The study population included all infants with a birth weight ≤1500 grams and gestational age ≤32 + 6 weeks, born between January 1st and December 31st, 2023, who were admitted to BC Women's Hospital NICU.

Potentially eligible infants were identified via local data from the Canadian Neonatal Network registry(23), generating a list of every infant with a birth weight less than 1500 grams born in the year 2023. Individual records were then reviewed to confirm eligibility.

Infants were excluded if they had insufficient growth data, defined as lacking a minimum of two anthropometric measurements (weight, length or head circumference) at end of follow up.

During the study period, infants were managed according to the standardized unit feeding protocol. Mothers' own milk was the preferred source of enteral nutrition, with pasteurized donor human milk used when maternal milk was unavailable or insufficient. Enteral feeds were advanced according to the standardized unit protocol, with progression individualized only when clinically indicated. Human milk fortification using a liquid bovine milk based fortifier was routinely initiated once enteral feeding volume reached 80 mL/kg/day.

For infants with prolonged hospitalization who were over 44 weeks PMA, fortification was transitioned to preterm formula powder added to human milk according to the unit protocol. Infants who no longer qualified for donor human milk and whose mother's own milk was unavailable were transitioned to preterm formula.

Study data were collected and managed using REDCap (24, 25) electronic data capture tools hosted at the University of British Columbia. REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies.

B. Definitions and variables

Growth faltering (GF) was defined using the decline in z score between birth and the end of follow-up for weight, length, and head circumference. For infants who died before discharge (n = 10), the measurements obtained closest to the time of death were used. For infants who remained hospitalized beyond 50 weeks PMA (n = 9), measurements at 50 weeks PMA were used, corresponding to the upper limit of the Fenton growth charts. For all other infants, measurements at discharge were used.

A graded definition was used, defining no growth faltering as a Z score decline < 0.8, mild growth faltering as a Z score decline of ≥ 0.8 to < 1.2, moderate if it was ≥ 1.2 to < 2, and severe if it was ≥ 2, using the work of Goldberg et al as reference (14) for this classification.

We collected all available data from each infant’s admission on weight, length and head circumference, for each week of admission. Z scores were calculated using Fenton 2013(26) growth charts. We also collected demographic data such as Sex, Gestational Age (GA) at birth, Birth weight (BW). We defined small for gestational age as a weight percentile < 10 at birth, and large for gestational age as a weight percentile > 90 at birth.

Fetal growth restriction was defined as Pc < 3 at birth, diagnosis documented prenatally by the Obstetrics team, or Doppler studies indicating absent end diastolic flow or reverse end diastolic flow.

Other variables analyzed were total days NPO (Nil Per Os) and day of life when full enteral feeds were achieved (defined as the time when an infant is tolerating 150 ml/kg/day enterally).

For associated factors with growth faltering, we collected data on central line days, culture positive infections, neonatal cholestasis (direct bilirubin higher than 34 umol/ L), metabolic bone disease (alkaline phosphatase results higher than 600 U/L), use of steroids during admission (early before 7 days of life, late after 7 days of life), Necrotizing Enterocolitis (NEC) diagnosis (diagnosis of Stage 2 or greater included in discharge summary), requirement of surgery for NEC, Grade 3 or 4 intraventricular hemorrhage, presence of periventricular leukomalacia, Patent Ductus Arteriosus with medical or surgical treatment, presence of genetic syndromes, major congenital heart disease, other congenital anomalies, presence of Chronic Lung Disease (requirement of respiratory support at 36 weeks corrected gestational age), presence of Retinopathy of Prematurity Stage 1 or greater, death before discharge.

C. Statistical analysis

Continuous variables were summarized using medians and interquartile ranges, and categorical variables using frequencies and percentages. Changes in anthropometric Z scores were classified as normal, mild, moderate, or severe growth faltering according to the prespecified thresholds.

Separate univariable proportional-odds logistic regression models were performed to evaluate the association between each clinical factor and growth-faltering severity.

Two multivariable proportional-odds logistic regression models were fitted for the composite growth-faltering outcome. Model 1 included baseline characteristics: sex, gestational age at birth, and birth-weight z score. Model 2 additionally included clinical course variables: days to full enteral feeds, necrotizing enterocolitis, and length of hospital stay. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs), with ORs greater than 1 indicating higher odds of being in a more severe growth-faltering category. Analyses were performed using complete cases for the variables included in each model.

A prespecified sensitivity analysis classified growth-faltering severity using weight z-score change alone.

D. Sample size

The sample size was determined by the number of eligible infants admitted during the prespecified study period. All infants meeting the inclusion criteria between January 1 and December 31, 2023, were included; therefore, no formal a priori sample-size calculation was performed. The final cohort comprised 110 infants.

Results

A. Patient demographics and characteristics

A total of 129 infants were initially identified for this study using our local site Canadian Neonatal Network database. Following individual chart review, 19 infants were excluded: 2 had a birth weight greater than 1500 grams, 9 patients did not have enough growth data (a minimum of two parameters at birth and discharge/death or 50 weeks PMA), and 8 patients were over 33 + 0 weeks GA at birth.

The final cohort included 110 infants, 10 of whom died before discharge. Baseline characteristics of the cohort are summarized in Table 1.

Table 1
Population characteristics

Characteristics	N = 110
Sex	
Female	58 (52.7%)
Male	52 (47.3%)
Birth Weight	
< 749 gr	20 (18.2%)
750–999 gr	30 (27.3%)
1000–1249 gr	34 (30.9%)
1250–1500 gr	26 (23.6%)
GA	
< 25 + 6 weeks	28 (25.5%)
26–28 + 6 weeks	41 (37.3%)
29–32 + 6 weeks	41 (37.3%)
Size for GA	
AGA	90 (81.8%)
SGA	15 (13.6%)
LGA	5 (4.6%)
FGR	
Yes	31 (28.2%)
No	79 (71.8%)
Death before discharge	
Yes	10 (9.1%)
No	100 (90.9%)

Values are presented as n (%). AGA: appropriate for gestational age; SGA: small for gestational age; LGA: large for gestational age; FGR: fetal growth restriction.

The median length of stay among surviving infants (n = 100) was 74 days (IQR 37–114), compared with 23 days (IQR 11–33) among infants who died before discharge (n = 10). Excluding infants who died

before discharge did not meaningfully alter the prevalence of growth faltering, which remained approximately 70% among surviving infants (69% versus 71%).

Anthropometric data were collected from each infant at birth, discharge/death and for every week they were admitted. Z scores were calculated using Fenton 2013 (26) charts. Figure 1 shows the weight Z score trajectory for each infant in the cohort throughout their admission.

Most infants (70%) received maternal breast milk as their primary feed, with 30% receiving mostly donor breast milk, and all infants received cow milk based fortifiers as per our unit protocol

B. Prevalence of growth faltering

Using our predefined growth faltering definition, 76 of 110 infants (69.1%) met criteria in at least one anthropometric parameter. Of these, 21 infants (19.1%) met criteria for mild growth faltering, 38 (34.5%) for moderate growth faltering, and 17 (15.5%) for severe growth faltering.

The prevalence and severity of growth faltering varied according to the anthropometric parameter assessed (Fig. 2). Using weight alone, 55 of 110 infants (50.0%) were classified as having growth faltering, compared with 76 of 110 (69.1%) when any anthropometric parameter was considered. Among the 63 infants with complete data for all three anthropometric measures, 52 (82.5%) were classified as having growth faltering using multidimensional assessment, compared with 33 (52.4%) using weight alone.

Growth faltering was observed across all gestational age groups. The prevalence of growth faltering using any parameter was 71.4% among infants born at ≤ 25 + 6 weeks, 73.2% among those born between 26 and 28 + 6 weeks, and 63.4% among infants born between 29 and 32 + 6 weeks. Moderate and severe growth faltering were more common among infants born at lower gestational ages, affecting 60.7%, 56.1%, and 36.6% of infants in each respective gestational age category.

Similarly, growth faltering was common across different birth weights. The highest prevalence was observed among infants weighing 750–999 g at birth (80%), while prevalence ranged from 61.5% to 67.7% in the remaining birth weight categories. Moderate or severe growth faltering occurred in 63.3% of infants weighing 750–999 g and 50–53% of infants in the other birth weight categories.

Growth faltering affected 65.5% of female infants and 73.1% of male infants. Moderate and severe growth faltering were more common among males (63.5%) than females (37.9%).

Among infants with fetal growth restriction, the prevalence of growth faltering was 61%.

C. Factors associated with growth faltering

In univariable proportional-odds models, retinopathy of prematurity, necrotizing enterocolitis, cholestasis, and metabolic bone disease were associated with greater growth-faltering severity

(Table 2). The confidence interval included 1 for bronchopulmonary dysplasia, culture-positive sepsis, steroid exposure, and grade 3 or 4 intraventricular hemorrhage.

Table 2
Univariable associations between clinical factors and growth faltering severity

Exposure	N analyzed	Present n (%)	OR (95% CI)
DOL to regain birth weight	110	n/a	1.017 (0.950 to 1.091)
Total days NPO	110	n/a	1.021 (0.999 to 1.045
DOL to full enteral feeds	110	n/a	1.025 (1.010 to 1.042)
Days of parenteral nutrition	110	n/a	1.010 (1.002 to 1.019)
Retinopathy of prematurity	95	36 (37.9%)	3.463 (1.564 to 7.932)
Bronchopulmonary dysplasia	101	56 (55.4%)	1.669 (0.819 to 3.437)
Culture positive sepsis	107	44 (41.1%)	1.099 (0.544 to 2.224)
Cholestasis	102	24 (23.5%)	2.839 (1.194 to 6.966)
Metabolic bone disease	102	36 (35.3%)	2.541 (1.182 to 5.588)
Use of steroids	106	33 (31.1%)	1.271 (0.595 to 2.729)
NEC	108	17 (15.7%)	3.107 (1.161 to 8.596)
Grade 3 or 4 IVH	109	12 (11%)	0.957 (0.334 to 2.723)

Each exposure was evaluated in a separate proportional-odds logistic regression model. ORs greater than 1 indicate higher odds of worse growth faltering. For binary exposures, absence of the condition ("NO") was the reference category. Continuous estimates as per one day increase. Percentages were calculated among infants included in the corresponding model. CI, confidence interval; OR, odds ratio; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; NPO, nil per os; DOL, days of life; n/a, not applicable.

Infants classified as having severe growth faltering received parenteral nutrition for a median of 43 days (IQR 31–72), compared with 12 days (IQR 6–23) among infants in the normal-growth category. Each additional 10 days of parenteral nutrition was associated with 10% higher odds of being in a more severe growth category (OR 1.10, 95% CI 1.02–1.21). Each additional 5 days in achieving full enteral feeds was

associated with 13% higher odds of being in a more severe category (OR 1.13, 95% CI 1.05–1.23). There was no clear evidence of association with total NPO duration (OR per 5 days 1.11, 95% CI 0.995–1.25).

In the baseline multivariable model, each additional week of gestational age at birth was associated with lower odds of being in a more severe growth-faltering category (OR 0.83, 95% CI 0.70–0.98); while sex and birth weight Z-score were not significant. In the model additionally adjusted for NEC, length of stay, and time to full enteral feeds, the association with gestational age was more pronounced (OR per week 0.71, 95% CI 0.56–0.89).

Time to full enteral feeds remained associated with growth-faltering severity (OR per day 1.024, 95% CI 1.006–1.043), equivalent to an OR of 1.27 (95% CI 1.06–1.52) per 10-day delay. There was no clear evidence of association for NEC (OR 0.99, 95% CI 0.26–3.68) or length of stay (OR per day 0.997, 95% CI 0.989–1.004); the wide confidence interval for NEC indicates substantial imprecision.

In the sensitivity analysis using weight z-score change alone, the association with delayed achievement of full enteral feeds was attenuated and its 95% CI included 1 (OR per day 1.012, 95% CI 0.996–1.028). The gestational-age estimate was also closer to the null and imprecise (OR per week 0.923, 95% CI 0.736–1.155). The association between gestational age at birth and growth severity observed for the composite outcome was not observed in the weight-specific analysis.

D. Linear growth data quality

There were variations in the accuracy and completeness of anthropometric data throughout the infants' admissions. Weight measurements were available for all infants and were consistently documented. Head circumference was also frequently measured, although not as much as weight (72% of infants had birth and discharge data).

Length data was particularly limited, with only 5 infants having complete weekly length measurements from birth to discharge. Additionally, birth and discharge length data was available for only 66 out of the 110 infants (60%).

To assess the quality of length measurement data, we analyzed anthropometric longitudinal trajectories to assess for implausible patterns. Length measurements were classified as implausible if an infant demonstrated a decrease in measured length over time (shrinking), or if the change in Z score for length between two consecutive weekly measurements was larger than 1. Using these criteria, 48% of infants demonstrated at least one implausible longitudinal length measurement.

Discussion

Applying a longitudinal growth faltering definition across all anthropometric measurements, 69.1% of infants were classified as having growth faltering, compared with 50% using weight alone. The difference was especially marked for severe growth faltering (a decline larger than 2 points in Z score): 15.5% using

any parameter versus 5.5% using weight. These findings emphasize the importance of incorporating length measurements and head circumference as part of a multidimensional growth assessment in premature infants. This difference persisted in the sensitivity analysis restricted to infants with complete data for all three anthropometric measurements, suggesting that the finding was not explained by differential availability of length and head-circumference.

Lower gestational age and delayed achievement of full enteral feeds were associated with greater severity. Each 10- day delay of achieving full feeds was associated with 27% higher odds of greater severity. Delayed feeds may contribute to cumulative nutritional deficits, but they may also reflect feeding intolerance, NEC, or illness severity. Time to reach full feeds was correlated with parenteral nutrition duration, which was also associated with growth faltering in our univariable analysis. Similar associations between delayed enteral feeding, prolonged parenteral nutrition, and postnatal growth faltering have been reported by Radmacher et al.(27), Lee et al.(28), and Sun et al(29). After sensitivity analysis, the trend was generally consistent in direction for delayed achievement of full enteral feeds, although associations were attenuated when growth faltering was defined using weight z-score change alone. On weight-specific analysis, the association between gestational age at birth and growth severity was not observed.

Retinopathy of prematurity, NEC, neonatal cholestasis, and metabolic bone disease were associated with more severe growth faltering. This may reflect a shared pathway involving illness burden, inflammation, and longer time on parenteral nutrition. For retinopathy of prematurity in particular, the relationship between nutrition and Insulin-like growth factor binding protein 3 has been described in the literature. This growth factor was lower in infants with ROP(30, 31), which can potentially relate to the association between growth faltering and ROP found in this study.

More infants were classified as growth faltering using any anthropometric parameter despite these measurements not being complete for all infants. All infants have birth and discharge/ 50 weeks PMA weight available, but data for both points was available in 60% for length, and 72% for head circumference. Another large cohort(11) had similar results with weight available for 98% of infants, length for 70% and head circumference for 85%. Given the retrospective nature of our study, we cannot estimate accuracy, however when considering implausible changes from one week to another in length, we found that 48% of infants demonstrated at least one implausible longitudinal length measurement. Measurement error has both the potential of overclassifying infants as growth faltering, as well as missing infants who can potentially benefit from nutritional interventions. These findings underline the importance of applying standardized protocols for accurate length measurement, providing periodic training for staff, and incorporating practice changes that support timely, complete and accurate growth measurements.

This study has several strengths. We included all eligible very-low-birth-weight infants admitted to a single tertiary neonatal intensive care unit during a prespecified calendar year. Serial weight, length, and head-circumference data allowed us to assess growth longitudinally and apply a graded definition that

retained information on the severity of growth faltering. Direct comparison with a weight-only definition demonstrated the additional infants classified as growth faltering through multidimensional assessment. The proportional-odds models also preserved the ordered nature of the outcome, while the weight-only sensitivity analysis assessed whether the observed associations depended on the growth definition used. Finally, including infants who died before discharge and explicitly evaluating the completeness and plausibility of anthropometric measurements increased the transparency of the analysis.

Limitations of this study include its retrospective, single-centre design and modest sample size which limit causal inference and generalizability. Sparse events produced wide confidence intervals for some clinical factors. Missing, and potentially inaccurate length and head circumference data may have introduced misclassification, particularly as the composite outcome was based on the most severe change observed. Additionally, the definition used is an expert recommendation and has not been fully validated to determine the clinical significance of Z score changes. Another limitation is based on the use of birth weight and not weight after the initial weight loss, which is the recommended parameter(19) as this was unavailable for many infants in our cohort; this may have overestimated early growth decline. Similarly, using discharge or 50 weeks PMA parameters as our end point may not be representative of these infants' subsequent growth trajectories, and may be influenced by the timing and length of hospitalization. Finally, we lacked body-composition, nutrient intake information, and long term neurodevelopmental data to determine the clinical significance of the identified growth patterns.

Future prospective studies should focus on clinical validation of the different definitions against neurodevelopment, body composition, and growth later in infancy. Future cohorts should also include sufficient numbers of extremely low-birth-weight infants, particularly those weighing less than 500 g, to evaluate whether current definitions are appropriate for this population. Ultimately, developing thresholds that can inform intervention during hospitalization, providing a comprehensive growth assessment can be helpful for clinicians treating very low birth weight infants

Declarations

Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval and consent statement

This study was approved by The University of British Columbia / Children's and Women's Health Centre of British Columbia Research Ethics Board (UBC C&W REB), #H24-02915. Owing to the retrospective nature of the study and the use of previously collected clinical data, the requirement for consent was waived for this study.

Data availability

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

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Author contributions

JC contributed to conceptualization and study design. JC, RE, SA and YS contributed to methodology. JC performed data collection and data curation. YS performed the formal statistical analysis. JC, SA, RE and YS contributed to interpretation of the results. JC prepared the original draft of the manuscript. SA, RE and YS contributed to critical review and editing of the manuscript. SA and RE provided supervision. All authors read and approved the final manuscript.

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Figures

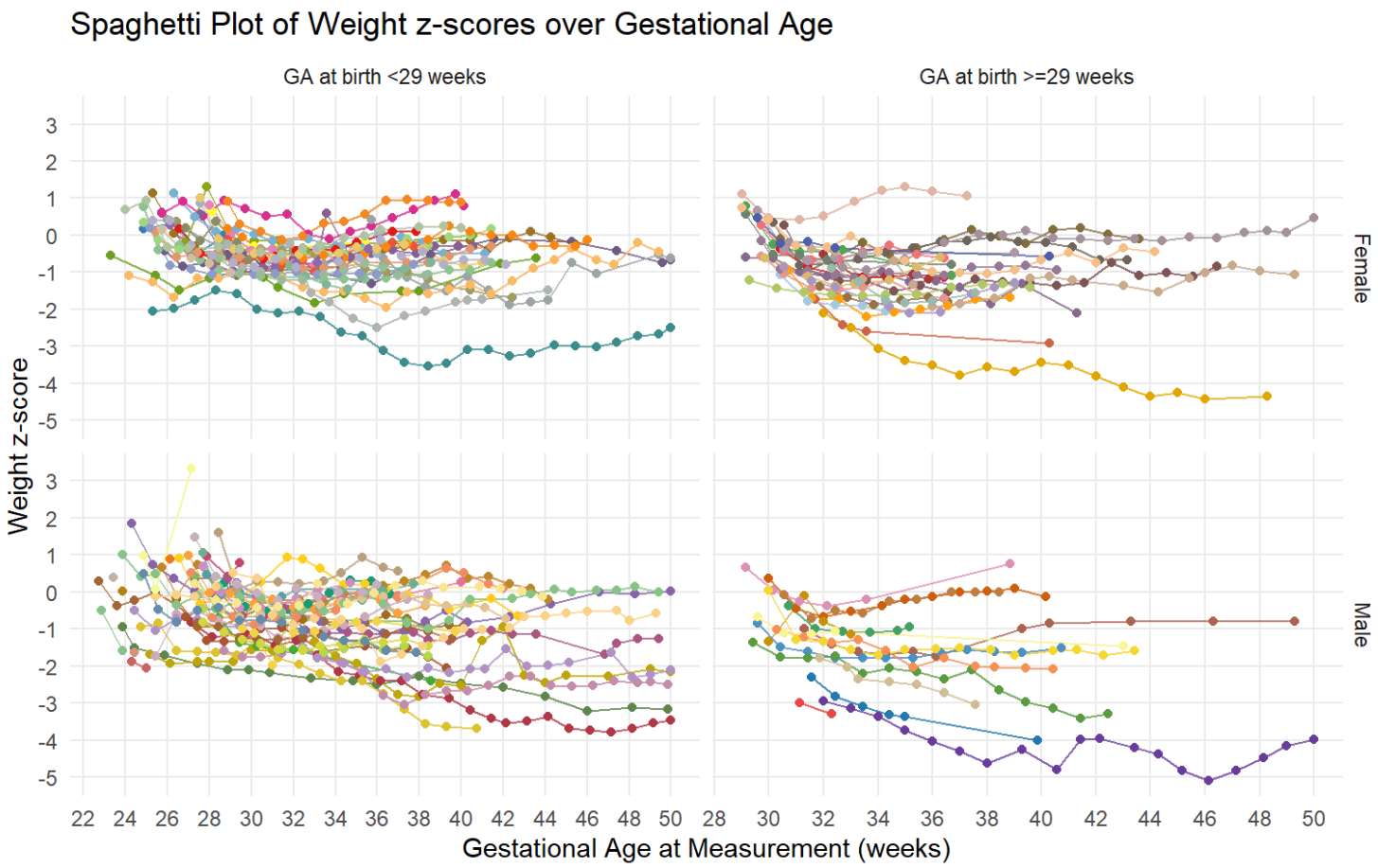


Figure 1

Spaghetti Plot of Weight Z- scores over Gestational Age

This graph represents the growth trajectories of infants in this cohort. Each line is a unique infant, and each point corresponds to weight Z score for each week the infant was admitted, using Fenton 2013 growth charts.

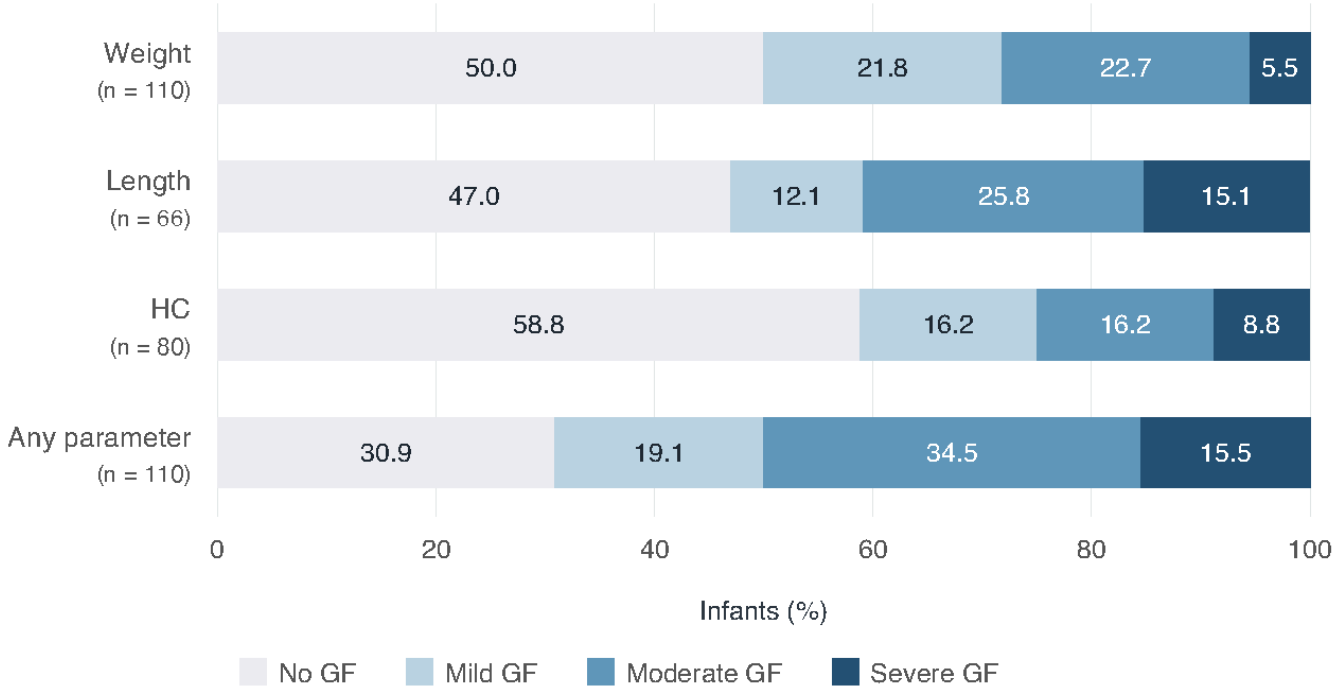


Figure 2

Distribution of growth faltering according to anthropometric parameter

Proportions of infants with no, mild, moderate, or severe growth faltering (GF) according to weight, length, head circumference (HC), or any anthropometric parameter. The denominator for each anthropometric parameter reflects infants with measurements available at birth and the end of follow-up.