Nutritional Outcomes in Bronchopulmonary Dysplasia: Identifying High-Risk Phenotypes Beyond Disease Severity

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Disclosure Statement

Speaker: Matthew Marcelino

Matthew Marcelino has documented that he has nothing to disclose

Learning Objectives

1. Describe longitudinal growth patterns in infants with bronchopulmonary dysplasia and their relationship to disease severity

2. Describe emerging evidence of unique growth phenotypes among patients with BPD

Introduction

Bronchopulmonary dysplasia (BPD) is the most common long-term complication of prematurity, affecting **40–50% of infants born <28 weeks GA** who survive to 36 weeks PMA.

BPD reflects **arrested lung and vascular development** driven by ventilation, oxygen exposure, inflammation, and extreme immaturity.

Its impact extends beyond the lungs: infants with BPD face **prolonged hospitalization, rehospitalization, pulmonary hypertension, neurodevelopmental impairment**, and **growth failure**

Introduction

Growth failure is especially pronounced in severe BPD and reflects high metabolic demand from increased work of breathing and chronic inflammation. This occurs during a *critical window for lung and brain development.*

Despite similar caloric intake, i**nfants with BPD show disproportionate growth patterns**, suggesting **disease burden—not nutrition alone—drives outcomes.**

Hypothesis

We aimed to determine, in patients with ***established BPD***, whether **growth velocity after 36 weeks post-menstrual age differs by BPD severity**, and whether distinct growth phenotypes exist *beyond* standard diagnostic labels

Methods

Study Type: Retrospective, electronic medical record chart review

Inclusion criteria:

1. Diagnosis of BPD at 36 weeks PMA using 2019 NRN (Jensen) Criteria
2. Weight measurements available for at least 4 weeks **after 36 weeks post-menstrual age** (to establish a trend)

Exclusion criteria:

1. Cardiac (other than PDA), genetic or syndromic abnormalities that can influence growth and lung development

Methods

197 infants with a diagnosis of BPD at CHLA NICU in the years 2022-2025. Of these, 149 patients met the study inclusion/exclusion criteria

The full data set of **197 patients had 24,314 weight measurements**. The **149 infants included in our study had 9,670 weight measurements.**

Multiple weights within a week were averaged to give *1,167 observations (one average weight per week) that were included in the final analysis*

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Analysis plan

Longitudinal growth trajectories of weight Z-scores were evaluated using linear mixed-effects models (LMM) to account for the hierarchical structure of the data

LMM was selected as the primary analytical tool because it provides within-subject correlation, effectively handles unbalanced data/missing observations, and is common in neonatal research.

Analysis plan

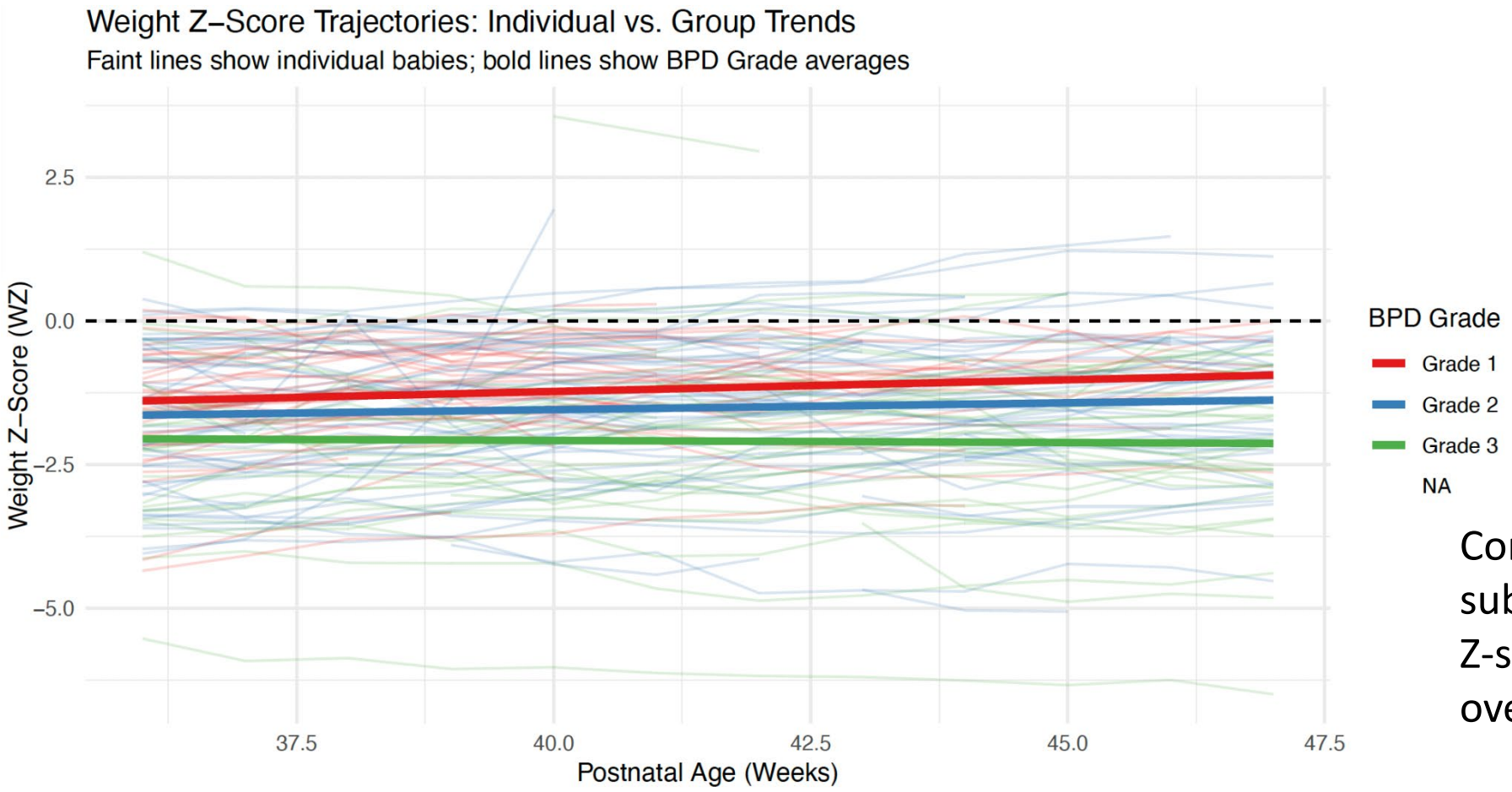
Standards for Z scores were derived from the recently published systematic review by Fenton et al (*Paediatr Perinat Epidemiol, 2025)*

All statistical analyses were performed in R (version 4.5.2) using the lme4 and lmerTest packages, with p-values for fixed effects derived via Satterthwaite's approximation for degrees of freedom.

Results

Patient Baseline Characteristics	
Characteristic	N = 149[1]
Birth gestational age (weeks)	26.19 (3.20)
Birth weight (grams)	850.15 (308.70)
Sex	
Female	58 (39%)
Male	91 (61%)
Deceased	16 (11%)
Length of stay (days)	130.21 (88.46)
BPD Grade	
Grade 1	39 (26%)
Grade 2	64 (43%)
Grade 3	45 (30%)
Unique Weeks Recorded (36-48)[2]	8 (4,12)
[1]Mean (SD); [2]Weeks recorded: Median (range); n (%)	

Results



Considerable within-subject heterogeneity in Z-scores was observed over time

Adjusted Linear Mixed Model of Weight Z-score Trajectories (adjusted for sex and birth weight)

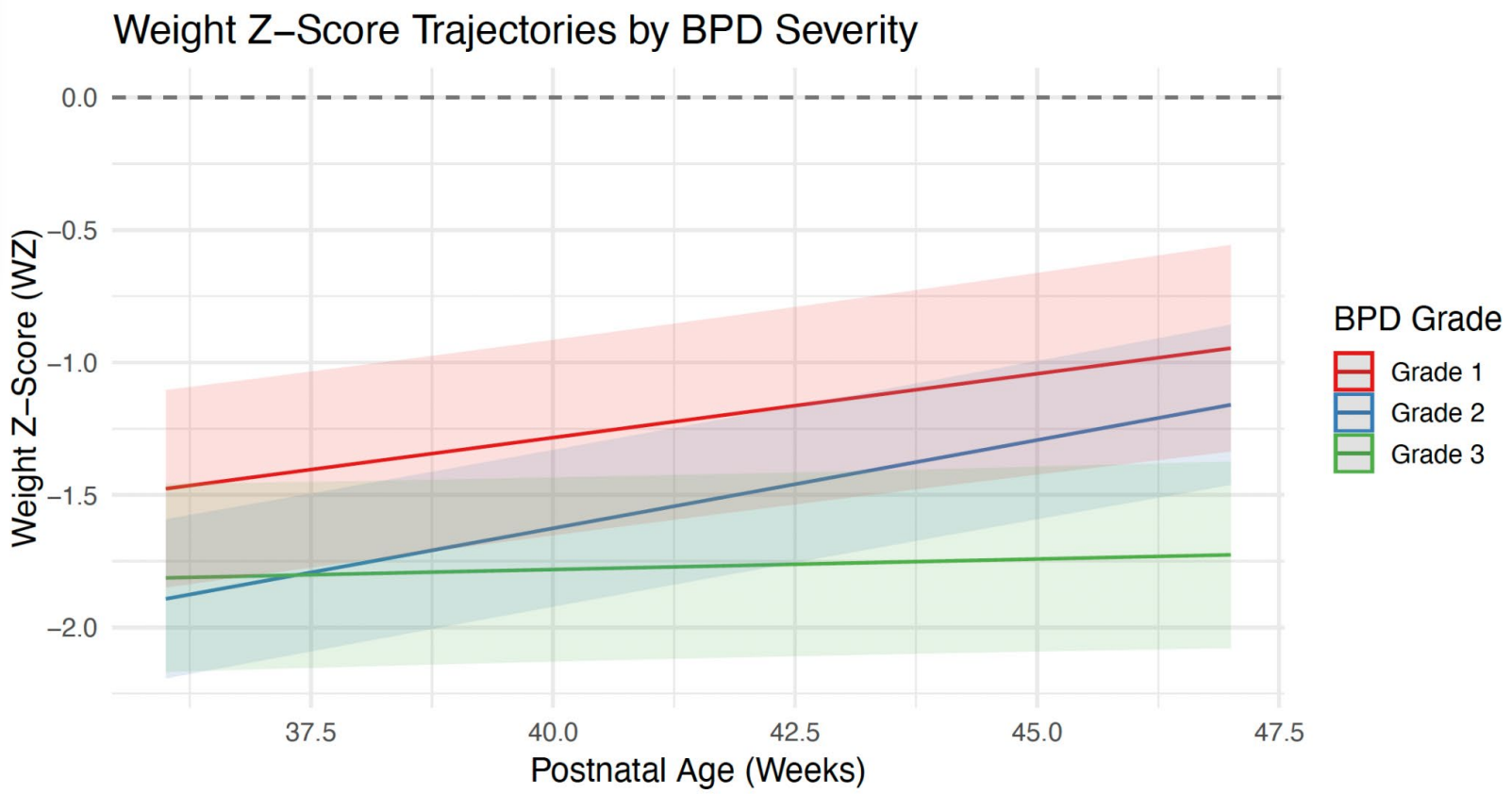
Characteristic	Beta	95% CI	p-value
(Intercept)	-4.3	-5.2, -3.3	<0.001
Postnatal Time (Weeks)	0.05	0.03, 0.06	<0.001
BPD Severity Grade (Weight Z score at 36 weeks PMA)			
Grade 1	—	—	
Grade 2	-1.0	-1.9, -0.12	0.027
Grade 3	1.3	0.37, 2.3	0.007
Sex			
Female	—	—	
Male	-0.28	-0.70, 0.14	0.2
Birth Weight (grams)	0.00	0.00, 0.00	<0.001
Postnatal Time (Weeks) * BPD Severity Grade			
Postnatal Time (Weeks) * Grade 2	0.02	0.00, 0.04	0.067
Postnatal Time (Weeks) * Grade 3	-0.04	-0.06, -0.02	<0.001

Abbreviation: CI = Confidence Interval

Results

The most critical finding was a highly significant interaction between **postnatal time (after 36 weeks PMA) and Grade 3 BPD severity (β=−0.04,p<0.001).**

This negative interaction indicates that while Grade 1 and Grade 2 infants exhibited positive growth trajectories, infants with Grade 3 BPD experienced relative growth stagnation.



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Discussion

These findings suggest that infants with the **highest severity of BPD (Grade 3) suffer from a profound growth velocity deficit that is independent of their initial birth weight or sex.**

Despite an initial WZ advantage at the start of the study period, the nearly flat trajectory of **Grade 3 infants leads to a progressive decline in weight status relative to their peers with less severe disease.**

Discussion

To evaluate whether growth patterns extend beyond BPD severity labels, we performed **Latent Class Growth Analysis (LCGA)**.

Given sample size limitations, these results are **preliminary and hypothesis-generating**.

A **two-class model** was selected based on **Bayesian Information Criterion (BIC)** and clinical interpretability.

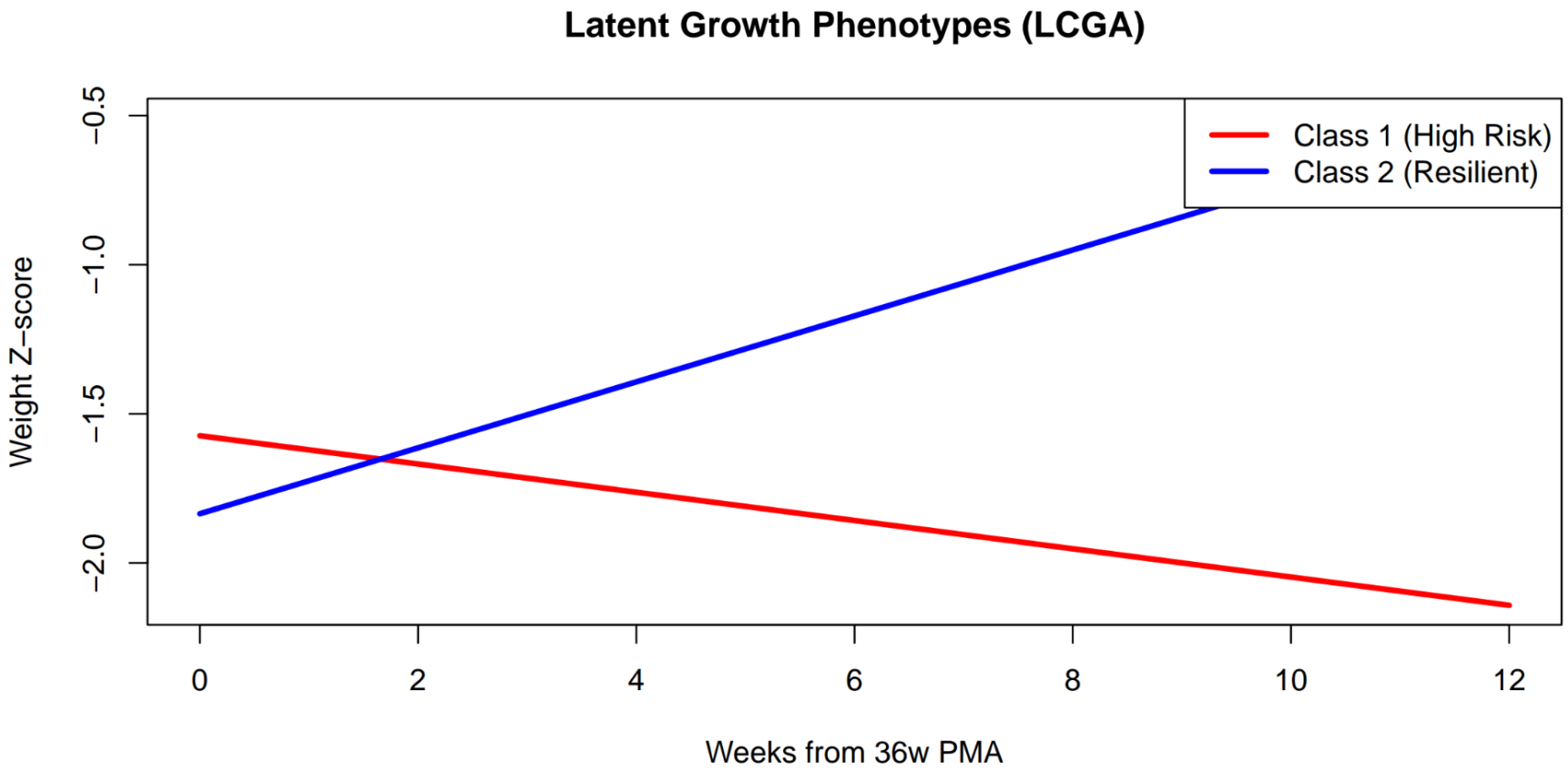
Class 1: "High-Risk" Growth Phenotype, *n = 62,* Included **58% of infants with Grade 3 BPD**

Class 2: "Resilient" Growth Phenotype, *n = 86,* Included **72% of infants with Grade 1 BPD**

Results

Class 1: "High-Risk" Growth Phenotype, *n* = *62,* Included **58% of infants with Grade 3 BPD**

Class 2: "Resilient" Growth Phenotype, *n* = *86,* Included **72% of infants with Grade 1 BPD**



Notably, **<u>42% of infants</u> with Grade 3 BPD** followed the **<u>resilient growth trajectory</u>**, demonstrating growth velocities comparable to infants with milder disease

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Limitations

The study's **observational, retrospective design** limits causal inference between BPD severity and growth velocity.

While models adjusted for **birth weight and sex**, key clinical contributors to growth—including **postnatal steroid exposure, nutritional composition, and comorbidities** (e.g., NEC, PDA)—were not included.

Data reflect a **single-center NICU experience**, which may limit generalizability to units with different respiratory or nutritional practices.

Future Steps

We plan to:

1. Extend analyses to length, head circumference, and BMI Z-score trajectories

2. Evaluate the impact of race/ethnicity and human milk exposure on growth phenotypes

3. Use trajectory-based risk stratification to inform targeted nutritional interventions

Summary

BPD Grade 3 is a major risk factor for growth failure

However, growth trajectories are heterogeneous:

- 42% of Grade 3 infants demonstrate resilient growth
- Some Grade 1 infants exhibit poor growth

Takeaway: Growth phenotype—not BPD diagnosis alone—may better identify infants who need early, targeted nutritional support.

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Appendix – Statistical analyses

The **Bayesian Information Criterion (BIC)** is a statistical measure used for model selection that balances model fit (goodness of fit) with model complexity. It penalizes the inclusion of additional parameters to reduce overfitting, with lower BIC values indicating a more parsimonious model that better explains the data. In the context of latent class growth analysis, BIC is commonly used to compare models with differing numbers of classes and to guide selection of the optimal model.

Appendix – Statistical analyses

Linear mixed-effects models (LMMs) are regression models designed for longitudinal and hierarchical data that include both **fixed effects**, which estimate population-level associations, and **random effects**, which account for subject-specific variability and correlation among repeated observations within individuals. By incorporating random intercepts, LMMs allow each subject to have a unique baseline value while estimating overall growth trajectories across the cohort. This approach is particularly well suited for neonatal longitudinal data, as it accommodates **unequal numbers of observations, irregular measurement intervals, and missing data** without requiring exclusion of subjects with incomplete follow-up.

Appendix – Statistical analyses

Latent Class Growth Analysis (LCGA) is a person-centered, longitudinal modeling approach used to identify unobserved (latent) subgroups within a population that share similar developmental or growth trajectories over time. LCGA assumes that within each latent class, individuals follow a common trajectory defined by fixed growth parameters, with **within-class variability constrained to zero**, allowing the model to focus on between-class differences in trajectory shape. This method is particularly useful for uncovering heterogeneity in longitudinal data and for identifying distinct growth phenotypes that may not be captured by traditional diagnostic or severity-based classifications.