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

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Background: Bronchopulmonary dysplasia (BPD) is the most common long-term complication of extreme prematurity, affecting 40–50% of infants born before 28 weeks' gestation who survive to 36 weeks post-menstrual age (PMA). Although traditionally conceptualized as a pulmonary disease, BPD has systemic consequences, including prolonged hospitalization, pulmonary hypertension, neurodevelopmental impairment, and growth failure. Growth impairment is most pronounced in severe BPD and is thought to reflect high metabolic demand driven by increased work of breathing and chronic inflammation during a critical window of lung and brain development. Despite similar prescribed caloric intake, infants with BPD demonstrate heterogeneous growth patterns, suggesting that disease burden rather than nutrition alone influences post-NICU growth outcomes.

Objectives: We aimed to determine whether post–36-week PMA growth velocity differs by BPD severity and whether distinct growth phenotypes exist beyond traditional BPD severity classifications.

Methods: We conducted a retrospective electronic medical record review of infants with BPD cared for in the Children's Hospital Los Angeles NICU between 2022 and 2025. Inclusion criteria required a diagnosis of BPD at 36 weeks PMA using the 2019 NICHD Neonatal Research Network (Jensen) criteria and availability of weight data for at least four weeks after 36 weeks PMA. Infants with major cardiac, genetic, or syndromic conditions known to affect growth were excluded. Longitudinal weight trajectories were analyzed using linear mixed-effects models (LMMs) to account for within-subject correlation and unbalanced data. Weight was expressed as Z-scores derived from Fenton's third-generation preterm growth charts. Models were adjusted for birth weight and sex. Latent class growth analysis (LCGA) was performed as a hypothesis-generating approach to identify distinct growth phenotypes.

Results: Of 197 infants with BPD identified, 149 met inclusion criteria, contributing 9,670 weight measurements, aggregated into 1,167 weekly observations. LMM analysis demonstrated a significant interaction between postnatal time and Grade 3 BPD severity ($\beta = -0.04$, $p < 0.001$), indicating relative growth stagnation among infants with severe disease, while infants with Grade 1 and Grade 2 BPD exhibited positive growth trajectories. Despite an initial weight Z-score advantage at 36 weeks PMA, infants with Grade 3 BPD experienced a progressive decline in relative weight status over time. LCGA identified two growth phenotypes: a high-risk phenotype and a resilient phenotype. Notably, 42% of infants with Grade 3 BPD followed the resilient growth trajectory, while a subset of infants with mild BPD demonstrated poor growth.

Conclusions: Severe BPD is strongly associated with impaired growth velocity; however, growth trajectories among infants with BPD are heterogeneous. Growth phenotype, rather than BPD severity alone, may better identify infants at risk for post-NICU growth failure and may inform earlier, individualized nutritional interventions.

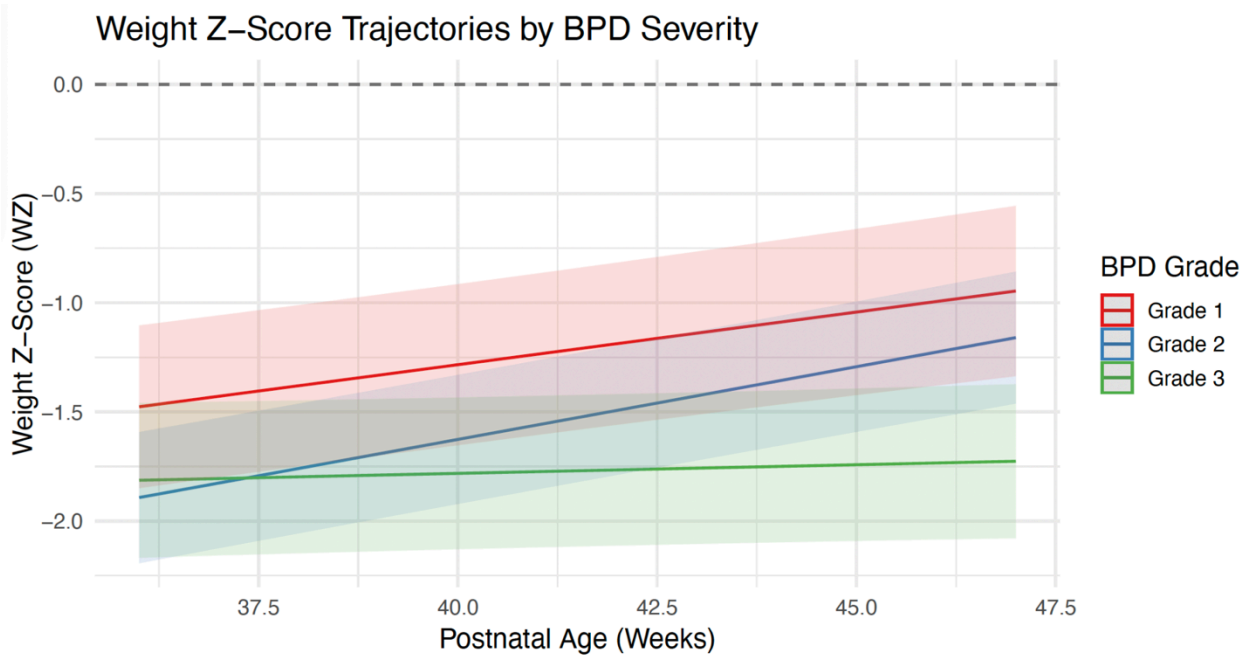

Figure 1. Adjusted linear mixed-effects model–derived trajectories demonstrate divergent postnatal growth patterns by BPD severity grade. Infants with Grade 1 and Grade 2 BPD show progressive improvements in weight Z-scores over time, whereas infants with Grade 3 BPD exhibit relative growth stagnation with a nearly flat trajectory. Shaded bands represent 95% confidence intervals. Models are adjusted for birth weight and sex, indicating that observed differences in growth velocity reflect ongoing disease burden rather than baseline size alone.

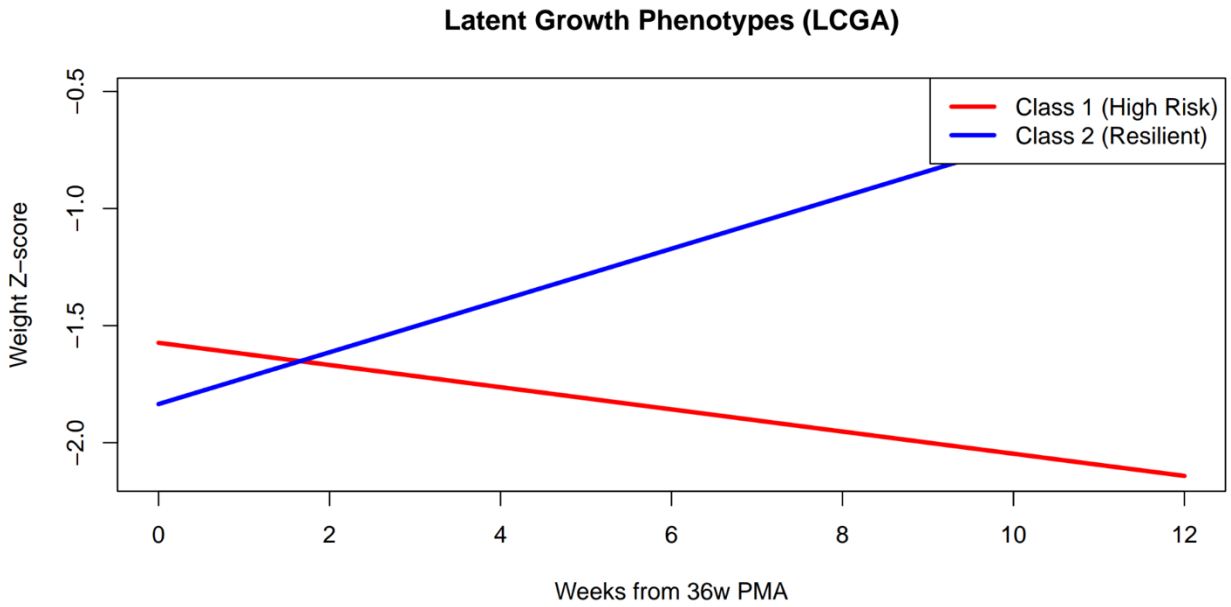

Figure 2. Latent class growth analysis identifying distinct post–36-week weight growth phenotypes in infants with bronchopulmonary dysplasia.

Latent class growth analysis (LCGA) revealed two distinct longitudinal weight Z-score trajectories following 36 weeks post-menstrual age. The high-risk phenotype (Class 1, red) demonstrates progressive decline in weight Z-scores over time, indicating worsening relative growth, whereas the resilient phenotype (Class 2, blue) exhibits sustained improvement in weight Z-scores, reflecting preserved growth velocity. These findings highlight clinically meaningful heterogeneity in post-NICU growth patterns that is not fully captured by traditional BPD severity classifications.

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