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# Catch-Up Growth in Extremely Low Birth Weight Infants at a Tertiary Hospital in South Africa: A Retrospective Cohort Study

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**Research Article**

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# Catch-Up Growth in Extremely Low Birth Weight Infants at a Tertiary Hospital in South Africa: A Retrospective Cohort Study

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## Abstract

### *Background*

Data on catch-up growth of extremely low birth weight infants (ELBWI) in low- and middle-income countries (LMICs) are scarce. Multiple factors affect growth in this vulnerable population, and catch-up growth has important implications for neurodevelopmental outcome.

### *Methods*

This was a retrospective descriptive study of surviving ELBWI seen at the neonatal follow-up clinic of Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), a tertiary referral centre in Gauteng, South Africa. Infants with birth weight <1000 g born between 1 January 2015 and 31 December 2020 were included. Growth data (weight, length, and head circumference) were plotted against World Health Organization (WHO) reference charts at corrected ages up to 24 months. Catch-up growth was defined as attaining a standard deviation (SD) score >−2 SD of the WHO reference population. Neurodevelopmental assessment used the Bayley Scales of Infant and Toddler Development III (BSID-III) at 9–12 and 18–24 months corrected age. Logistic regression identified risk factors for failure to achieve catch-up growth by 18 months.

### *Results*

Ninety-seven ELBWI were included (mean gestational age 27.5 weeks; mean birth weight 877 g; 65% female). At 18 months corrected age, catch-up growth (>−2 SD) was achieved by 90% of females and 76% of males for weight, 79% and 67% for length, and 92% and 88% for head circumference. Sepsis was significantly associated with failure to achieve catch-up growth for length (OR 5.47, 95% CI: 1.54–26.34; p = 0.016) and showed a trend towards significance for weight (OR 4.64, 95% CI: 1.12–31.71; p = 0.059). At 9–12 months, infants with normal BSID-III scores were significantly heavier (mean difference 919 g, 95% CI: 297–1541) and taller (mean difference 2.3 cm, 95% CI: 0.4–4.3) than those with abnormal scores.

### *Conclusions*

The majority of ELBWI at this South African tertiary centre achieved catch-up growth above −2 SD for weight, length, and head circumference by 18 months corrected age, with overall good neurodevelopmental outcomes. Sepsis was the principal risk factor for impaired catch-up growth. These findings must be interpreted with caution given significant loss to follow-up. Multicentre prospective studies in resource-limited settings are urgently needed.

**Keywords:** extremely low birth weight; catch-up growth; neurodevelopment; Bayley scales; South Africa; low- and middle-income countries; neonatal follow-up; sepsis; prematurity

## Background

Advances in neonatal care, including the introduction of surfactant therapy for respiratory distress syndrome (RDS) in the late 1980s and broader implementation of antenatal corticosteroids, have substantially improved survival among extremely premature infants [1]. Extremely low birth weight infants (ELBWI, birth weight <1000 g) are among the most vulnerable neonates, experiencing prolonged hospitalisation and heightened risk of growth faltering and neurodevelopmental impairment [2,3].

Catch-up growth is a complex, multifactorial process, defined as attaining a standard deviation (SD) score >−2 SD of a reference population, or a change in SD score of >0.67 between birth and two years of age [4]. Most very preterm infants achieve catch-up growth by two years of age, yet they remain shorter and lighter in adulthood compared to term-born peers [4]. Early catch-up growth before two years is considered beneficial, with recognised improvements in neurodevelopmental outcomes, immunity, and childhood survival [5]. However, rapid or excessive catch-up growth has been associated with later metabolic, cardiovascular, and renal disease risk [5,6].

The prevalence of preterm birth in LMICs is poorly characterised, with estimates of approximately 12.4 per 1000 live births [2]. In South Africa (SA), socio-economic adversity is widespread, and family income is an established determinant of infant growth monitoring [7]. ELBWI are additionally predisposed to conditions such as RDS, necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and sepsis, all of which impair growth and neurodevelopment [8]. Data on medium- and long-term growth outcomes of ELBWI in SA remain limited [2,9].

The Bayley Scales of Infant and Toddler Development, third edition (BSID-III), is a well-validated tool for neurodevelopmental assessment in the first three years of life. A composite score <70 denotes developmental delay, while 70–85 indicates risk for developmental delay. Cognitive, language, and motor delays are disproportionately common in ELBWI [10].

The aims of this study were to determine the rate of catch-up growth in surviving ELBWI after discharge at CMJAH and to assess the relationship between catch-up growth and neurodevelopmental outcome at two years corrected age.

## Methods

### *Study design and setting*

This was a retrospective descriptive study conducted at CMJAH, a tertiary academic hospital in Johannesburg, Gauteng Province, SA. The neonatal unit comprises a 35-bed neonatal high care (NHC), a 15-bed neonatal intensive care unit (NICU), and kangaroo mother care (KMC)/low care facilities.

### *Participants*

All infants with a birth weight <1000 g (ELBWI) born at CMJAH or referred from regional facilities between 1 January 2015 and 31 December 2020, who survived to discharge and attended the neonatal follow-up clinic, were eligible for inclusion. Infants were excluded if they had chromosomal abnormalities or major congenital anomalies, or if follow-up data were insufficient.

### *Data source*

Data were extracted from the REDCap (Research Electronic Data Capture) neonatal database, hosted by the University of the Witwatersrand and used for clinical audit [11]. Variables collected included gestational age; birth weight, length and head circumference (HC); discharge weight; Apgar score at 5 minutes; presence of RDS, NEC, patent ductus arteriosus (PDA); culture-proven early-onset sepsis (EOS, on or before day 3) and late-onset sepsis (LOS, after day 3); invasive ventilation; breastfeeding at discharge; maternal HIV status; antenatal care attendance; antenatal steroid receipt; maternal employment; and child support grant (CSG) receipt. BSID-III scores were obtained from a prospective sub-study of ELBWI surviving to discharge between 1 July 2013 and 31 December 2017, assessed at 9–12 and 18–24 months corrected age [12].

### *Growth assessment*

Anthropometric measurements at each follow-up visit were plotted using WHO reference charts [13], with corrected age applied throughout. For preterm infants up to 50 weeks post-menstrual age, the Fenton growth chart was used as a reference [14]. Catch-up growth was defined as achieving a weight, length, or HC SD score >−2 SD of the WHO reference population [4].

### *Statistical analysis*

Data were imported into R version 4.0.2. Categorical variables are presented as frequencies and proportions; continuous variables as mean ± SD. Fisher's exact test assessed associations between categorical variables. A linear mixed-effects regression model characterised anthropometric trajectories over time. To assess the association between growth parameters and abnormal BSID-III scores, linear mixed-effects models were fitted with fixed effects including BSID-III status (normal/abnormal), sex, linear and quadratic terms for corrected age, and sex-by-age interaction terms. Logistic regression identified risk factors associated with failure to achieve catch-up growth (<−2 SD) at 18 months corrected age using stepwise variable selection. A p-value <0.05 was considered statistically significant.

### *Ethics*

Ethics approval was granted by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (reference: M210730). Parental consent for data collection was obtained as part of routine clinical care and the neonatal database sub-study.

## Results

### *Sample characteristics*

Of 380 ELBWI who survived hospitalisation during the study period, 114 attended follow-up. After exclusion of 17 infants (12 with missing data, four who did not meet weight criteria, one who died during follow-up), the final sample comprised 97 infants (Figure 6). Patient and maternal characteristics are presented in Table 1, alongside characteristics of the 283 infants lost to follow-up.

**Table 1. Maternal and infant characteristics**

| Characteristic | Study sample (N=97) | Lost to follow-up (N=283) |
|---|---|---|
| Mean gestational age (weeks) | 27.5 ± 1.8 | 27.8 ± 1.9 |
| Mean birth weight (g) | 877 ± 91 | 903 ± 95 |
| Mean birth HC (cm) | 26.1 ± 1.7 | 25.9 ± 1.9 |
| Mean discharge weight (g) | 1727 ± 256 | 1736 ± 309 |
| Female sex | 63 (65%) | 151 (53%) |
| Multiple gestation | 5 (5.2%) | 26 (9.2%) |
| Antenatal care | 87 (89.7%) | 217 (76.7%) |
| Antenatal steroids received | 60 (61.9%) | 92 (32.5%) |
| Maternal HIV positive | 23 (23.7%) | 90 (31.8%) |
| Apgar score <5 at 5 minutes | 6 (6.2%) | 21 (7.4%) |
| Respiratory distress syndrome | 91 (93.8%) | 269 (95.1%) |
| Invasive ventilation | 19 (19.6%) | 59 (20.8%) |
| NCPAP | 77 (79.4%) | 231 (81.6%) |
| Surfactant administered | 48 (49.5%) | 234 (82.7%) |
| Grade 3–4 IVH | 2 (2.1%) | 20 (7.1%) |
| Bronchopulmonary dysplasia | 70 (71.2%) | 184 (65.0%) |
| Necrotising enterocolitis | 10 (10.3%) | 21 (7.4%) |
| Patent ductus arteriosus | 12 (12.4%) | 54 (19.1%) |
| Early-onset sepsis (≤day 3) | 3 (3.1%) | 14 (4.9%) |
| Late-onset sepsis (>day 3) | 55 (56.7%) | 157 (55.5%) |
| Meningitis | 2 (2.1%) | 3 (1.1%) |
| Breast milk only on discharge | 41 (42.3%) | 115 (40.6%) |
| Mother employed | 27 (27.8%) | — |

| | | |
|---|---|---|
| Child support grant (index patient) | 36 (37.1%) | — |

*HC head circumference, IVH intraventricular haemorrhage, NCPAP nasal continuous positive airway pressure.*

### *Growth trajectories*

Growth trajectories for weight, length, and HC plotted against WHO reference standards are shown in Figures 1–3. Most infants started below the −2 SD threshold at discharge and demonstrated progressive catch-up over the follow-up period. Female infants showed a trend towards slightly higher rates of catch-up growth across all three parameters compared to males.

**Figure 1. Weight for corrected age versus WHO reference standards**

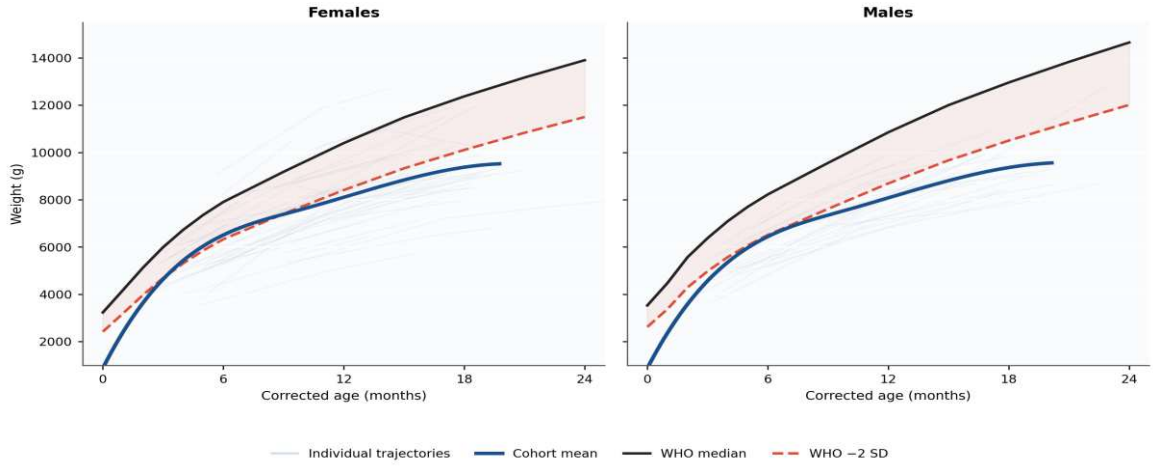



*Figure 1. Weight for corrected age versus WHO reference standards (females left, males right). Individual trajectories in blue-grey; cohort mean in navy; WHO median in black; WHO −2 SD in red dashed line.*

**Figure 2. Length for corrected age versus WHO reference standards**

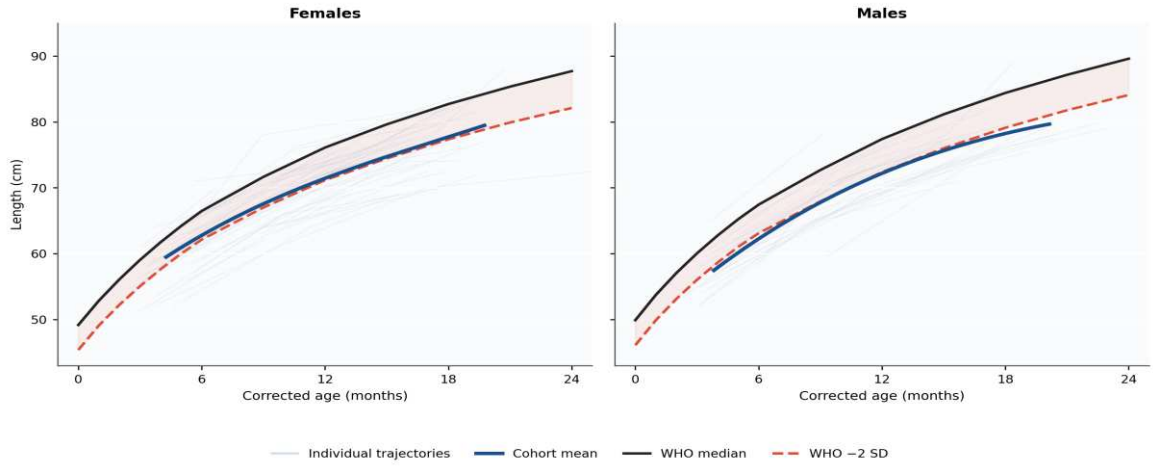



*Figure 2. Length for corrected age versus WHO reference standards.*

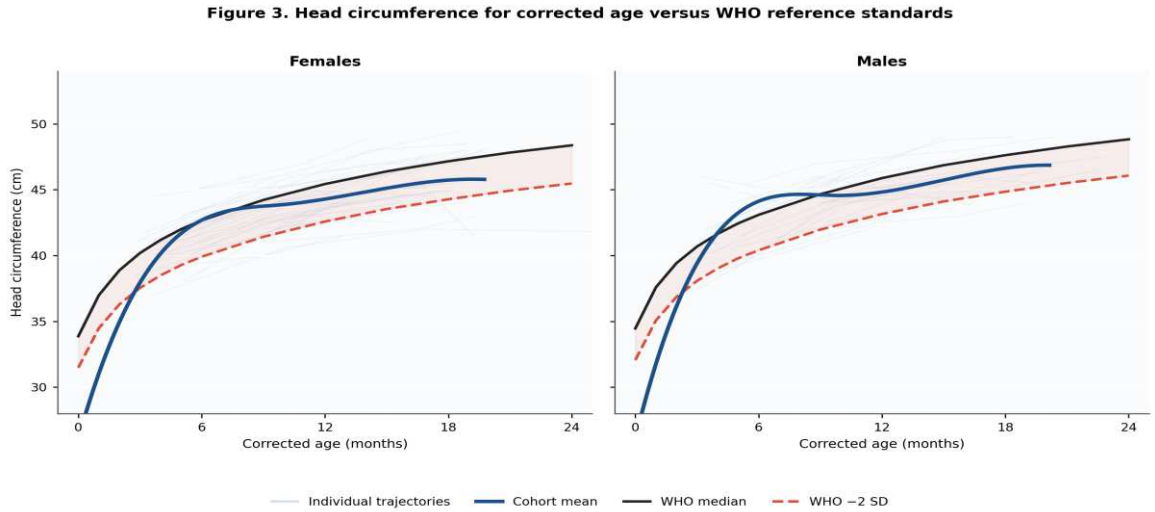



*Figure 3. Head circumference for corrected age versus WHO reference standards.*

### *Catch-up growth rates at 18 months corrected age*

At 18 months corrected age, catch-up growth (>−2 SD) was achieved by 90% of females and 76% of males for weight, 79% and 67% for length, and 92% and 88% for HC.

### *Risk factors for failure to achieve catch-up growth*

Logistic regression identified sepsis as the principal risk factor for failure to achieve catch-up growth. Sepsis was significantly associated with length remaining below −2 SD at 18 months (OR 5.47, 95% CI: 1.54–26.34; p = 0.016). A borderline association was observed for weight (OR 4.64, 95% CI: 1.12–31.71; p = 0.059). No significant associations were found for HC.

### *Neurodevelopment and growth*

Of 97 infants, 46 had BSID-III assessment at 9–12 months; 14 (30%) had abnormal scores. At 18–24 months, 26 infants had BSID-III scores; 9 (35%) were abnormal. Two infants were diagnosed with cerebral palsy.

Linear mixed-effects modelling demonstrated that at 9–12 months, both weight and length were significantly associated with BSID-III scores. Infants with normal BSID-III scores at 9–12 months weighed on average 919 g more (95% CI: 297–1541) and were 2.3 cm taller (95% CI: 0.4–4.3) than those with abnormal scores. No significant associations were demonstrated at 18–24 months, most plausibly reflecting the small sample size at that assessment (Figures 4 and 5).

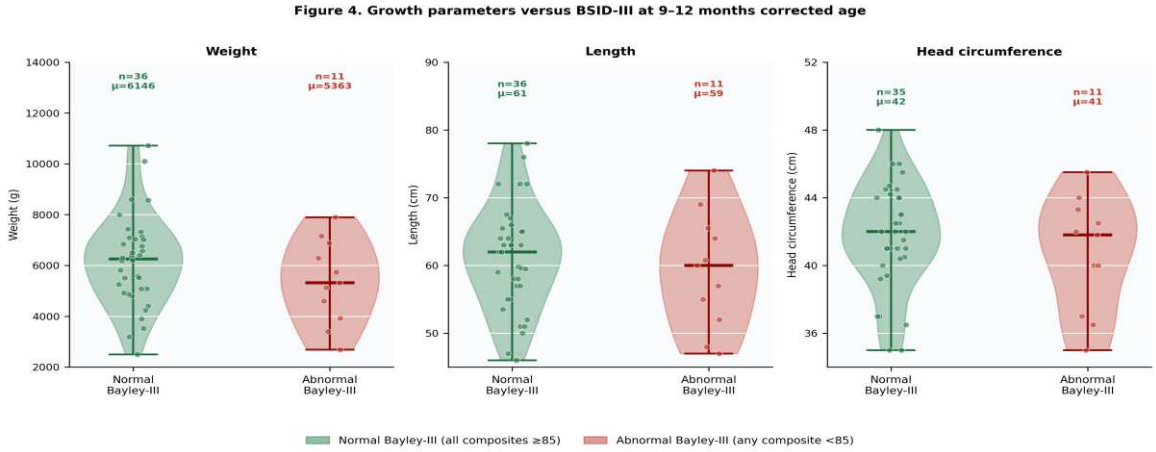



*Figure 4. Weight, length, and head circumference stratified by BSID-III score at 9–12 months corrected age. Violin plots with individual data points overlaid. Forest green = normal Bayley-III (all composites ≥85); Crimson = abnormal Bayley-III (any composite <85). n and group means annotated.*

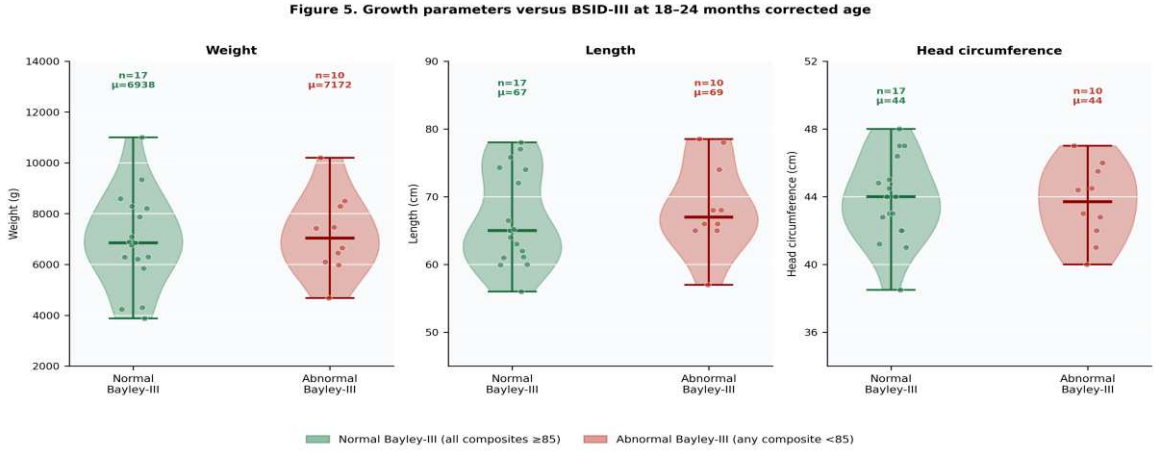
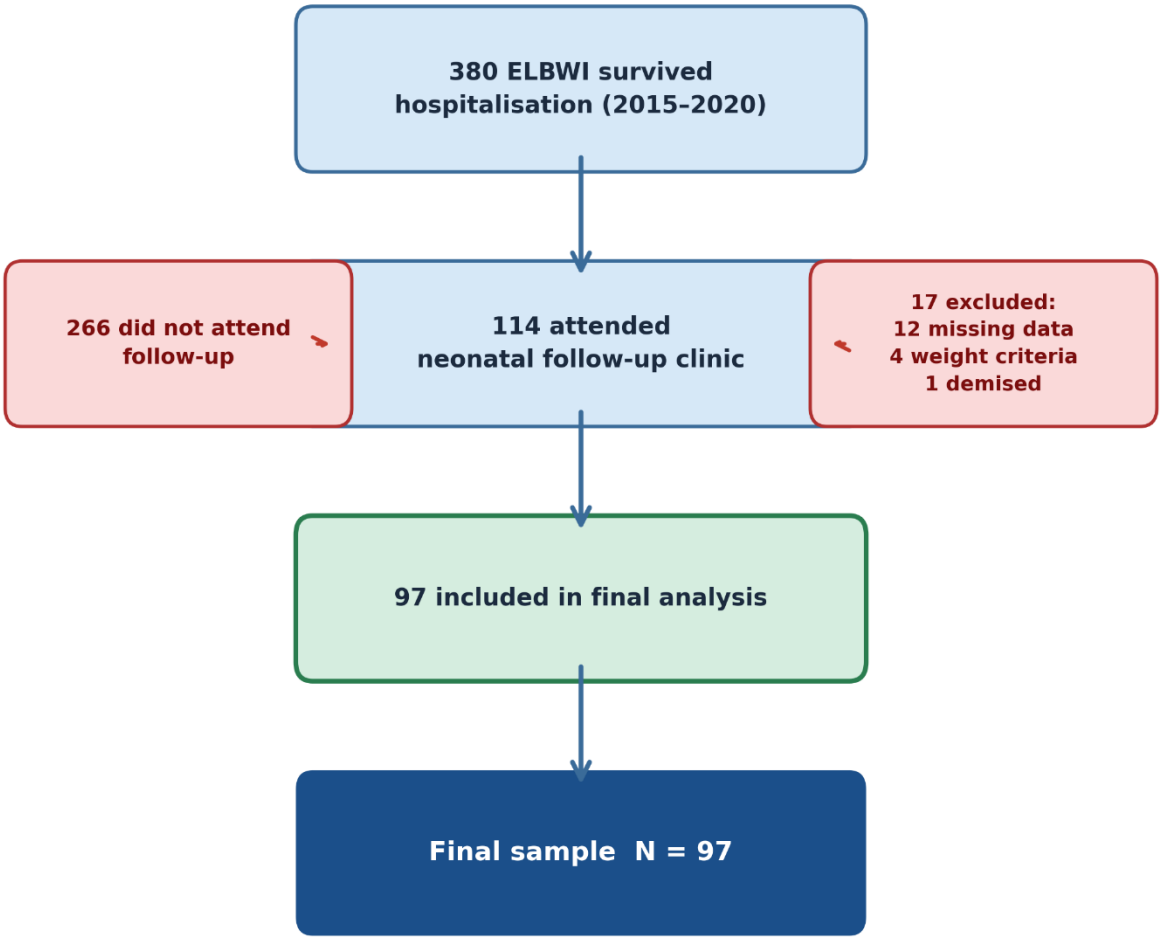



*Figure 5. Weight, length, and head circumference stratified by BSID-III score at 18–24 months corrected age.*

**Figure 6. Study participant flow diagram**




*Females: 63 (65%)  Males: 34 (35%)*

*Mean GA: 27.5 weeks  Mean BW: 877 g*

*Figure 6. Study participant flow diagram.*

## Discussion

This study describes catch-up growth trajectories and neurodevelopmental outcomes in a cohort of ELBWI at a South African tertiary hospital, an area where such data are scarce. The mean gestational age was 27.5 weeks and mean birth weight 877 g, consistent with published ELBWI cohorts [1,4].

The majority of infants achieved catch-up growth by 18 months corrected age across all three anthropometric parameters, consistent with the Euser et al. definition [4]. This is particularly noteworthy given the prolonged and often complicated hospital admissions typical of ELBWI and the well-described postnatal growth restriction during such stays [4,9,15]. A previous study from the same institution in a predominantly VLBW cohort (15% ELBWI) found gradual but incomplete catch-up for length by 20 months [9].

A notable feature of the study sample was the high rate of antenatal care attendance (89.7%), relatively low maternal HIV prevalence (23.7%), and high rate of antenatal steroid receipt (61.9%). These favourable antenatal factors may have contributed to better growth outcomes. Critically, only 32.5% of those lost to follow-up had received antenatal steroids compared to 61.9% in the study sample, a potentially important selection bias.

Sepsis emerged as the most significant modifiable risk factor for impaired catch-up growth, significantly associated with failure to achieve catch-up growth for length and trending for weight. This is consistent with the well-established consequences of neonatal sepsis on growth and neurodevelopment [16,17]. Velaphi et al. identified sepsis as the second most common cause of death in VLBWI in South Africa, after prematurity [17]. A multicentre study in China identified family income, regular healthcare attendance, and breast milk supplementation as additional modifiable risk factors [7].

At 9–12 months corrected age, both weight and length were significantly associated with BSID-III scores. This aligns with existing literature linking early postnatal growth to brain development and cognitive outcomes in preterm infants [8]. The absence of a detectable association at 18–24 months is most plausibly attributable to the very small sample size at that assessment (n=26), rather than a true biological divergence.

The long-term consequences of rapid catch-up growth, including cardiometabolic risk, have been described in high-income settings [1,6], but no studies to this effect have been conducted in the South African context [2].

## Strengths and limitations

This study provides a rare description of growth and neurodevelopmental trajectories in ELBWI from a LMIC setting, with rigorous data collection via a validated REDCap database.

BSID-III assessments were performed by trained paediatricians and neonatologists. A direct comparison with infants lost to follow-up was possible, allowing some characterisation of selection bias.

The most significant limitation is the substantial loss to follow-up: only 97 of 380 surviving ELBWI (25.5%) formed the final sample, a major source of selection bias. Reasons for non-attendance were multifactorial, including relocation, difficulty accessing the hospital, poor socio-economic circumstances, and inability to attend due to employment constraints — findings consistent with earlier reports from this institution [18]. The retrospective design and reliance on a clinical database resulted in missing data for several variables. Gestational age was frequently estimated using the Ballard score rather than early ultrasound, introducing potential inaccuracy. The distinction between small-for-gestational-age (SGA) and appropriate-for-gestational-age (AGA) ELBWI was not made, precluding assessment of SGA status as a predictor, an important gap given the well-described association between SGA and poorer neurodevelopmental outcomes [8]. Follow-up in the majority of infants was limited to 18 months corrected age rather than the intended 24 months.

## Conclusions

Most ELBWI at this South African tertiary centre achieved catch-up growth above −2 SD for weight, length, and HC by 18 months corrected age, with overall favourable neurodevelopmental outcomes. Sepsis was the principal risk factor for impaired catch-up growth, underscoring the importance of robust infection control policies in neonatal units. These findings should be interpreted with caution in the context of substantial loss to follow-up and likely selection bias. Larger multicentre prospective studies in resource-limited settings are urgently needed to accurately characterise growth and neurodevelopmental outcomes in this vulnerable population.

## List of abbreviations

AGA: Appropriate for gestational age; BSID-III: Bayley Scales of Infant and Toddler Development III; BPD: Bronchopulmonary dysplasia; CMJAH: Charlotte Maxeke Johannesburg Academic Hospital; CSG: Child support grant; ELBWI: Extremely low birth weight infants (<1000 g); EOS: Early-onset sepsis; HC: Head circumference; HIV: Human immunodeficiency virus; IVH: Intraventricular haemorrhage; KMC: Kangaroo mother care; LMIC: Low- and middle-income country; LOS: Late-onset sepsis; NEC: Necrotising enterocolitis; NCPAP: Nasal continuous positive airway pressure; NICU: Neonatal intensive care unit; PDA: Patent ductus arteriosus; RDS: Respiratory distress syndrome; REDCap: Research Electronic Data Capture; SA: South Africa; SD: Standard deviation; SGA: Small for gestational age; VLBWI: Very low birth weight infants; WHO: World Health Organization.

## Declarations

### *Ethics approval and consent to participate*

This study was conducted in accordance with the Declaration of Helsinki. Ethics approval was obtained from the Human Research Ethics Committee (Medical), University of the Witwatersrand (reference M210730). Written informed parental consent was obtained for participation in the neonatal follow-up database at the time of enrolment; as this study is a retrospective secondary analysis of routinely collected, de-identified data from that database, the requirement for additional study-specific consent was waived by the same committee.

### *Consent for publication*

Not applicable.

### *Availability of data and materials*

The datasets analysed during the current study are held within the REDCap neonatal database at the University of the Witwatersrand. Data are available from the corresponding author on reasonable request and subject to institutional data governance approval.

### *Competing interests*

The authors declare that they have no competing interests.


### *Funding*

No external funding was received for this study.


### *Authors' contributions*

SMK conceptualised and designed the study, performed data extraction and statistical analysis. OA drafted the manuscript, provided critical intellectual input, and assisted with data interpretation. TR supervised the study, provided critical intellectual input, and reviewed and approved the final manuscript. All authors read and approved the final version.


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### *Clinical Trial number*

Not applicable.

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