



## Original article

# Individualised growth charts for preterm infants based on a cohort with healthy neurodevelopment



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## SUMMARY

**Background & Aims:** Early growth of very preterm infants is associated with later neurodevelopmental outcome. Current growth charts are based on in utero growth rather than a growth pattern associated with good outcomes. This study aimed to generate growth standards using infants who were developing normally.

**Methods:** Data were obtained from the National Neonatal Research Database. Logistic regression identified associations of in-hospital and post-discharge weight gain and head circumference growth with the chance of healthy development at two years. The LMS method was used to construct centile curves reflecting the growth of very preterm infants with a positive developmental outcome. Infants with surgical necrotising enterocolitis or a significant brain injury were excluded from the cohort used to generate growth charts.

**Results:** Growth data were available for 37700 infants, of whom 14120 had a documented developmental assessment. Healthy development was positively associated with three factors: In-hospital weight gain (adjusted OR 1.09 per unit z-score change, 95 % CI: 1.02–1.17), weight gain from discharge to two-year assessment (aOR 1.08, 1.04–1.12) and in-hospital head growth (aOR 1.12, 1.04–1.21). A web app is available ([www.bit.ly/preterm-plotter](http://www.bit.ly/preterm-plotter)) to generate individualised growth charts for preterm infants, conditioned on their weight and head circumference at birth, to plot their growth and indicate whether their growth was expected to align with that of healthily developing infants.

**Conclusion:** This study presents a novel method of forming individualised growth charts. It can be implemented using a web app or by integration with clinical information systems to allow an infant's growth to be compared to a cohort of infants with a favourable developmental outcome.

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## 1. Introduction

Promoting healthy growth is fundamental to the care of preterm infants. Such infants are beset by challenges to their growth: the sudden cessation of placental supply, gut and metabolic immaturity impairing tolerance of nutrition, prevalent comorbidities and very high nutrient requirements [1,2]. A growing body of data confirms an association between the quality of early growth and later neurodevelopmental outcome [3–5].

Current growth charts such as the UK Newborn Infant Close Monitoring chart [6] and the Fenton chart [7] are based on measurements of preterm infants at birth. Therefore, they reflect in-utero growth. However, it has long been recognised that the ex-utero growth of preterm infants does not follow this trajectory [8]. Most obviously, body water loss in the first week of life causes early weight loss or stasis which is not reflected in current growth charts for preterm infants (although charts for term-born infants omit the first two weeks of life in recognition of this effect) [9,10]. The practical result of this discrepancy is that clinicians expect deviation from growth charts and it is unclear whether or not this deviation is pathological for an individual infant. It cannot be assumed that tracking centiles based on birthweight data

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represents the optimal growth trajectory of an individual preterm infant ex utero.

Individualised charts aim to tailor a growth trajectory to an individual infant. Such charts have been created using an understanding of the physiological basis for early weight change and assessment of effects of growth on body composition [11]. A relationship between this growth trajectory and neurodevelopmental outcome has not been established. This technique has allowed an individualised chart to be created for an infant using an interactive website, with the day of life as the independent variable and early weight loss integrated into the model used to create it. The current study aims to use national data to create growth charts which reflect the pattern of weight gain and head growth associated with positive developmental outcome. Length data were too sparse to include. A web app allows the user to generate individualised growth charts for infants on which to plot their growth.

## 2. Material & Methods

Data for all infants born in England before 32 weeks of gestation and cared for during the period from 2014 to 2018 were obtained from the National Neonatal Research Database (NNRD) which collects data about all admissions to neonatal units in Great Britain and makes them available for research upon application [12].

Data included gestation, sex, serial measurements of weight and head circumference, and daily diagnoses from birth until discharge, and a developmental assessment made at around two years corrected age. The assessment is based on a clinician answering yes or no to four questions:

- “Is development normal (<3 months delay)?”
- “Is there mild delay (3–6 month delay)?”
- “Is there moderate delay (6–12 month delay)?”
- “Is there severe delay (more than 12 month delay)?”.

For this study, infants were included if the clinician selected yes for the first statement “Is development normal (<3 months delay)?” and did not answer yes to any of the other statements.

Errors in weight and head circumference produced by transposing the two or misplacing the decimal point were corrected. Measurements were examined in triplets and extreme velocity outliers were identified and excluded (using the *sitar* package for R) [13]. Descriptive data were used to explore the differences between infants with and without a developmental assessment.

### 2.1. Logistic regression modelling

Logistic regression was used to model the probability of having a normal developmental assessment (compared to delayed) in relation to growth in hospital and post-discharge. Weight gain and head circumference growth were summarised as the change in z-score (based on UK-WHO growth charts [14]) from birth to hospital discharge (35–37 weeks postmenstrual age (PMA), in-hospital growth) and from discharge to the two-year assessment (post-discharge growth). The model was adjusted for gestation, sex, small for gestational age (SGA) status, Apgar score at 5 minutes, necrotising enterocolitis requiring surgery, and significant brain injury (intraventricular haemorrhage grade 3/4 or post-haemorrhagic hydrocephalus). The *glm* function of R was used to perform logistic regression with a logit link [15].

### 2.2. Growth centile modelling

Infants assessed as “development normal (<3 months delay)” were selected for growth chart development. Infants suffering from surgically managed necrotising enterocolitis (NEC) or from severe intraventricular haemorrhage (IVH) (grade III, grade IV or causing posthaemorrhagic hydrocephalus) were excluded as these conditions were available in the source data and were found to influence growth in the logistic modelling step. For weight, separate charts were created for infants at each gestational week (i.e. one chart for infants born at 23<sup>+0</sup> to 23<sup>+6</sup> weeks gestation, one for infants born at 24<sup>+0</sup> to 24<sup>+6</sup> weeks gestation etc.). Charts were set to end just before 36 weeks PMA for the most mature infants in each group as most infants remained in hospital (and therefore in the dataset) at that point. As head circumference data were sparser, charts were made for wider gestation groups (23<sup>+0</sup> to 25<sup>+6</sup>, 26<sup>+0</sup> to 27<sup>+6</sup>, 28<sup>+0</sup> to 29<sup>+6</sup> and 30<sup>+0</sup> to 31<sup>+6</sup> weeks gestation).

Growth chart centiles were calculated using the LMS method with the Box–Cox Cole and Green distribution in GAMLSS [16–18]. Centile lines were placed two-thirds of a z-score apart, at 0.4th, 2nd, 9th, 25th, 50th, 75th, 91st, 98th and 99.6th (rounded) centiles.

In order to reflect the early weight and head circumference changes seen in preterm infants, the day of life was taken as the independent variable and the weight or head circumference was taken as the dependent variable. By aligning all infants by day of life, early weight loss and head circumference change were captured. LMS modelling was performed using the *gamlss* package [18] for R.

### 2.3. Growth trajectory predictions

Healthy growth is not expected to follow a centile line on the charts produced in this way. It has long been observed that when a growing child is measured to two occasions, the centile of the second measurement tends to be closer to the median than the first [19]. Considering that there will not be perfect correlation between centiles on two occasions, the measurement centile is bound to experience regression to the mean. The extent of this regression to the mean is measured by calculating the correlations between z-scores at different ages. The resultant prediction of future z-scores (i.e. the predicted growth trajectory) can then be conditioned on the z-score at birth (in the manner first described by Cole [19] and recently implemented by van Buuren [20]).

Tables calculating the time-to-time correlations for weight and head circumference were formed. These correlations were smoothed slightly using cubic B-splines and were then used to predict the growth trajectory, conditioned on the size at birth. In the case of this project, only the measurement at birth is known at the time of generating the predicted trajectory and therefore only the correlations with birth measurements are used (i.e. the top row of the correlation matrix in [Supplementary Table 2](#)). A confidence interval was calculated around this prediction interval by calculating the measurement value at +1.15 SD and –1.15 SD of the prediction interval, determining a range within which 75% of infants would be expected to grow.

### 2.4. Web app

A web application was created using the *shiny* package [21] for R. The app allows the user to enter gestation and sex for an infant, along with serial weight and head circumference measurements and the corresponding ages. The app generates an individualised growth chart for the infant based on their gestation and birth-weight. The chart illustrates the expected growth trajectory and

the range within which 75% of infants would be expected to grow. The infant's birthweight and birth head circumference centiles (based on UK-WHO reference) are also given to indicate the size (and SGA status) at birth.

This project was approved by the Oxford A research ethics committee (20/SC/0073).

### 3. Results

Data were obtained for 37700 infants born before 32 weeks of gestation. The number of infants included in each stage of analysis is shown in Fig. 1. Of those infants, 14120 had documented neurodevelopmental assessments around two years corrected age. Assessed infants differed systematically from those who were not assessed; they had an earlier median gestation, and were more likely to: be small for gestational age, be born in NICU and suffer a significant brain injury (Table 1).

#### 3.1. Association of growth with developmental outcome

Complete weight data were available for 9359 infants who subsequently underwent developmental assessment. After adjustment, the chance of normal neurodevelopment was positively associated with in-hospital change in weight z-score (adjusted OR 1.09 per unit z-score change, 1.02–1.17) and with the post-discharge change in weight z score (adjusted OR 1.08, 1.04–1.12) (Table 2A). Head circumference data were available for 1322 infants who had undergone developmental assessment. After adjustment, the in-hospital change in head circumference z-score was positively associated with a higher chance of normal neurodevelopment (adjusted OR 1.12 per unit z-score change, 1.04–1.21) (Table 2B). The association with post-discharge change in head circumference z score was not statistically significant (adjusted OR 1.09, 1.00–1.20) (Table 2B).

**Table 1**  
Comparison of infants with and without a developmental assessment.

	Developmental Assessment Performed	Developmental Assessment Not Performed	p value
n	14120	23580	
Male	7575 (53.6 %)	12960 (55.0 %)	0.013 <sup>f</sup>
Gestation (weeks + days, median (IQR))	28 <sup>+5</sup> (27 <sup>+0</sup> - 29 <sup>+6</sup> )	30 <sup>+0</sup> (27 <sup>+4</sup> -31 <sup>+1</sup> )	<0.001 <sup>c</sup>
SGA (<10th centile)	2212 (15.7 %)	3431 (14.6 %)	0.0045
Born at a NICU	8443 (59.8 %)	12343 (52.3 %)	<0.001 <sup>b</sup>
Surgery for NEC	338 (2.4 %)	631 (2.7 %)	0.097 <sup>b</sup>
Severe brain injury <sup>a</sup>	743 (5.3 %)	1072 (4.5 %)	0.002 <sup>b</sup>

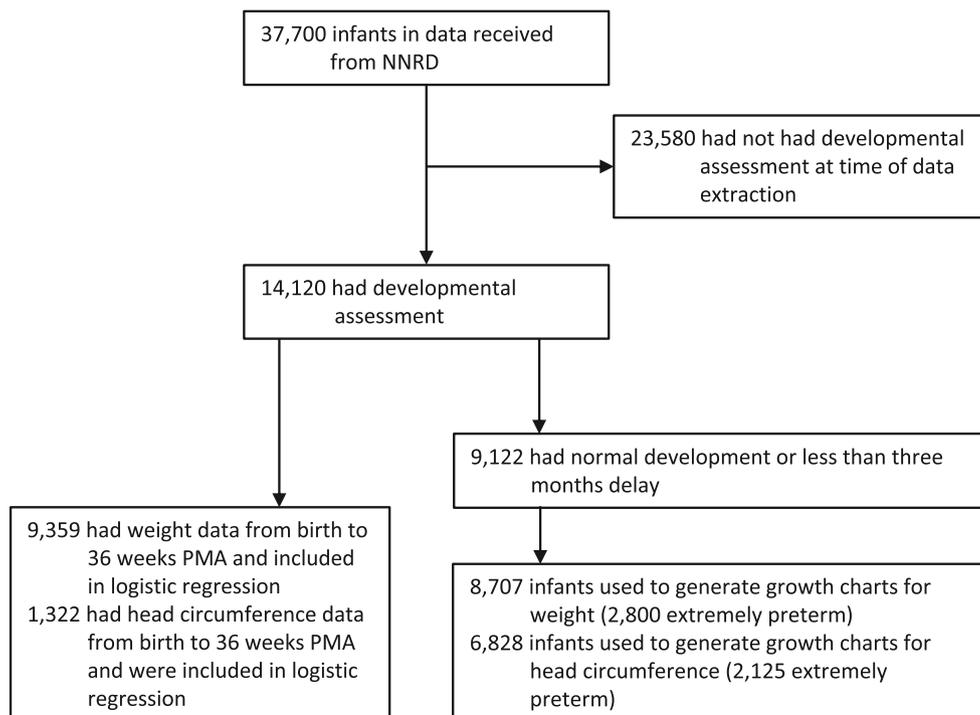
<sup>a</sup> Intraventricular haemorrhage of grade 3 or 4, or post-haemorrhagic hydrocephalus.

<sup>b</sup> Two-sample t-test.

<sup>c</sup> Chi-squared test.

#### 3.2. Growth charts

After data cleaning and excluding infants with an adverse neurodevelopmental outcome, 77564 weight measurements of 2795 extremely preterm infants, 102517 weight measurements of 5912 very preterm infants, 8663 head measurements of 2125 extremely preterm infants and 15619 head measurements of 4701 very preterm infants were available. Fewer infants were included at the most preterm gestations due to fewer infants being born in these groups and a lower proportion experiencing favourable neurodevelopment (see Supplementary Table 1). Fig. 2 shows growth charts for weight and head circumference versus postnatal age for each gestation group. As previously identified, early weight loss was more pronounced in the more mature infants [22,23]. An analogous pattern of head circumference loss was seen at 30–31 weeks.



**Fig. 1.** Flow chart of infants included in analysis. PMA – postmenstrual age.

**Table 2**

Multivariable logistic regression for the influence of selected clinical variables on the chance of normal development including **A.** change in weight z-score between birth and 35–37 weeks postmenstrual age (PMA) (in-hospital weight gain) and change in weight z-score between 35 and 37 weeks PMA and two-year follow-up (post-discharge weight gain) (n = 9359); and **B.** change in head circumference z-score in-hospital and post-discharge (n = 1322).

A- Weight gain				
	Unadjusted OR (95 % CI)	Unadjusted P Value	Adjusted OR (95 % CI)	Adjusted P Value
Gestation (weeks)	1.17 (1.14–1.19)	<0.001	1.12 (1.09–1.14)	<0.001
SGA	0.88 (0.8–0.98)	0.022	0.76 (0.67–0.85)	<0.001
Female	1.54 (1.42–1.67)	<0.001	1.52 (1.39–1.66)	<0.001
Apgar at 5 min	1.12 (1.1–1.15)	<0.001	1.06 (1.03–1.08)	<0.001
Surgical necrotising enterocolitis	0.44 (0.34–0.55)	<0.001	0.63 (0.48–0.82)	<0.001
Significant brain injury <sup>a</sup>	0.3 (0.25–0.35)	<0.001	0.37 (0.3–0.44)	<0.001
In-hospital weight gain	1.06 (1–1.13)	0.033	1.09 (1.02–1.17)	0.013
Post-discharge weight gain	1.09 (1.06–1.13)	<0.001	1.08 (1.04–1.12)	<0.001
B- head growth				
	Unadjusted OR (95 % CI)	Unadjusted P value	Adjusted OR (95 % CI)	Adjusted P value
Gestation (weeks)	1.13 (1.08–1.2)	<0.001	1.07 (1.01–1.14)	0.029
SGA	0.89 (0.68–1.18)	0.42	0.79 (0.59–1.06)	0.11
Female	1.39 (1.12–1.73)	0.003	1.35 (1.07–1.71)	0.012
Apgar at 5 min	1.09 (1.02–1.16)	0.007	1.02 (0.95–1.09)	0.66
Surgical necrotising enterocolitis	0.73 (0.37–1.49)	0.38	0.98 (0.45–2.24)	0.96
Significant brain injury <sup>a</sup>	0.19 (0.12–0.29)	<0.001	0.21 (0.13–0.34)	<0.001
In-hospital head growth	1.13 (1.06–1.21)	<0.001	1.12 (1.04–1.21)	0.003
Post-discharge head growth	1.08 (1–1.18)	0.054	1.09 (1–1.2)	0.064

<sup>a</sup> Intraventricular haemorrhage of grade 3 or 4, or post-haemorrhagic hydrocephalus.

### 3.3. Time-to-time correlations

Supplementary Table 2 sets out the time-to-time correlations for weight and head circumference z-scores as infants grew. Correlations between measurements at birth and at all later ages were used to formulate projected trajectories for infants. As expected, the correlation between birth z-score and later z-scores weakened with advancing age, making the growth trajectory prediction less precise as the infant aged. Correlations for weight were generally stronger than those for head circumference.

### 3.4. Web app

A web app is available at [www.bit.ly/preterm-plotter](http://www.bit.ly/preterm-plotter). Examples of the web app with sample infants are given in Fig. 3.

The red line indicates the expected growth trajectory, based on a gestation-appropriate growth chart using infants with normal neurodevelopment as its basis, conditioned on the size of the infant at birth and calculated using time-to-time correlations of z-scores. The red shaded areas indicate regions above and below the expected trajectory within which 75% of such infants would be expected to grow.

Figure 3A provides an example of the weight gain of an SGA infant born at 26 weeks gestation. The weight gain trajectory falls below the expected shaded area, indicating that the infant is gaining weight more slowly than would be expected. This deviation below the expected trajectory should trigger a clinical review of the patient's nutritional care and consideration for enhanced nutritional monitoring and support [1]. Conversely, Fig. 3B demonstrates the case of an extremely preterm infant whose head is growing at the expected rate for a child likely to experience normal neurodevelopment, reassuring the clinician that nutritional care is likely to be sufficient to support normal development.

## 4. Discussion

This study created individualised growth charts, accessible via a web app, which reflect growth patterns of preterm infants assessed as having normal development or less than three months

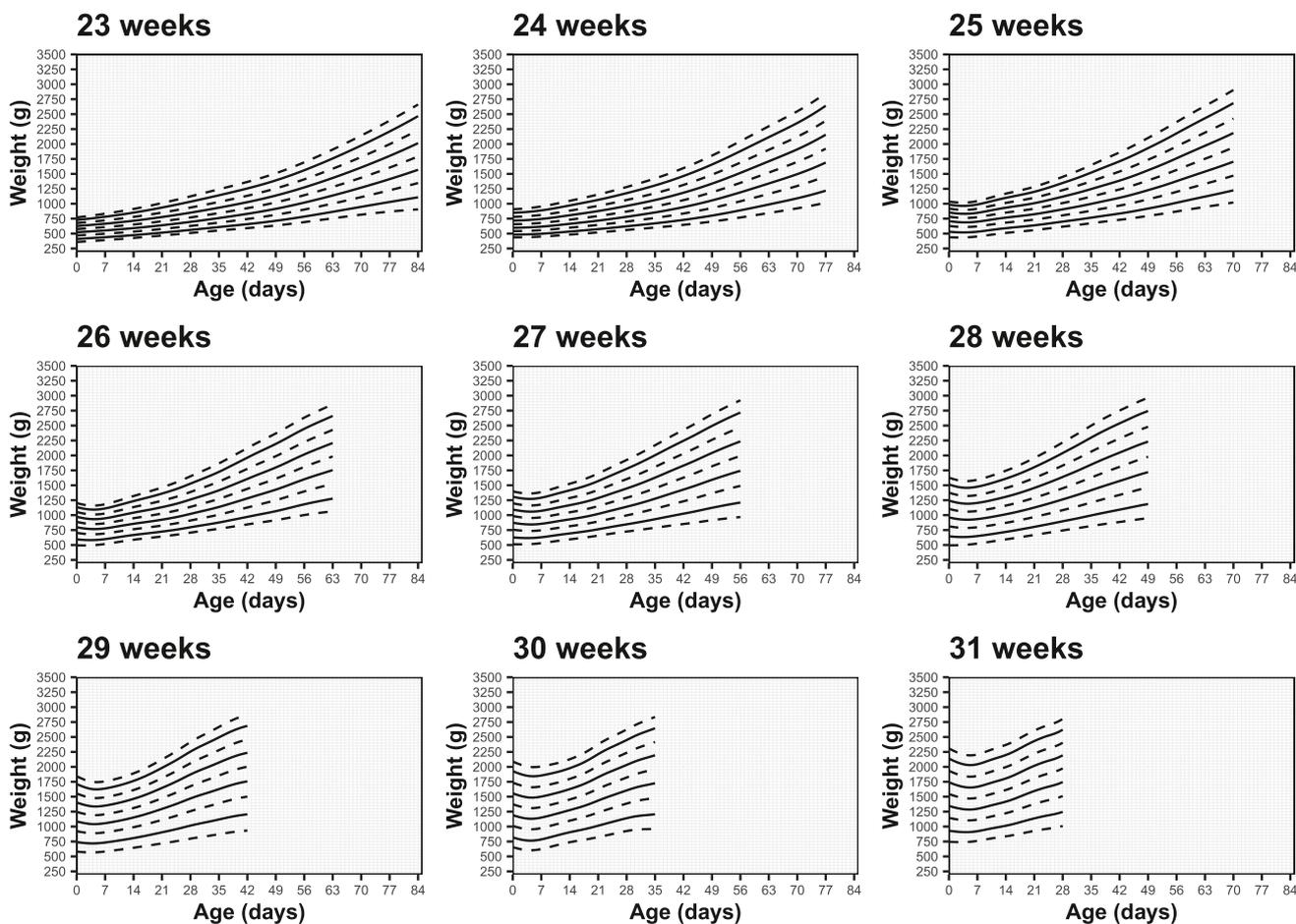
delay at two years of age. Time-to-time correlations between z-scores are used to illustrate the growth trajectory which would be expected for most infants who go on to demonstrate normal neurodevelopment. This conditional growth approach ensures that the predicted trajectory is based on the longitudinal growth patterns of infants with a good neurodevelopmental outcome.

This study confirms findings in earlier cohorts that faster growth during the neonatal period is associated with more favourable neurodevelopmental outcomes, with a small but statistically significant effect size. The underlying reason for this association is difficult to discern from the available data. It is likely that those infants who receive more effective nutritional support (or those who are able to tolerate and utilise nutrition most effectively) also experience better brain development. The exact causal pathway between growth and neurodevelopment is uncertain. There may be a straightforward causal link of good growth leading to a good outcome, or growth may be a marker of which infants are thriving and are therefore more likely to meet their developmental potential, or both may be true. It must be remembered that only around 45% of growth is explained by nutritional intake [24] and a wide range of comorbidities exert an influence on growth [25]. Other care decisions, for example the use of postnatal steroids, will also be influential. Therefore, a nuanced exploration of all the factors influencing growth must inform care decisions, as we have previously recommended [1]; unthinkingly increasing nutritional intake in the absence of such a review is unlikely to influence growth and even less likely to improve later neurodevelopmental outcome.

Furthermore, an excess intake of macro- and micro-nutrients may have unwanted effects. For example, unusually high protein intakes have been associated with some short and long term adverse outcomes, albeit not always reaching statistical significance [26]. International guidance provides clear guardrails for nutrient intakes, recommending that higher intakes are provided only within a research setting [27]. This study did not assess whether faster growth was associated with any other positive or negative effects.

The results of the current study show weight gain patterns by gestation that are broadly consistent with trajectories previously

### A. Weight



### B. Head Circumference

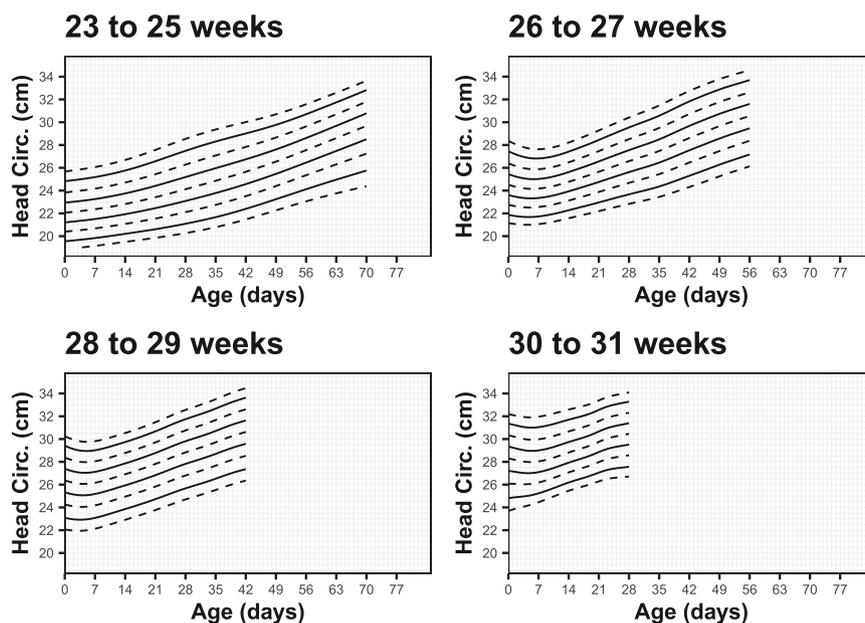
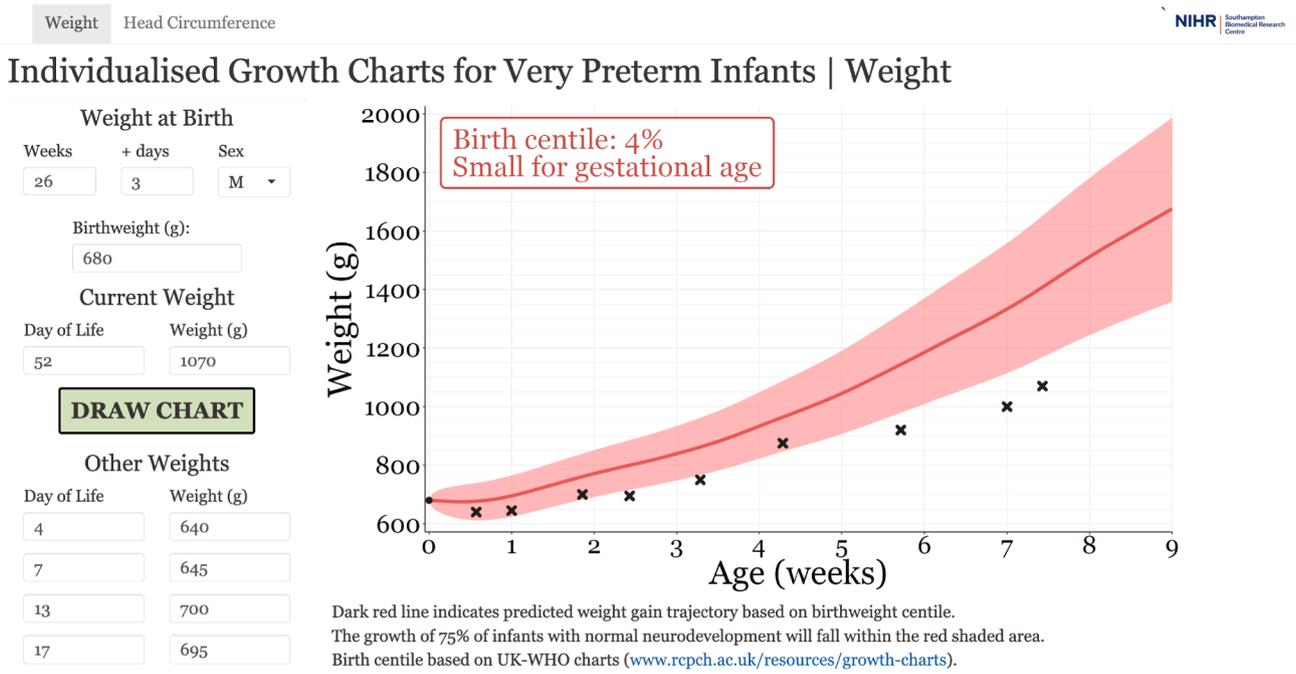
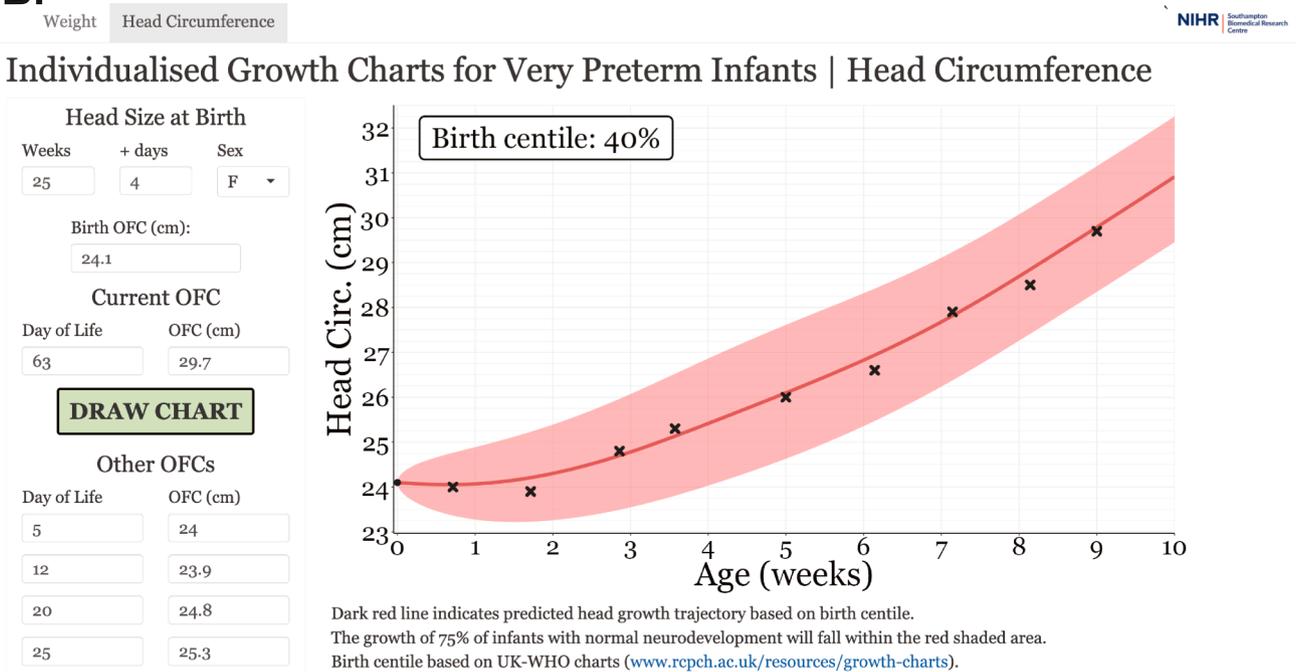


Fig. 2. Growth charts for weight (A) and head circumference (B) versus postnatal age by completed week(s) of gestation at birth based on very preterm infants with a positive developmental outcome. Centile lines are spaced two-thirds of a z-score apart at 0.4th, 2nd, 9th, 25th, 50th, 75th, 91st, 98th and 99.6th centiles. [NB Available as SVG but online system would not accept SVG format for figures].

**A.**



**B.**



**Fig. 3.** Screenshots from the web application published at [www.bit.ly/preterm-plotter](http://www.bit.ly/preterm-plotter) for **A.** weight gain for an SGA infant who is gaining weight more slowly than expected and **B.** head growth for an extremely preterm infant with normal head growth.

identified using the SITAR method, where early weight loss was absent in extremely preterm infants and progressively more evident in more mature infants [22,23]. The reason for this absent weight loss is difficult to discern, especially considering the strong physiological reasoning to expect early weight loss [10]. Differences in fluid management or artefacts arising from intermittent weighing may contribute to this effect. It is interesting to note a

similar pattern of early reduction in head circumference at later gestations. In clinical practice it is known that head circumference changes as the effects of delivery on the flexible preterm skull wane. In fact, a study performed in 1976 recorded early head circumference loss in preterm infants [28].

The findings of this study are limited by the quality and coverage of developmental outcome data. Weight and head

circumference measurements ceased at discharge from hospital, meaning that the growth trajectory could be assessed only up to that point. Developmental data were limited to a clinician's classification of "normal development or less than a three month delay", "mild delay", "moderate delay" or "severe delay" at two years corrected age. It may be that the pattern of growth in infants with completely normal development, with no delay, is different. Furthermore, the data were available for only a subset of the cohort which was not representative of the whole group. Large-scale data collection on preterm infants will rely on consistent application of a standardised and practical neurodevelopmental assessment. Whilst gold standard scores such as the Bayley Scale of Infant and Toddler Development are available [29], their implementation is limited by the time and expense required to administer them. The INTER-NDA package may provide a more practical means to obtain reliable neurodevelopmental outcome measures at scale [30].

Growth standard charts are derived from a cohort of healthy individuals. For example, WHO growth standards for term-born children are derived from a population of healthy breastfed infants [31]. Developing growth standards for preterm infants is conceptually challenging as they are, by definition, not normal and most of them are not completely healthy, for example a degree of respiratory distress syndrome is near-inevitable. Furthermore, preterm infants require supplementation of breastmilk to meet their nutritional requirements [2]. Infants included in this study are likely to have experienced comorbidities, some of them serious, and therefore do not represent a truly healthy population.

Figure 4 shows the UK's Newborn Infant Close Monitoring chart [6] (pink centiles) overlaid by two individualised growth trajectories for an example extremely preterm infant, one from this study (in black) and the other from Landau-Cringle et al. (in green) [11], along with the median growth trajectory for infants born at this gestation in the UK between 2014 and 2018 from work published by our group (in blue) [22]. Landau-Cringle's work used a deep understanding of the physiology of preterm infants to generate predicted healthy growth trajectories. The example trajectory from the current study (in black) crosses centiles downwards on the standard growth chart, and it also (reassuringly) matches the median trajectory (in blue). However, the growth

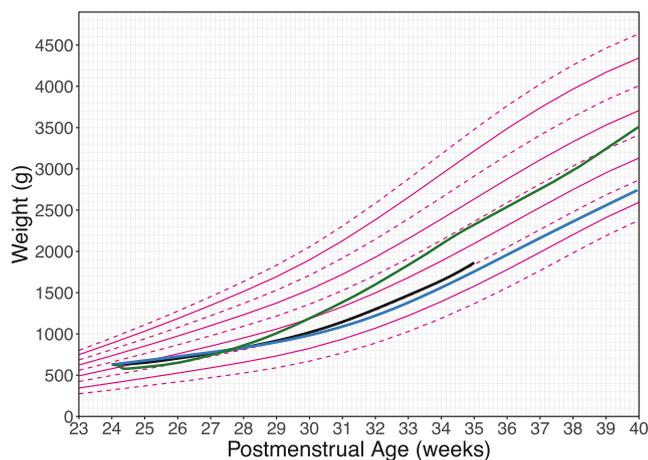
pattern differs materially from that of Landau-Cringle, with less early weight loss and slower later weight gain. This raises the possibility that infants in the current cohort systematically grew more slowly than their potential, even when their development was good. Smaller cohorts subjected to very precise nutritional care have been shown to exhibit more early weight loss and grow faster overall [32].

It is notable that, despite the association between weight gain and neurodevelopment, infants with normal development were much smaller at term-corrected age than an equivalent cohort of infants born at full-term, and they gained weight only slightly faster than the median. The growth trajectories in Fig. 4 demonstrate that weight gain in this cohort of normally developing infants was significantly slower than the healthy trajectory posited by Landau-Cringle and co-workers. There are several plausible theories to explain this effect. Firstly, the trajectories identified in the current paper may truly represent a growth pattern which is associated with normal neurodevelopment, and growth which complies with physiological theories is not required to optimise neurological outcome. It is important to note that growth patterns identified in this paper were conditioned purely on neurodevelopmental outcome, and other important outcomes such as cardiovascular health were not considered. There is some evidence that rapid growth after hospital discharge is associated with poorer later cardiovascular health, and it is plausible that faster weight gain during initial hospital care would prevent the need for such catch-up growth [33]. Secondly, the cohort used to develop these curves may not have met their full growth potential, limiting the maximal growth seen. Applying the approach used here to other cohorts who have overall greater growth may show that better neurodevelopmental outcomes are associated with faster growth than that seen in the current study. Finally, the neurodevelopmental follow-up data may have been insufficiently detailed to detect true developmental outcomes, and development could have been enhanced further by a different growth trajectory.

The method presented here provides a model to predict and present growth trajectories for infants based on their size and gestation at birth which are consistent with a cohort of infants with normal development at two years of life. This novel concept posits that growth may be monitored with a view to optimising outcome rather than basing growth expectations on fetal norms or physiological principles. However, such approaches can only form one element of a comprehensive care approach, which includes careful attention to all the causes of poor growth and especially to maintaining appropriate body composition and proportionality between different growth measurements. The most effective application of this method would require growth data from a large cohort of infants for whom comprehensive outcome data were available, ideally involving multiple body systems and monitoring outcomes later into childhood. Such data are not currently readily available, but the digitisation of health records, linkage with educational records and advances in the use of routine data may increase access to the kind of comprehensive follow-up data which would be required.

## Conclusions

Monitoring the growth of preterm infants is not as simple as it seems [19]. The method presented here provides a model for producing plausible target growth trajectories, conditioned on normal neurodevelopment and on size at birth in very preterm infants. Such an approach may form one element of improving the nutrition and growth of preterm infants. With the advent of bedside clinical information systems and ubiquitous computer access, these trajectories can be used to benchmark an infant's



**Fig. 4.** Centile lines from the female UK Newborn Infant Close Monitoring (NICM) growth chart for preterm infants (pink lines at 0.4th, 2nd, 9th, 25th, 50th, 75th, 91st, 98th and 99.6th centiles) [6] with projected growth trajectories for a girl born at 24 + 4 weeks gestation near the median birthweight: from the current study in black, from Landau-Cringle and coworkers [11] in green and the median growth curve of English infants in 2014–2018 in blue [22].

growth against a reference population to guide their nutritional care.

### Authorship declaration

No one eligible for authorship has been excluded from the list of authors.

### Ethical approval, study registration and permissions

This study received UK NHS Health Research Authority ethical approval via the Oxford A research ethics committee (ref: 20/SC/0073).

This study was sponsored by University Hospital Southampton NHS Foundation Trust (ref: CHI1013).

Use of the National Neonatal Research Database was approved by application to the Neonatal Data Analysis Unit, Imperial College London.

### Author contributions

Aneurin Young: Conceptualisation, Data curation, Formal analysis, Visualisation, Writing (original draft).

Tim Cole: Conceptualisation, Methodology, Supervision, Writing (review and editing).

James Ashton: Conceptualisation, Supervision, Writing (review and editing).

Mark Beattie: Conceptualisation, Supervision, Writing (review and editing).

Mark Johnson: Conceptualisation, Funding acquisition, Supervision, Writing (review and editing).

### Data sharing statement

All data used for this project are held by the UK National Neonatal Research Database (NNRD) and are available from the NNRD upon application.

### Declaration of Generative AI and AI-assisted technologies in the writing process

No generative AI or AI-assisted technologies were used in any way in conducting this study, analysing these data or preparing this manuscript.

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### Conflict of interest

Aneurin Young, Mark Johnson, R Mark Beattie and Tim J Cole declare no conflicts of interest. James Ashton is an SAB member for Orchard Therapeutics and is a member of the Personalisation of IBD Care Think Tank (sponsored by Takeda).

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2025.106551>.

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