Appendix H.4 — Evidence to Decision: Monitoring Nutrition and Growth

EtD 51. What is the definition of faltering growth that requires attention or nutritional intervention for preterm infants?

POPULATION:	Preterm infants
INTERVENTION:	What is the definition of faltering growth that requires attention or nutritional intervention
COMPARISON:	(no comparison)
MAIN OUTCOMES:	**Critical outcomes** Mortality Faltering growth/body composition Neurodevelopmental impairment Adverse effects Fully breastmilk feeding at hospital discharge **Important but not critical** Time to full enteral feeds Necrotising enterocolitis Sepsis: proven or suspected Duration of initial hospital stay Time to full sucking feeds Bronchopulmonary dysplasia Retinopathy of prematurity Anaemia of prematurity Cost: cost of intervention, cost of neonatal care and life-long cost
SETTING:	Neonatal care
PERSPECTIVE:	Clinical recommendation
BACKGROUND:	Whilst growth is considered a critical measure of preterm infant progress and development, faltering growth is poorly defined with significant variation in definition, method of assessment, and threshold for intervention. Evaluating the evidence in relation to defining faltering growth is important to establish a consensus definition to guide clinical practice.
CONFLICT OF INTERESTS:	The following authors of the secondary analysis within a RCT (Nyakotey *et al) are guideline group members:* Barbara Cormack and Frank Bloomfield

Assessment

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	There is no direct evidence to answer this clinical question. We provide a narrative summary of some additional supporting evidence. **Growth assessment** Serial measurements of weight, length and head circumference and knowledge of expected growth patterns are crucial for making accurate growth assessments in preterm infants. Z-scores and changes in z-scores are useful for standardising and quantifying infants' sizes, losses and growth, and for determining at which threshold faltering growth is associated with adverse outcomes. **Expected growth patterns** ESPGHAN [1] and the American Academy Pediatrics [2] agree that after early postnatal weight loss, the best goal for preterm infant growth is growth similar to the fetus and then term-born infants, which translates to growth approximately parallel to growth chart curves. A large, international longitudinal observational study [3] reported that even infants with uncomplicated postnatal adaptation transitioned to a weight gain trajectory 0.8 z-scores below birthweight at day 21 after birth. Maximum weight loss was 11% for infants with gestational age of 25-29 weeks and 7% for those between 30-34 weeks' gestation. This means that if an infant loses weight, as expected after birth, and then grows parallel to the growth chart, their weight z-score will be **0.8 z-score below their birth z-score**, which may also apply to their length and head circumference. If an infant's growth is slower than growth chart curves, further investigation is needed to explore nutrition, morbidity, intrauterine or genetic reasons, with the actions required depending on the cause [4,5]. **Existing consensus faltering growth/malnutrition criteria** 1. **American Academy of Dietetics:** Consensus faltering growth/malnutrition criteria for preterm infants or neonates up to age 1 month were developed by eight experienced neonatal dietitians [4]. They proposed:	**Evidence of benefit from nutrition and growth studies** A systematic review of 6 clinical trials by Ong [7] showed consistent positive associations between postnatal weight or head growth and neurodevelopmental outcomes. For ELBW infants, achievement of head circumference **z-score ≥-2 by term-equivalent age** is associated with better cognitive outcome at 5.5 years of age when compared with those with a head circumference z-score <-2 [8]. For preterm infants, head circumference growth is more closely related to neurodevelopment than weight gain [9,10]. In VLBW infants assessed at **25 years of age,** it was found that, after adjustment for demographic factors and neonatal complications, only **faster head circumference growth between birth and term-corrected age** was significantly associated with improvements in IQ and its components, performance and verbal IQ, with effect sizes ranging between 0.33-0.42 standard deviations per z-score increase in head growth [11]. There were no statistically significant associations with faster weight or length growth. Aotearoa New Zealand: Secondary analysis of RCT [12]: Extremely low birthweight infants (n=327). Canada: Cohort study [3]: Gestational age 25-29 weeks and 30-34 weeks (n=981).

Table 1. Primary indicators of neonatal malnutrition

Indicator	Mild malnutrition	Moderate malnutrition	Severe malnutrition	Use of indicator
Primary indicators requiring 1 indicator				
Decline in weight-for-age *z* score[a]	Decline of 0.8-1.2 SD[b]	Decline of >1.2-2 SD	Decline of >2 SD	Not appropriate for first 2 wk of life
Weight gain velocity[a]	<75% of expected rate of weight gain to maintain growth rate	<50% of expected rate of weight gain to maintain growth rate	<25% of expected rate of weight gain to maintain growth rate	Not appropriate for first 2 wk of life
Nutrient intake	≥3-5 consecutive days of protein/energy intake ≤75% of estimated needs	≥5-7 consecutive days of protein/energy intake ≤75% of estimated needs	>7 consecutive days of protein/energy intake ≤75% of estimated needs	Preferred indicator during the first 2 wk of life
Primary indicators requiring 2 or more indicators				
Days to regain birth weight	15-18	19-21	>21	Use in conjunction with nutrient intake
Linear growth velocity[a]	<75% of expected rate of linear gain to maintain expected growth rate	<50% of expected rate of linear gain to maintain expected growth rate	<25% of expected rate of linear gain to maintain expected growth rate	Not appropriate for first 2 wk of life May be deferred in critically ill, unstable infants Use in conjunction with another indicator when accurate length measurement available
Decline in length-for-age *z* score[a]	Decline of 0.8-1.2 SD	Decline of >1.2-2 SD	Decline of >2 SD	Not appropriate for first 2 wk of life May be deferred in critically ill, unstable infants Use in conjunction with another indicator when accurate length measurement is available

[a]Expected weight gain velocity, expected linear growth velocity, and *z* scores can be determined using the online calculator PediTools (www.peditools.org).
[b]SD=standard deviation.

2. **NICE Recommendations:** The National Institute for Health and Care Excellence (NICE) published recommendations in 2017 on a similar question to ours for *term infants* [6].
Consider using the following as thresholds for concern about faltering growth in infants and children (a centile space being the space between adjacent centile lines on a growth chart):
a fall across 1 or more weight centile spaces, if birthweight was below the 9th centile
a fall across 2 or more weight centile spaces, if birthweight was between the 9th and 91st centiles
a fall across 3 or more weight centile spaces, if birthweight was above the 91st centile
current weight is below the 2nd centile for age, whatever the birthweight

The 10th percentile in a growth chart equates to a z score of -1.28 points. The 90th percentile also corresponds to a z-score of 1.28 points.

Undesirable Effects

How substantial are the undesirable anticipated effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	Research indicates a link between faltering growth in preterm infants and subsequent neurodevelopment up to age 19 years [4,5]. **Evidence from observational studies** In a cohort born at <28 weeks' gestation [13] tested the predictive performance of 36-week gestational age weight measures <10th percentile, <3rd percentile, >1 z -score loss from birth and >2 z-scores loss from birth. Only a **loss of >2 z-scores for weight related to adverse neurodevelopmental outcomes** at 18-24 months CA. A secondary analysis within a RCT [12] examined associations between faltering growth and neurodevelopment in Aotearoa New Zealand and Australian extremely low birthweight infants. Faltering growth was defined as a **z-score decrease ≥0.8 for weight/length, >1 for head circumference** between birth, 4 weeks', 36 weeks' postmenstrual age and 2 years' corrected age. **Faltering growth in all measures between 4–36 weeks** (OR 2.0–4.7) compared with other time intervals (OR 1.7–2.7) **were more strongly associated with developmental delay, particularly motor delay (OR 2.0–4.7)** but faltering growth was poorly predictive of developmental delay at 2 years (AUC ≤ 0.62). In 168 VLBW infants [14] reported **every 1-point loss in weight z-score to 36 weeks** was associated with a 5.6 point (95% CI 1.7 to 9.4) decrease in the Bayley- II Mental Development Index. However, a **weight z-score <−1.5 at 36 weeks was not associated with a worse mental or psychomotor result.** In a USA cohort study [15], infants who **lost >1 z-score for length from birth to discharge or 120 days** had no difference in Bayley-III cognitive scores but had **lower Bayley-III language scores.** In summary, several studies have observed associations between losses of z-scores in neonatal care with suboptimal neurodevelopment [7,10,14,16,17]. Single studies that examined associations between z-score losses and neurodevelopmental outcomes found that losses of **>1 z-scores for head circumference** [10,17,18], **weight [19] or length** [20] **or >2 z-scores for weight** [21,22] were predictive. However, determining an appropriate z-score loss guideline that requires nutrition intervention requires further validation.	Over diagnosing faltering growth could lead to overfeeding preterm infants, which could increase their risks for obesity and cardiovascular disease in later life, doubt among practitioners about the adequacy of current preterm infant nutrition recommendations and damaging messages to parents about their infant's growth. If parents are told that their infant has faltering growth, distress on the part of parents could lead to discontinuing breastmilk feeding and possibly to inappropriate nutrition intervention. Nutrition intervention to limit perceived faltering growth, e.g. decrease of <0.8 z-scores from birthweight after the first 21 days after birth, especially if this involves increasing energy intake without the addition of protein and other nutrients. This type of intervention may not be beneficial because increasing fat mass without increasing fat-free mass may be harmful for later cardiovascular health outcomes.

Certainty of evidence

What is the overall certainty of the evidence of effects?		
JUDGEMENT	**RESEARCH EVIDENCE**	**ADDITIONAL CONSIDERATIONS**
○ Very low ○ Low ○ Moderate ○ High ○ No included studies	No included studies	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ● Possibly important uncertainty or variability ○ Probably no important uncertainty or variability ○ No important uncertainty or variability	Possibly important uncertainty or variability	

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison ○ Probably favours the intervention ○ Favours the intervention ○ Varies	**Definition of faltering growth that requires attention or nutritional intervention - moderate certainty evidence** Until there is a clearer definition of when nutritional intervention is required with faltering growth in preterm infants, it is reasonable to use the recommendations suggested by (Goldberg et al., 2018) [4]and NICE to screen for and characterise faltering growth.	Head circumference growth may be more important than weight or length growth for neurodevelopment

○ Don't know		

Resources required

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	Negligible costs and savings	

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies	No studies were identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favour the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favours the comparison ○ Probably favours the comparison ○ Does not favour either the intervention or the comparison	No included studies	

○ Probably favours the intervention ○ Favours the intervention ○ Varies ● No included studies		

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	**Equity for Māori** Preterm pēpi Māori are more likely to experience challenges that contribute to faltering growth, due to the cumulative impact of social determinants of health, including colonisation, racism, income inequality, education, employment and housing. These factors may affect access to antenatal care, the quality of postnatal nutrition, breastfeeding support and continuity of care after discharge. Whānau Māori may face systemic barriers to timely identification and response to growth concerns, particularly if definitions are inconsistently applied or not communicated clearly. A lack of culturally grounded engagement can delay trust and limit opportunities for early intervention. A clear, equitable and nationally consistent definition of faltering growth is critical to ensuring that pēpi Māori receive timely and appropriate nutritional support. **Equity for Pacific families** Pacific infants are overrepresented in the preterm population and may be at greater risk of growth faltering due to overlapping clinical and social vulnerabilities. These include higher rates of early hospital discharge, limited culturally relevant post-discharge support and variability in how growth concerns are identified or addressed. Standardising the definition of faltering growth that requires intervention, alongside culturally appropriate engagement, can support equitable recognition and management of growth issues for Pacific infants. **Equity for underrepresented groups** Indian infants and infants from other underrepresented groups (including Middle Eastern and Asian backgrounds) are increasingly present in the preterm population in Aotearoa New Zealand. Risk factors for faltering growth may be compounded by language barriers, low health literacy, cultural food practices (such as vegetarianism or veganism) and limited familiarity with the New Zealand health system. Migrant, refugee and rural families may not consistently receive timely explanations or follow-up regarding growth patterns, particularly if the definition of faltering growth is not well understood across settings. An inclusive, clearly defined approach to identifying faltering growth is essential to enable consistent nutritional care and empower all families to participate meaningfully in their	

	infant's growth and care planning.	

Acceptability
Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	Nutrition intervention when there is faltering growth - probably yes	

Feasibility
Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ○ Varies ○ Don't know	Nutrition intervention when there is faltering growth - yes if there is a neonatal dietitian	

Summary of judgements

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	**Possibly important uncertainty or variability**	Probably no important uncertainty or variability	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	**Low**	Moderate	High			No included studies
COST EFFECTIVENESS	Favours the comparison	Probably favours the comparison	Does not favour either the intervention or the comparison	Probably favours the intervention	Favours the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

Type of recommendation

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
○	○	○	●	○

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Back to question list