

# How quickly should we aim for full milk feeds?



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Every year in the UK around 8,000 infants are born so prematurely that they cannot initially be fed nutritional volumes of milk and require intravenous nutrition. Milk feeding is then gradually increased as the immature gut begins to tolerate milk, and intravenous nutrition is correspondingly reduced. There is, however, little evidence to guide clinicians on how quickly this is best achieved<sup>1</sup>.

One of the most serious complications of intravenous feeding is late onset sepsis, which occurs in 27% of babies born weighing less than 1,500g at birth or under 29 weeks' gestation<sup>2</sup>. It is also known to cause poor long-term cognitive

outcomes, liver damage and sudden death from cardiac problems resulting from misplaced catheters<sup>3-5</sup>. One of the commonest late onset infections is 'catheter-related bloodstream infection'; the risk of which is directly related to the time the catheter is present in the blood stream<sup>6-8</sup>. While infection-control and catheter-management bundles have successfully reduced rates, they have not yet eliminated such infections<sup>9-11</sup>. In order to further reduce infection rates, there is a need to identify methods to reduce exposure to parenteral nutrition (PN).

It can be anticipated that more rapid advancement of enteral feeds will, in principle, cause infants to reach full milk feeds (tolerating 150mL/kg/day) a few days earlier than slower advancement. In the Speed of Increasing milk Feeds Trial (SIFT), the intention is to reduce exposure to parenteral nutrition and catheters by an estimated four days per infant, equating to 1,000 catheter days in 250 infants. This is possibly an underestimate of the reduction, since infection risk increases with the length of time a catheter is in place<sup>12,13</sup>.

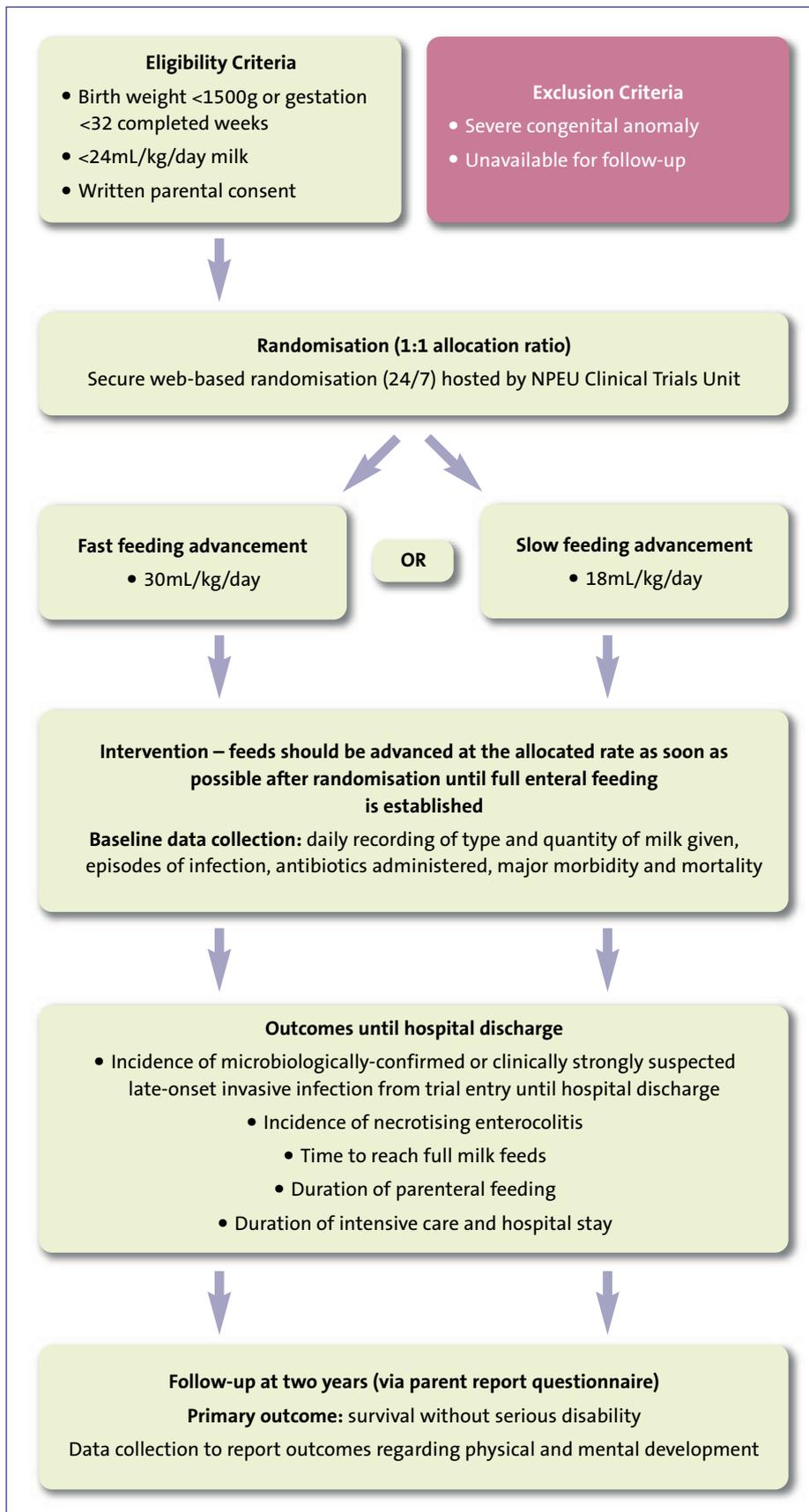
Potential benefits must, however, be confirmed in a clinical trial as faster increases in milk feed volumes may be countered by an increase in the likelihood of a serious bowel infection known as necrotising enterocolitis (NEC). This condition, aside from being potentially fatal, may provoke gut intolerance resulting in *longer* times to achieve full feeds rather than shorter.

The Cochrane review of studies examining rates of feed increase was updated in March 2011<sup>1</sup>. It included 496 infants from four trials, which all showed a reduction in time to full feeds of between two and five days in the faster increase groups, clearly demonstrating that this intervention could feasibly affect late onset sepsis. Unfortunately, none of the studies reported the effect on infection or long-term outcomes, nor were they powered to assess any effects on NEC. This proposed study will use survival without serious disability at two years of age as the primary outcome and will also evaluate the effect on key short-term outcomes including sepsis, NEC, growth and resource utilisation.

The 'SIFT' trial will be a multi-centre randomised controlled trial to assess whether the speed of increasing milk feed volumes, fast increase (30mL/kg/day) vs slow increase (18mL/kg/day), in very low birthweight infants (under 1,500g at birth) or significantly preterm infants (born before 32 weeks' gestation) has any

<b>Trial design</b>	Multicentre, randomised controlled trial, 2500 participants, duration 72 months
<b>Trial participants</b>	Infants who are either (i) very preterm (<32 weeks) or (ii) very low birth weight (<1500g)
<b>Inclusion criteria</b>	<p>Infants will be eligible to participate if:</p> <ul style="list-style-type: none"> <li>■ Gestational age at birth &lt;32 weeks, or &lt;1,500g birthweight</li> <li>■ The infant is receiving &lt;24mL/kg/day of milk at randomisation</li> <li>■ Written informed consent is obtained</li> </ul> <p>To ensure the widest applicability to preterm infants across the UK we will include those exclusively breast milk fed, formula milk fed, or receiving mixed feeds.</p>
<b>Exclusion criteria</b>	<ul style="list-style-type: none"> <li>■ Infants with severe congenital anomalies</li> <li>■ Infants who, in the opinion of the treating clinician, have no realistic chance of survival</li> <li>■ Infants who are unlikely to be traceable for follow-up at 24 months of age (eg infants of non-UK residents)</li> </ul>
<b>Follow-up duration</b>	Participants will be followed up at two years of age via a parent report questionnaire.
<b>Objectives</b>	<p>To assess and compare the effects of a fast (30mL/kg/day) and a slow (18mL/kg/day) increase in milk feed volumes in very low birthweight (&lt;1,500g at birth) or significantly preterm (born before 32 weeks) infants with respect to:</p> <ol style="list-style-type: none"> <li>1. survival without serious disability at 24 months of age corrected for prematurity</li> <li>2. the incidence of invasive nosocomial infection before hospital discharge</li> <li>3. the time taken to reach full milk feeds (tolerating 150mL/kg/day)</li> <li>4. growth (weight and head circumference)</li> <li>5. duration of parenteral feeding</li> <li>6. length of time in intensive care</li> <li>7. length of hospital stay</li> <li>8. the incidence of necrotising enterocolitis</li> </ol>

**FIGURE 1** Summary of the SIFT trial.



**FIGURE 2** Study flow diagram: the ‘SIFT’ trial for very preterm or VLBW infants.

effect on survival without serious disability at 24 months of age (corrected for prematurity). Further information is provided in the summary and flow diagram (FIGURES 1 and 2).

The trial (subject to a contract being agreed between NIHR HTA and University of Oxford) will recruit 2,500 infants from approximately 30 neonatal units within the UK and Ireland over three years commencing in the first few months of 2013.

**References**

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