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## Faster growth comes with increased risks of severe bowel problems when using formula rather than donor breast milk in preterm or low birth weight infants

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### Question

Does feeding preterm or low birth weight infants with formula rather than donor breast milk affect digestion, growth or the risk of severe bowel problems?

### Context

In preterm and low birth weight infants, enteral feeding with the mother's own breast milk is recommended. However, when a mother's own breast milk is not available or insufficient, infant feeds can be supplemented or replaced with formula or donor breast milk. Artificial formula is thought to have a more stable consistency and to contain more nutrients than donor breast milk, but could be harder to digest for the infants. Donor breast milk on the other hand may deliver some immunoprotective and growth factors to the immature gut mucosa of the infants which might prevent necrotising enterocolitis and serious gut infections. This donor breast milk is, however, expensive and is thought to sometimes lack the necessary nutrients for growth and development.

### Criteria for study selection

The Cochrane review included trials comparing enteral feeding of formula versus donor breast milk in preterm (<37 weeks' gestation at birth) or low birth weight (<2500g) infants. The formula or donor breast milk could be a supplement to maternal breast milk or could form the sole diet. The main outcomes reported by the review were short-term and long-term growth, death and neurodevelopmental outcomes including severe neurodevelopmental disability, neurodevelopmental scores in children of at least 12 months of age and cognitive and educational outcomes in children over 5 years old.

### Summary of the results

The review included eleven randomized controlled trials and one quasi-randomised trial. The twelve trials with a total of 1879 infants were all conducted in neonatal units in Europe or North America. The donor breast milk was pasteurised in all but one trial. Four trials compared term formula to donor breast milk and eight trials compared nutrient-enriched preterm formula to donor breast milk. Five trials used breast milk from women who had delivered at term, one trial used preterm donor milk and another used a combination. Five trials did not specify the type of donor breast milk. Four trials, all performed after 2000, used donor breast milk with multinutrient fortifier.

Infants receiving formula had higher rates of weight gain (mean difference: 2.51 g/kg/day higher (95% CI 1.93-3.08); 1028 infants, 9 studies, moderate-certainty evidence), linear growth (mean difference: 1.21 mm/week higher (95% CI 0.77-1.65); 820 infants, 8 studies, moderate-certainty evidence) and head growth (mean difference: 0.85 mm/week higher (95% CI 0.47-1.23); 894 infants, 8 studies, moderate-certainty evidence). The meta-analyses contained high levels of heterogeneity for the effect estimates and this lowered our confidence in the effect estimate. Post-hospital discharge growth was measured in only two trials but did not show differences in weight, length or head circumference at 9 months, 18 months or 7.5 to 8 years post-term. There is also no evidence of an effect on mortality (donor breast milk: 86 per 1000 vs formula: 94 per 1000 (95% CI: 69-128); 1527 infants, 7 studies, moderate-certainty evidence) or the prevalence of neurodevelopmental disability (donor breast milk: 73 per 1000 vs formula:

88 per 1000 (95% CI: 45-171); 400 infants, 2 studies, moderate-certainty evidence). The number of infants developing necrotising enterocolitis was higher when formula was used compared to donor breast milk (donor breast milk: 36 per 1000 vs formula: 67 per 1000 (95% CI: 44-102); 1675 infants, 9 studies, moderate-certainty evidence).

### Conclusion

Feeding preterm or low birth weight infants with formula compared to donor breast milk, either as a supplement to maternal breast milk or as the sole diet, probably increases short-term growth rates. However, it probably makes little or no difference to long-term growth, survival and neurodevelopment. Using formula compared to donor breast milk probably leads to an increase in infants with necrotising enterocolitis.

### Implications for practice

The evidence shows that using formula compared with using donor breast milk leads to faster in-hospital growth in preterm and low birth weight infants, but is also associated with a near-doubling of the risk of developing necrotising enterocolitis. Only a few of the trials included in the review compared using formula with using nutrient-fortified donor breast milk. As the fortification of donor breast milk has become standard practice, this does limit the implications for practice from this review. The inclusion of several ongoing trials in future updates will generate more precise effect estimates and strengthen the applicability of the data for practice.

### REFERENCE:

Quigley M, Embleton ND, McGuire W. Formula versus donor breast milk for feeding preterm or low birth weight infants. Cochrane Database of Systematic Reviews 2019, Issue 7. Art. No.: CD002971.

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<sup>^</sup> CI: confidence interval