

Emerging Evidence for Amino Acid Formula Containing Synbiotics in the Management of Infants with Cow's Milk Allergy



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The proposed role of synbiotics in the management of cow's milk allergy

Cow's milk allergy (CMA) is one of the most common food allergies in infants. When exclusive breastfeeding is not possible, guidelines recommend hypoallergenic formula as part of clinical management.¹ Gut dysbiosis is common in CMA and has been associated with its development,^{2,3} and an elevated risk of developing additional allergies in later life.⁴ In light of these findings, the gut microbiome has been identified as a therapeutic target in the clinical management of CMA.⁵ This has led to the development of hypoallergenic formula containing synbiotics (a synergistic mixture of pre- and probiotics). This article summarises the emerging clinical and real-world evidence of the use of amino acid formula (AAF) containing synbiotics (AAF-Syn) in the management of formula fed infants with CMA.

Evidence from robust clinical trials suggests AAF-Syn could improve clinical outcomes

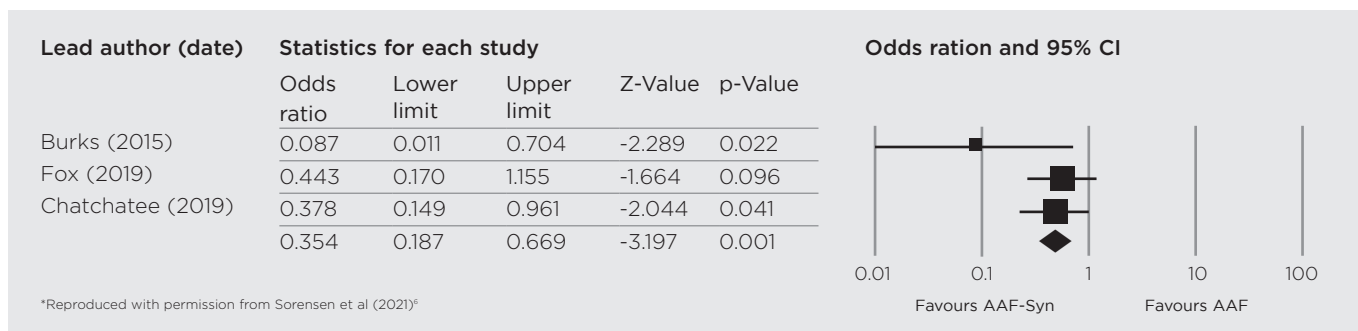
A systematic review and meta-analysis published in 2021 collated the findings from four randomised controlled trials (RCTs) comparing the clinical outcomes of infants with CMA who received either AAF-Syn or AAF.⁶ Both formulas were effective in managing allergic symptoms and promoting normal growth. Compared to AAF, AAF-Syn was associated with:⁶

- Significantly fewer infections (**Figure 1**).

- 55% reduction in the number of infants requiring antibacterial or antibiotic medications.
- 78% reduction in the number of infants requiring gastrointestinal (GI) medications.
- 69% reduction in the number of infants requiring emollients or dermatological medications.
- 56% reduction in hospital admissions, with potential cost savings.

These clinical benefits were attributed to changes in the gut microbiome observed with AAF-Syn, which was closer to that found in healthy breast-fed infants.⁶

Figure 1: Forest plot displaying results of a meta-analysis of three RCTs showing significantly lower rates of infection with AAF-Syn vs. AAF.*



Are these benefits being observed in clinical practice across the U.K.?

In a recent GP database study, data were extracted from The Health Improvement Network (THIN, A Cegedim Proprietary Database)⁷ for infants with CMA prescribed either AAF-Syn or AAF. In line with findings from clinical trials, compared with infants prescribed AAF, infants who were prescribed AAF-Syn experienced:⁸

- Significantly fewer infections (-35%),
- Significantly fewer medication prescriptions (-19%),
- Lower rates of clinical symptoms (-37%),
- Being free of CMA symptoms and no longer requiring a hypoallergenic formula 31% sooner (1.35 years vs. 1.95 years, see **Figure 2**).

As a result of these clinical benefits, the use of AAF-Syn was found to be associated with potential cost savings of £452.18 per infant over the clinical course of symptoms.⁸

Similar findings were reported in a survey of 20 HCPs (10 dietitians and 10 GPs) who prescribed AAF-Syn as part of their clinical management of CMA, and 10 parents of infants recently prescribed AAF-Syn.^{9, 10} Upon initiation of AAF-Syn, survey respondents observed:^{9, 10}

- Reductions in the incidence of infections, medication prescriptions and visits to the GP surgery or hospital amongst infants (**Figure 3**).
- Symptom improvement (observed by 100% of HCPs and 89% of parents).
- Improved sleep of child (observed by 70% of parents).
- Improved quality of life (QoL) of infants and their families (observed by 100% of HCPs and parents).

Perhaps most importantly, 100% of HCPs agreed that AAF-Syn made the management of CMA easier.^{9, 10}

Summary and take-away messages

The evidence from both clinical trials and real-world studies of infants with CMA suggest that an amino acid formula containing synbiotics may be associated with significantly improved clinical outcomes, reduced healthcare use, and cost savings, with positive impacts on perceived quality of life for infants and families, and the ease of clinical management among HCPs.

Figure 2: The adjusted Cox proportional hazard regression model showing the decreased combined probability of symptom persistence and ongoing hypoallergenic formula prescription over time associated with AAF-Syn vs. AAF*

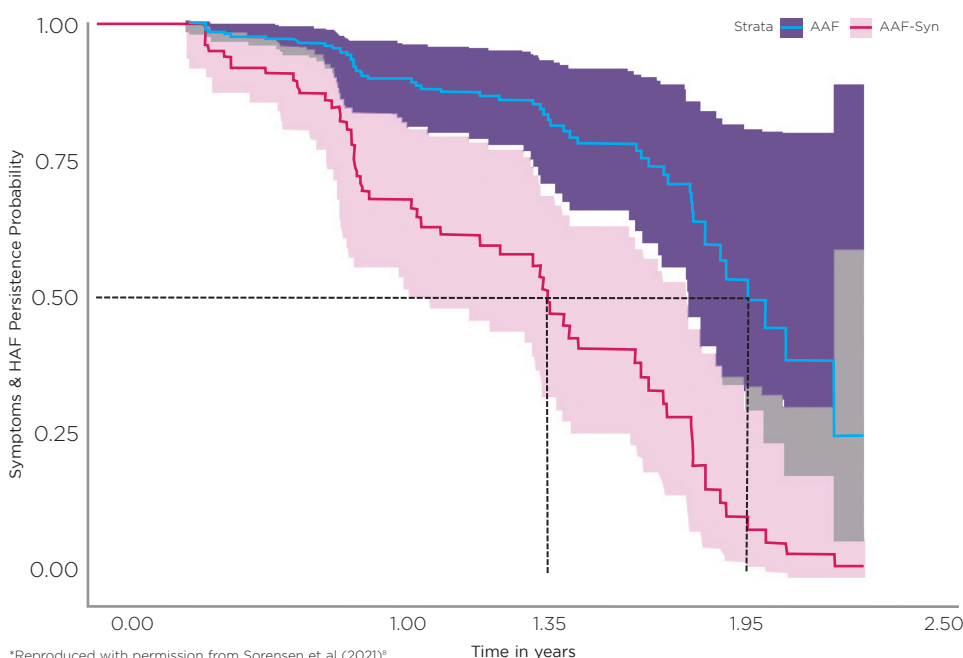
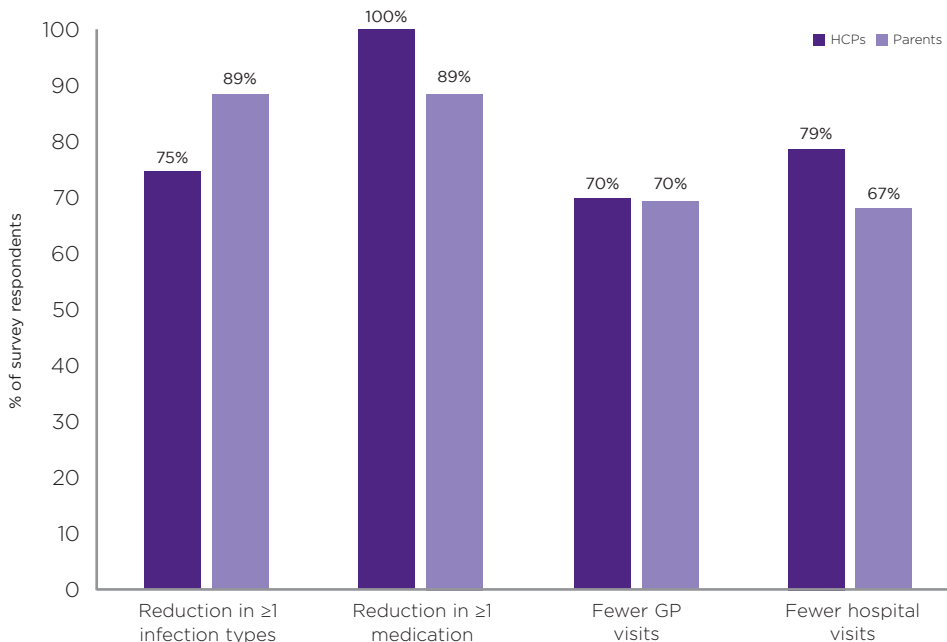


Figure 3: Percentage of survey respondents (HCPs and parents) observing a reduction in healthcare usage following initiation of AAF-Syn*



References: 1. Luyt D, et al. (2014). BSACI guideline for the diagnosis and management of cow's milk allergy. *Clin Exp Allergy*; 44 (5): 642-672. 2. Thompson-Chagoyan OC, et al. (2010). Changes in faecal microbiota of infants with cow's milk protein allergy—a Spanish prospective case-control 6-month follow-up study. *Pediatr Allergy Immunol*; 21(2 Pt 2): e394-400. 3. Shreiner A, et al. (2008). The "Microflora Hypothesis" of allergic disease. *Adv Exp Med Biol*; 635: 113-34. 4. Bisgaard H, et al. (2011) Reduced diversity of the intestinal microbiota during infancy is associated with increased risk of allergic disease at school age. *J Allergy Clin Immunol*; 128(3): 646-52. 5. Fox A, et al. (2019). The potential for pre-, pro- and synbiotics in the management of infants at risk of cow's milk allergy or with cow's milk allergy: An exploration of the rationale, available evidence and remaining questions. *World Allergy Organ J*;12(5): 100034. 6. Sorensen K, et al. (2021). Amino Acid Formula Containing Synbiotics in Infants with Cow's Milk Protein Allergy: A Systematic Review and Meta-Analysis. *Nutrients*; 13: 935. 7. Blak BT, et al. (2011). Generalisability of The Health Improvement Network (THIN) database: Demographics, chronic disease prevalence and mortality rates. *Inform Prim Care*; 19: 251-255. 8. Sorensen K, et al. (2021). The Use of an Amino Acid Formula Containing Synbiotics in Infants with Cow's Milk Protein Allergy—Effect on Clinical Outcomes. *Nutrients*; 13(7): 2205. 9. Kinnear FJ, et al. (2021). Insights into the Role of an Amino Acid Formula Containing Synbiotics in the Clinical Management of Infants with Cow's Milk Protein Allergy. *Complete Nutrition*; 21(3): 69-71. 10. Kinnear FJ, et al. (2021). Healthcare professional and parental survey exploring the effects of an amino acid formula containing synbiotics in the management of cow's milk allergy. E-poster at the Nutrition & Growth Congress 2021.