

# COST-EFFECTIVENESS OF USING AN EXTENSIVELY HYDROLYSED FORMULA COMPARED TO AN AMINO ACID FORMULA AS FIRST-LINE TREATMENT FOR COW MILK ALLERGY IN THE UNITED KINGDOM

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## INTRODUCTION

- Cow milk allergy (CMA) is an abnormal immune response to milk proteins [1], with an estimated incidence in infancy in western industrialised countries of 2-3% [2].
- Clinical nutrition preparations for infants with CMA include soy-based formulae, extensively hydrolysed formulae, such as Nutramigen, and amino acid formulae, such as Neocate.
- In the UK, clinical guidelines and protocols recommend that formula-fed infants <6 months of age are initially given an extensively hydrolysed formula (eHF) [3,4].
- An increasing proportion of infants are being initially prescribed an amino acid formula (AAF), which should be reserved for those who remain symptomatic after being fed an eHF or those with severe symptoms.
- This study estimated the cost-effectiveness of using an eHF (Nutramigen) compared to an AAF (Neocate) as a first-line treatment for CMA in the UK, from the perspective of the UK's National Health Service (NHS).

## METHODS

- **Study Population**
  - The Health Improvement Network (THIN) database is a nationally representative database of 5 million patients registered with general practitioners (GPs) in the UK.
  - The study population comprised all the patients in the THIN database (n=145) who were <1 year of age, were first diagnosed with CMA between 1 Jan 2003 and 31 Dec 2008, received a prescription for an AAF as their first formula for CMA, and had at least 12 months follow-up data from the initial GP visit.
  - The AAF-treated patients were matched with a randomly selected cohort of 150 eHF-treated patients from the THIN database.
  - Ethics approval for this study was obtained from The South West 1 Research Ethics Committee.
- **Health Economic Modelling**
  - Using the case records of the matched patients, a decision model was constructed depicting the treatment paths and

- associated resource use attributable to first-line management of CMA with the two formulae.
- Unit costs at 2008/09 prices [5-7] were assigned to the estimates of healthcare resource use in the model to determine the NHS cost of managing patients in both treatment groups.
- The measure of clinical effectiveness following treatment with either formula was the number of symptom-free weeks during the 12 months following the initial GP visit.
- The cost-effectiveness of using an eHF compared with an AAF was calculated as the difference between the expected costs of the two treatment strategies divided by the difference between the expected outcomes of the two strategies (i.e. the number of symptom-free weeks). If the number of symptom-free weeks was the same in both groups, the analysis would focus solely on costs, and the cheaper treatment strategy would be the preferred option.
- Sensitivity analyses tested the uncertainty of the results by changing the model's inputs.

## RESULTS

### Patient Characteristics

- Patients were well matched as there were no significant differences between presenting symptoms, weight at the time of starting diet and disease severity, using the incidence of reflux, failure to thrive and anaphylaxis as a proxy (Table 1).

	eHF	AAF
Gender (percent female)	51%	45%
Mean age and 95% confidence intervals (months)	2.62 (2.33; 2.91)	2.76 (2.44; 3.07)
Mean weight and 95% confidence intervals (kg)	4.42 (3.98; 4.86)	4.43 (3.91; 4.95)
Percent with eczema and gastrointestinal symptoms	44% (*6%)	44% (*6%)
Percent with gastrointestinal symptoms alone	39% (*3%)	39% (*3%)
Percent of patients with gastrointestinal symptoms who also had reflux	36%	46%
Percent with eczema alone	13% (*5%)	11% (*6%)
Percent with urticaria and other symptoms	4% (*2%)	5% (*2%)
Percent of patients with urticaria who had anaphylaxis	33%	50%

Table 1: Characteristics of CMA patients in the data set. \*Percent of patients in group who also had failure to thrive.

### Patient Management

- In both groups, it took a mean 2.2 months from initially seeing a GP before a patient received their first prescription for a formula (Table 2).

	eHF	AAF
Mean length of time between the first GP visit and starting a formula*	2.15 (1.76; 2.53) (months)	2.17 (1.77; 2.57) (months)
Patients' mean age at the time of starting a formula*	4.76 (4.28; 5.25) (months)	4.93 (4.45; 5.40) (months)
Patients' mean weight at the time of starting a formula*	5.53 (4.85; 6.21) (kg)	5.37 (4.51; 6.23) (kg)
Percent of patients remaining symptomatic after the initial formula*	26%	19%
Percent of patients prescribed a topical dermatological drug*	61%	62%
Percent of patients prescribed a gastrointestinal drug**	46%	59%
Percent of patients prescribed an antihistamine*	15%	14%
Percent of patients with anaphylaxis prescribed adrenaline (Epipen)*	76%	100%
Time to symptom resolution*	1.2 (0.5; 2.7) (months)	1.2 (0.5; 2.3) (months)

Table 2: Prescribed treatments to CMA patients in the THIN data set and outcomes. 95% confidence intervals in parentheses. \* p = ns; \*\* p < 0.03.

- There was no significant difference in the mean time to symptom resolution between the eHF and AAF groups (Table 2).
- There was no significant difference in the percent of patients remaining symptomatic after starting an eHF or AAF (26% versus 19% respectively).
- Of the eHF-treated patients who remained symptomatic, 9% were prescribed a different eHF, 25% a soy formula, 51% an AAF and 15% an antacid, H<sub>2</sub> receptor antagonist or proton pump inhibitor a mean 2 months after starting an eHF.
- All 19% of AAF-treated patients who remained symptomatic were prescribed either an antacid, H<sub>2</sub> receptor antagonist or proton pump inhibitor.

### Healthcare Resource Use Associated with Patient Management

Healthcare Resource	eHF	AAF
GP visits**	13.10 (12.53; 13.67)	17.54 (16.46; 18.63)
GP home visits*	0.28 (0.27; 0.29)	0.20 (0.19; 0.21)
Practice nurse visits*	0.06 (0.05; 0.07)	0.01 (0.00; 0.02)
Dietician visits*	0.22 (0.21; 0.23)	0.12 (0.11; 0.13)
Health visitor visits*	0.33 (0.31; 0.36)	0.18 (0.17; 0.19)
Outpatient visits (percent of patients)*	65%	59%
Outpatient visits*	1.62 (1.55; 1.69)	1.94 (1.83; 2.06)
Accident and emergency visits*	0.25 (0.23; 0.26)	0.27 (0.25; 0.29)
Hospital admissions*	0.17 (0.16; 0.18)	0.21 (0.20; 0.22)
Length of hospital stay (days)*	2.96 (2.27; 3.65)	2.48 (2.10; 2.87)
Diagnostic tests*	0.34 (0.32; 0.36)	0.52 (0.48; 0.55)

Table 3: Mean amount of healthcare resource use (per patient) associated with managing the CMA patients in the THIN data set in the 12 months following the initial GP visit. 95% confidence intervals in parentheses. \* p = ns; \*\* p < 0.0001.

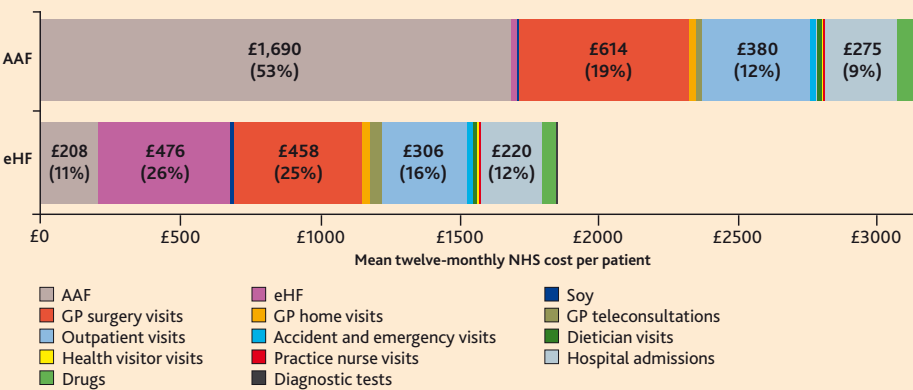


Figure 1: Distribution of twelve-monthly NHS costs (£ at 2008/09 prices) following initial presentation to a GP. (Percent of total cost is in parentheses.)

## DISCUSSION

- A review of published literature suggests this to be the first study assessing the cost-effectiveness of alternative treatments for CMA.
- The advantage of using the THIN database is that the treatment patterns and associated resource use were based on actual clinical practice, although patients were not randomised to the treatment they received and resource use, whilst collected prospectively, was analysed retrospectively.
- The results were censored at twelve months and excluded the costs and consequences of managing patients beyond this period. However, all infants in the study population were symptom-free by twelve months and most of them would have outgrown their allergy to cow milk by two years of age [8-10].
- Patients in the data set had to have a diagnosis of CMA, although the diagnosis may not be secure in all cases. Nevertheless, all patients were managed by their GP as if they had

- CMA. Hence, the estimates in this analysis were derived from actual cases and perceived cases of CMA. This is a reflection of actual clinical practice, and all patients became symptom-free during the year of follow-up after receiving a formula.
- There was no apparent reason why the AAF-treated patients in the data set started with this formula rather than an eHF. There was no significant difference in the distribution and severity of symptoms, age and body weight between the two groups. Accordingly, if patients in the AAF group had been initially treated with an eHF it would have resulted in 4.4 fewer GP visits per patient over the 12 months which could have been used by other patients with other conditions. This equates to 17,000 fewer GP visits when considering the estimated 19,900 newly-diagnosed infants with CMA in the UK per annum [2,11]. Clearly, improving GP education on managing CMA has the potential to increase the use of cost-effective interventions and release healthcare resources for alternative use within the system.

## CONCLUSION

- First-line treatment of newly-diagnosed infants with CMA with an eHF instead of an AAF affords a cost-effective use of NHS resources. Moreover, in the absence of published evidence showing superiority of one formula over the other, an eHF is the preferred first-line treatment in newly-diagnosed infants receiving their first formula, except in the most severe cases.

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