

ORIGINAL ARTICLE

Modelling the resource implications and budget impact of managing cow milk allergy in Australia

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Key words: Amino acid formula – Australia – Cost – Cow milk allergy – Extensively hydrolysed formula – Soy

ABSTRACT

Objective: To estimate the resource implications and budget impact of current clinical practice for managing cow milk allergy (CMA) in Australia, from the perspective of the publicly funded healthcare system.

Methods: A decision model was constructed using published clinical outcomes and clinician-derived resource utilisation estimates. The model was used to estimate the expected 6-monthly levels of healthcare resource use and corresponding costs attributable to managing 6150 new CMA sufferers following referral to a specialist.

Results: The expected 6-monthly costs of managing 6150 newly-diagnosed infants with CMA following referral to a specialist was an estimated (Australian dollars, AU\$) AU\$6.5 million at 2006/07 prices. Clinical nutrition

preparations were found to be the primary cost driver accounting for 62% of the total 6-monthly cost and clinician visits were the secondary cost driver accounting for up to a further 28% of the total 6-monthly cost. Sensitivity analysis showed there would be fewer visits to hospital-based paediatric gastroenterologists and paediatric immunologists/allergists if all newly-diagnosed patients were prescribed an amino acid formula (AAF) following referral to a specialist, instead of being managed according to current practice.

Conclusion: CMA imposes a substantial burden on the publicly funded healthcare system in Australia. However, using an AAF as the initial treatment for CMA can potentially release limited hospital resources for alternative use within the paediatric healthcare system.

Introduction

Cow milk allergy (CMA) is an immunologically-mediated adverse reaction to cow milk protein, with an estimated incidence in infancy of 2–3% in western industrialised countries^{1,2}. Symptoms generally appear within the first few months of life and can also occur in exclusively breast-fed infants. CMA presents with a broad range of syndromes either immediately or up to several days after milk ingestion^{3–5}. There are three types of allergic reactions to cow's milk: immediate, intermediate and delayed responses^{3–5}. In quick onset

(immediate) reactions^{3–5}, infants develop symptoms within minutes to 1 hour after ingestion of small volumes of cow's milk. These are typically acute IgE-mediated reactions and symptoms may include urticaria, eczema, facial swelling, vomiting, diarrhoea and wheeze. In severe cases, anaphylaxis may occur. In slow onset (intermediate) responses^{3–5}, infants may develop vomiting or diarrhoea several hours after ingestion of moderate amounts of cow's milk. In late onset (delayed) reactions^{3–5}, infants may develop eczema, vomiting, bloody stools, colic, diarrhoea or irritability after ~24 hours, or up to several days after ingestion of

normal volumes of cow's milk. These are generally T-cell mediated reactions. Most children will outgrow cow milk allergy by 2 years of age.

A correct diagnosis is critical and depends on appropriate immunological and morphological investigations. In all cases a diagnosis should be confirmed by observing remission of the symptoms following elimination of cow milk protein from an infant's diet. If the diagnosis remains uncertain, further confirmation should be obtained by observing relapse following challenge with cow milk protein. As a number of the conditions may remit with time, rechallenge with cow milk protein after a period of avoidance will be indicated in some cases.

Mothers of affected infants who are being breast-fed are advised to eliminate dairy products from their diet under the close supervision of a dietician, because a strict diet must be followed to ensure adequate intake of nutrients while eliminating cow milk protein. However, in practice, this is not always done. Clinical nutrition preparations for infants with CMA include soy-based formulas, extensively hydrolysed formulas (eHF) and amino acid formulas (AAF). Soy-based formulas contain proteins found in soybeans, but the same vitamins and minerals as those found in cow milk-based formulas⁶. Extensively hydrolysed formulas (eHF) contain milk proteins which have been pre-digested, making them less allergenic than the whole proteins contained in regular formulas⁷. Elemental formulas contain only amino acids in the absence of any protein and thus are not allergenic⁸⁻¹⁰. Partially hydrolysed formulas are not recommended for use in infants with CMA since they can provoke a significant allergic reaction¹¹.

An analysis of Australian prescribing practices¹² suggests that these formulas are not being prescribed in accordance with the Australian Pharmaceutical Benefits Advisory Committee (PBAC) guidelines¹³. Since November 2006, the PBAC guidelines recommend the use of eHF to those who have an intolerance to cow milk protein and AAF to those who have a combined intolerance to cow milk protein and eHF¹³.

Against this background, the aim of this study was to determine (1) how infants with CMA are managed in clinical practice in Australia, and (2) the resource implications and budget impact of managing CMA, from the perspective of the publicly funded Australian healthcare system.

Methods

Study objective

This study estimated how infants with CMA are currently managed in Australia and the associated resource

implications and budget impact. In Australia, hospital care is funded by individual State Governments, whereas community-based care is funded by the Federal Government (i.e., the Commonwealth). Hence, this study was conducted from the combined perspective of the States and Commonwealth of Australia.

Decision model

A decision model was constructed in TreeAge Pro 2007, depicting the treatment patterns and associated resource use attributable to managing newly-diagnosed infants < 1 year of age at the time of presentation with CMA following referral to a paediatric specialist (Figure 1). Within the model, infants are stratified according to whether they initially present with bloody stools, gastrointestinal symptoms, failure to thrive, eosinophilic oesophagitis, eczema, urticaria or anaphylaxis. The model was used to simulate the management of an annual cohort of new CMA sufferers over the first 6 months following referral to a specialist.

Model inputs – clinical outcomes

Based on the findings of an epidemiological study the authors have undertaken among 1000 infants < 1 year of age with CMA in the UK, it was estimated that 9% of infants would be intolerant to soy and 29% would be intolerant to eHF¹⁴.

Model inputs – resource use

The gaps in the published evidence base on healthcare resource use pertaining to managing CMA in Australia was estimated following a series of interviews with Australian clinicians. Fifteen paediatricians (three per State), ten paediatric gastroenterologists and ten paediatric immunologists/allergists with experience of managing CMA were identified and invited to participate in the study. All paediatricians who were contacted agreed to an interview. Three paediatric gastroenterologists declined because of lack of time ($n=1$), no interest in the study ($n=1$) or no longer managed infants with CMA ($n=1$). Two paediatric immunologists/allergists declined because of lack of time ($n=1$) or no interest in the study ($n=1$). Hence, the sample of interviewees comprised paediatricians ($n=15$), paediatric gastroenterologists ($n=7$) and paediatric immunologists/allergists ($n=8$) who were based in the following States: New South Wales, Queensland, Victoria or Western Australia. The interviews used a structured questionnaire and interviewees were asked objective questions about diagnosis, patient management, resource utilisation, use of prescribed

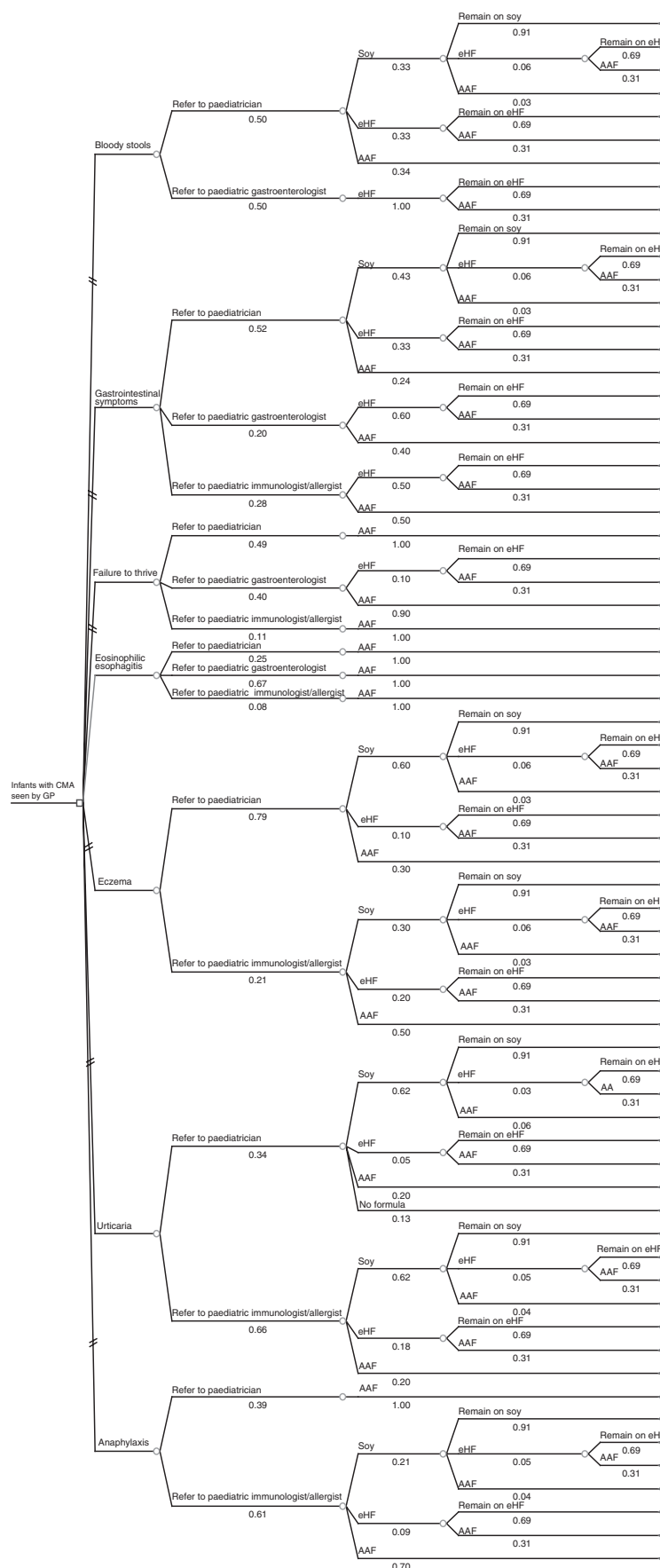


Figure 1. Decision tree depicting the management of infants < 1 year of age at the time of presentation with CMA, who require a clinical nutrition preparation following referral to a paediatric specialist. Breast-fed infants who are not prescribed a clinical nutrition preparation are not shown, since the treatment would be their mothers being placed on a cow's milk elimination diet. Numbers denote the probability of an infant following a particular path according to current practice

Table 1. Estimates of healthcare resource use incorporated into the model

	Estimated percent of patients using the following resources when managed by:		
	Paediatricians	Paediatric gastroenterologists	Paediatric immunologists/allergists
Initial diet for breast-fed infants			
Soy	0	0	0
EHF	1	6	6
AAF	19	25	19
Initial diet for bottle-fed infants			
Soy	41	0	15
eHF	20	59	31
AAF	39	41	54
Follow-up visits at			
1 month	35	48	62
3 months	44	57	15
6 months	65	65	61

clinical nutrition preparations, use of prescribed drugs and time to symptom resolution based on their own practice and not Pharmaceutical Benefits Scheme (PBS) criteria¹³.

According to the interviewees, all affected infants would initially be seen by their GP. Using information obtained from published literature¹⁵ and clinician interviews, the model assumes that GPs refer 50% of their CMA infants to a paediatrician, 32% to a paediatric gastroenterologist and 17% to a paediatric immunologist/allergist. Additionally, paediatricians subsequently refer 20% of their CMA referrals to a paediatric gastroenterologist and 20% to a paediatric immunologist/allergist.

The model also assumes that most breast-fed infants would continue to be breast-fed, although their mothers would be placed on a cow milk elimination diet. In some instances the infant would have their diet supplemented with eHF or AAF (Table 1). Use of clinical nutrition preparations for breast-fed and bottle-fed infants is summarised in Table 1. CMA sufferers who are intolerant to a particular formula would have a follow-up visit with their specialist to receive a prescription for an alternative formula. Those who are intolerant to soy have an 80% and 20% chance of being switched to an eHF and AAF, respectively by paediatricians. In contrast, paediatric gastroenterologists would generally switch all infants who are intolerant to soy to an eHF, whereas paediatric immunologists/allergists would generally switch 85% of infants to an eHF and 15% to an AAF. All clinicians would switch infants to an AAF if they are intolerant to an eHF. Notwithstanding this, based on information provided by the interviewees, the model assumes that 20% of infants presenting to a paediatrician with bloody

stools and 25% of those presenting with gastrointestinal symptoms would be initially treated with a proton pump inhibitor for 2 weeks before cow's milk was eliminated from the diet. Similarly, 99% of infants presenting to a paediatrician with eczema would be initially treated with moisturisers and steroid cream for 6–8 weeks before cow's milk was eliminated from the diet.

Infants can undergo a range of tests, and depending on the nature of the presenting symptoms these may include a RAST test, skin prick test, stool culture, urine culture, white blood cell/IgE count. In addition, two centres were also using patch tests. Those presenting with suspected eosinophilic oesophagitis are also expected to undergo an endoscopy.

The frequency of follow-up visits to each specialist is shown in Table 1. However, infants presenting to a paediatrician with failure to thrive, suspected eosinophilic oesophagitis or anaphylaxis would be referred either to a paediatric gastroenterologist or a paediatric immunologist/allergist and subsequently managed by that physician. Additionally, mothers of affected infants would only see a dietician as part of a clinic visit to 15% of paediatric gastroenterologists and 40% of paediatric immunologists/allergists.

According to the interviewees, all infants are expected to be on an appropriate clinical nutrition preparation and be symptom-free at 6 months after the initial referral.

Model outputs

The number of infants born per annum in Australia was estimated to be 246 000¹⁶. The estimated incidence of CMA among infants is 2.5%^{1,2}. Hence, the annual

Table 2. Unit resource costs at 2006/07 prices
(in Australian dollars, AU\$)^{13,17}

Resource	Unit cost (AU\$)
Amino acid formula (Neocate (400 g can))	46.40
Extensively hydrolysed formula (Pepti-Junior (450 g can))	13.25
Endoscopy	130.00
Faecal blood count	25.00
Faecal occult test	21.00
Follow-up dietician visit	31.90
Follow-up paediatric allergist/ immunologist visit	55.60
Follow-up paediatric gastroenterologist visit	55.60
Follow-up paediatrician visit	55.60
Initial dietician visit	63.85
Initial paediatric allergist/immunologist visit	111.05
Initial paediatric gastroenterologist visit	111.05
Initial paediatrician visit	111.05
RAST test	22.55
Skin prick test	36.00
Stool culture	18.00
Urine culture	18.00
White blood cell count	25.00

number of new CMA sufferers in Australia was estimated to be 6150 infants.

The model estimated the expected 6-monthly levels of healthcare resource use attributable to managing 6150 new CMA sufferers following referral to a specialist. National unit resource costs¹⁷ (Table 2), drug costs¹³ and costs of clinical nutrition preparations¹³ (Table 2) at 2006/07 prices were applied to the resource utilisation estimates within the model to estimate the expected 6-monthly healthcare costs following referral to a specialist, from the perspective of the publicly funded healthcare system. The cost of hospital-based outpatient visits was assumed to be reimbursed by individual State Governments, whereas the cost of community-based visits to paediatricians was assumed to be re-imbursed by Medicare, a Federal Government Agency. The costs of soy formulas were excluded from the analysis as these formulas are not listed on the PBS¹³.

Sensitivity analysis

Probabilistic sensitivity analyses were undertaken using Monte Carlo simulations (6150 iterations of the model) by simultaneously varying the probabilities, resource-use values and unit costs within the model. The probabilities were varied randomly according to a beta distribution by assuming a 20% standard deviation around the mean. The resource use estimates and unit

costs were varied randomly according to a lognormal distribution by assuming a 20% standard deviation around the mean. Large standard deviations were used to reflect the uncertainties surrounding the inputs of our model. Additionally, deterministic sensitivity analyses were performed to assess how the costs of current practice would change by varying different assumptions in the model (as described in Table 4).

Sensitivity analysis also assessed the budget impact of implementing two alternative treatment strategies:

- Strategy 1: Infants with suspected eosinophilic oesophagitis or failure to thrive are referred to a paediatric gastroenterologist and treated with an AAF. Infants with anaphylaxis are referred to a paediatrician and treated with an AAF. All other infants are initially referred to a paediatrician and initially treated with an eHF.
- Strategy 2: Infants with suspected eosinophilic oesophagitis or failure to thrive are referred to a paediatric gastroenterologist and all other infants are initially referred to a paediatrician. All infants are initially treated with an AAF.

Results

Resource implications and expected healthcare costs

Based on information obtained from published literature¹⁵ and the interviewees, the model estimated that 20% of CMA sufferers present with bloody stools, 39% with gastrointestinal symptoms, 5% with failure to thrive, 10% with eosinophilic oesophagitis, 11% with eczema without gastrointestinal involvement, 14% with urticaria and 1% with anaphylaxis. On the basis of this distribution of presenting symptoms, the expected 6-monthly healthcare cost per CMA infant managed according to current practice following the initial specialist visit was estimated to be (in Australian dollars, AU\$) AU\$1150 (95% CI AU\$966, AU\$1558). However, this varied according to the presenting symptoms. Probabilistic sensitivity analyses highlighted the differences in cost and time to symptom resolution between the different symptomatic groups.

Clinician visits collectively accounted for 40–50% of the 6-monthly cost of managing those presenting with bloody stools, gastrointestinal symptoms and eczema, but < 15% of the 6-monthly cost of managing those presenting with failure to thrive, eosinophilic oesophagitis and anaphylaxis (Table 3). Clinical nutrition preparations were found to be the primary cost driver in all symptomatic groups, except those presenting with eczema, accounting for between 51% (gastrointestinal symptoms) and 87% (anaphylaxis) of the total

Table 3. Expected 6-monthly costs (in Australian dollars, AU\$ at 2006/07 prices) per infant following referral to a specialist, stratified according to presenting symptoms. Percentage of total cost is in parentheses

	Expected 6-monthly cost (in AU\$ at 2006/07 prices) per infant presenting with:						
	Bloody stools	Gastrointestinal symptoms	Failure to thrive	Eosinophilic oesophagitis	Eczema	Urticaria	Anaphylaxis
Paediatrician visits	123.6	143.0	54.4	27.7	140.1	60.4	43.3
Paediatric immunologist/allergist visits	0.0	79.8	25.1	18.8	170.3	168.3	205.4
Paediatric gastroenterologist visits	141.4	88.3	281.9	310.2	0.0	0.0	0.0
Dietician visits	5.4	12.1	11.3	10.8	15.5	21.2	25.5
Clinical nutrition preparations	370.3	384.1	2219.5	2223.4	223.9	603.0	2188.0
Tests	15.4	48.7	73.0	367.1	41.1	46.2	42.7
Symptomatic drugs	2.6	3.4	0.0	158.9	31.7	0.0	0.0
TOTAL	658.8	759.5	2665.2	3117.0	622.5	899.2	2504.9
	(19%)	(19%)	(2%)	(1%)	(23%)	(7%)	(2%)
	(0%)	(11%)	(1%)	(1%)	(27%)	(19%)	(8%)
	(21%)	(12%)	(11%)	(10%)	(0%)	(0%)	(0%)
	(1%)	(2%)	(<1%)	(<1%)	(2%)	(2%)	(1%)
	(56%)	(51%)	(83%)	(71%)	(36%)	(67%)	(87%)
	(2%)	(6%)	(3%)	(12%)	(7%)	(5%)	(2%)
	(<1%)	(<1%)	(0%)	(5%)	(5%)	(0%)	(0%)
	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)	(100%)

6-monthly cost of managing an infant following referral to a specialist. Clinician visits were the primary cost driver among those presenting with eczema.

The length of time for a CMA sufferer to be put on an appropriate diet and achieve symptom resolution was estimated to be 12 (95% CI 6, 19) days. However, this varied according to presenting symptoms, ranging from as little as 7 (95% CI 2, 16) days for those presenting with bloody stools to 25 (95% CI 7, 45) days for those presenting with eczema (Figure 2).

Budget impact of managing CMA

The expected 6-monthly cost of managing 6150 newly-diagnosed infants with CMA following referral to a specialist was estimated to be AU\$6.5 million. Of this, clinical nutrition preparations were the primary cost driver accounting for 62–65% of the total 6-monthly cost and clinician visits were the secondary cost driver accounting for up to a further 28%.

Sensitivity analyses

Sensitivity analyses (Table 4) showed that the expected cost of current practice is very sensitive to the probability of an infant being breast-fed at the time of presentation. This is because the primary cost drivers are clinical nutrition preparations, and fewer breast-fed infants are likely to receive a formula compared to bottle-fed infants (See Table 1). Sensitivity analyses also showed the cost of current practice is more sensitive to the probability of being intolerant to eHF than to soy. This is because those who are intolerant to eHF are switched to AAF, which is a more expensive formula than eHF. Changing the probability of a mother seeing a dietician as part of a clinic visit to a paediatric gastroenterologist or immunologist/allergist has negligible effect on the expected cost of current practice. Hence, cost should not be an obstacle to proportionally more mothers seeing a dietician when visiting a paediatric gastroenterologist or immunologist/allergist or to dieticians participating in more paediatric clinics. Changing the frequency of follow-up visits to paediatric gastroenterologists or immunologists/allergists has a greater effect on the expected healthcare costs than changing the frequency of follow-up visits to paediatricians. However, no other changes to the model's inputs affected the expected cost of current practice.

Additionally, the length of time for a CMA sufferer to be put on an appropriate diet and achieve symptom resolution was not affected by changes to any of the model's inputs with the exception of (1) the probability of infants presenting to a paediatrician with bloody stools or gastrointestinal symptoms and being initially treated with a proton pump inhibitor for 2 weeks

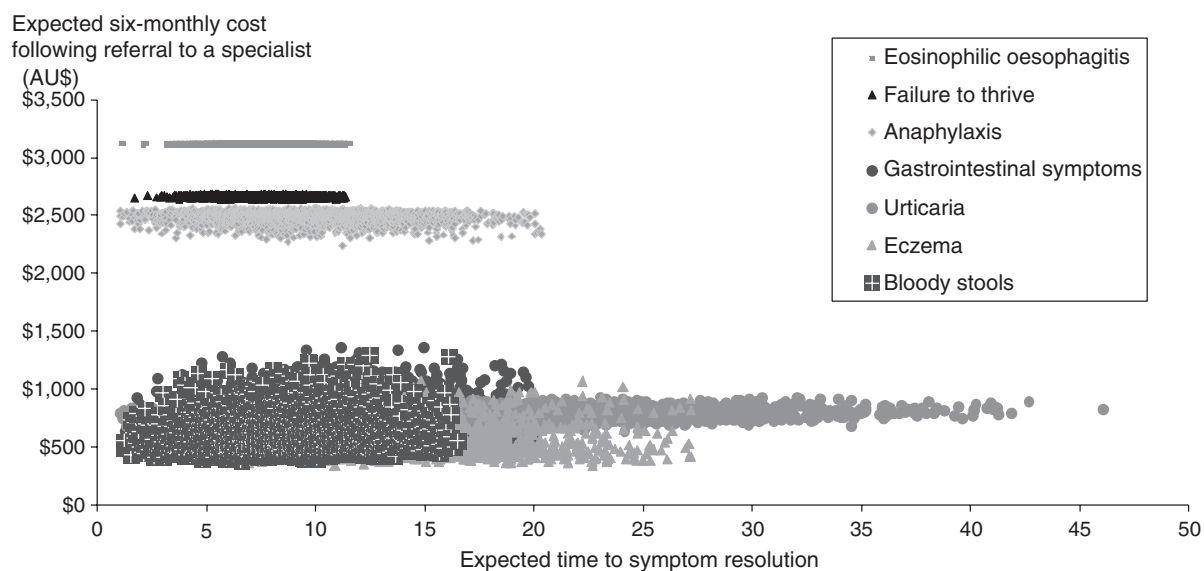


Figure 2. Distribution of expected costs (in Australian dollars, AU\$) and time to symptom resolution ($n = 2000$ iterations of the model) for each symptomatic group

Table 4. Sensitivity analyses

Scenario	Base case value	Healthcare cost (Australian dollars US\$)*
Probability of being intolerant to soy ranges from 5% to 25%	8%	6.5–6.6 million
Probability of being intolerant to eHF ranges from 5% to 35%	29%	6.3–6.5 million
Probability of newly-presenting infants being breast-fed ranging from 60 to 90%	80%	7.4–6.0 million
Probability of seeing a dietician as part of the clinic visit to a paediatric immunologist/allergist ranges from 0 to 1	0.4	6.5–6.6 million
Probability of seeing a dietician as part of the clinic visit to a paediatric gastroenterologist ranges from 0 to 1	0.15	6.5–6.6 million
Number of follow-up visits to a paediatric immunologist/allergist ranges from 50% below to 100% above the base case value	100%	6.4–6.7 million
Number of follow-up visits to a paediatric gastroenterologist ranges from 50% below to 100% above the base case value	100%	6.3–6.9 million
Number of follow-up visits to a paediatrician ranges from 50% below to 100% above the base case value	100%	6.3–6.8 million

*Expected range of 6-monthly healthcare costs (in AU\$ at 2006/07 prices) associated with treating an annual cohort of 6150 newly-diagnosed infants with CMA following referral to a specialist

before cow's milk was eliminated from the diet, and (2) the probability of infants presenting to a paediatrician with eczema and being initially treated with moisturisers or steroid cream for 6–8 weeks before cow's milk was eliminated from the diet.

Budget impact of alternative treatment strategies

Sensitivity analyses modelled the impact of treating 6150 newly-diagnosed infants with CMA following referral to a specialist with two other treatment strategies, as outlined below, instead of current practice.

Strategy 1 assumes that infants with suspected eosinophilic oesophagitis or failure to thrive would be referred to a paediatric gastroenterologist and treated with an AAF. Infants with anaphylaxis would be referred to a paediatrician and treated with an AAF. All other infants would be initially referred to a paediatrician and treated with an eHF. Those who are intolerant to an eHF would have a follow-up visit with their specialist to receive a prescription for an AAF. Additionally, none of those presenting with eczema or GI symptoms would be initially treated with topical dermatologicals or proton pump inhibitors, respectively. This strategy also assumes that the

range and frequency of tests and the frequency of follow-up visits with the relevant specialist would be as described for current practice.

Strategy 2 assumes that infants with suspected eosinophilic oesophagitis or failure to thrive would be referred to a paediatric gastroenterologist and all other infants would be initially referred to a paediatrician. All infants would be initially treated with an AAF and none of those presenting with eczema or gastrointestinal symptoms would be initially treated with topical dermatologicals or proton pump inhibitors, respectively. Since AAFs are hypoallergenic, this scenario assumes that none of the infants would be intolerant to this formula and therefore would not require additional follow-up visits to switch their diet. The range and frequency of tests and the frequency of follow-up visits with the relevant specialist would be as described for current practice.

The analyses found that the total 6-monthly cost of managing 6150 newly-diagnosed infants with CMA with either an eHF (Strategy 1) or an AAF (Strategy 2) following referral to a specialist were both an estimated AU\$7.1 million (Table 5).

Nevertheless, managing a newly-diagnosed cohort with an AAF (Strategy 2) following referral to a specialist is expected to result in fewer visits to hospital-based paediatric gastroenterologists and paediatric immunologists/allergists than the other treatment strategies (Table 6), because none of the infants on an AAF are expected to require follow-up visits to switch their diet. Nevertheless, initially treating all CMA infants with an AAF (Strategy 2) instead of current practice is expected to result in 10 300 additional visits to paediatricians, but 1400 fewer visits to paediatricians when compared to initially treating all CMA infants with an eHF (Strategy 2). Conversely, initially treating all CMA infants according to clinical practice or with an eHF is expected to result in more visits to hospital-based paediatric gastroenterologists and immunologists/allergists when compared to initially treating all CMA infants with an AAF.

Additionally, initially treating all CMA infants with an AAF is expected to reduce the length of time for a CMA sufferer to be put on an appropriate diet and achieve symptom resolution. This was estimated to be a mean 3 (95% CI 1, 5) days, ranging from as little as 1 day for those presenting with bloody stools to 7 days for those presenting with eczema.

Discussion

Food allergy represents an important source of patient morbidity and healthcare utilisation. Nevertheless, our

Table 5. Distribution of expected 6-monthly healthcare costs (in Australian dollars, AU\$ at 2006/07 prices) associated with treating an annual cohort of 6150 newly-diagnosed infants with CMA following referral to a specialist. Percentage of total cost is in parentheses

	Expected 6-monthly healthcare costs (in AU\$ at 2006/07 prices) associated with treating an annual cohort of 6150 newly-diagnosed infants with CMA following referral to a specialist according to:		
	Current practice	Strategy 1	Strategy 2
Paediatrician visits	678 589	1 325 044	1 244 048
Paediatric immunologist/allergist visits	479 058	289 931	253 359
Paediatric gastroenterologist visits	654 587	473 085	415 250
Dietician visits	75 294	46 874	40 666
Clinical nutrition preparations	4 034 990	4 439 773	4 599 063
Tests	452 137	440 353	422 351
Symptomatic drugs	130 724	96 826	96 826
TOTAL	6 505 378	7 111 886	7 071 564
		(100%)	(100%)
		(62%)	(65%)
		(7%)	(6%)
		(100%)	(1%)
		(2%)	(1%)
		(62%)	(65%)
		(1%)	(1%)
		(7%)	(6%)
		(4%)	(4%)
		(19%)	(18%)

Table 6. Expected number of 6-monthly clinician visits associated with managing a cohort of 6150 newly diagnosed infants with CMA following initial referral to a specialist

	Expected number of 6-monthly clinician visits associated with managing a cohort of 6150 newly diagnosed infants with CMA following initial referral to a specialist according to:		
	Current practice	Strategy 1	Strategy 2
Paediatrician visits	6 200	17 900	16 500
Paediatric immunologist/allergist visits	4 400	2 700	2 300
Paediatric gastroenterologist visits	6 000	4 400	3 800
Total number of hospital-based clinician visits	10 400	7 100	6 100

literature search did not find any health economic studies on CMA, apart from one previous study in Finland¹⁸. Hence, we believe this to be one of the first health economic studies on CMA.

The Australian PBAC guidelines recommend using an eHF as first-line treatment in those who have an intolerance to cow milk protein and an AAF in those who have a combined intolerance to cow milk protein and eHF¹³. However, our study suggests that these formulas were not being prescribed in accordance with the PBAC guidelines as an AAF was being used as a first-line treatment in more than 39% of infants presenting with the symptoms of CMA.

There are ~440 consultant general paediatricians in Australia and only ~30 consultant paediatric gastroenterologists and ~20 consultant paediatric immunologists/allergists¹⁹. Waiting times to see a paediatrician is only a matter of days, whereas there may be a delay of 3–6 months to see a paediatric gastroenterologist and 4–12 months to see a paediatric allergist. At the time of performing this study there were only two paediatric immunologists/allergists in Queensland and waiting times to see them was typically > 12 months. Hence, any treatment strategy that can reduce the number of visits to these two clinical specialties has the potential to increase the efficiency of paediatric healthcare delivery in publicly funded hospitals in Australia. Consequently we consider that treating new CMA sufferers with an AAF has the potential to afford health economic benefits to the paediatric healthcare system in Australia, since this strategy is expected to generate fewer visits to the ~50 consultant paediatricians specialising in gastroenterology and immunology/allergy in Australia's paediatric departments when compared to (1) current practice and (2) using eHF as the initial treatment, albeit for an additional cost.

There are approximately 2000 registered dietitians in Australia²⁰. However, less than 200 specialise in infant feeding, paediatrics, or maternal health²¹. Additionally, according to our interviewees, mothers of affected infants would only see a dietitian as part

of a clinic visit to 15% of paediatric gastroenterologists and 40% of paediatric immunologists/allergists. Consequently, access to a dietitian by a mother of affected infants is restricted. Hence, using an AAF in CMA infants should ease the pressure to see the limited number of dietitians who specialise in infant feeding, paediatrics, or maternal health.

In the aforementioned Finnish study¹⁸, the authors reported that Finland's Social Insurance Institution adopted new guidelines as the basis for reimbursing clinical nutrition preparations for the treatment of CMA. However, the guidelines had not been validated in clinical practice and were found to increase the use (and corresponding cost) of paediatric healthcare resources in Finland's public hospitals, which could have been used elsewhere within the system¹⁸. Clinical guidelines are systematically developed statements designed to help clinicians and patients make informed decisions about appropriate healthcare for specific circumstances²². The benefits of usable clinical guidelines enabling patients, practitioners, scientists and purchasers to make more informed decisions and share information more effectively has been well documented²³. However, before healthcare organisations adopt guidelines, they have an onus of responsibility to validate them and ensure they are clinically effective and cost-effective. Adopting recommendations from guidelines without appropriate validation can lead to a waste of resources²⁴. In 2007, consensus guidelines for the use of clinical nutrition preparations in managing CMA in Australia were developed by a panel of clinicians specialising in the management of infants with this allergy²⁵. However, based on our modelling of these guidelines, they are likely to require adaptation before they can afford health economic benefits to the paediatric healthcare system in Australia.

Our results may be confounded by certain limitations within the model. The rates of intolerance to soy and eHF were based on a 1-year follow-up epidemiological study among 1,000 infants with CMA who were managed in the community in the UK¹⁴ and not on

previously published rates which have been derived from studies undertaken in secondary care involving a sub-group of patients who had been referred to specialists, involving smaller sample sizes (typically 20–30 patients) and shorter periods of follow-up (typically 2–3 months). There was a lack of published data assessing healthcare resource use attributable to the management of CMA in Australia. Therefore, this was obtained retrospectively by interviewing 30 paediatricians with experience of managing CMA. Consequently, treatment patterns and associated healthcare resource use for the ‘average patient’ throughout Australia may not be the same as for those patients who are managed by this study’s interviewees. In particular, no clinicians from the Northern Territory were invited to be interviewed. Nevertheless, many of the key paediatric specialists involved in managing CMA in Australia have participated in this study. The inherent variability and uncertainty of using data from sources, other than that collected prospectively, is depicted by the Monte Carlo simulations. The period of the study is limited to 6 months following presentation to a paediatrician, and does not consider the impact of CMA beyond this period.

The model only considered resource use and corresponding costs for an ‘average patient’ and doesn’t take into account such factors as patient characteristics, disease severity, co-morbidities etc. The model estimated direct healthcare costs borne by the publicly funded healthcare system and not those borne by patients or society. The model excluded changes in quality of life and improvements in general well-being of sufferers and their parents as well as parents’ preferences. Also excluded are changes in patients’ behaviour. Consequently our study may have underestimated some of the impact of the treatment strategies that were evaluated.

The authors have also been estimating the budget impact of managing CMA in Finland¹⁸, the Netherlands, New Zealand, South Africa, UK^{14,26} and US. Based on these experiences, we concluded that it is difficult to generalise the findings from this study to other countries because treatment patterns for CMA vary between all seven countries, including the clinicians who manage CMA sufferers, referral patterns, diagnostic procedures and prescribing patterns. For example, GPs are primarily involved in managing CMA in the UK, whereas it is a combination of GPs and Youth Healthcare Doctors in the Netherlands, key opinion leaders at tertiary referral centres in Finland and paediatricians at secondary care centres in New Zealand, the US and South Africa. In the UK any physician can prescribe an AAF, whereas only a paediatrician would do so in South Africa or the Netherlands.

Moreover, while clinical nutrition preparations were found to be the key cost driver in Australia, primary care clinician visits were found to be the primary cost driver in the UK²⁶, whereas it was tertiary care clinician visits in Finland¹⁸.

Conclusion

CMA imposes a substantial burden on the publicly funded healthcare system in Australia. However, using an AAF as the initial treatment for CMA could potentially release limited hospital resources for alternative use within the paediatric healthcare system.

Acknowledgements

Declaration of interest: This study was sponsored financially by SHS International Ltd, Liverpool, UK, manufacturers of the AAF, Neocate. However, the authors have no other conflicts of interest that are directly relevant to the content of this manuscript.

The authors would like to thank the following paediatricians for their contributions: Dr J Brereton, Sydney; Dr P Egan, Adelaide; Dr G Ford, Melbourne; Dr C Hughes, Sydney; Dr P Lang, Adelaide; Dr D Levitt, Brisbane; Dr J Mel, Melbourne; Dr B Lewis, Brisbane; Dr L Lubitz, Melbourne; Dr D McCrossin, Brisbane; Dr S Ong, Sydney; Dr R Power, Adelaide; Dr D Roberts, Perth; Dr J Scurlock, Perth; Dr M Slattery, Perth.

The authors would also like to thank the following paediatric gastroenterologists for their contributions: Dr D Cameron, Melbourne; Dr A Day, Sydney; Dr L Ee, Brisbane; Dr P Hammond, Adelaide; Dr P Lewindon, Brisbane; Dr D Moore, Adelaide; Dr W Hardikar, Melbourne.

Last, but not least, the authors would also like to thank the following paediatric immunologists/allergists for their contributions: Dr R Heine, Melbourne; Dr D Hill, Melbourne; Dr M Gold, Adelaide; Prof. A Kemp, Sydney; Dr J Peake, Brisbane; Dr S Prescott, Perth; Dr P Smith, Sunshine Coast; Dr M Tang, Melbourne.

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<http://www.cmrojournal.com>
 Paper CMRO-4562A_5, *Accepted for publication*: 28 November 2008
Published Online: 16 December 2008
 doi:10.1185/03007990802594685