In conclusion, partially hydrolysed infant formula was cost effective versus standard formula for infants at risk in the prevention of atopic dermatitis and cost saving compared with EHF when used in prevention.

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**Partially Hydrolysed 100% Whey-Based Infant Formula and the Prevention of Atopic Dermatitis: Comparative Pharmacoeconomic Analyses**

by Jörg Spieldenner et al.

**Key insights**

Atopic dermatitis is a common complaint in young children and it is often associated with the development of other allergic disorders. This article investigates the relative health and cost benefits of using partially hydrolysed infant formula (PHF) for preventing atopic dermatitis in at-risk newborns who were not exclusively breastfed.

**Current knowledge**

Childhood atopic dermatitis places a significant economic burden on healthcare systems, the families of affected children, and on society. Few European economic evaluations have addressed this issue, but a German study found that the annual cost of treating atopic dermatitis was USD 219 per child in 2003, while in Italy the average cost to the family was EUR 1,254 in 2006. It is therefore important to consider the financial, as well as the clinical impact of interventions aimed at preventing or treating atopic dermatitis.

**Practical implications**

Based upon clinical findings and economic analyses, PHF has been shown to be a suitable alternative to cow’s milk-based formulas for preventing atopic dermatitis in at-risk children. European data indicate that from a societal perspective the additional costs associated with using the PHF will be more than compensated for by significantly reduced healthcare costs and time losses for the families. Families with at-risk children will on average save between EUR 624 and 2,200 by using PHF over cow’s milk-based formula.

**Recommended reading**

Partially Hydrolysed 100% Whey-Based Infant Formula and the Prevention of Atopic Dermatitis: Comparative Pharmacoeconomic Analyses

Jörg Spieldenner a Dominique Belli b Christophe Dupont c Ferdinand Haschke a Michael Iskedjian d Santiago Nevot Falcó e Hania Szajewska f Andrea von Berg g

Key Words
- Allergy prevention
- Atopic dermatitis
- Cost-effectiveness analysis
- Cost-minimization analysis
- Infant formula
- Infant nutrition

Abstract
Clinical trials have demonstrated that the risk of developing atopic dermatitis is reduced when using hydrolysed infant formulas to feed infants with a documented risk of atopy (i.e. an affected parent and/or sibling) when breastfeeding is not practised. However, little is known about the cost-effectiveness of using hydrolysed formulas. Consequently, economic analyses in 5 European countries (Denmark, France, Germany, Spain and Switzerland) have evaluated the costs and cost-effectiveness of a specific brand of 100% whey-based partially hydrolysed infant formula, NAN-HA® (PHF-W) compared with a cow’s milk-based standard formula (SF), and comparable to extensively hydrolysed infant formulas (EHF), in the prevention of atopic dermatitis in at-risk infants.

Key Messages
- Atopic dermatitis is a common skin disease in infants and children, and places a substantial economic burden on families and the healthcare system.
- In infants that are not exclusively breastfed, atopic dermatitis can be prevented by using a hydrolysed infant formula to reduce the risk of allergy. A specific 100% whey-based partially hydrolysed formula (PHF-W) has been shown to be more effective than a cow’s milk-based standard formula (SF), and comparable to extensively hydrolysed infant formulas (EHF), in the prevention of atopic dermatitis in at-risk infants.
- Based on data from 5 European countries, PHF-W appears to be a feasible option for the prevention of atopic dermatitis, being cost effective from the perspective of public healthcare systems when compared with SF, and associated with substantial cost savings for public healthcare systems and society when compared to EHF.
Hydrolysed Infant Formula

Economic Evaluations of Partially Hydrolysed Infant Formula

Introduction

Atopic dermatitis is one of the most common skin diseases in infants and young children [1]. In addition to having an adverse effect on the quality of life of the child and their family [2], it is often associated with the subsequent development of other atopic disorders [1]. The prevalence of atopic dermatitis among children aged 6–7 years varies from 0.9 to 22.5% in different countries worldwide, with Latin America and Asia having comparatively high rates [3]. In Europe, the prevalence of atopic dermatitis in children is approximately 10–20% [4, 5]. The prevalence of the condition has increased over the last few decades, particularly in developing countries [6–8]. Atopic dermatitis often develops within the 1st year of life; one study found the onset was within 6 months in 45% of affected children and within 1 year in 60% [5]. Infants with a family history of atopy are at increased risk of developing atopic dermatitis [9].

It is recommended that infants are exclusively breastfed for the first 4–6 months of life [10–15]. However, when this is not possible or desired they are given an infant formula instead of, or in addition to, breast milk. Formulas are usually based on cow’s milk (standard formula, SF). There is some evidence that early exposure to dietary allergens may increase the risk of developing food allergies and atopic dermatitis [16, 17]. In an effort to reduce the potential risks associated with cow’s milk proteins, formulas have been developed that contain proteins which have been hydrolysed in order to reduce allergenicity.

In an effort to reduce the potential risks associated with cow’s milk proteins, formulas have been developed that contain proteins which have been hydrolysed in order to reduce allergenicity.

An alternative approach is to use amino-acid-based formulas, but these are considerably more expensive [18]. It has been shown that using hydrolysed formulas can reduce the incidence of allergic manifestations and atopic dermatitis compared with cow’s milk formulas [19–21].

Hydrolysed formulas are differentiated by the degree of hydrolysis (extensively or partially hydrolysed) and by the protein source (whey or casein). Partially hydrolysed formulas (PHF) are thought to have hypoallergenic properties similar to extensively hydrolysed formulas (EHF), but a better taste and texture [19]. One specific brand of 100% whey-based partially hydrolysed infant formula (PHF-W) manufactured by Nestlé, NAN-HA®, and branded under NIDAL HA® in France, NAN Excel® in Spain, BEBA HA® in Germany and Switzerland and NAN HA® in Denmark, has been shown to be effective in the prevention of atopic dermatitis in meta-analyses of randomised trials [21, 22]. It was found to be more effective than SF and similar in efficacy to EHF for preventing atopic dermatitis in infants who were not exclusively breastfed, and who were deemed at risk of allergy because of a family history of atopy [22, 23].

Atopic dermatitis is associated with a significant economic burden for healthcare systems, the families of affected children and for society as a whole [24–31]. Only a few European economic evaluations have focused specifically on children: a German study found that the annual cost of treating atopic dermatitis was USD 219 per child in 2003 [26], while in Italy the average cost to the family amounted to EUR 1,254 in 2006 [25]. It is therefore important to consider the financial, as well as the clinical, impact of interventions aimed at preventing or treating atopic dermatitis.

Health economics is a discipline that analyses the economic aspects of health and healthcare, including both prevention and treatment approaches [32]. Health economics usually focuses on the costs and the consequences of healthcare interventions, incorporating both medi-
Table 1. Pharmacoeconomic terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>Alternative interventions are compared in terms of the cost per unit of effectiveness for a specific outcome (e.g. deaths avoided, cases detected).</td>
</tr>
<tr>
<td>Cost-minimisation analysis</td>
<td>Assumes the alternative interventions are equally effective in terms of the outcome, and, therefore, only costs are considered.</td>
</tr>
<tr>
<td>Decision-analytic modelling</td>
<td>Pharmacoeconomic models combine information on therapeutic strategies, clinical outcomes and/or quality-of-life data, epidemiological data and costs. Decision analytical models reflect a sequence of chance events and decisions over time and are particularly useful for acute episodes of illness.</td>
</tr>
<tr>
<td>Discounting</td>
<td>Procedure used to express those costs and benefits that will occur in future years as ‘present values’.</td>
</tr>
<tr>
<td>Dominance</td>
<td>An intervention is considered dominant if it is more effective and less costly than the alternative intervention. An intervention is dominated if it has a worse outcome and higher costs.</td>
</tr>
<tr>
<td>ICER</td>
<td>Ratio of (the difference in the costs of the intervention of interest compared with an alternative) to (the difference in outcomes between the two interventions). Indicates the cost per unit of effect from switching from intervention A to intervention B.</td>
</tr>
<tr>
<td>Sensitivity analysis</td>
<td>Performed to examine the effect on the results of uncertainty in some of the inputs. The analysis is repeated while varying the assumptions used.</td>
</tr>
<tr>
<td>Time horizon</td>
<td>Time span that reflects the period during which the main differences in effects and use of resources are expected to occur.</td>
</tr>
<tr>
<td>Utility</td>
<td>Measure of preference for one health state in relation to another on a numerical scale where 0 = death and 1 = optimal health.</td>
</tr>
</tbody>
</table>

One type of health economic evaluation that is widely used is cost-effectiveness analysis (CEA). In CEA, the costs and consequences of two alternative strategies are compared, with the results expressed as an incremental cost-effectiveness ratio (ICER), representing the difference in costs in relation to the difference in consequences [33]. This can be interpreted as the cost that will be incurred in order to obtain an additional success, if one treatment is selected over the other (e.g. cost per avoided complication) [33]. Costs that might be considered include direct medical costs associated with the treatment pathway, such as the cost of the intervention (e.g. drug, or in the case of PHF-W, the formula), physicians, hospitalisation and laboratory tests. Indirect costs, such as productivity losses incurred through absence from work, may also be taken into account.

Other terms that are relevant in the field of health economics and the analyses discussed in this paper are summarised in table 1.

Until recently, there has been no research into the cost-effectiveness of PHF-W for the prevention of atopic dermatitis in Europe. However, a series of pharmacoeconomic analyses evaluating the use of PHF-W in 5 European countries has now been performed. These analyses determined the costs, consequences and cost-effectiveness of PHF-W in the prevention of atopic dermatitis in at-risk children when compared with SF. An additional analysis compared PHF-W with EHF. The aim of this article is to summarise and compare the results from these European pharmacoeconomic analyses of PHF-W.

**Methods**

Pharmacoeconomic analyses exploring the use of PHF-W for the prevention of atopic dermatitis were performed in 5 European countries. CEA were performed as the main analysis in France [23], Germany [34], Spain [35, 36] and Switzerland [37]. In Denmark, a cost-minimisation analysis was performed [36, 38]. Cost-utility assessments (evaluating the relationship between costs and health utility, expressed as quality-adjusted life years) were not performed due to a lack of published data on health utilities for atopic dermatitis in infants.

Similar methodology was applied for each of the CEA. Predictive decision-analytic modelling was used to determine treatment pathways, resource utilisation and costs associated with the management of atopic dermatitis in healthy at-risk children (newborn to 3 years of age) who were not exclusively breastfed. At risk was defined as children with at least 1 parent or sibling with a confirmed medical history of allergies.

The main comparator used was SF for all countries except Denmark, for which EHF-whey (EHF-W) and EHF-casein (EHF-C) were used. For France, Germany, Spain and Switzerland, PHF-W was compared with one or both types of EHF in a secondary analysis.

Three different perspectives were applied to the analyses: those of the public healthcare system (Ministry of
Health; MOH), the child’s family and society as a whole (which incorporated both of the other perspectives). The time horizon for the base-case analyses was 12 months, including a 6-month period of formula consumption. Twelve months was chosen because it covered the period during which most cases of atopic dermatitis first develop and also went beyond the usual period of milk consumption.

The structure of the decision-analytic model is summarised in figure 1. The model applied a series of 3-month cycles starting from the birth cohort. Clinical and cost inputs were obtained from medical literature, government publications, official formularies, pharmacy surveys and expert opinions.

The initial cohort entering the model (i.e. at-risk newborns not exclusively breastfed) was determined using the following equation: 

\[
\text{Initial cohort} = \left( \text{birth cohort of country} \times (1 - \text{average exclusive breastfeeding rate}) \times \text{rate of at-risk infants} \right)
\]

The main clinical input, the incidence of atopic dermatitis, was obtained from a meta-analysis of randomised controlled trials, which reported that PHF-W was more effective than SF at preventing cases of atopic dermatitis, and that there was no statistically significant difference in efficacy between PHF-W and EHF-W or EHF-C [22, 23]. For the CEA, the final clinical outcome of the model was the number of avoided cases of atopic dermatitis when using PHF-W compared with SF.

A panel of expert clinicians was convened in each country in order to define and validate treatment pathways, and to identify and value the resources consumed in the management of atopic dermatitis. Depending on the clinical practice patterns applicable to each country, treatment pathways could encompass dietary management (change in infant formula), medical treatment (topical emollients, corticosteroids or immunosuppressants, depending on the country), or a combination of both approaches.

The costs that were considered are summarised in table 2. The cost of the comparator formula was based on the brand with the largest market share or the average cost of two dominant brands in the relevant country. The base-case CEA assumed that all infant formulas were reimbursed at the same rate by the relevant MOH (65% in France, 60% in Spain, 100% in Germany, 90% in Switzerland and 60% in Denmark). This enabled a direct comparison to be made between the different formulas. Costs beyond 1 year were discounted.

The principal analysis for the studies in France, Germany, Spain and Switzerland assessed cost-effectiveness, with the main outcome being...
the expected incremental cost per avoided case of atopic dermatitis (ICERs) when comparing PHF-W with SF. ICERs were calculated as the difference in costs between PHF-W and SF divided by the negative value for the difference in the number of cases of atopic dermatitis between PHF-W and SF. The aggregated cost associated with each perspective was an intermediate economic outcome. In these studies, a secondary analysis was performed to compare PHF-W with one or both types of EHF, using a cost-minimisation approach.

The main analysis in Denmark was a cost-minimisation analysis comparing PHF-W with EHF-W and EHF-C. This approach was applied based on the lack of significant difference in efficacy for the prevention of atopic dermatitis between PHF-W and EHF. The analysis assumed that all costs would be similar between comparators with the exception of the acquisition cost for the infant formulas themselves. Even though differences in efficacy were not statistically significant, the nominal differences that existed were taken into account in sensitivity analyses by performing a CEA to produce ICERs for the expected cost per avoided cases of atopic dermatitis when comparing PHF-W with either type of EHF [38].

One-way sensitivity analyses tested the effect of variations in individual key parameters on the outcome of the modelled CEA, and probabilistic sensitivity analyses using a set of 10,000 Monte Carlo simulations (simultaneously varying multiple parameters in a random fashion) tested the robustness of the overall model. The main parameters varied in one-way sensitivity analyses are listed in table 3 [23].

### Results

In the base-case analyses comparing PHF-W with SF for the prevention of atopic dermatitis, the number of avoided cases of atopic dermatitis achieved when PHF-W was used instead of SF ranged from 1,653 to 13,356 among at-risk birth cohorts of 22,933 (Switzerland) to 185,298 (France) infants (table 4) [23, 34–38].

Incremental costs and ICERs for PHF-W versus SF are shown in table 5 [23, 34–36]. From the perspective of the MOH and society, the main driver of overall costs was the cost of the infant formula, while from the family perspective, the main cost driver was loss of time [see table 6 for data from Germany (consistent with data from the other countries studied)]. Expected ICERs (ICER per avoided case of atopic dermatitis for PHF-W compared with SF) ranged from EUR 982 to 1,343 from the MOH perspective, from EUR –2,202 to –624 from the family perspective (indicating savings), and from EUR 1,220 to 719 from the societal perspective (table 5) [23, 34–36]. One-way and probabilistic sensitivity analyses confirmed the robust-
ness of the model, with most producing ICERs that were consistent with those obtained in the base-case analysis (table 7) [36].

In the analyses comparing PHF-W with EHF-W for the prevention of atopic dermatitis, PHF-W was associated with potential cost savings ranging from EUR 1.3 million (Denmark) to 64 million (France) from the MOH perspective, and savings of EUR 4.3 million (Denmark) to 120 million (Germany) from the perspective of society as a whole (table 8) [23, 34–36, 38].

In the comparisons of PHF-W with EHF-C, PHF-W was associated with potential savings of EUR 1.3 million (Denmark) to 76 million (France) from the MOH perspective, and savings of EUR 3.8 million (Denmark) to 116 million (France) from the societal perspective.

In the Danish study, sensitivity analyses confirmed that PHF-W was dominant over EHF-W, and found that EHF-C showed unattractive ICERs against PHF-W, with no likelihood that EHF-C would dominate PHF-W [38].

As seen in table 7, Monte Carlo simulations indicated probabilities of PHF-W being cost effective against SF (gain in efficacy with a cost increase) of between 45 and 92% and probabilities of it being dominant (cost savings with a gain in efficacy) of between 8 and 55%, with negligible probabilities of being dominated (≤0.2%).

### Discussion

Atopic dermatitis places a substantial economic burden on the families of affected children and on the healthcare system [24–26]. In Germany, it has been estimated that the total annual cost of atopic dermatitis is EUR 1.2–3.5 billion [39]. It has been shown that in infants who are not exclusively breastfed, the use of hydrolysed formulas reduces the risk of developing atopic dermatitis [19–22]. Given the economic impact of the disorder, it is impor-

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**Table 5. Cost and ICERs for PHF-W versus SF in base-case analyses**

<table>
<thead>
<tr>
<th>Setting</th>
<th>Incremental cost, EUR</th>
<th>ICER, EUR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MOH</td>
<td>family</td>
</tr>
<tr>
<td>France</td>
<td>17,941,352</td>
<td>–8,338,537</td>
</tr>
<tr>
<td>Spain</td>
<td>7,319,916</td>
<td>–7,673,628</td>
</tr>
<tr>
<td>Germany</td>
<td>11,634,350</td>
<td>–14,910,733</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1,623,775</td>
<td>–3,639,795</td>
</tr>
</tbody>
</table>

CHF were converted into EUR using the exchange rate from June 24, 2011. Negative values indicate savings.

**Table 6. Costs in the base-case analysis for Germany (in EUR)**

<table>
<thead>
<tr>
<th>Item</th>
<th>PHF-W</th>
<th>SF</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOH perspective</td>
<td>Formula</td>
<td>62,653,435</td>
</tr>
<tr>
<td>Physicians</td>
<td>632,178</td>
<td>1,120,485</td>
</tr>
<tr>
<td>Treatment</td>
<td>279,597</td>
<td>562,087</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>611,387</td>
<td>1,083,633</td>
</tr>
<tr>
<td>Hospitalisation</td>
<td>305,051</td>
<td>540,678</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td>121,338</td>
<td>215,062</td>
</tr>
<tr>
<td>Total cost</td>
<td>64,602,986</td>
<td>52,968,636</td>
</tr>
<tr>
<td>Family perspective</td>
<td>Treatment</td>
<td>191,701</td>
</tr>
<tr>
<td>Time lost</td>
<td>18,081,614</td>
<td>32,121,375</td>
</tr>
<tr>
<td>Travel</td>
<td>930,969</td>
<td>1,653,868</td>
</tr>
<tr>
<td>Total cost</td>
<td>19,204,284</td>
<td>34,115,016</td>
</tr>
<tr>
<td>Societal perspective</td>
<td>Total cost</td>
<td>83,807,270</td>
</tr>
</tbody>
</table>

* Combination of costs from MOH and family perspectives.

**Table 7. Probabilistic sensitivity analyses for PHF-W versus SF from the societal perspective**

<table>
<thead>
<tr>
<th>Country</th>
<th>Distribution of simulation results per quadrant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>quadrant 1</td>
</tr>
<tr>
<td>France</td>
<td>91.5%</td>
</tr>
<tr>
<td>Spain</td>
<td>78.8%</td>
</tr>
<tr>
<td>Germany</td>
<td>74.8%</td>
</tr>
<tr>
<td>Switzerland</td>
<td>44.6%</td>
</tr>
</tbody>
</table>

Quadrant 1 = Gain in efficacy but with a cost increase (incremental cost-effectiveness for PHF-W); quadrant 2 = increase in cost and decrease in efficacy (SF dominant); quadrant 3 = cost savings but with a reduction in efficacy; quadrant 4 = cost savings and gain in efficacy (PHF-W dominant).

* Based on 10,000 Monte Carlo simulations.

Economic Evaluations of Partially Hydrolysed Infant Formula

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tant to examine the cost-effectiveness of using these formulas for the prevention of atopic dermatitis.

This review discusses the 5 studies, either published as articles or presented as posters, which are the first 5 economic evaluations of Nestlé NAN-HA, the PHF-W used in this study, for the prevention of atopic dermatitis in at-risk infants in Europe. In 4 of the studies, a CEA compared PHF-W with SF, while in the 5th study (and in secondary analyses in the other studies), PHF-W was compared with EHF in a cost-minimisation analysis.

Under the set of assumptions used, and taking into account the robustness of the economic modelling results, PHF-W was shown to be the highly cost-effective option compared with SF for the prevention of atopic dermatitis in infants from the perspective of the MOH in all 4 countries analysed – France, Spain, Germany and Switzerland. From the MOH perspective, incremental costs per avoided case of atopic dermatitis ranged from EUR 982 to 1,343. Furthermore, PHF-W was dominant over SF (more effective and associated with cost savings) in all 4 countries from the perspective of the family, and in 3 countries – Spain, Germany and Switzerland – from the perspective of society. Sensitivity analyses confirmed the robustness of the results, with only 1 scenario providing a notably different outcome from the base case in each study.

Denmark is the only one of the 5 countries studied where EHF are currently approved, and partly reimbursted, for use in the prevention of cow’s milk and food allergy in at-risk infants. Therefore, a comparison between PHF-W and both EFH-W and EFH-C formed the basis of the economic evaluation for this particular country. It is also possible that EHF might be used for prevention in some clinical practice situations in other countries studied, and it was appropriate to perform secondary analyses comparing PHF-W to EHF in these settings, too.

Given that there was no significant difference in preventive efficacy between PHF-W and EHF, a cost-minimisation approach was used for all of these analyses.

In the setting of atopic dermatitis prevention, PHF-W was associated with cost savings compared with EHF in all 5 countries studied, including Denmark, both from the perspective of the MOH and from that of society as a whole. In Denmark, the savings with PHF-W were similar in the comparisons with both EFH-W and EFH-C, which was because the acquisition costs of the two types of EHF were almost identical [38]. These data suggest that PHF is preferable to EHF in the preventive setting, which is consistent with guidelines that recommend using PHF (or reduced allergenicity formulas) for the prevention of allergic manifestations in at-risk infants who are not exclusively breastfed [17, 40–42].

Few other economic evaluations of hydrolysed formulas in the prevention of atopic dermatitis have been reported. A study in Germany, which used a longer time frame (6 years) and a fairly low discount rate of 3%, found that from the societal perspective PHF and EHF-C were cost effective or cost saving, while from the perspective of the German statutory health insurance EHF-C was cost effective and PHF was cost saving [39]. The ICER per avoided case for PHF-W compared with SF was EUR –6,358 from the societal perspective and EUR –792 from the German statutory health insurance perspective [39].

Throughout the current analyses, one of the main drivers of cost was that of the infant formulas themselves; loss of time was also an important consideration from the perspective of the child’s family. Atopic dermatitis has an adverse effect on the quality of life of both the child and the parents; however, there are few published data on quality of life or health utilities associated with atopic dermatitis in young children, and, consequently, it was not possible to

<table>
<thead>
<tr>
<th>Country</th>
<th>PHF-W vs. EHF-W</th>
<th>PHF-W vs. EHF-C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>society</td>
<td>MOH</td>
</tr>
<tr>
<td>France</td>
<td>98</td>
<td>64</td>
</tr>
<tr>
<td>Spain</td>
<td>26</td>
<td>26</td>
</tr>
<tr>
<td>Germany</td>
<td>120</td>
<td>120</td>
</tr>
<tr>
<td>Switzerland</td>
<td>11.4</td>
<td>10.2</td>
</tr>
<tr>
<td>Denmark</td>
<td>4.3</td>
<td>1.3</td>
</tr>
</tbody>
</table>

CHF and DKK were converted into EUR using the exchange rate from June 24, 2011. N/A = Not applicable.
incorporate a formal cost-utility analysis into the studies discussed here. Nonetheless, a hypothetical cost-utility analysis was performed as a sensitivity analysis in the Spanish study [35]. Utility values of 0.9, 0.8, 0.7 and 0.9 were applied to mild, moderate, severe and relapsing cases, respectively, for 3-month cycles. Applying time horizons of 1 and 3 years, this analysis indicated dominance from the family and society perspectives and produced ICERs of less than EUR 22,000 per quality-adjusted life year from the MOH perspective, which is well below the commonly accepted threshold of EUR 35,000 per quality-adjusted life year [35].

All economic evaluations have limitations, and the predictive model used in the analyses discussed here is no exception. However, whenever possible the bias was set against the treatment of interest, PHF-W, in the base-case analyses, in order to make the evaluations as conservative as possible.

Incidence rates came from a meta-analysis which included a range of studies of different sizes; however, using a meta-analytic approach to analysis should reduce any bias associated with data from different studies. An equal incidence of atopic dermatitis was assumed for adjoining 3-month intervals in the periods from 0 to 6 and from 6 to 12 months, although, in reality, incidence rates for atopic dermatitis tend to be higher earlier in life. Flare-ups were assumed to occur at 3-monthly intervals, although, in practice, they are likely to happen more frequently. It was assumed that the same quantity was consumed daily for each type of formula, although this may not be the case in reality. In addition, after discontinuing one brand of formula it was assumed that the next brand used was of equal price.

The effect of altering the assumptions made for these and other parameters was tested individually using one-way sensitivity analyses. In addition, the overall model was tested using probabilistic sensitivity analysis, and the boundaries assigned to parameters in Monte Carlo simulations meant that this probabilistic analysis was more conservative than the base-case analysis.

In summary, a series of European analyses based on predictive modelling have established the cost-effectiveness of PHF-W over SF in the prevention of atopic dermatitis in healthy at-risk infants who were not exclusively breastfed. PHF-W generally demonstrated dominance over SF from the family and societal perspectives, and attractive cost-effectiveness from the MOH perspective. PHF-W was also dominant over EHF-W from the MOH perspective. These findings should be of interest to public healthcare systems and reimbursement agencies when considering the role of PHF-W in the prevention of atopic dermatitis.

Disclosure Statement
This study was funded by Nestlé Nutrition Institute (NNI). M.I. is employed by PharmIdeas, which performed this study under contract with NNI; J.S. and F.H. are employed by NNI; D.B., C.D., S.N.F. and A.v.B. have received honoraria for their participation. H.S. has participated as a clinical investigator, and/or advisory board member, and/or speaker for Arla, Biocodex, Danone, Nestlé Nutrition Institute, Nutricia, and Mead Johnson.

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