Cost-effectiveness of Emollients in the Prevention of Relapse among French Patients with Atopic Dermatitis

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Atopic dermatitis affects up to 20% of children and quite frequently persists in adulthood. Follow-up, treatment, and prevention of relapses have an impact on healthcare spending. The aim of this study was to assess the cost-effectiveness of different emollients prescribed for patients with atopic dermatitis in France. A 3-health state Markov model was designed, using French data for resource utilization, price and transition probabilities. The effects of the use of 5 different emollients (A, B, C, D, E) or no emollient were compared. The selected outcome was time (years) without flare-up. The 5-year cost for emollient A is 1,575.64€, and the effectiveness is 3.89 years without flare-up. Strategy A is the most effective. Compared with treatment E, which was the least expensive emollient, A is more expensive (+481.84€) and more effective (0.082 years without flare-up). The incremental cost-effectiveness ratio is 5,877.48€/years without flare-up. In conclusion, treating atopic dermatitis with emollients is a cost-effective strategy.

Key words: dermatitis; atopic; secondary prevention; cost-benefit analysis.

Accepted Jul 6, 2021; Epub ahead of print Jul 7, 2021

Acta Derm Venereol 2021; 101: adv00509.

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SIGNIFICANCE

Emollients are recommended as treatment for atopic dermatitis. The model used in this study aims to assess the cost-effectiveness of different emollients in the French setting. The effectiveness of the treatment was evaluated by measuring the relapse-free period. When accounting for consultation, hospitalization, and medication costs, as well as productivity losses, the use of emollients was found to be cost-effective compared with no emollient. The strategy of using of no emollients was worse based on 2 of the 4 selected comparators: it is both more expensive and less effective. Dominant cost-effective strategies should be preferred by physicians.

Atopic dermatitis (AD) is an inflammatory skin condition affecting up to 20% of children (1, 2). Air pollution is a main driver of prevalence in industrialized countries. The prevalence of AD has tripled over the last 30 years (2). AD is a chronic, remitting-relapsing, pruritic, inflammatory, immune-mediated skin condition. Skin symptoms are common and can vary, including: erythema, lichenification, xerosis with scaly plaques, bleeding, oozing, cracking, and flaking (3). Pruritus is the most disruptive symptom, and the frequency and intensity of itching can cause sleep issues, anxiety and depression (4). Itching may also affect work performance and learning abilities, thereby having an important impact on patients' quality of life. AD is characterized by the remission-flare-up cycle, which is an acute inflammatory flare-up phase, followed by a period that is nearly symptom-free (3).

While acute symptoms are treated with topical glucocorticosteroids, AD relapses are primarily prevented by the daily use of emollients (5–7). To delay flare-ups, health authorities recommend daily applications of emollients and topical glucocorticosteroids to manage acute phases (8). While this therapy aims only to manage symptoms, quality of life is increased, with a lower number of practitioner consultations and less frequent and severe flare-ups.

An emollient is a substance applied externally that protects against skin dryness. Most emollients are composed of at least mixtures of oils and water (in some cases, thermal spring water) in different proportions. Water allows the keratinized tissue to be plasticized. The oils first smooth the skin by covering the external layer with a thin, oily film. Then, water evaporation is discouraged, thus maintaining skin flexibility (9). Recently, some emollients have also been supplemented with specific microbiotic extracts to increase the skin microbial diversity altered in patients with AD (10).

Many emollients are available on the market. However, their effectiveness is not well demonstrated. To our knowledge, few cost-effectiveness studies have been published (11, 12), and none have compared the overall set of emollients in the French market.

The aim of this study was to evaluate the cost-effectiveness of the use of 5 different emollients (A, B, C, D, and E) and no emollient for AD relapses. The study considers the health outcomes and costs of intervention from the perspective of the French healthcare system.

doi: 10.2340/00015555-3873
Acta Derm Venereol 2021; 101: adv00509

METHODS

Modelling

A cost-effectiveness study was designed. Five emollients and a no treatment strategy were compared. Two dermo-cosmetic emollients (A and D) were compared with a mass-market emollient (emollient B). The generic version of the mass-market emollient was included in the study (emollient E) as well as a medical device (emollient C). No emollient use was also tested for comparison.

A 3-state Markov model was implemented to mimic the course of the disease (**Fig. 1**). Health states include "flare-up", "post-corticoid", and "maintenance". Patients in the maintenance and post-corticoid states were considered to have mild AD; however, when they were in the flare-up state, they were considered to have moderate AD. The flare-up state was defined by an over 20% decrease in the SCORing Atopic Dermatitis (SCORAD) score.

Modelled patients entered the model in the post-corticoid state. Patients could either relapse to a flare-up state or enter the maintenance state. Pf was the transition probability for the transition from the post-corticoid state to the flare-up state; thus, 1 – Pf was the probability for transition from the post-corticoid state to the maintenance state. In the maintenance state, the patient might remain stable or could relapse and transition to the flare-up state. This transition probability is named Mf. Once the patient entered the flare-up state, it was assumed that he or she would use topical glucocorticosteroids to manage the disease. At the end of the cycle, the patient will automatically transition to the post-corticoid state.

Van Zuuren et al. (7) reported 15 randomized clinical trials (RCTs). The review assessed progression-free survival before flare-ups, as well as the quality of the study according to selection bias risk, detection bias, attrition bias and reporting bias. Using data from this review, transition probabilities were computed. The Declining Exponential Approximation of Life Expectancy (DEAL) (13) method was used to compute transition probabilities and match them to the 4-week time-frame. Patient data were extracted from published RCTs (14–16). The A-RCT was based on a study of both adult patients and children. A total of 99 patients aged 6 months to 63 years with mild AD were recruited (mean age 11.5 ± 12.6 years). Twenty-six percent of patients were older than 16 years. Women represent 56.6% of the sample.

The SCORAD scale was used to measure the severity of AD. Fifteen days before the beginning of the trial, the SCORAD scale was administered. The mean SCORAD score was 20.81, corresponding to mild AD. When in relapse, the SCORAD score decreased by 25%, corresponding to moderate AD.

Population similarities to other RCTs (B, C, D, Es) regarding age and sex were assessed. No differences were found between populations; therefore, patients were modelled from the A-RCT (14).

The following working assumption was adopted to construct the model: transition probabilities between the maintenance state and flare-up state and between the post-corticoid state and flare-up state were equal. Expert opinion supports this assumption. Although seasonal reductions in flare-up are probable, this variation has not yet been quantified. Therefore, it is not possible to account for this variation in the model.

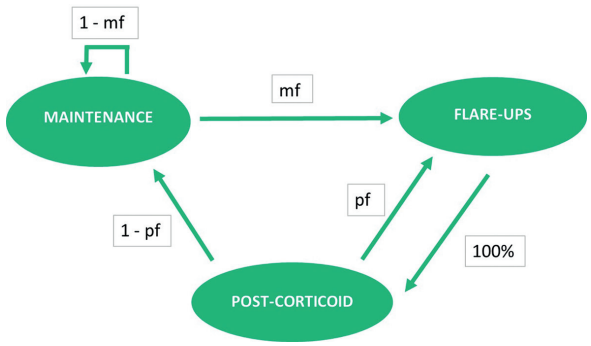

Fig. 1. Markov model used to model the cost efficiency of different emollients.

Five emollients were compared. The International Nomenclature of Cosmetic Ingredients compositions of different emollients are available from Appendix S1[1]. In addition, an absence of emollient and the generic form of one emollient were chosen as comparators.

The base case was designed using a 5-year time horizon. The mean AD persistence level was reported to be 6.1 years (17). As the studied population consists of both adults and children, treatment will not be taken for life. The RCT used to model the transition probabilities for different emollients lasted 4 weeks; therefore, a cycle of 28 days was chosen to emulate the cohort. Half-cycle correction was applied (18).

A discount rate of 3.5% was applied to efficacy, and a rate of 2.5% was applied to costs following French high health authority recommendations (19).

Effectiveness

Effectiveness was derived from RCTs. The marker of effectiveness is time without relapse expressed in years without flare-ups (YWFU). Time without relapse was defined as the time in years each patient spent in a state different than flare-up.

Because emollient E is the generic medication of emollient B, effectiveness was considered similar when the same quantity was used.

Costs

The costs used in the base case model were treatment costs: emollients, topical glucocorticosteroids, hospitalization costs, and follow-up costs of medical practitioners (i.e. generalists and specialists). Other out-of-pocket expenditures were added. Due to the specific route of administration used, no administration or transportation costs were considered.

A health system perspective using contributions from statutory health insurance, voluntary health insurance and out-of-pocket payments was retained. Out-of-pocket payments are defined by the cost to the patient for health goods and services after payments from health insurance. Therefore, all direct costs are included in the model.

Costs were computed in Euro 2019. Data from the French National Statistics Institute (INSEE) were used to correct the price from inflation. The inflation rate from 2018 to 2019 was 1.8%, and from 2017 to 2018 it was 1%.

Emollient prices were derived from different sources. Most (A, B, C, and D) were extracted from an IQVIA® panel in the absence of treatment, and the cost was equal to zero. The price of emollient E is fixed by health authorities and documented in the red book (the French drug dictionary). Reimbursement rates are set by French authorities and were considered.

RCTs describe the daily quantity needed to achieve an alleviating effect (14–16). **Table I** reports the quantity and price per cycle for all emollients. The quantities of B and E are identical to achieve similar effectiveness at a different price.

During flare-ups, treatment involved the application of a topical glucocorticosteroid. A mean quantity of 5.9 g per application was reported by Akerstrom et al. (20). Topical glucocorticosteroids should be used according to guidelines: 20 applications per cycle are needed to soothe relapse. To remain agnostic to which steroids were used, the mean price weighted by the prescription rate of the top 12 topical glucocorticosteroids used in France was computed

[1]https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3873

Table I. Cost of emollients per cycle in 2019

Emollient	Daily applications, *n*	Mean quantity/ application, ml	Mean quantity/ day, ml	Mean quantity/ cycle, ml	Price/ ml (€) (2019)	Price/ cycle (€) (2019)
A	2	3.42	6.84	191.6	0.0621	11.90
B	2	5.35	10.7	299.6	0.0419	12.55
C	3	5.687	17.06	477.75	0.1119	53.46
D	2	5.687	11.37	318.5	0.0405	12.90
E	2	5.35	10.7	299.6	0.01	3.00

from an IQVIA panel. Prices were derived from the French drug dictionary. A price of 0.1064€/ml was computed.

Other costs were included in the analysis. Medical costs, such as hospitalization and visits to general practitioners and/or specialists, were considered. Healthcare utilization was extracted from the dupilumab (21) (a monoclonal antibody drug for AD treatment) health technology assessment for the French setting. Dupilumab Health Technology Assessment (HTA) was submitted to French healthcare authorities and mentions the frequency of patient visitation to healthcare providers. However, data from this HTA were not published, hence the study had to rely on their own dichotomy between mild and moderate AD. With moderate AD, in the model flare-up state, the patient visits his or her general practitioner (GP) a mean of once and a specialist 3.6 times per year. During the maintenance or post-corticoid states, a patient consults a GP and specialist a mean of 3.1 and 1.8 times per year, respectively.

Costs were derived from the French national healthcare cost database. The cost of a consultation can vary; indeed, some supplementary costs can be added by the practitioner, for instance, at home consultation. To obtain the mean cost of a consultation, the total amount paid by the health insurance to GPs and dermatologists for 2019 was divided by the number of acts realized by the practitioners. Thus, a cost of consultation of 35.91€ for general practitioners and 63.71€ for dermatologists was withheld.

The Eczema Cohorte Longitudinale Adultes (ECLA) study revealed that 1.8% of patients with AD were fully hospitalized almost twice per year, and 0.4% were hospitalized for one day (22). Costs of hospitalization were derived from disease-related groups: AD corresponded to 09M07 on the French national cost scale, and the included cost was 2,019.38€ per hospitalization.

Launois et al. (23) showed that patients do not buy the same alleviating products (food supplements, cotton clothes, or bandages) whether they have mild or moderate AD. Data from this study were used to estimate the indirect out-of-pocket expenditure of patients with AD. While these items are not mandatory to treat AD, most patients resort to them to ease the symptoms and to improve their quality of life. **Table II** shows out-of-pocket expenses for patients with AD.

Incremental cost-effectiveness ratio

The aim of the analyses was to compute the incremental cost-effectiveness ratio (ICER) using the following formula (24):

$$ICER = \frac{Cost_b - Cost_a}{Efficacy_b - Efficacy_a}$$

The ICER represents the incremental cost between 2 strategies divided by the incremental efficacy. The ratio is a decision support tool that makes it possible to estimate the cost that the community must be willing to pay to obtain an additional health unit thanks to the intervention being evaluated compared with alternative strategies.

Cost-effectiveness evaluation is a type of economic evaluation that identifies the efficiency frontier and estimates the ICER of the interventions that make it up. The efficiency frontier is made up of all non-dominated health interventions.

Table II. Out-of-pocket repartition

Item	Mild AD		Medium AD	
	Mean spending/ year (€)	Frequency of patients using this item (%)	Mean spending/ year (€)	Frequency of patients using this item (%)
Clothes	43.60	2.80	91.10	19.20
Bandages	38.00	5.30	55.00	25.20
Hygiene products	44.20	33.70	63.90	70.90
Sunscreen	36.00	24.80	39.10	39.10
Food supplement	48.20	5.30	88.00	20.60
Other products	29.60	4.60	68.40	19.70

Dominance is a situation in which a health intervention is less costly for the same or greater efficacy of its comparator, or a situation in which an intervention is more effective for the same or lower cost than its comparator.

In the base case, it is not possible to obtain a confidence interval or at least to characterize the uncertainty around the ICER due to its construction (ratio of 2 differences). It is with this in mind that sensitivity analyses are conducted (25).

Sensitivity analysis

Every decision is made in a situation of uncertainty, i.e. there is a risk of making the wrong decision. It is therefore essential to assess this risk using sensitivity analysis (26) by testing the robustness of the conclusions and identifying the key parameters. However, when carrying out a sensitivity analysis, the parameters included in the model are modified. Changing parameters allows us to account for interindividual variability.

First, each parameter was set to a define value. By fixing values to a realistic extremum, typically of ±20%, the parameters with the most influence on the results could be found. This method is known as deterministic sensitivity analysis. Then, a probabilistic sensitivity analysis (PSA) was set up (27, 28). A PSA is a multiparametric Monte Carlo analysis of type II. The principle is that each parameter of the model is characterized by a parametric probability distribution. To carry out this analysis, a probability distribution is associated with each uncertain parameter. A normal distribution was used for all parameters relating to quantities, such as the quantity of emollient used in each cycle. All frequencies (such as hospitalization) and transition probabilities (such as Mf transition and Pf transition) were modelled by a beta distribution. The different costs were associated with a gamma distribution. All distributions were specified from the initial value and standard deviation of the parameter. A total of 1,000 simulations using randomly valuated parameters according to the chosen parametric distribution were carried out, allowing us to strengthen the current results.

Launching these simulations allowed us to compute the probability of efficiency according to the willingness to pay (WTP) value, i.e. the number of times among all simulations carried out where the ICER is lower than the WTP. The WTP is the sum of money society is ready to spend for greater efficacy. The WTP varies by country. In France, no threshold of maximum WTP exists. Therefore, we had to use a range of WTP values to compute the probability of a treatment being the most efficient for a given WTP. For each simulation run, this estimation was repeated.

In a complementary analysis, the perspective was changed and all expenditures were taken into account. The cost of productivity losses from a societal perspective was added. For paediatric patients, it was assumed that the productivity loss originates from the caring parent who cannot work while nursing his or her child. The ECLA study was used to assess the frequency of sick leave (22). The human capital method was used to account for costs of productivity loss (29). Both sick leave in general and time spent in physician waiting rooms was accounted for.

Table III. Costs and effectiveness of the use of 5 different emollients (A, B, C, D and E) and the no emollient strategy in the 5-year period

Emollient	A	NE	B	C	D	E
Effectiveness						
Time without relapse, years	3.89	3.38	3.80	3.57	3.48	3.80
Costs, €						
Glucocorticosteroids	115.67	200.37	129.42	167.99	184.37	129.42
Hospitalization	312.93	410.39	328.75	373.14	391.99	328.75
Consultations	208.35	360.91	233.11	302.59	332.10	233.11
Medical expenses total	636.96	971.66	691.28	843.72	908.46	691.28
Emollients (drugs)	0.00	0.00	0.00	0.00	0.00	27.45
Emollients (medical device)	0.00	0.00	0.00	566.20	0.00	0.00
Emollients (patients/VHI)	726.87	0.00	766.87	2 699.66	788.01	155.57
Total emollients	726.87	0.00	766.87	3 265.86	788.01	183.02
OOP (excluding emollients)	211.82	259.13	219.49	241.04	250.19	219.49

OOP: out-of-pocket; VHI: voluntary health insurance; NE: no emollient.

RESULTS

Effectiveness

From a health system perspective, emollient A was the most effective. Effectiveness findings are reported in **Table III**. Patients using emollient A lived 3.89 YWFU over a 5-year period. The second-best emollients are B and E under the assumption that both have equal effectiveness of 3.80 YWFU, which is 0.09 YWFU less than that of emollient A. These results are summarized in **Table IV**.

As expected, using no emollient was the least effective strategy. Indeed, with this strategy, the benefit was only 3.38 YWFU. Therefore, emollient A provided 0.51 YWFU more than that obtained by using no emollient. The difference between emollient A and using no emollient was more than 6 months of effectiveness with 15% fewer flare-up cycles, thus leading to an improved quality of life. Emollients C and D were less effective than emollients A, B, and E.

Costs

Emollient E was the least expensive strategy, costing 1,093.80€. Hospitalizations (328.75€) and consultations (233.11€) were the main expenses for this strategy. Emollient expenses amounted to 183.02€ for the 5-year period.

No emollient strategy was more expensive than emollient E, but it was still cheaper than other emollient strategies. Over the course of 5 years, total medical expenses amounted to 1,230.79€. Among them, 971.66€ are medical expenses, accounting for the highest expenses.

Emollient A, the most effective strategy, was not the most expensive treatment (1,575.64€). While it was more expensive than emollient E (Δ=+481.84€) and using no emollient (Δ=+344.84€), it was less expensive than less effective strategies such as emollients B (Δ=–102.01€), D (Δ=–371.03€) and C (Δ=–2,774.98€).

Emollient C, the medical device, was the most expensive strategy (4,350.62€) due to the combined effect of emollient C having both the highest emollient cost (0.1119€/ml, 80% more than the next most expensive approach) and the highest emollient quantity required per cycle for a soothing effect (477.75 ml, + 50% more than the next most expensive approach).

Table IV. Incremental cost-effectiveness ratio (ICER) computation table for all comparators

	Costs, €	ΔC, €	Benefit	ΔB	ICER
Emollient E	1,093.80		3.803		
No emollient	1,230.79	136.99	3.380	–0.423	Dominated
Emollient A	1,575.64	481.84	3.885	0.082	5,877.48
Emollient B	1,677.65	102.01	3.803	–0.082	Dominated
Emollient D	1,946.67	371.03	3.475	–0.410	Dominated
Emollient C	4,350.62	2,774.98	3.573	–0.312	Dominated

ΔC and ΔB are computed from the last non-dominated comparator.

Incremental cost-effectiveness ratio

The 6 strategies were listed in ascending order of cost. The first was emollient E, the cheapest strategy, costing 1,093.80€ and 3.803 YWFU in efficacy (Table IV). No emollient was the next cheapest strategy, with a cost differential of +136.99€ compared with emollient E. The no emollient strategy is, however, less efficient than emollient E, with an efficacy differential of –0.423 YWFU. Thus, the no emollient strategy was dominated by emollient E insofar as it is more expensive and less effective.

In ascending order of cost, the next strategy was emollient A. This strategy was more expensive (+481.44€) and more effective (+0.082 YWFU) than emollient E. The computed incremental cost-effectiveness ratio (ICER) is 5,877.48€/YWFU.

The 3 following strategies in ascending order of cost, emollients B, D and C, were more expensive than emollient A (+102.01€, +371.03€, +2,774.98€, respectively). They are also all less effective than emollient A strategy (–0.082 YWFU, –0.410 YWFU, –0.312 YWFU, respectively). Thus, emollients B, D and C, are all strongly dominated by emollient A.

Emollients E and A are both on the efficiency frontier (**Fig. 2**).

Sensitivity analysis

For the deterministic sensitivity analysis, variability in the results has mainly attributable been to probabilities of Mf transition. Product cost variation was also an important source of variability in the cost of treatment.

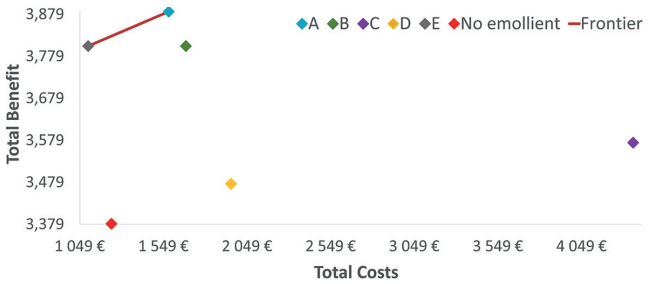

Fig. 2. Efficiency frontier of atopic dermatitis treatments.

Other probabilities of transition were reasons for variability in the efficiency of treatment.

When comparing emollient A with using no emollient in the probabilistic sensitivity analysis, emollient A was the most effective treatment in all simulations. In 23% of the simulations, emollient A was less expensive; therefore, it was the dominant strategy in 23% of the simulations.

In 89% of the simulations, emollient A was more effective than emollient E, and in 14% of simulations, emollient A was less expensive than emollient E. In 13%, emollient A was both less expensive and more effective than emollient E, making it the dominant strategy. However, in 11% of simulations, emollient E was more effective and less expensive than emollient A, thus making emollient E dominant.

Fig. 3 presents acceptability curves. From a willingness to pay (WTP) below 6,000€, applying emollient E maximized the net monetary benefits. From a WTP of 6,000€ and up, using emollient A maximized the net monetary benefits. At WTP values above 30,000€, the efficiency probability is more than 80%.

Strategies using emollients C and D were never efficient: in all simulations, they were more expensive and less effective than strategies using emollient A. For all WTPs, the probability of efficiency was null. Emollient B had a probability of efficiency below 0.5% for all WTPs. Indeed, the effectiveness of emollient B was equal to that of emollient E, while being more expensive.

Using no emollient could have been cost effective from a null WTP (11%), but the probability of efficiency rapidly decreases to 0 from 2,000€.

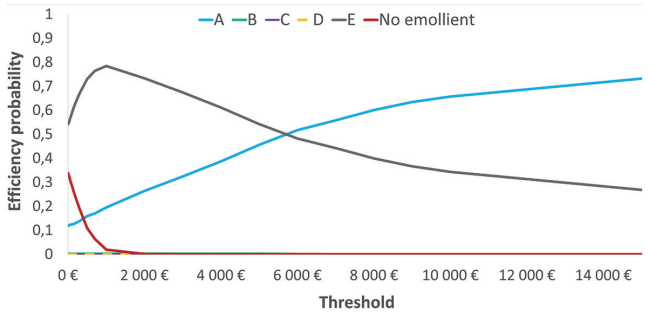

Fig. 3. Acceptability curve of different strategies in atopic dermatitis treatment.

Finally, a societal perspective was chosen instead of a healthcare system perspective. From this new perspective, all treatment strategies were costlier. However, the ranking of the strategies remained the same. From this perspective, effectiveness was equal to that obtained from a health system perspective. Therefore, no change in the dominance relationship was observed.

Changing the healthcare system perspective to the societal perspective did not modify the results. In addition, only strategies A and E constituted the efficiency frontier. The computed ICER was reduced to 5,725.30€. The productivity losses due to absenteeism were reflected in a smaller cost increase for the most effective treatment: 113.64€ for emollient A and 126.11€ for emollient E. Indeed, the more effective a treatment is, the less sick a patient is, and less time they need to be absent from work. The least effective strategy (no emollient) accounts for 190.50€ of productivity losses.

DISCUSSION

To our knowledge, this study was the first cost-effectiveness analysis of emollients used in the French healthcare setting. The use of the health system perspective in this study was justified, as it includes both treatment and medical costs.

The results are consistent with findings from the Eczema Society of Canada (30), which indicated that treating atopic dermatitis with an emollient is a cost-effective strategy. The results are also consistent with our previous findings in the UK (31). While the current results show that emollient A is superior to emollient B, a slight difference in efficacy should be noted. The ideal emollient should be safe, effective, inexpensive, and free of additives, fragrances, perfumes, and other potentially sensitizing agents (32).

The societal perspective was the most thorough and adapted to a study such as the current one. Indeed, multiple aspects of AD have often been silenced. The hidden out-of-pocket costs of AD, such as clothes and skincare products (i.e. cleansers, emollients, etc.) should be considered. Productivity losses due to absenteeism must also be considered. These costs reflected the reality of parents caring for children with AD and the difficulties faced by adults with AD in the workplace.

The link between AD and anxiety and depression strengthens the importance of using a societal perspective. There is a direct dose-effect relationship between the severity of AD and the appearance of depression and anxiety (33). Reducing the severity of AD with the use of emollients would avoid some indirect hidden costs. Currently, the model accounted for productivity losses due to AD, but not the consequences of anxiety and depression on both presenteeism and absenteeism. In addition, the model did not include the consumption of anti-anxiety medication.

Time without relapse has been used as a main outcome, and it is a good proxy for simulating patients' quality of life: patients in a relapse stage were more susceptible to sleep deprivation and anxiety, and itching was more intense during this stage.

Overall data have been lacking. Most data came from clinical trials with short durations. Therefore, hypotheses developed in this study are preliminary. Nevertheless, our sensitivity analysis results have strengthened our findings for the base-case scenario.

While the current study only used comparators from the French market, some important market-share comparators were not considered, due to a lack of data. With the exception of transition probabilities, this study only used data from the French healthcare setting.

Regarding treatment, this study exclusively incorporated topical glucocorticosteroids as a therapeutic treatment. While we had been aware of the use of topical calcineurin inhibitors as a treatment for AD, we chose not to include them. This choice was conservative: these treatments were more expensive, and introducing them would only increase cost differences. Differences in costs of treatment have been one of the main sources of result variability in the model.

Emollients A, B and E had similar effectiveness. However, emollient A was more effective in the management of patients with AD. In the current study base-case scenario and most of the probabilistic sensitivity analyses (89%), emollient A was the most effective.

Regarding costs, the main expenditure item was hospitalizations, followed by the costs of consultations. These hidden costs should be accounted for in the prescription of an emollient. The more effective an emollient was, the lower were the consultation and hospitalization costs. While no emollient had been the less costly option in terms of emollient expenditures, savings made from a lack of emollient use had been cancelled out by the higher number of consultations required.

Limitations also arose from the application of dupilumab HTA data to the French market. While these were the only data available concerning access to the healthcare system, we could not be certain that the definition of mild AD used had been the same as that used in our study. Dupilumab economic assessment's definition of mild AD was likely, based on a worse health state than ours. Therefore, healthcare access might have been overestimated in the current study, especially for the least effective strategies, thus increasing their costs. Nevertheless, as data on the frequency of consultations were accepted by an institution, we felt confident in using them.

The model developed in this study should also be confronted with real-world data. Indeed, patients tend to use emollients suboptimally, and tend to have subpar compliance with the treatment (34, 35). During RCT, patients are monitored closely, whereas in real life, when the patient obtains a prescription, what happens behind closed doors is unknown. In the developed model, using less emollient will decrease the cost of emollient and the efficacy. The differences between the comparators will be mitigated slightly. To promote the good use of emollients, the reimbursement of emollients should be implemented more widely. Purchasing emollients would have the detrimental effect of using a lower dose of emollients to spare, thinning the differences between treatment and no treatment.

Currently, in France within the Ma Santé 2022 (My Health 2022) guidelines, regulators are looking towards increasing medical time for practitioners (36). Promoting the good use of emollients will be a way to avoid consultations for AD and to allow practitioners to spend their medical time with other patients or other pathologies.

Emollient A was more expensive and effective than emollient E. For a 5-year period, a 5,877.48 €/YWFU ICER shows that, while being more expensive than a generic drug, emollient A is not that much more expensive.

Emollient C was the most expensive across all given perspectives. It should be noted that even though it was the only emollient that was partially reimbursed by social security, the out-of-pocket costs were the highest. This emollient is not a good candidate for daily application, due to its high price per unit.

It was also necessary to investigate the use of no emollient. While the general population exclusively has been foreseeing obvious costs, in the end, using no emollient has been a more expensive strategy than using emollient E. The current results suggest that the main costs of AD treatment are not obvious, and the value of questioning policies of statutory health insurance reimbursement. Even in the case of a 0€ WTP, using no emollient is unlikely to be the most efficient strategy.

Using an emollient is the best-known strategy to avoid relapse of AD. This strategy is cost-effective. Emollient A is the most effective; however, the difference from emollients B and E is small: 29 days over a 5-year period. This result was consistent with the literature.

ACKNOWLEDGEMENTS

Funding: This work was supported by La Roche-Posay Dermatological Laboratories, France.

Conflicts of interest: S. Seité and V. Delvigne are employees of La Roche-Posay, France. C. Taïeb has served as a consultant for L'Oreal/La Roche-Posay, REES France, and received funding from La Roche Posay for designing and carrying out the study.

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