Preface

This article was written by Esben Bo Boisen during the third semester of his master's degree, Medical Market Access, at Aalborg University. The article was developed in collaboration with Coloplast A/S, and is to be used as precursor for future research on the cost-effectiveness of InterDry in the treatment of intertrigo.

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Cost effectiveness of InterDry, a skin fold management product for patients suffering from intertrigo

A decision analysis

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Devised in collaboration with Coloplast A/S

Background – In the current treatment of intertrigo many patients suffer from persistent intertrigo as a results of ineffective treatment. The management of intertrigo includes addressing the causal factors of friction and moisture in opposing skin folds. In many intertrigo patients this process is associated with care from health care professionals (HCPs). Although the drugs used in the treatment of intertrigo are cheap, the associated care and persistence of the condition results in accumulated costs for the health care system. This decision analysis aims to investigate the cost pr. resolved case of intertrigo for the product InterDry textile with silver and the current treatment scheme.
Methods – A Markov decision tree, was constructed to compare the cost-effectiveness of the two interventions in a British care home setting. Effectiveness data for InterDry was extracted from an unpublished non-controlled multiple site trial, and effectiveness for the current treatment scheme was found in the literature. Drug costs were taken from Drug Tariff, and the effect of the model was cost pr. resolved case of intertrigo. A one-way sensitivity analysis and a probabilistic sensitivity analysis (PSA) was conducted to evaluate the validity of the outcome.
Results – The study estimated InterDry to provide a saving of 33.37 GBP pr. average case of intertrigo compared to the current treatment scheme. InterDry also provided an incremental effect of 0.43 resolved cases of intertrigo pr. year pr. average patient. The sensitivity analysis revealed that the outcome of the model was subject to change if the incremental nursing time of the current treatment fell below 2.1 minutes pr. day, or if the cm cost of InterDry exceeded 0.508 GBP. The PSA showed that in 75.08% of the iterations, InterDry was cost-saving.
Conclusion – The Markov model presented in the study, found InterDry to be cost-saving compared to the current treatment scheme. However, drawing a definitive conclusion from the results of this model is not possible. The model data used in this study is based on low quality clinical studies, and therefore the result of the model is questionable. In order to provide a definitive conclusion on the cost-effectiveness of InterDry and the current treatment, a RCT comparing the two interventions is needed.

Intertrigo (intertriginous dermatitis) is a cutaneous inflammatory process on opposing skin surfaces and is one of the four most prevalent moisture-associated skin damages. The condition initially presents with mild erythema as a result of moisture becoming trapped in skin folds due to poor circulation and friction. The erythema can progress to a more intense inflammation with maceration, erosion of skin (denudation) and secondary infections. The condition impacts the individual with symptoms of pain, itching, burning and

unpleasant odour, which affects the individual throughout life, as it is known to have a high recurrence rate. It is commonly found in the skin folds of the groin, axillae, inframammary folds and in obese individuals also under the abdominal or pubic panniculi [1-4]. Patients have also express discomfort, embarrassment/self-consciousness, depression/low mood and distress due to their condition, according to ward nurses [5].

Reports from The National Prevalence Measurement of Quality of Care (the LPZ), in the Netherlands, estimates that in 2014, 5.4% of the patients in the general hospital sector suffered from intertrigo and that in 2015, 6.7% of individuals in the care home sector suffered from intertrigo [6, 7]. The condition is linearly correlated with degree of obesity, as shown by Al-Mutairi and by Boza et al. [8, 9]. Boza et al. also found a prevalence of 44.7% among Brazilian obese, and Al-Mutairi found a prevalence of 22.2% among Kuwaiti obese and overweight [8, 9]. Other risk factors include age, hyperhidrosis, immobility, self-neglect, diabetes mellitus and poor hygiene [2, 4, 8].

The current treatment of intertrigo differs in relation to the type of intertrigo [1, 2, 4, 10, 11], see table 1. The initial treatment of intertrigo (simple intertrigo) is targeted at keeping the affected skin folds dry with drying agents such as bedlinen, cotton underwear or antimicrobial gauze, and at treating inflammation with a topical hydrocortisone/miconazole cream.

If the condition persists for more than two weeks, a treatment with Trimovate cream containing clobetasone, oxytetracycline and nystatin creams are recommended in addition to keeping the skin folds dry. Intertrigo infected by yeast (candidal intertrigo) is treated with topical antifungals such as imidazoles, allylamines, ciclopirox, nystatin or oral antifungals such as terbinafine, itraconazole[1, 10]. Although the drugs used in the treatment of intertrigo are cheap, the associated care and persistence of the condition results in accumulated costs for the health care system [7]. InterDry textile with silver (InterDry) is a medical absorbent fibre with a regulatory class 1 approval from the FDA. It is developed to treat both simple-, complicated- and candidal intertrigo by wicking away moisture, reducing friction and providing broad-spectrum antimicrobial action using ionic silver. InterDry has been tested in multiple unpublished case studies [12], and a single non-controlled multiple site trial of 25 subjects (19 with complete data) with hard to treat intertrigo and candidal intertrigo (MSF-study) [13].

Due to scarcity of resources in the British health care system, the aim of this study was to find the treatment of intertrigo which provides the best value money for the NHS, be measuring cost pr. resolved case of intertrigo in an British care home setting.

Table 1 The table explains the types of intertrigo, current treatment scheme and InterDry treatment. Current treatment is chosen from best available data in accordance to Primary Care Dermatology Society recommendations [10]. InterDry treatment is chosen in accordance to the recommendations from the MSF-study [13].

Type of intertrigo	Current treatment scheme	InterDry Treatment
Simple intertrigo	▪ Hydrocortisone 1%/Miconazole 2% cream (Daktracort)	▪ InterDry
Complicated intertrigo	▪ Tacrolimus 0.1% ointment (Protopic)	▪ InterDry
Candidal intertrigo	▪ Ketoconazole 2% cream (Nizoral) ▪ Hydrocorticone 1% cream (Daktacort)	▪ InterDry

Method

A decision model was constructed in TreeAge Pro Healthcare 2016 (TreeAge Software, Inc, Williamstowm, Mass.) to resemble the treatment pathway of intertrigo and include the associated costs of resolving intertrigo. The current treatment scheme consisted of three different treatments in relation to the type of intertrigo, see table 1. These were chosen on the grounds of best available data and recommendations from the Primary Care Dermatology Society (PCDS) [10]. Effectiveness data on Trimovat, the recommended treatment for complicated intertrigo, was not available and therefore effectiveness data for tacrolimus 0.1% ointment was used instead [14]. Treatment with InterDry, did not change in relation to type of intertrigo and consisted only of InterDry as the sole treatment.

A Markov model was constructed to capture the effect and cost of the types of intertrigo, and of transitioning between health states. The cycle length of the Markov model was five days, and continued for 74 cycles. The five-day cycle length, was chosen as it corresponded to the length of the treatment in the MSF-study. Effectiveness data for all other treatments were scaled down by determining the compounding curation rate. The effect of the model was *resolved cases of intertrigo*, and was chosen to make costs comparable between both interventions.

The study was based on best available data, and constructed in accordance with the NICE guidelines for health economic evaluation [15].

Markov model

The Markov cohort consisted of intertrigo patients with medicine/medical device usage patterns of the population from the MSF-study.

The model consisted of four health states: *simple intertrigo*, *complicated intertrigo*, *candidal intertrigo* and *resolved*, see figure 1. All

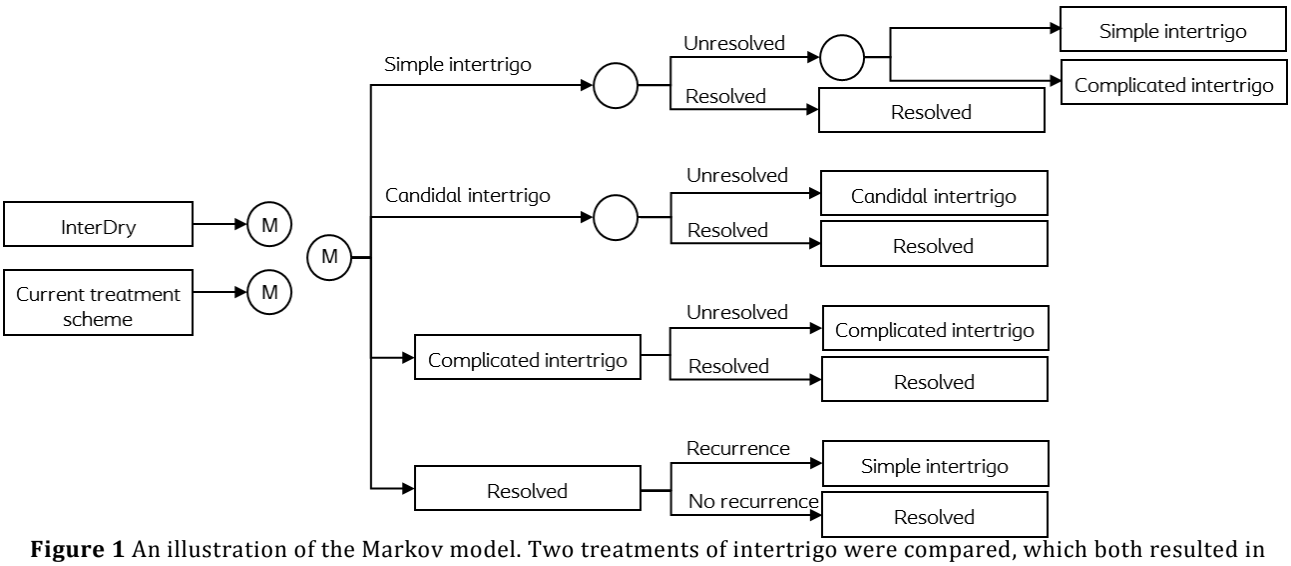

Figure 1 An illustration of the Markov model. Two treatments of intertrigo were compared, which both resulted in a Markov node. Following the Markov node, the structure of the branches of the tree was identical. All patients were distributed in either the simple- or candidal intertrigo health state. Following this, patients could either have their intertrigo resolved, or stay unresolved. If unresolved they would stay in the same health state, and if resolved they would move to the resolved health state, with a chance of having a recurrence. If patients in the simple intertrigo health state was not resolved after three cycles, they had a probability of being moved into the health state complicated intertrigo. The cycle length was 5 days and the model ran for one year. Graphic work constructed in Microsoft PowerPoint (Microsoft, Washington USA).

patients started in either simple- or candidal intertrigo. If assigned to the simple intertrigo health state, the patients could either receive treatment and be moved to the resolved health state or receive treatment and stay in simple intertrigo (unresolved). If the patients were not resolved within three cycles, they had a risk of being moved to the complicated intertrigo health state. For complicated intertrigo the patients could either receive treatment and be moved to resolved, or stay in complicated intertrigo (unresolved). After being assigned to candial intertrigo the patients could either receive treatment and be moved to the resolved health state or be treated and stay in the same health state (unresolved).

No serious adverse events were included in the model as none were described in the literature. Some patients described pain and burning when using Daktacort or tacrolimus, however the model did not take these events into account [13, 14, 16].

Model costs included medicine, medical devices and care. The costs were adjusted for the five-day cycle length, and usage of medicine and medical devices were adjusted to match the usage of the MSF-study population and the five-day cycle length. Due to the wicking effect of InterDry keeping the skinfolds dry, the daily care is assumed to decrease for the InterDry population. Therefore, an increment of 15 minutes of daily adult nurse care was added to all stages of the current treatment scheme.

Costs and effects were not discounted as the model did not run for more than a year.

Data Input, Probability

Probabilities for distribution between simple, and candidal intertrigo were calculated using a weighted mean from the LPZ reports from 2013-2015, see table 2.

All probabilities for InterDry were calculated from the MSF-study [13]. The effectiveness of simple intertrigo treatment was calculated from a clinical study investigating a 2-week treatment with hydrocortisone vs. hydrocortisone with miconazole [16]. The percentage of patients that did not respond to the treatment was used to indicate the risk of transitioning to complicated intertrigo. The clinical study included 3 patients with candial intertrigo which had to be included in the simple intertrigo group due to the raw data being unavailable. Probabilities for the treatment of complicated intertrigo was taken from a clinical study investigating a 6-week treatment period of 0.1% tacrolimus ointment in intertrigo patients with no comparator [14], and probabilities for candidal intertrigo was calculated from a study investigating 2% ketoconazole powder in a 6-week treatment period [17].

Data Input, Cost

All costs were taken from 2015-2016 levels.

Drug costs were extracted from Drug Tariff [18], except the cost of InterDry which was the retail price in Canada [19]. Canadian costs were converted with an exchange rate of 0,5256 (price for 1 unit of currency).

The usage of InterDry, tacrolimus, hydrocortisone/miconazole, hydrocortisone and ketoconazole was estimated from the average use investigated in the MSF-study [13].

The cost of care was taken from the NHS nursing pay scales, and an average of the adult nurse pay rate was implemented [21]. The model assumed 15 minutes of care pr. day designated to cleaning of the intertrigo site.

The study applied a care home setting, and it was therefore assumed that the population could not contribute to the labour market. Cost

attributed to loss of ability to work was therefore not included in the model.

A half cycle correction was used for costs.

Data Input, Effect

The effect was chosen to represent the average cost of resolving a patient with intertrigo. All patients that transitioned from an intertrigo health state to a resolved health state were given an effect of one, which was implemented as a transitional effect. All other patients were given an effect of zero.

Sensitivity analysis

A one-way sensitivity analysis of all variables was conducted and presented in a tornado diagram. This was done to test the robustness of the model and the outcome in relation to changes in the variables. The variables with the most impact on expected value were also investigated in a cost-effectiveness one-way sensitivity analysis plane. All probabilities that did not have confidence intervals provided from the literature were given a standard deviation (SD) of ±5%, and all costs were given a SD of

Table 2 Table describing probabilities, costs and effects included in the Markov model.

Input Variable, probability	Value (SD)	Reference
Intertrigo in care homes (%)	7.07 (6.72-7.42)	[6, 7, 20]
Simple Intertrigo (%)	96.27 (91.46-100)	[6, 7, 20]
Candidal Intertrigo (%)	3.73 (3.54-3.91)	[6, 7, 20]
InterDry treatment		
Simple intertrigo – resolved (%)	73.33 (69.66-77.00)	[13]
Simple intertrigo – complicated (%)	6.67 (6.34-7.00)	[13]
Complicated Intertrigo – resolved (%)	50.00 (47.50-52.5)	[13]
Candidal intertrigo – resolved (%)	50.00 (47.50-52.5)	[13]
Current treatment scheme		
Simple intertrigo – resolved (%)	42.15 (40.00-44.26)	[16]
Simple intertrigo – complicated (%)	2.89 (2.23-2.52)	[16]
Complicated Intertrigo – resolved (%)	23.98 (22.78-25.18)	[14]
Candidal intertrigo – resolved (%)	18.47 (17.55-19.39)	[17]
Input Variable, Cost	**Value (SD)**	**Reference**
InterDry treatment		
InterDry (cm of length/5-days)	67.56 (54.05-81.08)	[13]
InterDry, cost for roll (GBP/cm of length)	0.13 (0.104-0.156)	[19]
InterDry (GBP/5-days)	8.77 (7.02-10.53)	[19]
Current treatment scheme		
Incremental care (GBP/5-days)	15.94 (12.75-19.13)	[21]
Nursing care rate (GBP/hour)	12.75 (11.09-14.41)	[21]
Hydrocortisone 1%/Miconazole 2% cream (grams/5-days)	21.43 (17.14-25.72)	[13]
Hydrocortisone 1%/Miconazole 2% cream (GBP/5-days)	1.78 (1.42-2.14)	[18]
Tacrolimus 0.1% ointment – 5 day use (grams/5-days)	21.43 (17.14-25.72)	[13]
Tacrolimus 0.1% ointment – 5 day cost (GBP/5-days)	16.89 (13.51-20.27)	[18]
Ketoconazole 2% cream – 5 day use (grams/5-days)	21.43 (17.14-25.72)	[13]
Ketoconazole 2% cream – 5 day cost (GBP/5-days)	3.03 (2.42-3.64)	[18]
Hydrocortisone 1% cream (grams/5-days)	21.43 (17.14-25.72)	[13]
Hydrocortisone 1% cream (GBP/5-days)	1.34 (1.07-1.61)	[18]
Input Variable, Resolve	**Value**	**Reference**
Intertrigo resolved (Any Type)	1	
Intertrigo unresolved (Any Type)	0	

±20%. Nursing time was given a SD of ±100%, as the nursing time variable was related to high uncertainty.

A probabilistic sensitivity analysis (PSA) was also conducted using a 2nd order Monte Carlo Simulation of 10,000 iterations. For this analysis costs were given a gamma distribution using SD, and probabilities were given a beta distribution using SD. A cost-effectiveness scatterplot with a 95% iteration ellipses and an acceptability plot was conducted with a WTP of 0.

Results

Table 3 features all costs and effects associated with one patient for the current treatment scheme and for InterDry in a one-year perspective. As indicated in the table, the costs of resolving an average patient is 11.49 GBP with InterDry and 44.86 GBP with the current treatment scheme. By using InterDry instead of current treatment, a saving of 33.37 GBP pr. patient pr. average case of intertrigo could be achieved. The accumulated effect of 5.59 for InterDry, and 5.16 for the current treatment scheme, also showed that InterDry treated more cases of intertrigo in the one-year time span.

The tornado diagram of the one-way sensitivity analysis showed that multiple variables affected the robustness of the model, see figure 2. Nursing time was identified as the variable having the biggest impact on the expected value. A one-way sensitivity analysis with a cost-effectiveness plot of nursing time, revealed that the chosen intervention of the decision model changed at a value of 0.035, corresponding to an increment of 2.1 minutes of nursing time pr. day, see figure 3.

The cm cost of InterDry had the second biggest impact on the expected value. A one-way sensitivity analysis with a cost-effectiveness plot of the cm cost of InterDry revealed that the chosen intervention of the decision model changed at a value of 0.508 GBP, see figure 4.

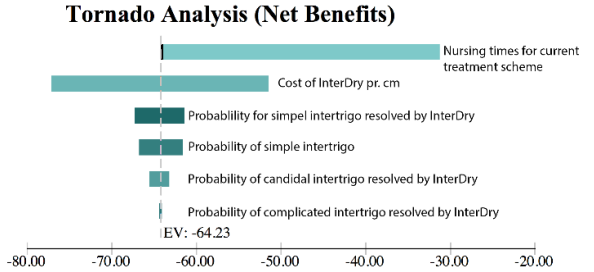

Figure 2 Tornado diagram sensitivity analysis. The figure displays the six most impactful variables on the expected value. The x axis represents the expected value of InterDry, and the size of the bars the impact the variable has on the expected value. Black mark indicates a change of chosen intervention.

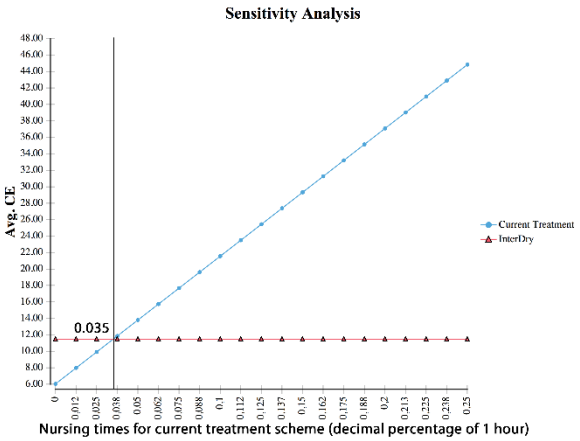

Figure 3 The graph indicates the average cost-effectiveness related to the nursing time for current treatment scheme variable. At a nursing time of 0.035 corresponding to 2.1 minutes of care, the current treatment scheme is more cost-effective than InterDry.

Table 3 The table displays the outcomes of the Markov model.

	Cumulative cost (GBP)	Cumulative effect (Resolved cases)	Cost/effect (GBP/resolved case)
Current Treatment Scheme	231.54	5.16	44.86
InterDry	64.23	5.59	11.49
Increment	-167.31	0.43	-33.37

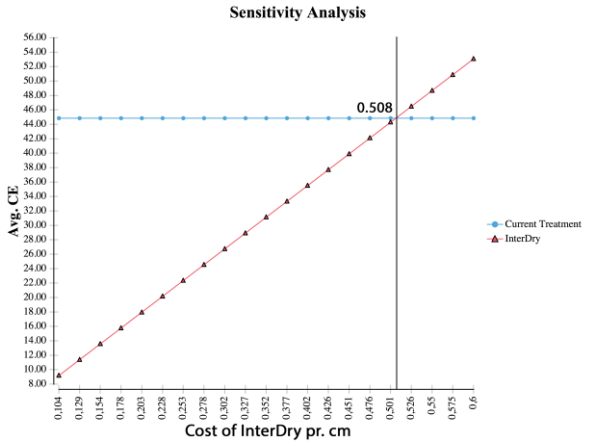

Figure 4 The graph indicates the average cost-effectiveness related to the cost in of InterDry pr. cm (GBP/cm) variable. The cost-effectiveness plot revealed that the preferred intervention of the Markov model changed at a value of 0.508 GBP.

The PSA incremental cost-effectiveness scatterplot showed that InterDry was more effective in all of the iterations, and cost-saving in the majority, see figure 5. This was further investigated in a cost-effectiveness acceptability diagram with a WTP of 0, which showed that in 75.08% of the iterations InterDry was cost-saving.

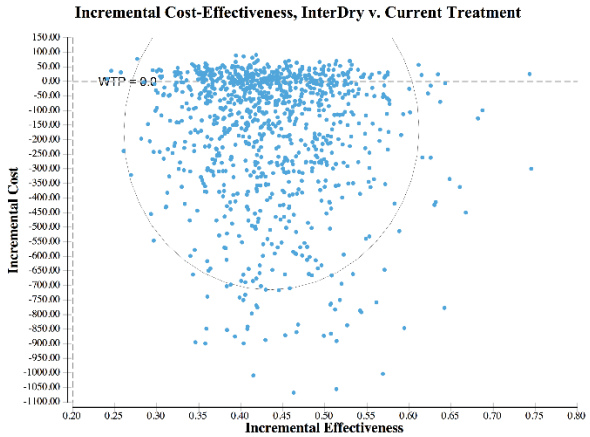

Figure 5 The graph shows the incremental cost-effectiveness plane with a scatterplot of 1000 iterations from the PSA. The ellipses represent the 95 % joint density on the cost-effectiveness plane. A WTP of 0 was applied, as the cheapest option was preferred.

Discussion

Intertrigo is a well-known condition among health care professionals (HCPs), but has received little attention by researchers, and as a result only three RCT's exist on intertrigo in PubMed. Treatment of the condition is mostly based on consensus statements, case studies and the expertise of the individual HCP [4, 22]. The lack of attention leads to many cases of intertrigo going unresolved, and the patients having to live with the symptoms for long periods of time. This was evident in the LPZ reports, where 29.4% of the intertrigo patients in care homes lived with unresolved cases of intertrigo for more than a year [7]. It is therefore evident that a more effective intervention is needed to treat intertrigo. This study revealed that despite the higher initial product cost of InterDry, it was not only more effective, but also cost-saving compared with the current treatment.

The sensitivity analysis' showed that InterDry was cost-saving as long as the incremental nursing time was above 2.1 minute of care pr. day, and if the cm price was below 0.508 GBP. Unfortunately, no real life data exists on nursing times related to intertrigo, and therefore the values were based on estimates.

The population in the MSF-study was chosen because they were hard to treat, and at inclusion of the study had a prior average treatment time of 226 days. Therefore, the population in the MSF-study was not representative of the general care home population, which implicates that the and the effect of InterDry could be underestimated.

The need for care from HCPs in the treatment of intertrigo can vary greatly from setting to setting, and therefore InterDry can only be assumed to be cost-saving for patients who depend on HCPs for care.

The current treatment scheme investigated in this study was recommended by the PCDS, but due to lacking evidence for the use of Trimovat in intertrigo, this had to be replaced with Tacrolimus. Many different approaches to the treatment of intertrigo exist, and this model only explores one of these treatment schemes. The construction of this model however opens the possibility to investigate multiple interventions by inputting the relevant data into the model.

Interdry was shown to be cost-saving in the care Home setting, however the prevalence of intertrigo among overweight and obese is known to be even higher than in care homes [8, 9]. These individuals often have intertrigo in hard to reach places, and depend on HCPs to facilitate the treatment. This segment of people would be interesting to investigate, and it is possible InterDry could provide an even greater benefit to this population.

The cost of the illness of intertrigo has not yet been investigated, however the high prevalence and the related costs indicates a significant drain on resources for the NHS.

Limitations

Several limitations apply to the outcome of this decision model. The model was based on best available data, however many of the studies included in the model were of low significance. The MSF-study only had complete data on 19 of the 25 patients included in the study, and only four of these patients had candidal intertrigo. A low significance was also evident in the ketoconazole 2% study which only investigated 22 patients, and the tacrolimus study which only investigated 10 patients. This is a significant hurdle for the relevance of the model, and an RCT including InterDry and the current treatment scheme should be conducted to strengthen the model input.

When investigating the effectiveness data for the current treatment, the resolve probabilities had to be scaled down in order to fit the cycle length. This was done using the compounding curation rate. The accuracy of this approach can be challenged, as this does not mimic the real life pathology of the disease. Using the compounding curation rate assumes that patients are resolved at a steady rate, spread out over multiple cycles, when in fact the majority of patients are resolved within the first week of treatment [16].

The model does not take into consideration the prevalence of bacterial intertrigo and the treatment hereof. The split between bacterial and candidal intertrigo was not described in the LPZ reports, and the treatment of bacterial intertrigo was not included in the MSF-study. Therefore, all cases of infected intertrigo presented by the LPZ were treated as candidal intertrigo. The model was also limited to transitioning from simple to complicated intertrigo, even though this isn't representative of the pathology of intertrigo. The model could have included the possibility of transitioning between all types of intertrigo, but was limited by the literature.

Conclusion

The study found InterDry to be cost-saving in a care home setting. InterDry provided an effective and cost-saving intervention by reducing the average treatment cost of intertrigo by 33.37 GBP, and treating 0.43 more cases of intertrigo pr. year pr. patient. The sensitivity analysis revealed that the outcome of the model only changed given that the incremental nursing time for the current treatment was below 2.1 minutes pr. day, or if the cm cost of InterDry was above 0.508 GBP pr. cm. The PSA revealed InterDry to be cost-saving in 75.08% of the iterations.

The results of the study rely on low quality data, and to many assumptions, and therefore the study cannot provide a definitive conclusion on the cost-effectiveness of InterDry. In order to provide a definitive conclusion, a RCT investigating the treatment of InterDry and the current treatment is needed.

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