A cost-effectiveness analysis of a hydration response technology dressing in the treatment of venous leg ulcers in the UK

Objective: Venous leg ulcers (VLUs) cause significant pain and suffering for patients. Additionally, they place considerable financial and service burden on the National Health Service (NHS). A large proportion of VLUs do not heal within the standard time frame of 16–24 weeks, resulting in static wounds which commonly have issues with increasing exudate production. As the NHS continues to face times of austerity, services need to find solutions to be able to reduce costs and release nursing time while maintaining standards of care. Cutimed Sorbion Sachet S, a hydration response technology dressing (HRTD), is a treatment option for the management of patients with a VLU. The objective of this study was to provide an update of the health economic analysis of HRTD in comparison with relevant comparators in the UK with current cost data.
Method: HRTD was compared against four different dressings, Zetuvit Plus (a super absorbent polymer dressing SAP), DryMax extra (a superabsorbent dressing, SADM), KerraMax Care (superabsorbent dressing, SAKM) and Eclypse (superabsorbent dressing, SAE) from a cost-effectiveness perspective. Clinical data were derived from literature and expert opinion. Cost input was utilised based on publicly available data and literature. The average patient in the model is assumed to be 65 years with a diagnosed VLU. It is assumed that patients in the different treatment arms have the same background mortality, hence the endpoint mortality is not included in the model. The analysis is based on a deterministic Markov model derived from Harding et al. with weekly cycles. The following assumptions are made: first, all patients start in a static health state with a non-healed but non-progressing VLU. It is assumed in the model that patients wounds can transition to a deteriorating state or one where a wound is improving or could progress. Additionally, VLUs could be healed from a progressed wound (i.e. improved wound), or they could develop into a severe wound with complications (infections) to be treated in hospitals. The time frame for the analysis was fixed for one year and no re-occurence after healing was assumed to happen.
Results: The cost-effectiveness analysis demonstrates health economic dominance of HRDT being more effective and cost-saving against all analysed comparators. When using literature-based input values, the incrementally higher healing rates for HRDT are 11.04 months (versus SAP), 29.04 months (versus SADM), 1.68 months (versus SAKM) and 11.04 months (versus SAE). Cost savings per patient were £37.60 versus SAP, £171.68 versus SADM, £3.13 versus SAKM and £43.63 versus SAE.
Conclusion: Clinical benefits and cost savings increase when real-life practice assumptions, based on expert opinion, are included. Based on the underlying health economic model, HRDT is more effective and less costly than other comparative products in VLUs in the UK.
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chronic wound • cost-effectiveness • Cutimed Sorbion Sachet S • health economics • venous leg ulcer

Patients with lower limb ulceration are common in clinical practice; within a one year period in the UK there were 730,000 leg ulcerations documented, equating to 1.5% of the adult population.[1] The most common cause of lower limb ulceration is attributed to venous hypertension with venous ulceration being reported to affect up to 1% of all adults, increasing to 1.7% for those aged over 65 years.[2,3] Furthermore, the prevalence of leg ulceration is known to increase with age,[4] with peak prevalence for the development of leg ulceration in patients aged between 60–80 years,[5] therefore, due to an aging population the number of patients affected by venous ulceration is likely to rise. Venous ulceration often takes weeks or months to heal and frequently recur. During the time of ulceration high volumes of exudate may be produced, it is painful and even malodorous, and all of these issues can negatively affect patient's quality of life (QoL).[6,7] The National Health Service (NHS) spends a substantial amount of money in the treatment of venous ulceration, mostly through community services; the annual spend on leg ulceration was estimated to be around £1.94 billion.[8]

It is acknowledged that the most important treatment for venous ulceration is compression therapy which is designed to improve venous return, reduce venous hypertension, and hence manage the underlying cause. However, it is also vital to ensure that venous leg ulcers (VLUs) are maintained in an ideal environment, which promotes wound healing, one of the most vital aspects

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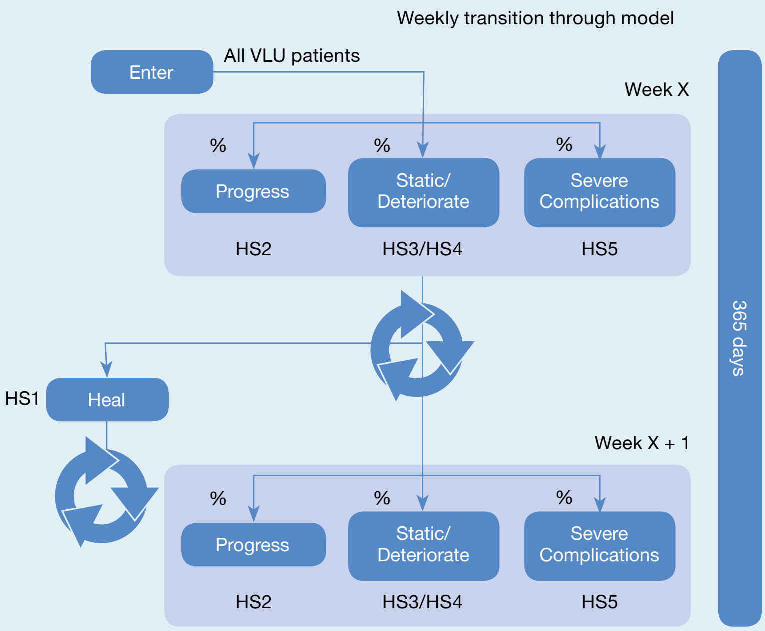
Fig1. Health states within the model based on the patient's pathway based on Harding et al.[19]



is the adequate management of wound exudate. If exudate is not adequately controlled this can negatively affect the wound bed and periwound skin, increasing the risk of infection resulting in delayed wound healing.[9] The use of advanced wound treatments such as Cutimed Sorbion Sachet S (Hydration Response Technology dressing, HRTD) could aid the management of VLUs by providing an ideal wound environment and ensuring effective exudate management, allowing for fewer dressing changes, resulting in less nursing visits and therefore providing overall cost savings.

Consideration of unit cost and comparing this with patient/service benefits is vital when trying to establish overall cost-effectiveness. Disease and health economic models can be adopted to demonstrate costs and patient benefits. Health economic modelling is a globally recognised technique based on well-documented, international standards.[10,11] Models are developed in order to demonstrate consequences of measurable effects which would only become clear in the future. By using health economic evaluation, the effects of cost reimbursement for new medical treatment methods may be quantified in relation to existing care modalities.[12]

HRTD has been evaluated as a treatment option to control exudate with the ability to progress patients from chronic or non-progressing wounds onto improving or healing wounds. In Panca et al.[13] an initial assessment of various wound dressings in the UK was published. The clinical basis as well as the cost basis might have changed since then. Hence, the objective of this study was to provide an update of the previously published health economic analysis of HRTD[13] in comparison with relevant comparators in the UK with current cost data. Analysis of HRTD was undertaken comparing with Zetuvit Plus (a super absorbent polymer dressing SAP), DryMax extra (a superabsorbent dressing, SADM), KerraMax Care (superabsorbent dressing, SAKM) and Eclypse (superabsorbent dressing, SAE) from a cost-effectiveness perspective.

The question under investigation was: 'Is HRTD cost-effective when compared to alternative treatments used to manage VLUs in the UK?'

Methods

To ensure a robust data base for the health economic model, a systematic literature search was conducted in the (standard) literature databases Medline through PubMed, INAHTA (International Network of Agencies for Health Technology Assessment), NHS Economic Evaluation Database and DIMDI (Deutsche Institut für Medizinische Dokumentation und Information; German Institute for Medical Documentation and Information) for Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews and DAHTA database (German HTA database). The research question was defined on the basis of the PICO criteria[14] literature search parameters. PICO criteria were as follows:

- Patient and intervention: chronic wounds, VLU, wound care, therapy, diagnostics
- Comparison: patients with or without medical therapy or therapy in support of medical devices, including dressing and bandages
- Outcomes: cost, cost-effectiveness, cost per quality-adjusted life year (QALY), cost minimisation, cost comparison, cost of illness, health economics, health economic model, statistical model.

The search was conducted over 12 years (2005–2017) in order to focus on the most relevant therapies (and models). Included languages were German and English. Inclusion criteria were health economic models and/or health economic analysis in the UK, ideally with a special focus and clear guidance for a health economic model. Overall, there were 831 hits across all included databases. After title selection and abstract review, full text evaluation was executed for 26 articles. Overall, there were six articles identified in which a UK analysis was provided in VLUs.[13,15–19] Of these six articles, one was a multinational analysis[17] and four were analyses on specific products without a recommendation on health economic modelling approaches.

Harding et al.[19] was the only article where a general approach, in terms of a new costing method, was recommended that can be used as a health economic modelling frame in chronic wounds, and was deemed to be appropriate for the underlying research question on which a Markov model was developed. Based on this deterministic Markov model with weekly cycles, a cost-effectiveness analysis was performed from the UK NHS payer's perspective. The time frame for the analysis was fixed for one year. The average patient in the model is assumed to be 65 years with a diagnosed VLU. It is

Table 1. Transition probabilities for the different treatment in the various health states of the underlying model

	Model path	Transition probability (per week)					Reference
		SAP	SADM	SAKM	SAE	HRDT	
Healed to unhealed grade 1 static	HS1 to HS3	0.0000	0.0000	0.0000	0.0000	0.0000	Assumption: no recurrence
Unhealed grade 1 progression to healed	HS2 to HS1	0.0180	0.0144	0.0200	0.0180	0.0204	Assumptions based on Panca et al. 2013[13]
Unhealed grade 1 static to unhealed grade 1 progression	HS3 to HS2	0.0600	0.0600	0.0600	0.0600	0.0600	Shannon et al. 2016[20]
Unhealed grade 1 static to unhealed grade 1 deteriorating	HS3 to HS4	0.0188	0.0188	0.0188	0.0188	0.0188	Walzer et al. 2016[21]
Unhealed grade 1 deteriorating to unhealed grade 2 severe	HS4 to HS5	0.0040	0.0040	0.0040	0.0040	0.0040	Shannon et al. 2016[20]
Unhealed grade 2 severe to unhealed grade 1 static	HS5 to HS3	0.8000	0.8000	0.8000	0.8000	0.8000	Walzer et al. 2016[21]

SAP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S

assumed that patients in the different treatment arms have the same background mortality, and hence it is not included in the model.

The health states in the model are defined as follows (Fig 1):

- Heal: skin is intact (HS1)
- Progress: ulcer is progressing towards healing (HS2)
- Static: ulcer is neither healing nor deteriorating (HS3)
- Deteriorating: ulcer is deteriorating (e.g. increasing in size, exudate or odour; surrounding skin is deteriorating) (HS4)
- Severe: ulcer is infected or with other complications which may require hospital admission and/or surgical intervention (HS5).

It is assumed that all patients' wounds start in the static health state (HS) with a non-healed and non-progressing VLU (HS3). Thereafter, patients' wounds can transition to a deteriorating health state (HS4) or one where a wound is improving or could progress (HS2). From (HS2) VLUs could be healed (HS1) or from a progressed wound they could develop into a severe wound with complications (infections) to be treated in hospital (HS5).

In other words, all patients in the model start with a currently non-healed wound which has not improved (HS3). At this stage in the model, the treating clinician chooses one of the dressings included in the model. Based on the probabilities for these dressings, the patient's wound could improve (HS2) or could worsen (HS4). Such changes in the wound are calculated on a weekly basis. The following week an improved wound (HS2) could be healed (HS1), whereas, a worsened wound (HS4) could improve (HS3) or even develop complications which would need to be treated in hospital (HS5).

Transition probabilities for the different health states and treatment options available in the model were derived from different sources (Table 1). No re-occurence of wounds after healing happen in this model (HS1 to HS3), however there is the flexibility analysing such an option in sensitivity analyses. Transition probabilities for moving patients from unhealed grade 1 progression (HS2) to healed were based on Panca et al.[13] For SAP and SAE, neither are included in Panca et al.[13] analysis, the average transition probability was assumed between SADM, SAKM and that HRTD as follows: HRTD efficacy in terms of healing was taken from Panca et al.[13] Transition probabilities for unhealed grade 1 static to unhealed grade 1 progression (HS3 to HS2), and unhealed grade 1 deteriorating (HS4) to unhealed grade 2 severe (HS5) were both taken from Shannon et al.[20] and assumed to be independent to the underlying treatment. The transition probability for unhealed grade 1 static to unhealed grade 1 deteriorating (HS3 to HS4) was based on Walzer et al.[21] Furthermore, it was assumed that all patients received two wound dressing changes per week, regardless of the underlying treatment.

Table 2. Utilities of individual health states in the model based on Shannon et al.[22]

Health State	Utility
Healed (HS1)	0.630
Progressing (HS2)	0.534
Static (HS3)	0.525
Deteriorating (HS4)	0.534
Severe (HS5)	0.130

The health state utilities were determined through investigation of EQ-5D data from a one-year pragmatic, randomised longitudinal VLU study (VenUS III) completed in the UK.[22] An EQ-5D five-dimension score (mobility, self-care, usual activities, pain/discomfort and anxiety/depression), recorded within zero to three weeks of each documented health state, was identified in the VenUS III dataset and then translated into a EQ-5D index score (utility value). Translation of five-dimension score to the index score was completed using an EQ-5D index calculator. The utilities for the health states 'progressing' and 'deteriorating' were assumed to be the same (Table 2).

The costs for the various health states were directly taken from Harding et al.[19] (Table 3). Once a patient is healed quarterly outpatient visits are assumed, costs derived from experts.

The individual costs of each therapy have been taken into account per dressing (Table 4). It was assumed, that each time a wound dressing was changed, a new dressing was applied (from the same manufacturer). The costs of additional wound care products have not been included in the calculations, assuming that similar products and consequently similar cost would arise.

Healing of the wound is the primary efficacy endpoint and is also the basis for the cost per QALY analysis in the model. Both the total costs and the respective cost of care per health state were determined as cost endpoints. Finally, the efficacy and cost endpoints of the model are compared to calculate the incremental cost-effectiveness ratio (ICER). The calculation is performed as the difference of the total costs between a HRTD therapy, and the respective treatment options SAP, SADM, SAKM and SAE, respectively. Analogically, the incremental efficacy was calculated based on the respective efficacy values. Finally, the incremental cost-effectiveness has been calculated, and both the costs per additional year of healing and the costs per QALY gained are determined.[12]

The ICER was calculated as follows:

$$\text{ICER} = \frac{(\text{HRTD costs}) - (\text{comparative therapy costs})}{(\text{HRTD efficacy}) - (\text{comparative therapy efficacy})}$$

Sensitivity analyses were executed on key variables of the model. Expert opinion (VLU clinician in cooperation with a wound nurse) on the transition probabilities for each health state were used in order to implement a 'real life' input into the model (Table 5). Within that process, experts were asked how many patients out of 100 patients would get one of the health states below. Health states were described for clinical personnel in order to get adequate responses.

Table 3. Cost input for the health economic model

Cost items	Cost per week	Reference
Healed (HS1)	£6.04	Harding et al.[19]
Progressing (HS2)	£87.59	Harding et al.[19]
Static (HS3)	£100.27	Harding et al.[19]
Deteriorating (HS4)	£159.45	Harding et al.[19]
Severe (HS5)	£637.15	Harding et al.[19]
Cost per outpatient visit ('administration cost')	£2.48	Expert opinion

Table 4. Package price input per therapy and week (package assumption for pack size: 10x10)

Product	Cost per package (use per wound dressing)	Reference
SAP	£0.64	Public UK price (April 2017)[23]
SADM	£0.87	Public UK price (April 2017)[23]
SAKM	£1.29	Public UK price (April 2017)[23]
SAE	£0.73	Public UK price (April 2017)[23]
HRTD	£1.49	Public UK price (April 2017)[23]

SAP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S

Table 5. Changed transition probabilities for the different treatments in the various health states of the underlying model in sensitivity analysis

	Model path	Transition probability (per week)					Reference
		SAP	SADM	SAKM	SAE	HRTD	
Unhealed grade 1 static to unhealed grade 1 progression	HS3 to HS2	0.5000	0.5000	0.5000	0.5000	0.5000	Expert opinion
Unhealed grade 1 static to unhealed grade 1 deteriorating	HS3 to HS4	0.3000	0.3000	0.3000	0.3000	0.3000	Expert opinion
Unhealed grade 1 deteriorating to unhealed grade 2 severe	HS4 to HS5	0.1000	0.1000	0.1000	0.1000	0.1000	Expert opinion
Unhealed grade 2 severe to unhealed grade 1 static	HS5 to HS3	0.1000	0.1000	0.1000	0.1000	0.1000	Expert opinion

SAP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S

Table 6. Cost comparison results in the treatment of venous leg ulcers in the UK Table 3. Cost input for the health economic model

Health state	SAP	SADM	SAKM	SAE	HRTD
Healed (HS1)	£56.49	£47.44	£61.22	£ 56.49	£62.07
Progression (HS2)	£1909.62	£2040.90	£1841.09	£ 1909.62	£ 1828.79
Static (HS3)	£1261.67	£1267.36	£1277.31	£ 1264.04	£ 1282.05
Deteriorating (HS4)	£1481.50	£1487.66	£1495.18	£ 1485.15	£ 1498.76
Severe (HS5)	£27.71	£27.71	£27.71	£ 27.71	£ 27.71
Total cost	**£4736.98**	**£4871.07**	**£4702.51**	**£ 4743.01**	**£ 4699.38**

SAP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S

Table 7. Cost-effectiveness results from a UK payer's perspective

Comparison	Incremental effect ('healed')	Incremental cost	Incremental utilities ('QALY')	Incremental cost-effectiveness	Incremental cost per QALY
HRTD versus SAP	0.92 years (11.04 months)	£37.60	0.0017	–£40.75	–£22,073.30
HRTD versus SADM	2.42 years (29.04 months)	£171.68	0.0045	–£70.90	–£38,403.23
HRTD versus SAKM	0.14 years (1.68 months)	£3.13	0.0003	–£22.28	–£12,065.77
HRTD versus SAE	0.92 years (11.04 months)	£43.63	0.0017	–£47.28	–£25,612.37

SAP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S; QALY—quality-adjusted life year

Table 8. Sensitivity analysis results on the cost-effectiveness a UK payer's perspective

Comparison	Incremental effect ('healed')	Incremental cost	Incremental utilities ('QALY')	Incremental cost-effectiveness	Incremental cost per QALY
HRTD versus SAP	1.27 years (15.24 months)	£3792.71	0.0023	–£73.02	–£39,552.51
HRTD versus SADM	3.35 years (40.2 months)	£265.38	0.0062	–£79.26	–£42,932.70
HRTD versus SAKM	0.19 years (2.28 months)	£13.24	0.0004	–£68.71	–£37,219.82
HRTD versus SAE	1.27 years (15.24)	£94.14	0.0023	–£74.15	–£40,163.92

AP—Zetuvit; SADM—DryMax extra; SAKM—KerraMax Care; SAE—Eclypse; HRTD—Cutimed Sorbion Sachet S; QALY—quality-adjusted life year

Results

The total costs per patient per year are reported in Table 6. According to the model, for a patient with HRTD the costs amount to £61.99. The main cost drivers are the costs in the progression (HS2) and deteriorating (HS4) health states, which account for more than 71% of the total costs (£4699.38). In contrast to this, the total annual costs with SAP, SADM, SAKM and SAE are £4736.98, £4871.07, £4702.51 and £4743.01 respectively.

The higher healing rates in the effect assumption (see Table 1 versus Table 5) for HRTD can also be affirmed in the higher incremental effect in the total calculation (Table 7). Given the higher utility values for the healed health state this advantage is also transferred into the incremental QALYs. The incremental cost-effectiveness, as reported in Table 7, is calculated from the modelled efficacy, calculated for an additionally healed patient, and the total costs accordingly. The difference in the incremental costs shows the difference in the total costs for the treatments to be compared. Finally, the incremental cost-effectiveness puts the difference in the costs in relation to the difference in the healings. According to the model, a HRTD therapy is more effective and cost-saving and can therefore be regarded as dominant in relation to the other four analysed therapies from a health economic's viewpoint.

The results of the base case analysis are also confirmed in the sensitivity analysis (Table 8). HRTD remains to be dominant from a health economic perspective. It is more effective and less costly against the four different other wound care therapies.

Discussion

The present analysis is an updated cost-effectiveness analysis related to HRTD in the UK.[13] The initial procurement costs of HRTD are negated when compared to the improved wound healing rates leading to reduced dressing changes, time for nurse visits and improved outcomes. However, as there are no randomised controlled trials (RCTs) available comparing different wound therapies against each other based on patient relevant endpoints such as healing, assumptions had to be taken between the therapies. The transition probabilities were assumed to be the same between the therapies for all health states except HS2 transitioning to HS1. These assumptions were taken from a published analysis by Panca et al.[13] and re-calculated into weekly probabilities. When changing the transition probabilities for the different health states from literature-based into real life expert opinions the results were quantitatively different, however the direction of the results remains the same. HRTD remains more effective and less costly.

Limitations

Markov models have been criticised as they might simplify reality further in comparison to other modelling approaches.[12] A key issue may be the exclusion of the majority of items included in the analysis, such as patient characteristics. In Markov models, cohorts are modelled instead of individual patients with specific characteristics and its correlation and covariates to clinical outcome parameters. Nevertheless, the underlying model is a well defined clinical snapshot of the reality including detailed health states during the different steps of a patient's journey.

Additionally, the clinical input values for the five therapies included in the analysis are based on assumptions and clinical data without direct evidence between those; similar to already published health economic evidence.[13] Based on the limited data availability also a network meta-analysis to derive the adjusted indirect evidence was not feasible.

Cost data are based on Harding et al.[19] However, their analysis mainly focused on testing a cost methodology even though the used data was derived directly from different treatment centres across the UK. In the analysis, it was shown that the key modelling parameter was the probability of healing, although healing was not proven in any of the underlying therapies. However, in Panca et al.[13] similar assumptions were used and also aligned with clinical experts in the UK who experienced similar numbers in real life settings.

Conclusion

The management of patients with VLUs is a daily challenge to many UK clinicians, the key to effective management is compression therapy, yet there are occasions when venous ulcerations fail to show signs of healing and issues with high volumes of exudate are common place. HRTD provides an ideal wound environment to allow healing to occur with the added advantage of being able to handle high volumes of exudate ensuring that the wound is protected from the damaging effects of uncontrolled moisture. Based on this health economic modelling, HRTD was more effective in promoting healing and less costly when compared with other comparative dressings within the UK. **JWC**

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