Journal of Tissue Viability 32 (2023) 262–269

Contents lists available at ScienceDirect

Journal of Tissue Viability

journal homepage: www.elsevier.com/locate/jtv

Cost-Effectiveness of PHMB & betaine wound bed preparation compared with standard care in venous leg ulcers: A cost-utility analysis in the United Kingdom

Dawn M. Cooper [a,c], Chris Bojke [b], Pinaki Ghosh [d,*]

[a] Centre for Health Social Care, Faculty of Health and Wellbeing, Sheffield Hallam University, UK
[b] Leeds Institute of Health Sciences, University of Leeds, UK
[c] B. Braun Medical UK, Sheffield, UK
[d] B. Braun Medical Industries, Pulau Pinang, Malaysia

ARTICLE INFO

Keywords:
Venous leg ulcer
Chronic wounds
Cost-effectiveness analysis
PHMB & betaine
Wound bed preparation

ABSTRACT

Background: Wounds cost £8.3 billion per year in the United Kingdom (UK) annually. Venous leg ulcers (VLUs) account for 15% of wounds and can be complicated to heal, increasing nurse visits and resource costs. Recent wound bed preparation consensus recommends wound cleansing and biofilm disrupting agents. However, inert cleansers such as tap water or saline are inexpensive, an evaluation of evidence is required to justify the higher upfront costs of treatment with active cleansers. We undertook a cost-effectiveness analysis of the use of a biofilm disrupting and cleansing solution and gel, Prontosan® Solution and Gel X, (PSGX) (B Braun Medical), as compared to the standard practice of using saline solution, for treating VLUs.

Methods: A Markov model was parameterised to one-year costs and health-related quality of life consequences of treating chronic VLUs with PSGX versus saline solution. Costs are viewed from a UK healthcare payer perspective, include routine care and management of complications. A systematic literature search was performed to inform the clinical parameters of the economic model. Deterministic univariate sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were undertaken.

Results: For PSGX an Incremental Net Monetary Benefit (INMB) of £1,129.65 to £1,042.39 per patient (with a Maximum Willingness to Pay of £30k and £20k per QALY respectively), of which cost savings are £867.87 and 0.0087 quality-adjusted life years (QALYs) gain per patient. PSA indicates a 99.3% probability of PSGX being cost-effective over saline.

Conclusions: PSGX for the treatment of VLUs is dominant compared with saline solution in the UK with expected cost-savings within a year and improved patient outcomes.

1. Introduction

Globally, chronic leg ulcers are highly prevalent [1]. The National Health Service in the United Kingdom manages 3.8 million wounds annually [2], and recent studies estimate that 1.1% of the adult UK population (over half a million adults) has a VLU [2]. Managing chronic wounds is complex, with only 49% of chronic wounds in the UK healing within a year, reducing to 37% when the wound is classified as a VLU, signs of infection further reduces the 12-month healing rate of VLUs to only 18% [26]. Resource use associated with managing unhealed wounds is substantially greater than managing healed wounds, the overall annual cost of managing unhealed VLUs (£7886.05), is considerably higher than that of managing VLUs which heal within a year (£2036.67); accurate diagnosis, prevention of infection and improving healing rates were outlined as strategies to manage these costs [2].

Chronic wounds have a delay in progression through the stages of healing, typically persisting in the inflammatory stage [3,4]. The inflammatory factors present in this stage of healing notably promote production of slough and exudate, the presence of which further exacerbates the host immune response, creating a recurring cycle of inflammation [5,6]. The presence of slough and excessive exudate delays wound healing, with slough supporting and harbouring biofilm [4,

Abbreviations: VLU, Venous Leg Ulcer; PSGX, Prontosan Solution and Gel X; QALY, Quality-Adjusted Life Years.

* Corresponding author.
E-mail address: pinaki.ghosh@bbraun.com (P. Ghosh).

https://doi.org/10.1016/j.jtv.2023.03.001
Received 5 April 2022; Received in revised form 3 November 2022; Accepted 9 March 2023
Available online 16 March 2023

7]. Biofilms are associated with chronic inflammation [8], further exacerbating the presence of slough and exudate [7,9]. Microbes present within biofilms demonstrate increased tolerance to antimicrobials and antibiotic therapy [10], and biofilms are an acknowledged source of wound infection [11]. Chronic wounds provide an ideal environment for the creation of biofilm, recently confirmed by a meta-analysis reporting the presence of biofilm in the majority of chronic wounds [12]. Hence, all non-healing chronic wounds, failing to respond to standard care, are considered to have biofilms as an underlying cause of delayed healing [11,13]. Recent wound biofilm consensus statements focus on cleansing as a strategy to address biofilms and recommend routine cleansing and disruption of biofilm at each dressing change [13]. The effects of the slough, excessive exudate, and biofilm within a chronic wound contribute to delay healing and must be removed to create an ideal environment for wound healing [7,14]. Although the usage of biofilm disrupting agents is increasing, in the UK saline and tap water is still predominantly in use nationally [15].

Prontosan® Wound Irrigation Solution and Gel X (PSGX) (B. Braun Medical Ltd) contain polyhexanide (PHMB) and a betaine surfactant. These ingredients work in combination to disrupt and remove biofilm as well as aiding the removal of debris and slough [16,17]. Betaine is an amphoteric surfactant, containing both hydrophilic and hydrophobic structures; hydrophobic sections bind to debris, slough and, biofilm; the hydrophilic element allows for removal and washing away due to the formation of micelles, having a disruptive effect on the biofilm extracellular polymeric substance (EPS) [18,19]. Once the EPS has been disrupted microbes within the biofilm are exposed and are no longer protected; PHMB helps to minimise bioburden [20]. The disruptive action on the EPS and reduction in bioburden prevent biofilm reformation [18]. By removal of slough and devitalised tissue, disruption, and prevention of biofilm, PSGX is thought to improve wound bed condition, removing barriers to wound healing through effective wound bed preparation, which supports and allows the wound to progress to healing [21]. PSGX has been reported to reduce time to healing by 1.1 months compared with saline in VLUs receiving compression [17].

Recent UK guidelines have introduced cleansing solutions, such as PHMB & betaine, into their wound care pathways due to positive outcomes and with the aim of reducing costs [22]. Current evidence has been focused on clinically relevant outcomes yet there is no evidence exploring the cost-effectiveness of specific wound cleansing pathways. With such “cleansing solutions” costing approximately three times the cost of saline to purchase [15], and “cleansing gels” likely to be an additional treatment in the care pathway, it is important, from the UK health system perspective, to understand the overall treatment cost and outcomes from implementing such changes. We undertook this analysis to identify all available literature comparing PSGX (Prontosan, B. Braun Medical Ltd) with saline in chronic wounds. We determined the whole treatment incremental cost and QALY differences of a wound bed preparation pathway, with PSGX as compared to saline solution in VLU patients, from a UK healthcare perspective and evaluated in a NICE reference case economic evaluation framework.

2. Methods

2.1. Model overview

A Markov model, representing patients with a chronic VLU, with finite wound states, was developed in MS Excel 2013®. In line with UK guidelines we performed a cost-utility analysis, using a provider perspective incorporating health system costs and benefits [23]. The model utilised monthly cycles with a one-year time horizon, to prevent projections that extrapolate significantly beyond the duration of the clinical trial data [24], no impact for discounting was applied due to short time horizon [25]. The results are reported in terms of total cost per patient treated with PSGX compared with saline solution and outcomes valued in terms of life years (LYs) and QALYs gained.

The Markov states were decided in consultation with wound care professionals treating chronic wounds, resulting in four finite health transition states in the model: open wound, closed wound, infected wound, and death. The influence diagram depicts patient transitions across the Markov states over time horizon (Fig. 1). An open wound can become infected. Infected wounds can resolve and return to the open state. An open wound can heal and become closed. A closed wound can reoccur and become open again. An infected wound cannot close until the infection has resolved and must move to the open state first before closing. In all health states patients have a risk of death by any cause (Fig. 1).

We modelled the overall costs and consequences of treating a VLU cohort with either of the two treatment options. We assumed that VLUs are on average 52.3 cm^2 in size and start in one of two wound states, open (70%) or infected (30%) [26]. Cycle length of 1 month was considered suitable based on available relevant literature and frequency of wound assessment in the UK [27], and we built in a half-cycle correction into the analysis, to account for the fact that events and transitions may occur at any point during the cycle, not necessarily at the start of each cycle [25]. Death was modelled based on all-cause mortality of UK patients with chronic wounds [28], which considered the patients who had died as censored, rather than a disease-related mortality.

2.2. Intervention and control

The intervention arm consists of PSGX (Prontosan®): wound cleansing agents (solution and gel) containing two active ingredients, a betaine surfactant (undecylenamidopropyl betaine) and an antimicrobial polyhexanide (polyhexamethylene biguanide, PHMB), is indicated for cleansing, irrigation, and moistening of acute/chronic wounds and the prevention of biofilm in the infected or non-infected state. The control arm is saline as it is common practice in the UK to irrigate chronic wounds with saline at each dressing change and is a suitable comparator for comparing a new intervention to standard practice in the NHS in the UK [15].

2.3. Clinical parameters

A systematic literature search was performed using EBSCO (CINHAHL Complete, Medline Complete, Biomedical Reference Collection, and STM), Cochrane database, and PubMed (2005–17th August 2020). Search terms used can be found in supplement 1. Participants included adults presenting to the primary or secondary care setting with chronic wounds. Interventions included all PSGX products, specifically wound irrigation Solution, Gel, and/or Gel X (Prontosan, B. Braun Medical Ltd). Comparators, were inert irrigation agents including saline, water, or Ringer’s solution. Outcomes: the primary outcomes of interest were the proportion of wounds with complete closure and time to complete wound closure, the incidence of infection, and infection resolution. Details of the systematic literature search details can be found in the PRISMA (supplement 2), data abstraction (supplement 3).

Based on the available literature the model is based on chronic VLUs, with all studies arising from Europe, these study results were considered appropriate for parameterisation of our model, given the studies were European and the patient profile of VLU in cases reported in the trials can be assumed similar to UK patients. Wound healing and infection rate parameters were derived from a comparative German study of 112 patients, aged 47–89 (mean 75 years) with a chronic VLU ($\geq$3 months in duration) treated with either PSGX or saline at each dressing change [17]. Patients received standardised compression therapy using under-padding and 2 layers of stretch bandages and followed until ulcer closure or for a maximum observation period of 6 months [17]. During the treatment patients were assessed for infections, defined as the presence of typical clinical signs of infection (e.g. redness, swelling) [17].

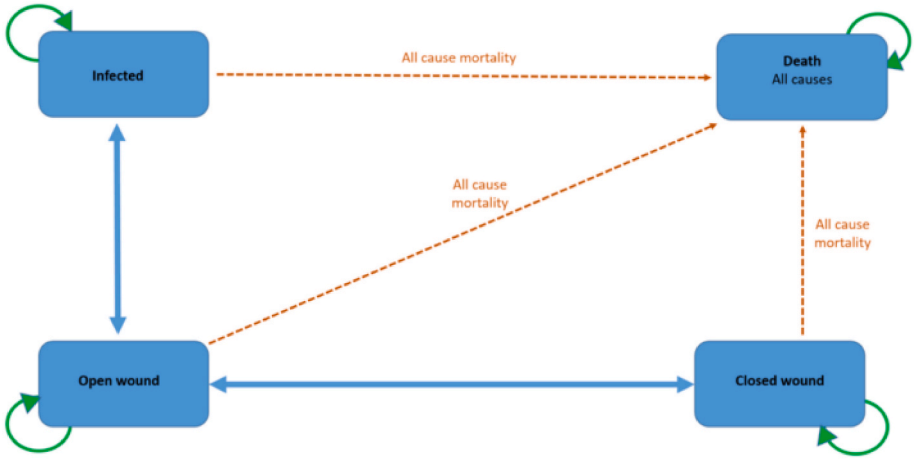

Fig. 1. Markov model to assess cost-effectiveness of PSGX.

We estimated a parametric wound healing survival model, applying multiple models to the reported monthly healing rate for PSGX and saline arm from the study [17], using Stata 14.1. The Weibull was the best fit according the Bayesian information criteria (supplement 4) and has been used previously for time to even healing hence used to deduce transition probabilities treating unhealed wounds as censored observations. Log relative hazard ratios were generated (supplement 5) and results indicated an estimated "hazard" ratio for healing equal to 2.2 (95% CI 1.48–3.26) for PSGX relative to saline, indicating a significant 120% faster healing rate with PSGX relative to saline. Estimated time sensitive monthly healing probabilities were calculated (Table 1). Over the 6 months, infection rate was reported in the two groups and converted to probability per month, a monthly infection probability of 0.57% for PSGX and 2.33% for saline were calculated (Table 1).

In a separate randomised control trial study in Spain, of 142 patients with chronic wounds, infection resolution occurred in 51.92% of wounds treated with PSGX and 33.33% and of wounds treated with saline over two weeks [29]. This data was converted to a rate of infection resolution per week and then to probability per month, resulting in a calculated monthly probability of infection resolution of 79.54% in the PSGX arm and 58.46% in the saline arm (Table 1).

Healed VLUs can reoccur; a large UK study (n = 1324) reports a 17% reoccurrence rate of a VLU within one-year of healing [30]. In the UK it is reported that 3% of patients with a chronic wound die within the year [28]. These annual data were converted into a monthly probability (1.54%: recurrence and 0.25%: all-cause mortality) and applied to both arms of the model (Table 1).

2.4. Utility

The primary effectiveness measure was QALY. In the absence of any utility data specifically comparing PSGX and saline in VLUs, Quality of life (QoL) values for each wound state (open, healed, and infected) were used as reported previously [31,32], open ulcer 0.75, infected ulcer 0.70

Table 1
Transition probabilities.

Parameter		Base Value	Lower value	Upper Value	Distribution	Source
Transition Probabilities						
All-cause mortality		0.00254	0.00228	0.00279	Beta	[28]
Healed to open		0.01541	0.01387	0.01695	Beta	[29]
PHMB & betaine	Infected to open	0.79542	0.59657	0.99428	Beta	[30]
	Open to Healed month 1	0.02140	0.01447	0.03158	Beta	[17]
	Open to Healed month 2	0.12824	0.01447	0.03158	Beta	[17]
	Open to Healed month 3	0.29612	0.01447	0.03158	Beta	[17]
	Open to Healed month 4	0.48146	0.01447	0.03158	Beta	[17]
	Open to Healed month 5	0.65011	0.01447	0.03158	Beta	[17]
	Open to Healed month 6	0.78317	0.01447	0.03158	Beta	[17]
	Open to Healed month 7	0.87633	0.01447	0.03158	Beta	[17]
	Open to Healed month 8	0.93497	0.01447	0.03158	Beta	[17]
	Open to Healed month 9	0.96843	0.01447	0.03158	Beta	[17]
	Open to Healed month 10	0.98583	0.01447	0.03158	Beta	[17]
	Open to Healed month 11	0.99412	0.01447	0.03158	Beta	[17]
	Open to Infected	0.00573	0.00401	0.00745	Beta	[17]
Saline	Infected to open	0.58460	0.43845	0.73075	Beta	[17]
	Open to Healed month 1	0.00979	0.00881	0.01076	Beta	[17]
	Open to Healed month 2	0.06048	0.05443	0.06653	Beta	[17]
	Open to Healed month 3	0.14754	0.13279	0.16230	Beta	[17]
	Open to Healed month 4	0.25811	0.23230	0.28393	Beta	[17]
	Open to Healed month 5	0.37961	0.34165	0.41758	Beta	[17]
	Open to Healed month 6	0.50090	0.45081	0.55099	Beta	[17]
	Open to Healed month 7	0.61334	0.55201	0.67468	Beta	[17]
	Open to Healed month 8	0.71132	0.64019	0.78245	Beta	[17]
	Open to Healed month 9	0.79215	0.71294	0.87137	Beta	[17]
	Open to Healed month 10	0.85561	0.77005	0.94117	Beta	[17]
	Open to Healed month 11	0.90316	0.81285	0.99348	Beta	[17]
	Open to Infected	0.02333	0.01633	0.03033	Beta	[17]

and healed ulcer 0.84, QoL values were adapted for monthly cycles (Table 2) and applied to both arms of the model. Incremental cost per QALY gained with the use of PSGX was calculated.

2.5. Costing

In line with UK guidelines, we performed a cost-utility analysis using a provider perspective, incorporating health system costs and benefits [23]. For both the treatment and control group the cost of healthcare resources has been assumed to be associated to wound condition, defined as: healed, progressing, static, deteriorating, or severe. Costs for different wound states were based on UK data [33]. From the study by Harding (2013), healed wound costs were used and directly adjusted to 2018/2019 prices, as were costs for "severe" wounds - used to indicate cost for the "infected" wound state in this model. For the "open" wound state, a weighted mean was calculated from "progressing, static and deteriorating" costs and then adjusted to 2018/2019 prices [33].

The study by Harding (2013) [33], reported weekly leg ulcer costs at 2008/2009 rates, consisting of cost for health care professional visits, dressings and bandages, skincare, compression hosiery, prescriptions, hospital visits, and equipment. Assuming practice nurse appointments are 15 min, and community nurse visits are 20 min [34], healthcare professional (HCP) costs were increased to the 2018/2019 Personal Social Services Research Unit (PSSRU) rate [35]. The remaining resource costs were inflated to 2018/2018 prices using the Hospital and Community Health Service Index (2008–2015) and NHS cost of inflation index from unit costs for health and social care (2015–2019) [36]. Recent UK wound care resource use papers [2], reported minimal hospital admissions for VLUs, hence the cost of hospital admissions was removed from this model; mostly impacting the infected wound cost by reducing costs and making this analysis more conservative. HRU costs used in the model are defined in Table 3.

An average cost per dressing change for PSGX solution was calculated based on 40 ml per application (24 × 40 ml £14.93, £0.62 per 40 ml ampoule). According to NHS drug tariff, saline is available in 20–25 ml sachets and clinical experts expressed that one sachet is used per dressing change, the average of these costs have been applied at £0.23 [15]. Each HCP visit was assumed to result in a dressing change application of either PSGX or saline. The number of HCP visits per month was determined by utilising 2008/2009 Personal Social Services Research Unit (PSSRU) costs [37], weekly costs from the study by Harding et al. [33], and assuming practice nurse appointments are 15 min, and community nurse visits are 20 min [34].

Cost of infection, an adverse event, is covered in the Markov model. No other adverse events are associated with either PSGX or saline solution as per the published literature and hence not included in the model schematic.

2.6. Sensitivity analysis

To assess the robustness of results over plausible ranges of inputs, univariate and multivariate sensitivity analyses were performed. Deterministic univariate sensitivity analyses were conducted to determine the effects of input parameters on the total cost differences.

Table 2
Clinical Utility for Assessing Cost-effectiveness of PSGX Versus saline.

Parameter	Base Value	Lower value	Upper Value	Distribution	Source
Utilities per month					
Open wound utility	0.063	0.056	0.069	Beta	[31, 32]
Healed wound utility	0.07	0.063	0.077	Beta	[31, 32]
Infected wound utility	0.058	0.053	0.064	Beta	[31, 32]

Table 3
Cost parameters for assessing cost-effectiveness of PSGX versus saline.

Parameter	Monthly cost	Lower cost	Upper cost	Distribution	Source
Heath care resource cost					
Healed wound	£33.96	£32.20	£35.72	Gamma	[33,35]
Open wound	£507.84	£500.43	£515.13	Gamma	[33,35]
Infected wound	£1,898.54	£1,197.96	£2,599.01	Gamma	[33,35]
PSGX treatment costs					
Open wound	£29.53	£22.41	£59.08	Gamma	Assuming lowest current NHS cost and +100% for upper
Infected wound	£36.47	£27.66	£72.93	Gamma	Assuming lowest current NHS cost and +100% for upper
Saline treatment cost					
Open wound	£2.69	£0.00	£5.39	Gamma	Assuming lowest is use of water and + 100% is upper
Infected wound	£3.33	£0.00	£6.65	Gamma	Assuming lowest is use of water and + 100% is upper

*Zero cost indicative of use of water instead of saline.

Probabilistic sensitivity analysis (PSA), using a Monte Carlo simulation, was conducted to assess the impact of individual and the joint uncertainty around key parameters. All cost and probability variables were included as well as mortality rate and utility values. Upper and lower transition probabilities for healing rate were calculated, replacing the incremental impact estimate β_1 value with the log relative upper and lower 95% CI (Table 1). Base case was varied by 30% for infection rate, 25% for infection resolution and 10% for wound reoccurrence, starting wound state, death rate and utility (Table 1).

Resource costs were varied by calculating the 95% CI from data provided by Harding (2013) [33], while technology costs were the lowest available cost of PSGX for the lower banding and the upper banding was cost of PSGX+100%, to stress test the model beyond typical price increases experienced by the NHS in wound care. The lower band of saline was £0.00; indicative of tap water usage and upper was +100% (Table 2). Gamma distribution was applied to all costs; and beta distribution was used for utilities and transition probabilities. The PSA was run for 1000 iterations, and incremental cost in Great British Pounds were plotted against incremental QALYs (Fig. 4). Probability for PSGX to be cost-effective was plotted on a cost effectiveness acceptability curve (supplement 6).

2.7. Time to cost neutral

The time taken for PSGX to become cost neutral with saline was estimated by plotting monthly incremental costs from the first 7 months from the Markov model, where data was linear, and fitting linear regression.

2.8. Validation

This model is based on the work by Andriessen and Eberlein [17],

and for validity the model was further performed using the unpublished RCT data [38], (supplement 7). In addition, the impact of no clinical effect of PSGX was explored to check robustness of analysis and potential risks of inaccuracies within this analysis.

3. Results

3.1. LYs, QALYs and health state distribution

Over 12 months modelled, as expected, LYs accrued per patient with PSGX and saline treatments were found to be 0.985 for both treatment groups. However, the number of QALYs accrued per patient increased for treatment with PSGX compared to saline arm (Table 4). The incremental health benefit of PSGX over 12 months was 0.0087 QALYs.

The time spent in the different health states varied; PSGX treated wounds spent less time in the open and infected state (3.29 and 0.25 months respectively) compared with the saline arm (4.18 and 0.554 months), with the PSGX treated wounds being in the healed wound state (8.26 months) for longer than the saline group (7.10 months) see Fig. 2. These changes in distribution of the health states will drive the differences in cost between the two treatment groups.

3.2. Costs

Overall, we found that the one year cost of treating chronic VLUs was reduced with PSGX treatment (Table 4), with a cost saving of £867.87 per patient following treatment using PSGX for one year. While the upfront purchasing cost of the wound cleansing agent was higher, healthcare resource costs accounted for the majority of one year costs therefore use of PSGX was cost saving overall, over a 12 month period. The predominant cost was on account of management of open wounds among both arms: PSGX (£1,766.64) and saline (£2,133.81). The cost of treatment of infection was reduced from 30% of the one year total cost of wound treatment with saline (£1,026.26), to 18% of the total one year cost of wound treatment with PSGX (£486.10).

3.3. Incremental impact

Based on these costs and consequences, the incremental cost and benefit gained from treating chronic VLUs with PSGX for 1 year, compared with saline, indicates an overall INMB £1,129.65 to £1,042.39 with a Maximum Willingness to Pay (WTP) of £30k or £20k per QALY respectively, of which cost savings are £867.87 per patient with a 0.087 quality-adjusted life years (QALYs) gain per patient.

3.4. Sensitivity analysis

The DSA investigated impact of individual parameter on the based case saving (£867.87), the parameter which had maximum influence on the savings per patient, were the values of health resource use of the infected state, (saving ranging from £1,068.86 to £665.22), followed by price of PSGX (saving from £892.70 to £760.79). The impact of the cost of saline had lesser influence on the expected incremental cost (Fig. 3). Of note, despite varying the parameters, treatment with PSGX continued to offer a saving per patient compared with saline.

Table 4
Costs, Effects and Cost Effectiveness of PSGX as compared with Saline over 12 months.

Finding	PHMB & betaine	Saline	Increment
Product cost	£106.25	£13.05	£93.20
HRU cost	£2,427.11	£3,388.18	-£961.07
Total cost	£2,533.36	£3,401.23	-£867.87
Health consequences per patient			
LYs	0.98	0.98	0
QALYs	0.799	0.790	0.0087

The PSA was run for 1000 iterations and plotted (Fig. 4), indicating that PSGX is the dominant technology. PSA indicates a cost saving of £874.88 and at a WTP of £20,000 indicates a 99.3% probability of PSGX being cost-effective over saline.

3.5. Time to cost neutral

The first month is the only month where PSGX is cost incurring compared with saline at an estimated cost of £28.73. Cumulatively, by month 1, the wound bed preparation pathway is estimated to be cost saving to a value of £53.51. The time for PSGX to become cost saving is estimated at 0.57 months.

3.6. Validation

Repeating the analysis with the pilot data from the unpublished UK RCT, returned very similar results estimating: £832.84 saving per patient over 12 months and 0.0081 QALY gain. In addition the INBM was estimated at £994.99 and £1,076.07 (WTP £20,000 and £30,000 respectively). The close alignment of results from analysis of two separate data sets adds strength and validity to the robustness of the results reported here.

4. Discussion

Management of chronic wounds poses an increasing burden to the NHS in the UK [2]. Whether to treat with standard care of saline or a change to a wound bed preparation pathway, defined as treatment with PSGX, is a decision to be made by clinicians responsible for local policies, on the balance of national consensus and guidelines and with health resource costs in mind.

Overall, we found that use of PSGX is cost effective and provides a net cost saving of £867.87 per patient over a 1 year period and 0.0087 quality adjusted life years (QALYs) per patient. Overall INMB £1,129.65 to £1,042.39 with a maximum WTP of £30k or £20k per QALY respectively, of which cost savings are £867.87 per patient with a 0.087 quality-adjusted life years (QALYs) gain per patient. Therefore, based on economic argument, use of PSGX is cost-effective in the UK NHS.

4.1. Findings in context of existing evidence

In our study, we used the data on effectiveness and other clinical parameters from a German study in VLUs, which was considered as representative of UK disease epidemiology [17]. Secondly, all our costing parameters were derived based on UK studies and data [33–35]. Hence, the results in our study were appropriately identified and costed for treatment of chronic VLUs in the UK with PSGX or saline to determine cost effectiveness of PSGX.

Costs calculated in the model utilise monthly resources costs, calculated and inflated from weekly costs for treating leg ulcers published by Harding, Vowden and Possnett (2013) are validated here with other literature specific for VLUs. Annual average costs for VLUs are reported in the literature as £7,600 on average, £3,000 for a healed VLU and ranging between £10,777 up to £14,475 for an infected VLU per year [26]. Costs used in this model correspond to £7,629.08 per year for an open wound, in line with published UK literature. VLUs are unlikely to spend 12 months in an infected state [39]. From costs used in this model, if a VLU spent any 4 month period in the infected state, and the remaining months in the open state, the annual cost would be £13,222, which is in line with the published UK data [2]. Literature around infection cost in the UK only describes wounds as having had an infection, duration and/or number of infections, per VLU, are not specified, therefore cost utilised here may be a conservative estimate. In VLUs which heal, average healing time is reported at 3 months in the UK [26], when monthly data used in this model is calculated for 3 months in the open state and 9 months in the healed state, the average annual cost of a

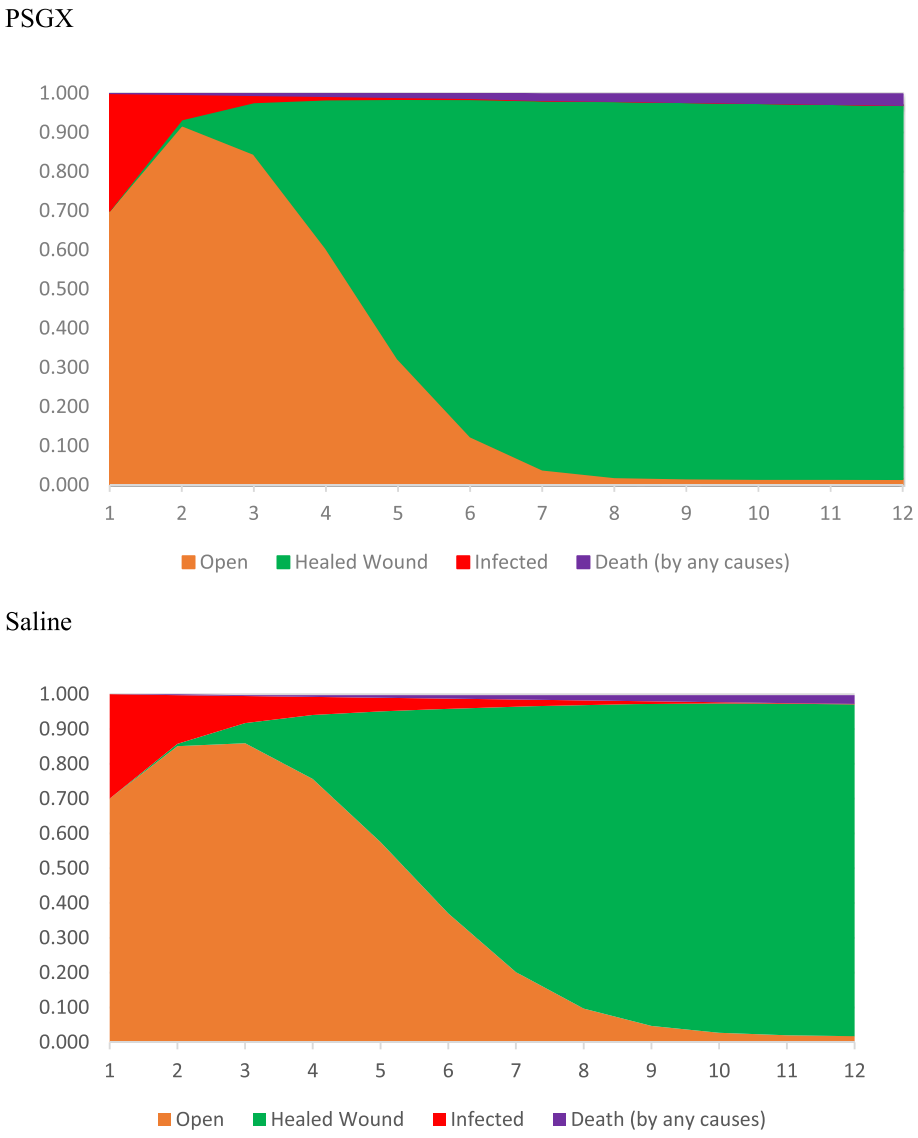

Fig. 2. Markov trace of time spent in wound states treated with PSGX or saline over 12 monthly cycles.

healed VLU in this model is £2,293.12. All resource costs used in this model align with other reported burden costs for VLUs in the UK and the resource cost used are robust.

4.2. Limitations

The main limitation of our study is lack of any UK data on wound healing and QoL impact of PSGX in VLUs. However, we feel that the results of studies within Europe are representative of the UK population in view of the similarities mentioned earlier. In addition, the source healing data is not from a randomised control trial and hence creates a level of uncertainty within the results, however the results from the pilot data supported the results reported here, strengthening the analysis presented.

4.3. Conclusion and policy implications

The UK health service is under increasing pressure from the economic and health resource burden of chronic wounds, the Guest 2020 Burden of Wounds study [2], recommended a focus on improving healing times and improving infection rates (as well as improving diagnosis). The results of this work demonstrate use of PSGX is cost effective for treatment of VLUs for 1 year compared with saline, with a cost saving of £867.87 per patient and gaining 0.0087 quality-adjusted life years (QALYs) per patient. PSA at a WTP threshold of £20,000 indicates a 99.3% probability of PSGX being cost-effective over saline. The cost savings are driven by faster wound healing and faster infection resolution, driving a reduction in healthcare professional visits and resource use. These results hold significant importance for setting standard treatment guidelines in the NHS, offering an option to reduce the burden of wound care and improve patients' lives.

In support of the National Wound Care Strategy Programme for lower limb, published in 2020, which recommends cleansing and debridement as immediate and ongoing care for all lower limb ulcers including VLUs [27], this work supports the use of an active cleansing agent (PSGX) as a cost-effective means of treating chronic VLUs. In terms of national impact, UK literature reports that 3.1% of the adult UK population (circa 1.8 million) has a chronic wound (defined as diabetic foot ulcer, leg ulcer of any kind or pressure ulcer), of which 51% are non-healing, due to hampering effects of slough, excessive exudate and biofilm [7,14,40]. In a geographic region with 250,000 patients, it would be estimated that 7,753 adults have a chronic wound, of which 3,954 would be non-healing. Implementation of PSGX, for all 7,753 chronic wounds could return a net cost saving of £6.7 million to the NHS,

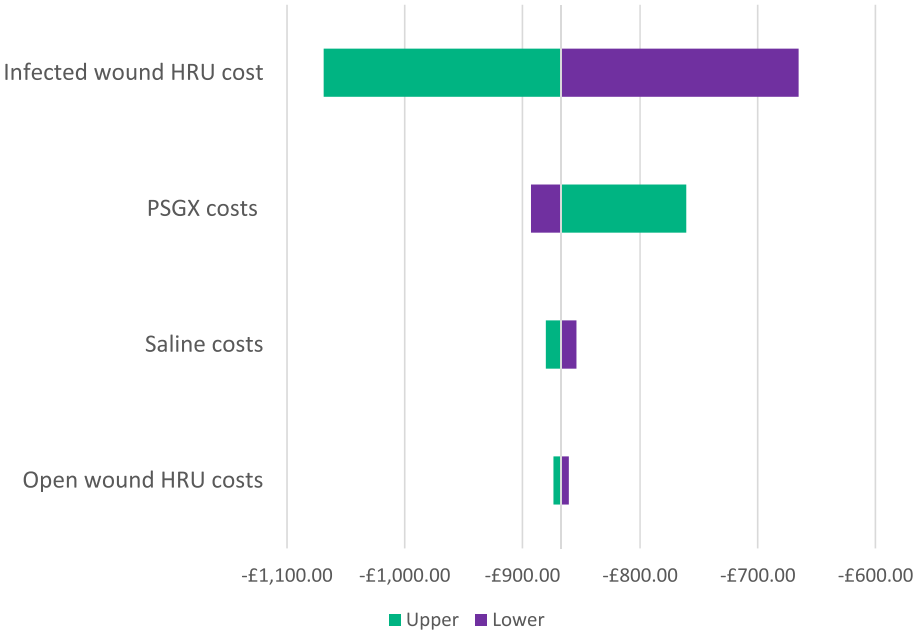

Fig. 3. Tornado showing influence of increasing or decreasing key cost variables over the base case incremental costs.

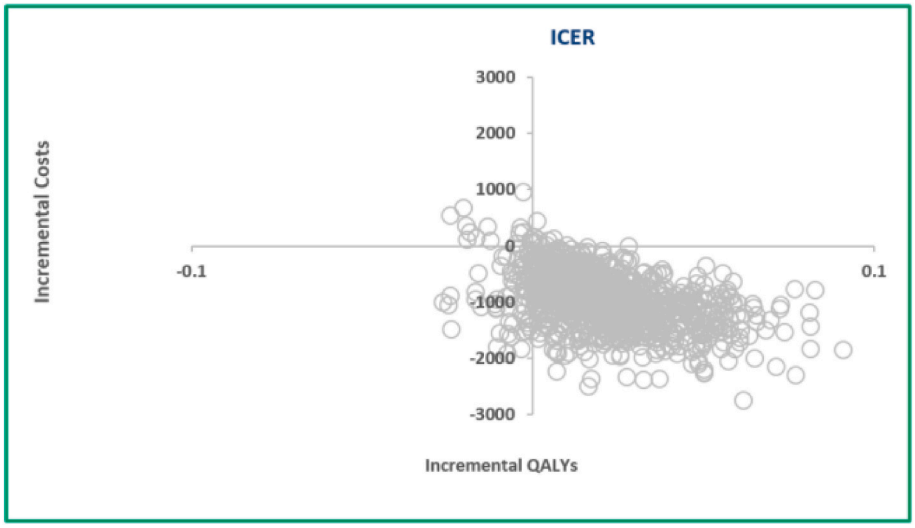

Fig. 4. Incremental cost and QALYs results from PSA for PSGX versus Saline.

whereas treatment of only the 51% on non-healing wounds (3,954) could return a net cost saving of £3.4 million to the NHS, reducing the burden of care by reducing time to healing and frequency of nursing visits. Such use of PSGX would be in accordance with current consensus documents including wound biofilm consensus statements and national guidance, which recommend use of active cleansing in the presence of biofilm, non-healing or chronic venous leg ulcers [14,22] and in line with wound cleansing and derbidement as recommended in national lower limb guidance [27].

Author contributions

D.M.C. and P.G. were involved in the design of the study. D.M.C., P.G and C.B., were involved in the acquisition, analysis or interpretation of data. D.M.C., P.G and C.B., were involved in drafting the work or revising it critically for important intellectual content.

Financial Support

No specific funding to report.

Acknowledgements

No other person has contributed to the work reported in the manuscript who do not fulfil the authorship criteria.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtv.2023.03.001.

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