

Cost-effectiveness and budget impact of topical antimicrobial polyhexamethylene biguanide with a surfactant betaine on wound bed preparation in venous leg ulcers: An analysis in Australia from a community perspective

Background and aim: Venous leg ulcers (VLUs) constitute 60–80% of leg ulcerations, often becoming chronic and imposing significant economic burdens, with Australia spending more than AUD\$3 billion annually on chronic wound care. This study evaluates the cost-effectiveness and budget impact of Prontosan Solution (PS), a biofilm-disrupting and cleansing agent, compared to standard saline solution for treating chronic VLUs from an Australian healthcare perspective.

Methods: A Markov model was developed in MS Excel to simulate 1-year costs and health-related quality of life (QALYs) for VLU patients treated with PS versus saline. The model used monthly cycles, incorporating clinical parameters from European studies, deemed applicable to Australia. Costs included routine care and complications, derived from Australian literature. Probabilistic sensitivity analysis (PSA) assessed parameter uncertainty, and the model was validated using unpublished randomised controlled trial (RCT) data and expert input.

Results: PS yielded 0.0087 additional QALYs and cost savings of \$295.23 per patient compared to saline. PSA indicated a 98.80% probability of PS being cost-effective at a \$25,000 WTP threshold. For 121,834 annual VLU cases, PS could save approximately \$35,969,051.82, or \$17,984,525.91 for non-healing wounds.

Conclusion: PS is cost-effective and cost-saving compared to saline for VLU treatment, offering improved patient outcomes and substantial budget impact in Australia.

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Key words

- Anti-infective agents
- Cost-effectiveness analysis
- QALYs
- Venous leg ulcers
- Wound healing

Venous leg ulcers (VLUs) are open lesions of the lower limb and represent between 60% and 80% of all leg ulcerations that occur in the presence of venous disease (Cushman, 2007; Nelson and Adderley, 2016). At least 60% of VLUs result in a chronic wound (Frykberg and Banks, 2015). VLUs are most prevalent among older people with concomitant chronic venous insufficiency. They impact more women than men, those who are obese, immobile, with a congenital absence of veins, or a history of deep vein thrombosis (DVT) or phlebitis, resulting in reduced mobility, poor quality of life, and notable financial burden on patients and healthcare systems (Vasudevan, 2014; Barnsbee et al, 2019).

In Australia, the annual healthcare

costs of VLU treatment is estimated to be more than AUD\$3 billion (Weller and Evans, 2012). According to the Medical Technology Association of Australia (MTAA), chronic wounds place a significant economic burden on the Australian healthcare system. The burden of chronic wounds is expected to increase in the future due to: ageing population and increasing prevalence of chronic diseases (e.g. diabetes) (MTAA, 2020). Each year, more than 420,000 Australians are affected by a chronic wound, while \$3 billion of the nation's aged care and healthcare budget is spent on chronic wounds (Wounds Australia 2022). Each chronic wound patient spends over \$4,000 on out-of-pocket costs because in Australia, the financial cost of wound products is typically

carried by the individual as there is no national reimbursement system (Kapp and Santamaria, 2017; Wounds Australia, 2022).

A recent wound bed preparation consensus recommends the use of wound cleansing and biofilm disrupting agents (Schultz et al, 2017). However, inert cleansers, such as tap water or saline, are most commonly used and are seen to be inexpensive. Saline has no properties to reduce the wound bioburden, and the vials are not designed to exert the correct pressure for cleansing and cannot be sealed and reopened. An evaluation of evidence is required to justify the higher upfront costs of treatment with active cleansers.

We undertook a cost-effectiveness and budget impact analysis of the use of a biofilm-disrupting and cleansing solution, Prontosan® Solution (PS), from an Australian healthcare perspective. We compared PS to the standard practice of using saline solution for treating VLUs, and considered the effectiveness values from published evidence and costs from an Australian clinical practice perspective.

Methods

Model overview

To determine cost effectiveness, a Markov model was parameterised to 1-year costs and health-related quality of life consequences of treating chronic VLUs with PS versus saline solution [Figure 1]. The Markov model, representing patients with a chronic VLU, with finite wound states, was developed in Microsoft Excel 2013. The model utilised monthly cycles with a 1-year time horizon, to prevent projections that extrapolate significantly beyond the duration of the clinical trial data, no impact for discounting was applied due to short time horizon. A cycle length of 1 month

was considered suitable based on available relevant literature and frequency of wound assessment in Australia, 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. Death was modelled based on all-cause mortality of patients with chronic wounds (Guest et al, 2017), which considered the patients who had died as censored, rather than a disease-related mortality and this was assumed to be same as Australia. The results are reported in terms of total cost per patient treated with PS compared with saline solution and outcomes valued in terms of life years (LYs) and QALYs gained.

Intervention and control

The intervention arm consisted of PS wound cleansing agents (solution) containing two active ingredients, a betaine surfactant and an antimicrobial polyhexanide (polyhexamethylene biguanide, PHMB), which is indicated for cleansing, irrigation and moistening of acute/chronic wounds, as well as the prevention of biofilm in the infected or non-infected state. The control arm used saline because it is common practice in Australia to irrigate chronic wounds with saline at each dressing change and is a suitable comparator for comparing a new intervention to standard practice.

Clinical parameters

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

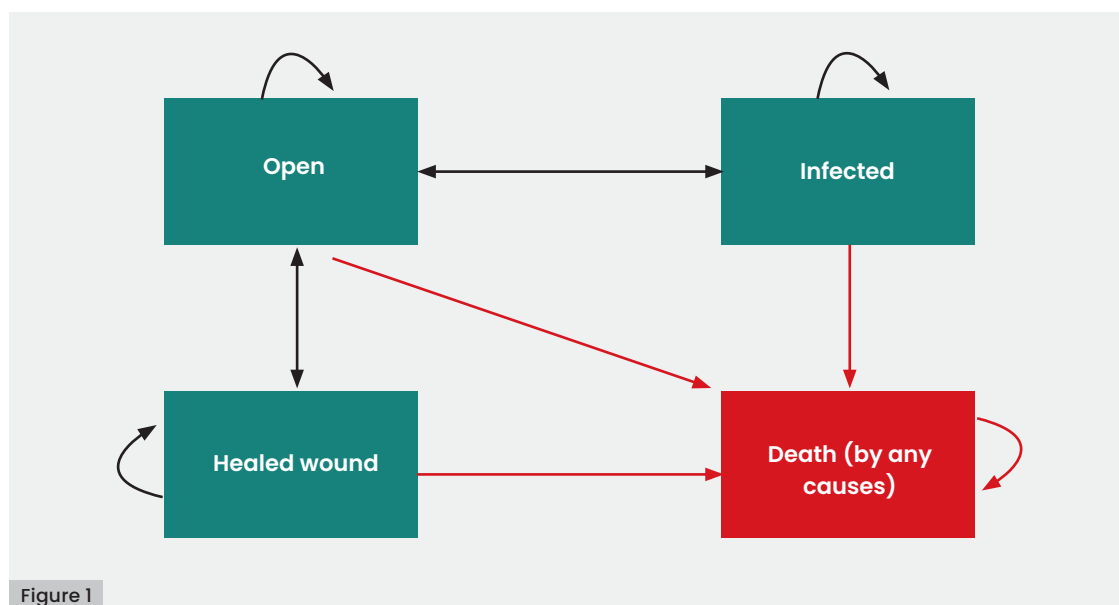


Figure 1

Figure 1. Markov model schematic to assess cost-effectiveness of Prontosan Solution versus saline in venous leg ulcers.

reported in the trials can be assumed similar to Australian 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 (≥ 3 months in duration) treated with either PS or saline at each dressing change (Andriessen and Eberlein, 2008). In a separate randomised control trial study in Spain, of 142 patients with chronic wounds, infection resolved in 51.92% of wounds treated with PS and 33.33% and of wounds treated with saline over 2 weeks (Valenzuela and Perucho, 2008). 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 PS arm and 58.46% in the saline arm [Table 1].

Healed VLUs can reoccur; a large UK study (n=1,324) reports a 17% reoccurrence rate of a VLU within 1 year of healing (Gohel et al, 2005). In the UK it is reported that 3% of patients with a chronic wound die within the year (Guest et al, 2018). 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. The clinical parameters from various publications converted to transition probabilities were referred from a recent publication by Cooper et al (2023) and have been outlined in Table 1 (Gohel et al, 2005; Andriessen and Eberlein, 2008; Valenzuela and Perucho, 2008; Guest et al, 2017).

Costs

Costs were calculated based on Australian healthcare community patient perspective

Table 1. Model inputs including probabilities, cost parameters, and utilities for assessing cost-effectiveness of Prontosan versus saline.

Model element	Value	Reference
PS All-cause mortality	0.00254	Cooper 2023, Guest 2017
PS Healed to open	0.01541	Valenzuela and Perucho, 2008; Cooper 2023
PS (Infected to open)	0.79542	Gohel 2005; Cooper 2023
PS open to healed (month 1)	0.02140	Andreissen 2008
PS open to healed (month 2–11)	0.79542	Cooper 2023, Gohel 2005
The transition probability values (month 2–11) have been mentioned in Appendix 1		
Saline All-cause mortality	0.00254	Cooper 2023, Guest 2017
Saline Healed to open	0.01541	Cooper 2023, Valenzuela 2008
Saline (Infected to open)	0.58460	Cooper 2023, Gohel 2005
Saline Open to Healed (month 1)	0.00979	Andreissen 2008
Saline Open to healed (month 2–11)	0.06048	Cooper 2023, Gohel 2005
The transition probability values (month 2–11) have been mentioned in Appendix 1		
GP Visit Cost	\$136	Brain 2019
Nurse Cost/visit (15 min)	\$5.2	Considering hourly rate of \$78 (Australia Nursing Services 2022)
Infected Wound	\$198.40	It was assumed that infected and complicated wound would need the basic GP visit and specialised nurse visits: ((12x\$5.2) + (\$136))

Table 1. Model inputs including probabilities, cost parameters, and utilities for assessing cost-effectiveness of Prontosan versus saline. (Continued)

Model element	Value	Reference
Cost of direct medical costs for leg ulcer treatment	\$399.70	Carville 2022
Saline Cost (ampoule, 30ml)	\$2.73	Market Data
Saline Cost per dressing (using ampoule)	\$2.73	As saline does not retain its sterility, a new ampoule each time needs to be used, and the volume of saline does not have any impact on cost savings
PS Cost (350 mL bottle)	\$31.50	Market Data
PS Cost per dressing (30 ml)	\$2.73	PS retains its sterility over 8 weeks, thus same bottle can be used multiple times
Dressings per week (PS/Saline)	3	Assumption (Clinical practice)
Monthly Cost PS	\$32.91	Considering 12 dressings per month and each dressing costing \$2.73
Monthly Cost Saline	\$5.88	Considering 12 dressings per month and each dressing costing \$2.273
PS Healed Wound	\$33	Brain 2019
Saline Healed Wound	\$33	Brain 2019
PS Open Wound	\$168.91	Considering \$32.91 + GP costs (\$136). It was assumed that Open wound is not complicated and would not need specialized nurse visits
Saline Open Wound	\$141.88	Considering \$5.88+ GP costs (\$136). It was assumed that Open wound is not complicated and would not need specialized nurse visits
PS Infected	\$631.01	Cost of wound treatment (\$399.70) + Infected Wound Costs (\$198.40) + Cost of PS treatment/month (\$32.91)
Saline Infected	\$603.9	Cost of wound treatment (\$399.70) + Infected Wound Costs (\$198.40) + Cost of PS treatment/month (\$5.8)

and include routine care and management of complications. To determine the costs of each health state, a bottom-up costing approach was followed. Details for each state are outlined in **Table 1**.

- *Infected state (PS and saline)*: The costs of management of venous leg ulcers in Australia (\$399) have been accrued from literature (Carville et al, 2022). The costs of infected wounds were derived by adding costs of Prontosan or saline to the published wound treatment costs in Australia along with the nurse costs (considering 15 minutes per dressing as per published literature (Phillips et al, 2016)).
- *Open state (PS and saline)*: For PS and

saline, this included the open wound general practitioner costs \$136 (Brain et al, 2019) and the respective costs of monthly usage of PS or saline.

- *Healed state (PS and saline)*: The costs of healed state for both PS and saline was referred from Brain et al (2019).

Utilities

The primary effectiveness measure was QALY. In the absence of any utility data specifically comparing PS and saline in VLUs, quality of life (QoL) values for each wound state (open, healed and infected) were used as reported previously: open ulcer 0.75, infected ulcer 0.70 and healed ulcer 0.84 (Redekop et al, 2004; Carter and Myntti, 2019). QoL values were adapted for monthly cycles and applied to both

arms of the model. Incremental cost per QALY gained with the use of PS was calculated.

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. A one-way sensitivity analysis was carried out and a tornado diagram was used to show the influence of increasing or decreasing key cost variables over the base case incremental costs.

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. Gamma distribution was applied to all costs; and beta distribution was used for utilities and transition probabilities. The PSA was run for 1,000 iterations, and incremental cost in Australian dollars were plotted against incremental QALYs.

Validation

This model is based on the work by Andriessen and Eberlein (2008). For validity, the model was further performed using the published cost-effectiveness analysis (Cooper et al, 2023). In addition, the impact of no clinical effect of PS was explored to check robustness of analysis and potential risks of inaccuracies within this analysis. The model structure was clinically validated by key opinion leaders and wound practitioners in Australia.

Results

Over 12 months modelled, as expected, life years (LY) accrued per patient with PS and saline treatments were found to be 0.985 for both treatment groups. The cost effectiveness analysis showed for PS an incremental net monetary benefit (INMB) of \$513.38 to \$469.75 per patient (with a maximum willingness to pay of \$25k and \$20k per QALY respectively), of which cost savings are \$295.23 and 0.0087 quality-adjusted life years (QALYs) gain per patient. Although the LY were similar in both treatment arms the QALYs were more in PS arm because the number of QALYs accrued per patient increased for treatment with PS compared to saline arm.

PSA indicates a 98.80% probability of PS being cost-effective over saline at WTP of \$25000. ICER scatter plot shows PS is more effective and less costly than saline in Australia. Considering a total incidence and recurrence of approximately 121,834 patients per year, the approximate savings could be \$35,969,051.82, if saline is replaced by PS (Kolluri et al, 2022). It has been also reported that approximately 51% of all wounds are non-healing, due to hampering effects of slough, excessive exudate and biofilm (Percival and Suleman, 2015; Murphy et al, 2019; Guest et al, 2020). Hence, implementation of PS for this subgroup could lead to a cost savings of \$17,984,525.91. The results of PSA are shown in **Figure 2**.

One-way sensitivity analysis was carried out to demonstrate the uncertainty in individual model cost parameters and how they affect the final results. The results of the one-way sensitivity analysis were visualised as a tornado diagram [**Figure 3**]. The tornado diagram ranks

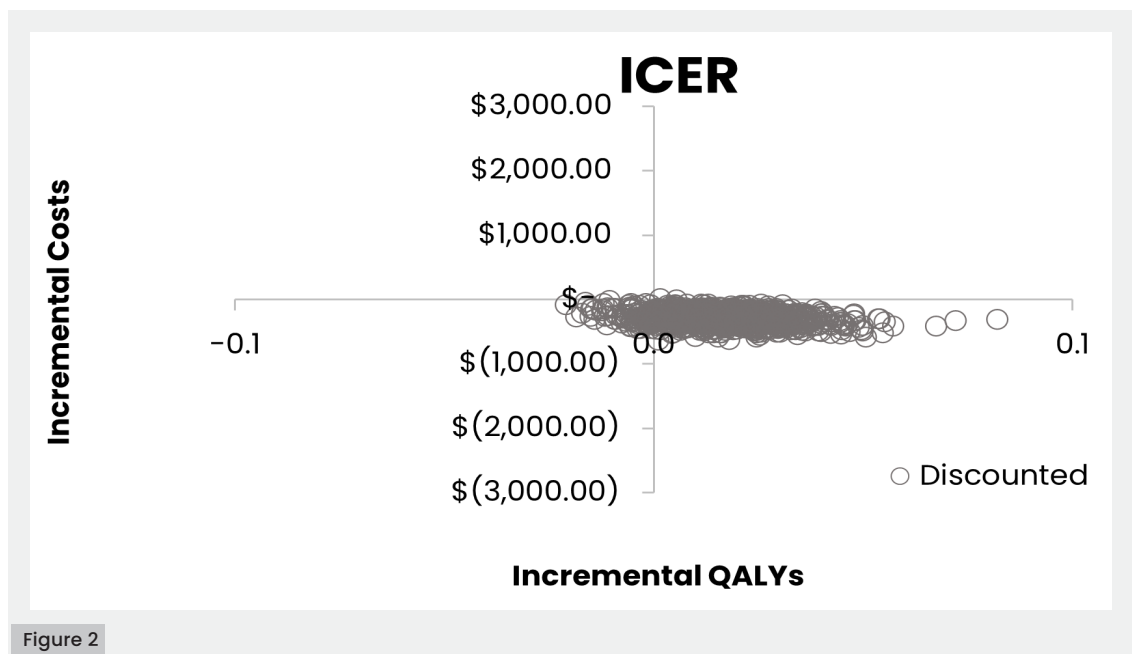


Figure 2. Incremental cost and QALYs results from probabilistic sensitivity analysis for Prontosan versus saline.

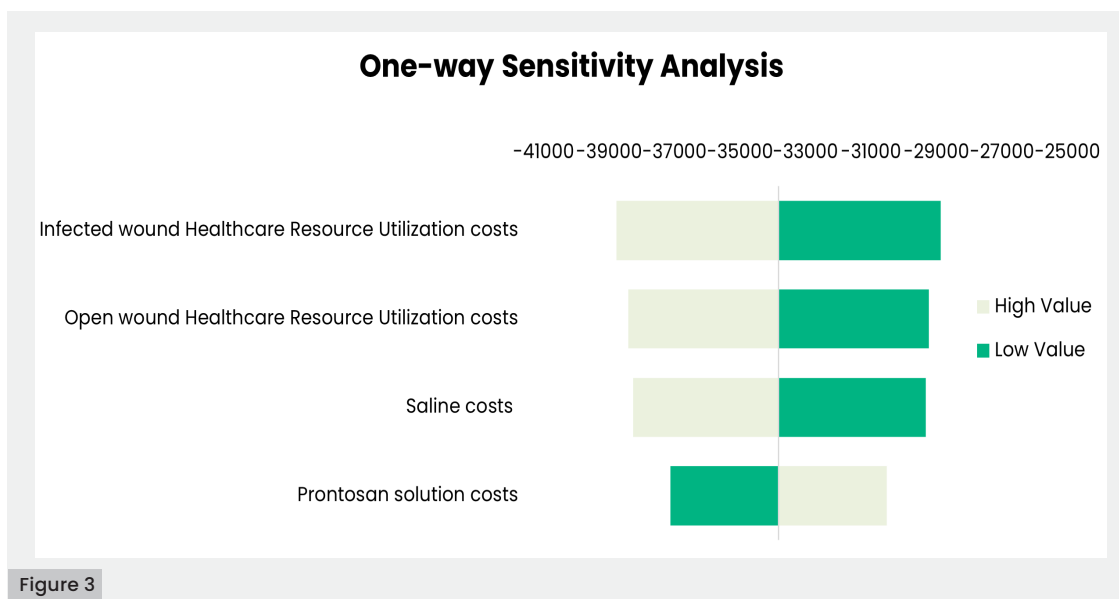


Figure 3. Tornado diagram presenting the one-way sensitivity analysis results

the parameters listed on the left in order of their influence on the incremental cost-effectiveness ratio (ICER). The results of one-way sensitivity analysis demonstrate the major drivers of cost effectiveness influencing ICER are the healthcare resource utilisation-related costs for infected and open wounds.

Discussion

The management of chronic wounds poses an increasing burden to the healthcare system in Australia (MTAA, 2020). Current provision of services for the care of chronic wounds in Australia is disjointed and costly (Brain et al, 2019). In Australia, chronic wounds present a significant financial cost to individuals who must self-fund their wound dressings and treatment-related expenses (Kapp and Santamaria, 2017). Continued attention is required to reduce the financial and personal costs experienced by people living with chronic wounds (Kapp and Santamaria, 2017).

Modern wound care devices include wound closure devices, antimicrobial wound dressings, negative pressure wound therapy, low-frequency ultrasound debridement and synthetic wound dressings (MTAA, 2020). There is only one federal funding scheme for these and only a limited number of people (<200 per year) receive subsidised dressings. Modern wound care devices are not funded in most Australian states and territories. Patients pay high out-of-pocket costs for dressings due to limited funding for chronic wound care in Australia, particularly in the community setting (MTAA, 2020).

Whether to treat with standard care of saline or a change to a wound bed preparation pathway, defined as treatment with PS, 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 PS is cost effective and provides a net cost savings over a 1-year period and along with a QoL gain.

Previous studies have provided empirical evidence suggesting PS is cost effective and saving across various countries in the world for wound closure as well as wound bed preparation as endpoints. A study by Mehl et al (2020) in Brazil reported cost effectiveness of PS in comparison to saline for wound bed preparation, under the scope of Brazilian private healthcare system perspective. Another study by Suh and Ghosh (2020) in South Korea demonstrated substituting 0.1% polyhexanide/betaine solution for sterile saline could lead to a lowering of the total cost for wound bed preparation by 63.6%. A recent study in the UK of PS and GelX demonstrated cost savings of £867.87 and 0.0087 QALYs gained per patient. PSA indicated a 99.3% probability of PS being cost-effective over saline (Cooper et al, 2023).

Our results are in accordance with the previous authors. However, the current study is the first study from a community healthcare perspective.

This analysis has several strengths. Firstly, the decision analytic model is based on bottom up costing methodology. Secondly, the rates of recurrence and mortality have been modelled equally across both the arms of the Markov model, thus avoiding overestimation of treatment effects of PS in comparison to saline in VLUs. Our analysis also has some limitations.

The primary limitation of our study is lack of Australian-specific clinical data on wound healing and quality of life impact of PS in VLUs in the model. The study is based on clinical

trials conducted in Germany (Gohel et al, 2005; Andriessen and Eberlein, 2008; Valenzuela and Perucho, 2008; Guest et al, 2017). However, the results of studies carried out in Europe are representative of the Australian population in view of the similarities in the healthcare quality standards and patient cohort. In addition, the source wound healing data is from a retrospective patient record analysis over a short duration of 6 months (Andriessen and Eberlein, 2008). This aspect creates a level of uncertainty within the results. However, the results from a previous cost-effectiveness study from UK which used the same clinical studies (Cooper et al, 2023) support the findings reported here, strengthening the validity of this cost-effectiveness analysis.

Conclusion

PS for the treatment of VLU is cost-effective (dominant) at the WTP threshold of Australia and has a favourable budget impact (cost saving) compared with saline solution as well as cost-savings within a year and improved patient outcomes. ●

References

- Adibelli S, Korkmaz F (2019) Pressure injury risk assessment
Andriessen AE, Eberlein T (2008) Assessment of a wound cleansing solution in the treatment of problem wounds. *Wounds* 20(6): 171–5
- Barnsbee L, Cheng Q, Tulleners R, et al (2019) Measuring costs and quality of life for venous leg ulcers. *Int Wound* 16(1): 112–21
- Brain D, Tulleners R, Lee X, et al (2019) Cost-effectiveness analysis of an innovative model of care for chronic wounds patients. *PLoS One* 14(3): e0212366
- Carter MJ, Myntti MF (2019) Cost-utility of a biofilm-disrupting gel versus standard of care in chronic wounds: a Markov microsimulation model based on a randomised controlled trial. *J Wound Care* 28(Suppl 7): S24–38. doi: 10.12968/jowc.2019.28.Sup7.S24
- Carville K, Alan J, Smith J (2022) Best practice, best products, best outcomes in community wound care: three descriptive cohorts. *Wound Pract Res* 30(4): 196–206
- Cooper DM, Bojke C, Ghosh P (2023) Cost-effectiveness of PHMB & betaine wound bed preparation compared with standard care in venous leg ulcers: a cost-utility analysis in the United Kingdom. *J Tissue Viability* 32(2): 262–9
- Cushman M (2007) Epidemiology and risk factors for venous thrombosis. *Semin Hematol* 44(2): 62–9
- Frykberg RG, Banks J (2015) Challenges in the treatment of chronic wounds. *Adv Wound Care* 4(9): 560–82
- Gohel MS, Taylor M, Earnshaw JJ, et al (2005) Risk factors for delayed healing and recurrence of chronic venous leg ulcers—an analysis of 1324 legs. *Eur J Vasc Endovasc Surg* 29(1): 74–7
- Guest JF, Ayoub N, McIlwraith T, et al (2017) Health economic burden that different wound types impose on the UK's National Health Service. *Int Wound J* 14(2): 322–30
- Guest, J.F, Fuller, G.W. and Vowden, P (2018) Venous leg ulcer management in clinical practice in the UK: costs and outcomes. *Int Wound J* 15(1): 29–37
- Guest JF, Fuller GW, Vowden P (2020) Cohort study evaluating the burden of wounds to the UK's National Health Service in 2017/2018: update from 2012/2013. *BMJ Open* 10(12): e045253
- Kapp S, Santamaria N (2017) The financial and quality-of-life cost to patients living with a chronic wound in the community. *Int Wound J* 14(6): 1108–19
- Kolluri R, Lugli M, Villalba L et al (2022) An estimate of the economic burden of venous leg ulcers associated with deep venous disease. *Vasc Med* 27(1): 63–72
- Mehl AA, Mensor LL, Bastos DF et al (2020) Cost-effectiveness of polyhexamethylene biguanide 0,1% and betaine 0,1% solution (Prontosan®) versus saline for cleansing of chronic wounds under the Brazilian private health system perspective. *J Bras Econ Saúde* 5(3): 135–46 [in Portuguese]
- Medical Technology Association of Australia (2020) Evidence for funding of the treatment and management of chronic wounds in Australia. Available at: <https://www.mtaa.org.au/sites/default/files/uploaded-content/website-content/Chronic%20Woundsv5.pdf> (accessed 17.03.2026)
- Murphy C, Atkin L, Dissemmond J, et al (2019) Defying hard-to-heal wounds with an early antibiofilm intervention strategy: 'wound hygiene'. *J Wound Care* 28(12): 818–22
- Nelson EA, Adderley U (2016) Venous leg ulcers. *BMJ Clin Evid* 2016: 1902
- Percival SL, Suleman L (2015) Slough and biofilm: removal of barriers to wound healing by desloughing. *J Wound Care* 24(11): 498–510
- Phillips CJ, Humphreys I, Fletcher J, et al (2016) Estimating the costs associated with the management of patients with chronic wounds using linked routine data. *Int Wound J* 13(6): 1193–7
- Redekop WK, Stolk EA, Kok E, et al (2004) Diabetic foot ulcers and amputations: estimates of health utility for use in cost-effectiveness analyses of new treatments. *Diabetes Metab* 30(6): 549–56
- Schultz G, Bjarnsholt T, James GA et al (2017) Consensus guidelines for the identification and treatment of biofilms in chronic nonhealing wounds. *Wound Repair Regen* 25(5): 744–57
- Suh J, Ghosh P (2020) Analysis of potential cost-savings after introduction of 0.1% polyhexanide/betaine solution for chronic wounds in reimbursement healthcare system of Korea. *Value Health Regional Iss* 22: S49
- Valenzuela AR, Perucho NS (2008) The effectiveness of a 0.1% polyhexanide gel. *Rev Enferm* 31(4): 7–12 [in Spanish]
- Vasudevan B (2014) Venous leg ulcers: pathophysiology and classification. *Indian Dermatol Online* 5(3): 366–70
- Weller C, Evans S (2012) Venous leg ulcer management in general practice – practice nurses and evidence based guidelines. *Austr Fam Physician* 41(5): 331–7
- Wounds Australia (2022) Pre-budget submission to fight Australia's chronic wound epidemic. https://treasury.gov.au/sites/default/files/2022-03/258735_wounds_australia.pdf (accessed 17.03.2026)