

CATEGORY: HARD-TO-HEAL WOUNDS

PROMOGRAN™ & PROMOGRAN PRISMA™

MAKING THE CASE

THE BURDEN OF HARD-TO-HEAL WOUNDS

The underlying pro-inflammatory biochemistry of a hard-to-heal wound must be rebalanced for healing to occur^[1]. Early recognition of stalled healing and subsequent implementation of an appropriate treatment strategy are vital to ensure wounds move from 'stalled' to 'healed'. Such wounds may be large in size (or there may be a failure to decrease in size); the wound bed may be in poor condition; there may be unexpectedly high levels of exudate, with surrounding maceration or ulceration; there may be evidence of critical colonisation or local infection; and there may be abnormal or persistent inflammation (often difficult to differentiate from infection in a chronic wound)^[2]. Recognition is critical, as delaying the right treatment can result in increased burden to patients, society and the economy^[3,4].

FOCUSING ON SHORT-TERM COSTS: A FALSE ECONOMY?

Chronic wound care can be both expensive and labour intensive. When wounds stall during healing, costs tend to rise as time-to-healing increases and there are more complications. A retrospective analysis of NHS costs (2012/2013) showed that £3.2bn was spent on treating wounds with delayed healing^[4], while another study estimated an annual spend of \$25bn on chronic wounds in the US^[5]. Where inappropriate care is provided, these costs are compounded as chronicity worsens.

There is an ever-increasing pressure to reduce costs in a challenged economy. However, a sole focus on the cost of dressings without thought for the total cost for a care 'episode' could represent a false economy, failing to consider long-term patient outcomes. Advanced wound dressings can help manage the wound environment, improve healing rates, reduce healing time and long-term disabling outcomes and, therefore, minimise the costs associated with care. Appropriate assessment, monitoring and use of advanced products are vital to address the economic and human costs of hard-to-heal wounds^[6].

PROMOGRAN™ PROTEASE MODULATING MATRIX & PROMOGRAN PRISMA™ WOUND BALANCING MATRIX

PROMOGRAN™ Matrix and PROMOGRAN PRISMA™ Matrix (Acelyty) are advanced topical therapies for hard-to-heal wounds, which maintain a moist microenvironment at the wound surface, conducive to formation of granulation tissue, epithelialisation and optimal wound healing.

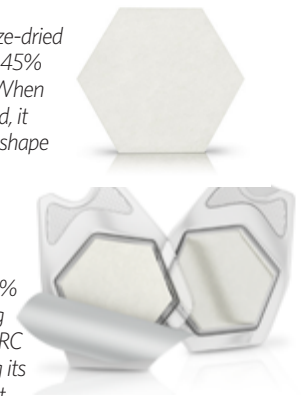
Figure 1: The properties of PROMOGRAN Matrix and PROMOGRAN PRISMA Matrix

PROMOGRAN Matrix

An absorbent, open-pored, sterile, freeze-dried matrix composed of 55% collagen and 45% oxidised regenerated cellulose (ORC). When the matrix is in contact with wound fluid, it forms a soft gel, which conforms to the shape of the wound.

PROMOGRAN PRISMA Matrix

Has additional silver for bacterial protection. The optimum formulation combines 1% silver-ORC containing 25% w/w ionically bound silver. This dressing has a higher amount of collagen and ORC than PROMOGRAN Matrix, increasing its overall density and extending the time it takes to biodegrade in the wound.



These dressings have been evaluated across numerous published RCTs, patient case studies and posters, with results showing enhanced outcomes across multiple wound types, specifically for hard-to-heal wounds (Table 1).

Table 1: Overview of clinical evidence for PROMOGRAN Matrix and PROMOGRAN PRISMA Matrix

Study overview
Diabetic foot ulcers (DFUs): In a 12-week RCT (n=276), more wounds achieved complete healing in the PROMOGRAN group compared with control (standard of care: saline moistened gauze). The difference was significant in wounds <6 months in duration (45% vs. 33%; p=0.056) ^[7]
DFUs: In a 6-week RCT (n=40), significantly more wounds (63% vs. 15%, p<0.03, OR 8.5) achieved complete healing with PROMOGRAN vs. control (standard of care: moist wound healing). Time to complete healing was significantly shorter in the PROMOGRAN group vs. control (23.3 vs. 40 days, p<0.01) ^[8]
DFUs: In a 14-week RCT (n=40), significantly more wounds achieved a >50% reduction in wound area vs. control at week 4 (79% vs. 43%, p=0.035). The number of wounds withdrawn due to infection was significantly greater in the control group (0% vs. 31%, p=0.012). At week 14, the number of healed wounds was 52% vs. 31% ^[9]
DFUs: In a 12-week RCT (n=32), significant differences were seen in wound area reduction on days 14 and 28 in the PROMOGRAN group vs. control (hydrocolloid dressing). Wound fluid biochemistry data indicated a more favourable moist wound environment in wounds in the PROMOGRAN group vs. control ^[10]
DFUs: In an 8-week RCT, PROMOGRAN (n=17) was more effective at reducing wound size than autologous growth factors (n=17). Wound size reduction in the group receiving both PROMOGRAN and autologous growth factors was significantly better (p<0.001) than either treatment alone ^[11]
Venous leg ulcers (VLUs): In a 2-week RCT (n=40), a significantly greater mean wound area reduction was seen with PROMOGRAN + good ulcer care vs. control (good ulcer care) (P<0.05). With PROMOGRAN, a significant reduction in pain was seen at week 2 (baseline mean pain score: 8.72 vs. 3.84) at week 2 (P<0.05) ^[12]
VLUs: In a 12-week RCT (n=73), more wounds (62% vs. 42%, p=0.0797) were healing/improved in the PROMOGRAN + compression group vs. control (non-adherent dressing + compression). Significantly greater wound area reductions were seen with PROMOGRAN + compression group vs. control (54.4% vs. 36.5%, p<0.0001) ^[13]
Surgical infection: In this study (n=98), there was no or reduced bacterial contamination in the second and third swab for 33 patients (66%) in the ORC group vs. 12 patients (25%) in the control group (gauze soaked in iodine). There were no cases of wound dehiscence in either group ^[14]
Pressure ulcers (PUs): In this 12-week study (n=23), significantly faster healing in the PROMOGRAN group vs. control (foam hydropolymer dressing) positively correlated with decreased elastase and plasmin activity in wound exudate, with no signs of infection or intolerance to PROMOGRAN ^[15]
PUs: In a 6-week RCT (n=80), more patients completely healed in the PROMOGRAN group vs. control (moist wound healing: vaseline gauze and hydropolymer patch) (90% vs. 70%). Time to complete healing was shorter in the PROMOGRAN group vs. control (360 days overall hospitalisation vs. 1164 days) ^[16]
DFUs: In an 8-day RCT (n=33), reduction in wound size was significantly greater (16% vs 1.65%, p=0.045) in the PROMOGRAN group vs. control (good standard of wound care). Wound fluid biochemistry data indicated a favourable moist wound environment in the PROMOGRAN group ^[17]

Explanation of how to use this guide: This document can be used to make the case for implementing effective prevention and management measures and may be supported by data from your own care setting. As well as economic impact, it is important to know the impact of interventions on patient quality of life and outcomes.

MAKING THE CASE

PATIENT BENEFITS OF PROMOGRAN MATRIX & PROMOGRAN PRISMA MATRIX

Living with a chronic wound, which may be painful, malodorous and exudative, can affect physical, mental and social wellbeing, including: daily living activities, productivity (i.e. work and income), and loss of sleep^[18,19]. The benefits of PROMOGRAN Matrix and PROMOGRAN PRISMA Matrix can be seen in a series of case studies on wounds with elevated protease activity over a 4-week period: the improved time to healing for patients with previously chronic wounds is especially pertinent, with improvements recognised within just a few weeks of beginning treatment^[20].

Previous duration of wound	Positive outcomes during 4-week period ^[20]
12 years	Elevated protease activity was lowered and healing improved (in a wound that had recurred after 8 months' ulcer-free)
12 years	Healing was activated, the wound was kept infection-free and protease activity was lowered
18 months	Protease levels were lowered, the wound reduced in size and there was a high percentage of healthy granulation tissue
14 months	The wound greatly decreased in size, the patient was very satisfied with treatment, as were the clinicians
8 weeks	The wound decreased in size and was healing well after 3 weeks; the dressing was discontinued due to this progression. Staff reported no problems with the dressing

Q COULD PROMOGRAN MATRIX OR PROMOGRAN PRISMA MATRIX IMPACT WOUNDS IN YOUR CARE?

ECONOMIC BENEFITS OF PROMOGRAN MATRIX & PROMOGRAN PRISMA MATRIX

A retrospective analysis was performed in a DFU population to assess cost-effectiveness using results of a 6-week RCT (n=40): patients were treated with either PROMOGRAN Matrix (n=20) or control (standard good wound care protocol with foam dressings and hydrating gels) (n=20). Effectiveness was defined as the percentage of patients whose wounds had healed by study end. *Table 2* outlines the cost of care and treatment outcomes with PROMOGRAN Matrix versus control. The cost savings shown below could be even greater across longer-term treatment programmes^[21].

The cost-effectiveness of PROMOGRAN Matrix compared with simple gauze dressing was confirmed in a retrospective chart study. Although simple gauze is less expensive than PROMOGRAN Matrix, it is actually

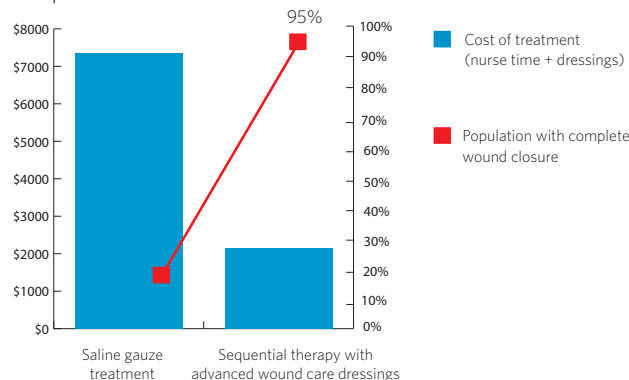
Table 2: Costs of care and treatment outcomes during the 6-week study^[21]

	Treatment group (PROMOGRAN)	Control group
Patients not healing (n/cost)	7 patients/\$17,537.68	16 patients/\$34,905.61
Patients healed (n/cost)	12 patients/\$17,835.95	3 patients/\$6,337.01
Total cost	\$35,373.3	\$41,242.63
Average cost per patient	\$1,861.76 ± \$717.91	\$2,170.65 ± \$32.75*
Effectiveness (% healed)	63%	16%
Average cost-effectiveness	\$561.48	\$2,577.65

*P=0.006, Student's t test

Q COULD YOU MAKE SAVINGS USING PROMOGRAN MATRIX OR PROMOGRAN PRISMA MATRIX?

Figure 2: Cost and healing of simple gauze versus PROMOGRAN over a period of 2 months^[16]



much less cost-efficient based on labour intensity: the cost of 2 months' treatment with saline gauze was \$7,350, but only 7.2% of patients achieved complete healing, whereas 95.0% achieved complete healing with PROMOGRAN Matrix at a cost of just \$2,145^[22]. These results were further demonstrated in an RCT that showed lower mean healing times and a greater frequency of complete healing with PROMOGRAN Matrix versus control^[16].

References

- Cullen B. Underlying biochemistry in non-healing wounds perpetuates chronicity. *Wounds International* 2016; 7(4):10-16
- Stacey M. Why don't wounds heal? *Wounds International* 2016; 7(1):16-21
- Dowsett C. Breaking the cycle of hard-to-heal wounds: balancing cost and care. *Wounds International* 2015; 6(2):17-21
- Guest JF, Ayoub N, McIlwraith T, et al. Health economic burden that wounds impose on the national health service in the UK. *BMJ Open* 2015; 5:12, e009283
- Fife CE, Carter MJ, Walker D. Why is it so hard to do the right thing in wound care? *Wound Repair Regen* 2010; 18(2):154-8
- Vowden P and Vowden K. The economic impact of hard-to-heal wounds: promoting practice change to address passivity in wound management. *Wounds International* 2016; 7(2):10-5
- Veves A, Sheehan P, Pham HT. A randomized, controlled trial of Promogran (a collagen/oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers. *Arch Surg* 2002; 137(7):822-7
- Lazaro-Martinez JL, Garcia-Morales E, Beneit-Montesinos JV, et al. [Randomized comparative trial of a collagen/oxidized regenerated cellulose dressing in the treatment of neuropathic diabetic foot ulcers]. *Cir Esp* 2007; 82(1):27-31
- Gottrup F, Cullen BM, Karlsmark T, et al. Randomized controlled trials on collagen/oxidized regenerated cellulose/silver treatment. *Wound Repair Regen* 2013; 21(2):216-25
- Ulrich D, Smeets R, Unglaub F, et al. Effect of oxidized regenerated cellulose/collagen matrix on proteases in wound exudate of patients with diabetic foot ulcers. *J Wound Ostomy Continence* 2011; 38(5):522-8
- Kakagia DD, Kazakos KJ, Xarchas KC, et al. Synergistic action of protease-modulating matrix and autologous growth factors in healing of diabetic foot ulcers. A prospective randomized trial. *J Diabetes Complications* 2007; 21(6):387-91
- Wollina U, Schmidt WD, Kronert C, et al. Some effects of a topical collagen-based matrix on the microcirculation and wound healing in patients with chronic venous leg ulcers: preliminary observations. *Int J Low Extrem Wounds* 2005; 4(4):214-24
- Vin F, Teot L, Meaume S. The healing properties of Promogran in venous leg ulcers. *J Wound Care* 2002; 11(9):335-41
- Alfieri S, Di Meceli D, Menghi R, et al. Role of oxidized regenerated cellulose in preventing infections at the surgical site: prospective, randomized study in 98 patients affected by a dirty wound. *Minerva Chir* 2011; 66(1):55-62
- Kloeters O, Unglaub F, de Laat E, et al. Prospective and randomized evaluation of the protease-modulating effect of oxidized regenerated cellulose/collagen matrix treatment in pressure sore ulcers. *Int Wound J* 2016; 13(6):1231-36
- Nisi G, Brandi C, Grimaldi L, et al. Use of a protease-modulating matrix in the treatment of pressure ulcers. *Chir Ital* 2005; 57(4):465-8
- Lobmann R, Zemlin C, Motzkau M, et al. Expression of matrix metalloproteinases and growth factors in diabetic foot wounds treated with a protease absorbent dressing. *J Diabetes Complications* 2006; 20(5):329-35
- Augustin M. Cumulative life course impairment in chronic wounds. *Curr Probl Dermatol* 2013; 44:125-29
- Green J, Jester R, McKinley R, et al. The impact of chronic venous leg ulcers: a systematic review. *J Wound Care* 2014; 23:12, 601-12
- Wounds International. *International case series: Using PROMOGRAN®/PROMOGRAN PRISMA® on wounds with elevated protease activity: case studies*. Available at: <http://bit.ly/2jTJMM> (accessed 20.01.17)
- Lazaro-Martinez J, Garcia-Morales E, Beneit-Montesinos J, et al. A retrospective analysis of the cost-effectiveness of a collagen-oxidized regenerated cellulose dressing in the treatment of neuropathic diabetic foot ulcers. *Ostomy Wound Management* 2010; 56(11A)
- Snyder R, Richter D, Hill ME. A retrospective analysis of the cost-effectiveness of a collagen-oxidized regenerated cellulose dressing in the treatment of neuropathic diabetic foot ulcers. *Ostomy Wound Management* 2010; 56(11A)