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Cost-effectiveness of adjunct haemoglobin spray in the treatment of hard-to-heal wounds in a UK NHS primary care setting

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Objective: To evaluate the cost-effectiveness of topical haemoglobin spray as adjunct therapy in the treatment of hard-to-heal wounds within a UK National Health Service (NHS) community setting.
Method: In a previously published comparative clinical evaluation, 50 consecutive patients treated with topical haemoglobin spray, as adjunct to standard care and followed up over 26 weeks, were compared with 50 consecutive retrospective controls from the same clinic treated with the same standard care protocol in the year prior to the introduction of adjunct topical haemoglobin spray. A de novo cost-effectiveness and break-even analysis were performed, using data from the previously published clinical evaluation, for all patients (intent-to-treat) and for patients with complete follow-up using a micro-costing approach and considering only wound care dressing costs.
Results: At 26 weeks, the total cost of dressings for all patients in the intervention group was £6953 with 874 cumulative weeks healed, compared with £9547 with 278 cumulative weeks healed for all patients in the control group. The incremental cost-effectiveness ratio (ICER), the incremental cost per additional week healed with adjunct topical haemoglobin spray, is therefore negative (dominant). Total treatment costs per week were lower from week six onwards, with break-even estimated to be at week 10.2. When considering only patients with complete follow-up, the results were similarly dominant, with a mean 10.9 more weeks healed, a mean dressing cost saving per patient of £81.83 by week 26 (–37%). Cost savings were realised from week five, and a break-even was estimated to occur at week 8.0.
Conclusion: Topical haemoglobin spray has the potential to restore the healing process, reduce healing times and reduce dressing costs in a NHS community setting, within a few weeks of adoption.
Declaration of interest: FE conducted all data analysis and wrote the paper, and GB provided guidance on overall design, results presentation and reviewed the manuscript. FE provides consulting services to pharmaceutical and medical device manufacturers, including but not limited to Mölnlycke Health Care AB. GB is an employee of Mölnlycke Health Care AB. The original clinical evaluation was supported by a grant from infirst Healthcare Ltd.

chronic wounds • cost-effectiveness • haemoglobin spray • hard-to-heal • wound healing

Wound treatment represents a significant cost to the National Health Service (NHS) in the UK and can severely impact the quality of life of patients.[1] A retrospective cohort analysis of data from The Health Improvement Network (THIN) estimated that the NHS treats more than two million patients annually at a cost of £4.5–£5.1 billion at 2012/13 prices.[2] Many of these wounds (39%) were not healed within the study period and the costs of treating these wounds ranged from £1719 to £5976 per patient within the observation period alone.

Hard-to-heal wounds are characterised by poor oxygen perfusion, such as in the case of arterial or venous insufficiency in arterial or venous leg ulcers (VLU), from complications associated with diabetes in diabetic foot ulcers (DFU), or from ischaemia and reperfusion damage in pressure ulcers (PU). A seminal prospective study suggested that 97% of wounds in limbs with low or very low oxygen levels (adjacent to the wound) failed to heal, while 95% of the wounds in limbs well perfused with oxygen in the same study went on to heal.[3] Later studies have demonstrated similar results.[4] Additionally, low wound oxygen levels ($TcPO_2$) have been identified as possibly the best predictor of wound chronicity.[5] However, hard-to-heal wounds can often be identified within 2–4 weeks without measuring wound oxygen levels, by just observing wound size reduction, and have been defined as wounds that fail to progress toward healing following 2–4 weeks of standard care.[6]

In order to address low wound oxygen levels, a number of topical oxygen therapies have been developed to support healing in hard-to-heal wounds.[7] Topical haemoglobin has been demonstrated to be an effective topical oxygen therapy, notably across a range of hard-to-heal wound types in a real-world evaluation where 90% of hard-to-heal wounds healed compared with 38% in the control group.[8] Haemoglobin has been shown to improve oxygen diffusion rates by more than 800% in a low oxygen environment under laboratory conditions.[9] Topical haemoglobin spray has been demonstrated to rapidly increase average oxygen concentration levels in wound tissue by more than 40% within 20 minutes in a pilot

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study involving five patients with hard-to-heal leg ulcers,[10] and by more than 7% within 20 minutes in a much larger sample of patients with VLUs.[11]

Healing rates more than double those of standard care were demonstrated in a randomised controlled trial (RCT) over six months in 28 patients with lower leg ulcers, where 1/14 ulcers healed with a standard care regimen versus 13/14 using a haemoglobin regimen.[12] This study, however, had several limitations and was followed by an RCT in 72 patients with VLUs which demonstrated a mean reduction in wound size of 53% versus a 21% mean increase in the control group over 13 weeks.[13] A simulation of expected long-term healing outcomes in hard-to-heal and non-healing VLUs was conducted showing 51% more wounds healed, and an overall reduction in wound care burden by 43%.[14] This prompted a series of long-term real-world evaluations of topical haemoglobin in a range of wounds with healing complications, including DFUs,[15] hard-to-heal wounds[8] and sloughy wounds.[16] These evaluations demonstrated substantially better wound healing outcomes and a combined meta-analysis confirmed these improvements across each wound type identified.[17]

Healthcare Improvement Scotland completed a cost-effectiveness evaluation of topical haemoglobin spray and reported expected average cost savings of £2330 per patient in DFUs, £1469 per patient in hard-to-heal wounds and £849 per patient in sloughy wounds over six months.[18] However this evaluation did not estimate cost-effectiveness when considering only dressing costs.

To provide clarity on the impact on dressing costs alone, this paper reports an analysis of the data from the hard-to-heal wound clinical evaluation above[8] on the potential impact of topical haemoglobin spray on the cost of dressings within a National Health Services (NHS) community setting.

Methods

The original clinical evaluation was carried out in a NHS community setting in 2015. It involved patients presenting with hard-to-heal wounds of any aetiology and demonstrating <40% wound size reduction after at least four weeks of standard care. The methodology and clinical results of this evaluation were reported previously.[8] The evaluation included the first 50 consecutive patients meeting the inclusion criteria in order of presentation. These wounds included wound types such as PUs, leg ulcers or DFUs, as well as burns, surgical and trauma wounds that had failed to heal normally. Exclusion criteria included wounds that were clinically infected and requiring antibiotics at baseline. Patients were treated with standard care plus topical haemoglobin spray (Granulox, Mölnlycke Health Care), applied with each dressing change in line with the manufacturer's instructions for use. Adjustments to dressing size and type were allowed as per standard care as dictated by the healing of each wound. Data were collected to 26 weeks follow-up.

A retrospective control group was constructed by selecting the first 50 consecutive patients, using the same inclusion and exclusion criteria, in the same NHS community setting, during the previous year. These patients were treated with the same standard care protocol but without the use of haemoglobin spray as adjunct therapy. Care in both the intervention and control groups was delivered by the same care team. The primary outcome measure was complete wound healing (complete re-epithelialisation).[17]

Data were collected from the regular medical records for each patient and information was recorded on all relevant wound attributes during each clinical contact. Wound attributes were transferred to a case record form, with weekly entries for the four-week run-in period and the first eight weeks from baseline, and then at least monthly up to week 26. Wound closure, adverse events, and any changes in wound care regimen or frequency were recorded for every week.[17]

Cost-effectiveness was evaluated for all patients and for patients with complete follow-up. Dressing costs were calculated for each patient from the dressing regimen and the number of dressing changes for each week of care using a micro-costing approach.[19] The prices of dressings and other materials used for debridement and dressing changes were extracted from the NHS Electronic Drug Tariff at 2018 prices[20] without additional dispensing charges. Costs of prescriptions for non-dressing items such as analgesics and antibiotics were not considered. Offloading device support such as boots, mattresses or seat cushions were invariably in place before baseline and were not included in the costing. Non-sterile water used for rinsing a wound was assumed at zero cost. On the rare occasion where no Drug Tariff price was available, the locally negotiated price at the time of the evaluation was used. The cost of the topical haemoglobin spray was based on the NHS tariff price for topical haemoglobin spray at £125 per can (£4.17 per application).

To provide a conservative estimate of the cost-effectiveness of topical haemoglobin spray as adjunct to standard care, the incremental cost-effectiveness ratio (ICER) of the adjunct haemoglobin spray treatment was calculated. This was calculated as the incremental total cost, considering only wound dressing consumables, for each additional week healed, compared with standard care alone within the observation period.

To provide insights into the possible budgetary effects of topical haemoglobin spray as adjunct to standard care within a NHS community setting, a break-even analysis was performed. This analysis aimed to estimate the number of weeks required for the cumulative cost of wound care dressings in the intervention group to be equal to that in the control group. Furthermore, the healing rate required in the intervention group for breakeven at 26 weeks was estimated.

Table 1. Wound healing (complete follow-up)

	Week	All hard-to-heal wounds		
		Haemoglobin	Standard	DIfference
Size reduction versus baseline*				
	Week 1	-31%	–5%	**–26%*** **
	Week 2	-48%	–8%	**–39%*** **
	Week 3	-63%	–11%	**–52%*** **
	Week 4	-73%	–12%	**–61%*** **
Wounds healed, by week, %†				
	Week 4	32%	10%	**–22%*** **
	Week 8	80%	14%	**–66%*** **
	Week 12	80%	28%	**–53%*** **
	Week 16	88%	33%	**–55%*** **
	Week 20	90%	43%	**–47%*** **
	Week 26	92%	48%	**–44%*** **

Statistically significant p<0.1, **p<0.05, ***p<0.01; †Percent for wounds with follow-up to that week or longer

All analysis was completed based on anonymised data and ethics committee approval for the analysis was not required, nor sought.

Results

As previously reported,[8] a total of 100 patients were included in the original evaluation, 89 with complete follow-up. No patients required exclusion (wound infection requiring antibiotics treatment at baseline). Trauma wounds were the most common wound type in both study groups (44% and 38% in the intervention and control groups, respectively) and 34% and 38% respectively were PUs, leg ulcers or DFUs. There were no significant differences between the intervention and control groups at baseline, with the exception of average wound duration before baseline, which were not considered as impacting the intended analyses.[17]

There was one patient lost to follow-up in the intervention group (one death at 12 weeks) and 10 in the control group (six deaths and four for other reasons). Hence, 26-week follow-up data were available for 89 patients: 49 and 40 in the intervention and control groups, respectively. After losses to follow-up, there were no significant differences between the intervention and control groups.[17]

More rapid wound size reduction was observed after the first week of adjunct topical haemoglobin spray (26% greater wound area reduction, t-test, p<0.01) (Table 1). At 26 weeks, the intervention group had a healing rate of 90% and the control group rate was 38%, Chi-square test p<0.001 (92% versus 48%, p<0.001, in the patients with complete follow-up, Table 1).[17]

Cost-effectiveness was evaluated as described. A higher rate of wound healing in the intervention group resulted in patients treated with adjunct topical haemoglobin spray benefiting from more weeks healed during the observation period. Overall, the intervention group recorded a total of 874 weeks healed, compared with 278 in the control group (Table 2). Despite the additional cost of the topical haemoglobin spray and fewer patients with complete follow-up in the control group, the total cost of dressings used in the intervention group was lower than in the standard care group, £6953 versus £9547. Together these findings were used to observe a negative ICER (–£4.35/week healed), indicating that with the topical haemoglobin spray better clinical outcomes can be obtained at a lower cost, suggesting adjunct topical haemoglobin spray to be dominant over standard care alone (Table 2). Additionally, the number of nurse visits required was lower in the intervention group (Table 2).

Cost savings were realised in line with the increased healing rate observed within the intervention group (Fig 1). Initially, the weekly cost of dressings were higher, £937.69 versus £642.52 at baseline, due to the use of the topical haemoglobin spray (Fig 2). However, the average weekly cost of dressings was reduced as wounds healed faster in the intervention group, with weekly cost of dressings per patient becoming lower in the intervention group from week six onwards (£377.52 versus £596.94 at week six). The break-even point, where the cumulative cost of dressings in the intervention group equals that in the control group, was estimated to occur at week 10.2 (Fig 3), using a least square regression (calculations not shown). The

Table 2. Cost-effectiveness outcomes after 26 weeks follow-up

	All patients				Complete follow-up only, average per patient			
	Healed (n, %)	Weeks healed (n)	Dressing costs (£)*	Nurse visits (n)	Healed (n, %)	Weeks healed (weeks/pt)	Dressing costs (£)*	Nurse visits (n/pt)
Haemoglobin	45/50 (90%)	874	£6953	997	45/49 (92%)	17.8	£139.56	19.8
Standard care	19/50 (38%)	278	£9547	2430	19/40 (48%)	7.0	£221.40	55.5
ICER (£/additional week healed)		Dominant†				Dominant†		

*Including primary and secondary dressings (including the cost of the haemoglobin spray, but not including nursing costs, drug, or surgical procedure costs); †Dominant means more weeks with complete healing at a lower total cost of dressings (including the cost of the haemoglobin spray applications); ICER—incremental cost-effectiveness ratio; pt—patient

healing rate required for break-even to occur only at the end of the observation period at week 26 was calculated to be 36/50 (72%) wounds.

However, more patients were lost to follow-up before healing in the control group, hence incurring dressing costs but without an opportunity to add to weeks healed. Therefore, the ICER analysis was repeated for patients with complete follow-up only. After 26 weeks, patients in the intervention group with complete follow-up had a mean of 17.8 weeks healed (874 total weeks healed) compared with seven weeks in the control group (278 total weeks healed), equating to a mean difference of 10.9 weeks. Correspondingly, patients received on average 8.2 and 19.1 weeks of treatment, respectively, at a mean cost of dressings of £139.56 (£6839 total) and £221.40 (£8856 total) (Table 2). Hence, the average saving per patient with complete follow-up was £81.83 after 26 weeks and, consistent with the analysis for the overall cohort, the ICER was found to be dominant (–£3.38/additional week heeled).

When excluding patients who were lost to follow-up, the expected break-even point was achieved at week eight, with average weekly costs of dressing changes lower in the intervention group from week five (data not shown). In the complete follow-up cohort, the healing rate required for break-even by week 26 was estimated to be 32/49 (65%) wounds.

Discussion

Adjunct topical haemoglobin spray was found to be dominant when considering wound care dressing costs, as compared with standard care in a NHS Community Setting. In this regard, dominance was obtained through achieving better wound healing outcomes at a lower cumulative cost of wound care dressings over a 26 week period.

Break-even analyses indicated the time in weeks required for the cumulative cost of wound care dressings in both groups to be equal and, therefore, signals the points beyond which overall dressing cost reductions can be gained in a NHS Community Setting. Whether an analysis was performed on an intent-to-treat or complete-follow basis, break-even was estimated to have been achieved after 10.2 and eight weeks, respectively. As these break-even points were estimated to occur relatively early within the observation period (39.2% and 30.8% of 26 weeks, respectively), this increases the likelihood of actual realisation of dressing cost reductions.

Furthermore, when assuming break-even to only occur at the very end of the observation period, it was estimated that 72% (intent-to-treat) and 65% (complete-follow) of wounds would be required to heal in the intervention group to account for the additional cost of the topical haemoglobin spray. As these rates are lower than the healing rates previously reported in literature,[8,15,16] these findings further support the likelihood of dressing cost savings with the adoption of adjunct topical haemoglobin spray in hard-to-heal wounds in a NHS Community Setting.

The cost-effectiveness and breakeven outcomes estimated were driven by a significantly increased

Fig 1. Cumulative wound closure rates to 26 weeks, all groups

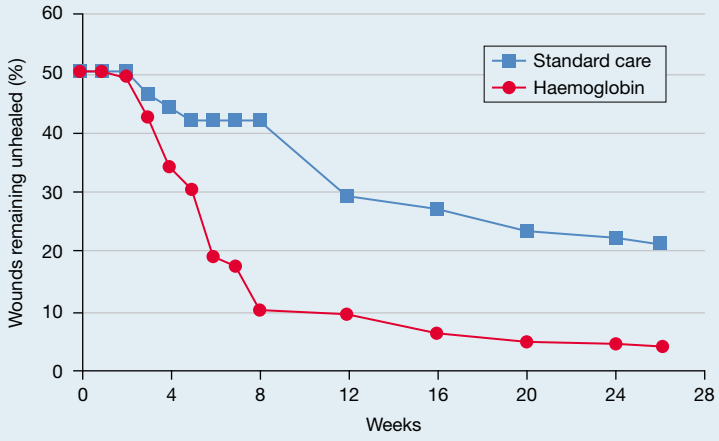


Fig 2. Cost of dressings per week (£)

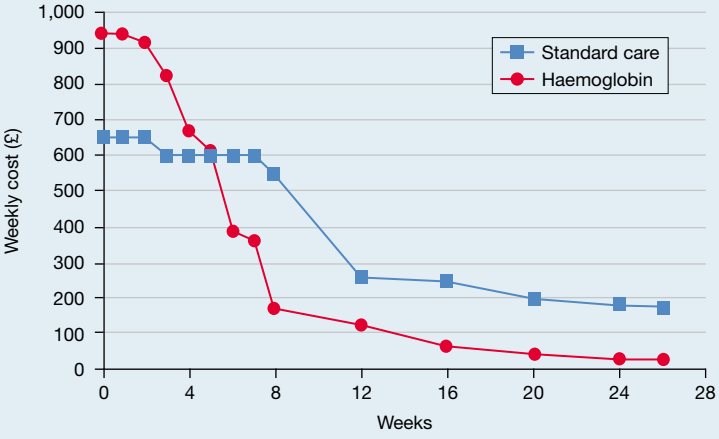
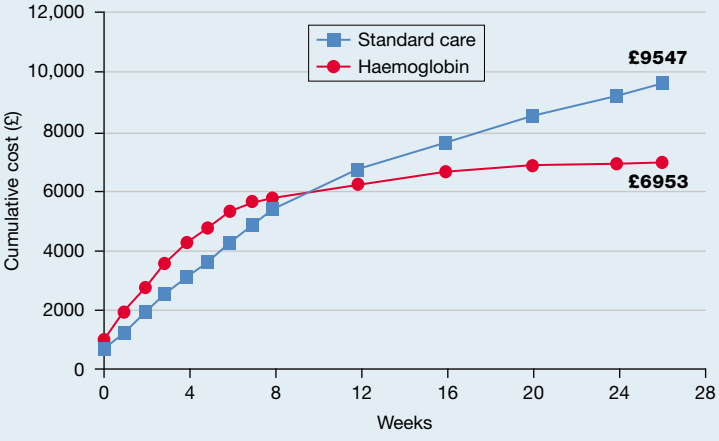


Fig 3. Cumulative cost of dressings (£)



Reflective questions

- If a group of wound clinics would switch all of their hard to heal wounds from standard of care to topical haemoglobin spray, how long would it take before cost savings are made?
- For every 50 patients with hard-to-heal wounds switched to topical haemoglobin spray, how much money is expected to be saved on dressings usage within six months?
- If the number of nurse visits required to care for 50 patients with hard-to-heal wounds is reduced from 2,430 nurse visits to 997 nurse visits, how much can quality of care be improved for remaining patients?

wound healing rate in the intervention group as compared with the control group. However, the possibility exists that cumulative dressing cost reductions were also driven by a reduction in dressing cost per clinical contact, as wounds that are on a healing trajectory might require fewer dressing layers, less expensive types of dressings, as well as smaller dressings. Our analysis did not allow us to examine this possibility and this could be the target of future evaluations.

The results of the current evaluation complements the results of the evaluation previously completed by the Healthcare Improvement Scotland[18] that suggested mean expected cost savings of £1469 per patient in hard-to-heal wounds, when also considering savings in nursing costs, drug costs and costs of surgical procedures.

Limitations

The clinical evaluation, on which the cost-effectiveness analysis was based, was carried out in a relatively small number of patients in England in a NHS community setting across a variety of hard-to-heal wound aetiologies,[8] and hence the estimated cost-effectiveness and break-even points in other clinical settings and in clinics with a different mix of wound aetiologies may vary. Future research should therefore aim to estimate these by specific wound aetiology and in different clinical settings.

Conclusion

The results of this evaluation supports the use of topical haemoglobin spray as an adjunct to standard care in hard-to-heal wounds that have not substantially reduced in size within four weeks with standard care within a NHS community setting. In these wounds, topical haemoglobin spray has the potential to restore the healing process, reduce healing times, and reduce dressing costs in a NHS community setting within a few weeks of adoption. JWC

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