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Submission For Senate Inquiry into Medicare funding for Hyperbaric Oxygen Treatment

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Information about Dr Hawkins:
I am a Specialist Anaesthetist and Hyperbaric Physician. I work as a Visiting Medical Officer Anaesthetist at Sutherland and Prince of Wales Hospitals in Sydney since 2006. I am also a Specialist Hyperbaric Physician having both the Diploma in Diving and Hyperbaric Medicine (from the South Pacific Underwater Medicine Society – SPUMS) and also the Certificate in Diving and Hyperbaric Medicine from the Australian and New Zealand College of Anaesthetists. These are the only two qualifications available in Australasia. I am also a Con-Joint Lecturer at the University of NSW and a member of the Australasian Diving and Hyperbaric Medicine Research group at UNSW. Currently I am Company Medical Director for Hyperbaric Health Pty Ltd looking after 52 Hyperbaric Chambers in 20 countries around the world including three Hyperbaric Hospitals in Australia.

Dear Committee Members,

I would like to submit several items of information in regard to the recent removal of funding by Medicare for Non-Diabetic Chronic Hypoxic Wounds (NDCHW) under CMBS Item number 10315.

I am a practicing Hyperbaric Physician and University Con-Joint Lecturer at the University of New South Wales.

I am also the lead author of the Australian and New Zealand Hyperbaric Medicine Group (ANZHMG) Wound Care Study that was initiated after the 2004 MSAC review (MSAC Report 1054) at their request and form the main data collection for the MSAC report that has currently in question (MSAC Report 1054.1).

I have attached several appendices of information that was made available to the committee and will explain their significance in this submission and a brief outlines as to why the MSAC committee process has failed both in the way it has assessed HBOT and also in the process itself which lead to the dissention of the two industry experts in the field (A/Prof Smart and A/Prof Bennett).

There are several points to summarise the issues were significant faults in the process has lead to the incorrect outcome being given to the Minister for approval.

1) The MSAC committee has made assumptions that are not valid with regard to the outcome benefit of standard wound care that has no basis in fact. A comparative study looking at standard wound care rates showed a 44.6% healing rate vs 68.3% in HBOT treatment at 6 months but the MSAC committee has stated and calculated cost effectiveness on both treatments having the same outcome percentage.

2) HBOT is stated as and is used clinically as a ***secondary treatment*** after standard wound care has failed. Treatment only starts after 3 months of standard wound care has not improved the wound (ie. 100% of patients have failed standard wound care treatment). In the ANZHMG wound care study the average time for a patient to present for HBOT was 19 months. So logically if the wound is not going to heal by 19

months of normal wound care then a 68.3% healing rate by 6 months post HBOT is quite remarkable.

3) The assumption that there is no difference in outcome between HBOT and wound care vs wound care alone means that the only difference between the two entities is the cost of HBOT. Therefore if other treatment modalities are assessed using this rationale, it is impossible for the new treatment to ever be cost effective. The assumption is that the outcome from standard wound care is the same as HBOT but this is a logical fallacy as it is ONLY initiated after the failure of standard wound care for 3 months.

4) MSAC requested that a study be done (in the 2004 review) and this was performed. It was a prospective outcome study of all people that presented to Hyperbaric Units for HBOT. It reflects actual clinical practice. While we do not deny that a randomised controlled trial is the best study for determining cause and effect it is difficult to do for non-diabetic wounds as the cause of the wounds is so variable that no control group can be established and the ethical issues surrounding withholding treatment for at least a year. The prospective study was therefore ethical and appropriate for the myriad of conditions that cause wounds (as HBOT fixes the underlying end point of the condition which is lack of small vessel blood flow to the skin).

INCLUDED DATA:

Several documents have been included in this submission and a short summary of their significance of each below:

Appendix 1 and 2:

These are reports looking at the MSAC report 1054.1 itself looking at the flaws and problems in depth. Appendix 1 is the primary report and Appendix 2 is the new data given to MSAC and NH&MRC for reconsideration of their assessment

Appendix 3 and 4:
The ANZHMG Woundcare reports from 2006 and 2011 referred to in the MSAC report. The 2011 report is unpublished as we wait for the final data for the patients to reach their 12 month assessment point (will finish in March 2013).

Appendix 5 and 6:
The original Gordon et al (2006) paper and the manuscript it came from. The addition of the manuscript is so that Table two (which looks at the outcomes of the treatment) was missing from the published paper due to Editorial control.

Appendix 7 and 8:
The paper (Hammarlund et al 1994) and corrospondence between Dr Glen Hawkins and Dr Christer Hammarlund regarding the non-diabetic wound RCT he performed in 1994 and how it should be interpreted.

Appendix 9:
Flow charts of Clinical Pathway, Economic Modelling Pathway and Actual Study Pathway.

Review of MSAC 1054.1

MSAC 1054.1 RESPONSE

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INTRODUCTION:

The Medical Services Advisory Committee (MSAC) is set up to evaluate ***new*** technologies and treatment modalities under three criteria:

1) Safety

2) Efficacy

3) Cost effectiveness

Assessment 1054.1 is the third attempt to assess the role of Hyperbaric Oxygen Therapy (HBOT) in the treatment of non-diabetic chronic non-healing wounds and non-neurological soft tissue radiation injury (STRI). MSAC assessment 1054.1 has approved the public funding of non-neurological STRI and we accept that assessment. Our concern is with the withdrawal of approval for public funding for non-diabetic chronic non-healing wounds and the methodology that was used in that assessment.

HISTORY OF PROCESS:

HBOT for non-diabetic non-healing chronic wounds is not a new treatment. The MSAC terms of reference and membership (as stated in Appendix A of the MSAC 1054.1 Report Page 119) state that:

> *"It advises the Minister for Health and Aging on whether a* ***new*** (my emphasis) *medical service should be publicly funded based on an assessment of its comparative safety, effectiveness, cost effectiveness and total cost, using the* ***best available evidence*** (my emphasis)*"*

Prior to 2001 non-diabetic, chronic hypoxic wounds were fully funded by Medicare. In 2001 an assessment process was started to look at the funding of other indications and the funding of non-diabetic hypoxic wounds was reassessed. This was MSAC assessment 1018-1020. The assessment concluded that there was ***insufficient evidence*** to support public funding and recommended that public funding should be withdrawn for this indication. This was not proceeded with as it was not the core issue being requested.

In 2004 MSAC review 1054 was performed. Further evidence of efficacy was presented in small studies and positive benefits were indicated, but still there was limited evidence. MSAC agreed to allow the development of a local prospective cohort collection of information that would prospectively look at the benefits of HBOT out to a year in individual patients with chronic wounds. The study was designed to follow each person out to 1 year at different stages, to see if HBOT improved healing rates in chronic non-healing wounds after three months of standard wound care. This design was deemed acceptable by MSAC and was extended in 2007 as the numbers of patients reaching a full years follow up were not sufficient to make an interpretation.

Due to evidence of benefit, the MSAC review committee stated

> *"…in the **absence of an effective alternative therapies** (my emphasis) and in view of local data collections and international trial, funding for HBOT should continue for existing MBS listed indications at eligible sites for a further three years."*

The current assessment (1054.1) is a continuation of this assessment with additional evidence from the MSAC approved study being available.

There is some concern expressed by the clinical experts that the current MSAC review process may not be applicable for HBOT as:

> *"Clinical expert opinion indicates that the current MSAC assessment process may not be appropriate for an established therapeutic intervention such as HBOT. The current assessment should determine the relative merits of the treatment options available rather than simply examining a single, existing treatment option in isolation. Clinical expert opinion is that a patient-centred approach, where all options for the treatment of the nominated conditions are examined, would be optimal." (MSAC 1054.1 Pg 17)*

The primary problem being that HBOT is a ***secondary*** treatment modality only used after three months of the primary treatment of 'usual care' has failed. It therefore limits options as well as restricting a clinical option that has been shown to enhance healing and terminating the long-term requirement for care.

POINTS:

•HBOT for non-diabetic non-healing wounds is **not a new technology** and should not be assessed under new treatment/technology guidelines as it was fully funded prior to 2001

•There is some concern that the MSAC assessment process is actually applicable to this therapy (as it is a secondary treatment modality when the primary treatment modality has failed already)

• MSACs prior reviews have recommended continuation of funding while studies were done and positive outcomes of those studies allowed further continuation of funding

• Due to the cost of developing and running a Randomised Controlled Trial (RCT) and the ethical dilemma of withholding treatment for at least a year, a prospective cohort study that was suggested and approved is the current best available evidence for HBOT

• The ANZHMG Woundcare study was accepted by MSAC as a study that would allow assessment of efficacy of the treatment and funding was extended based on the preliminary positive outcomes of this study

• The ANZHMG Woundcare study does not assess the rate of healing or failure of treatment in ‘usual care’ cases and therefore cannot be used to determine healing rates in patients that have not had HBOT

THE ASSESSMENT PROCESS:

The use of HBOT is listed as having 15,579 Medicare Services for the 2010-2011 financial year for all MBS numbers of which 8,910 Services were related to either non-diabetic chronic non healing wounds or STRI (the item number 13015 does not distinguish between the two).

HBOT was seen as a uniquely placed clinical modality in that it is used

> *"after primary interventions and conventional therapies have failed to promote wound or radiation injury healing." (MSAC 1054.1 Page 6).*

Therefore by definition, the treatment modality is a secondary intervention only introduced *after* conventional treatment has failed.

SAFETY ASSESSMENT:

In all three reviews (2001, 2004 and 2010) have found that

> *"Adverse events related to treatment with HBOT are generally minor and self-limiting, rarely lead to discontinuation of treatment, and where present usually resolve shortly after cessation of treatment" (MSAC 1504.1 Pg 113)*

In summary the MSAC committee found

> *"…based on absolute data HBOT can be considered to be a safe and well-tolerated intervention for which serious, life threatening adverse effects and fatalities are rare." (MSAC 1504.1 Pg 113).*

Therefore HBOT is considered to be a relatively safe and well-tolerated treatment in all three reviews.

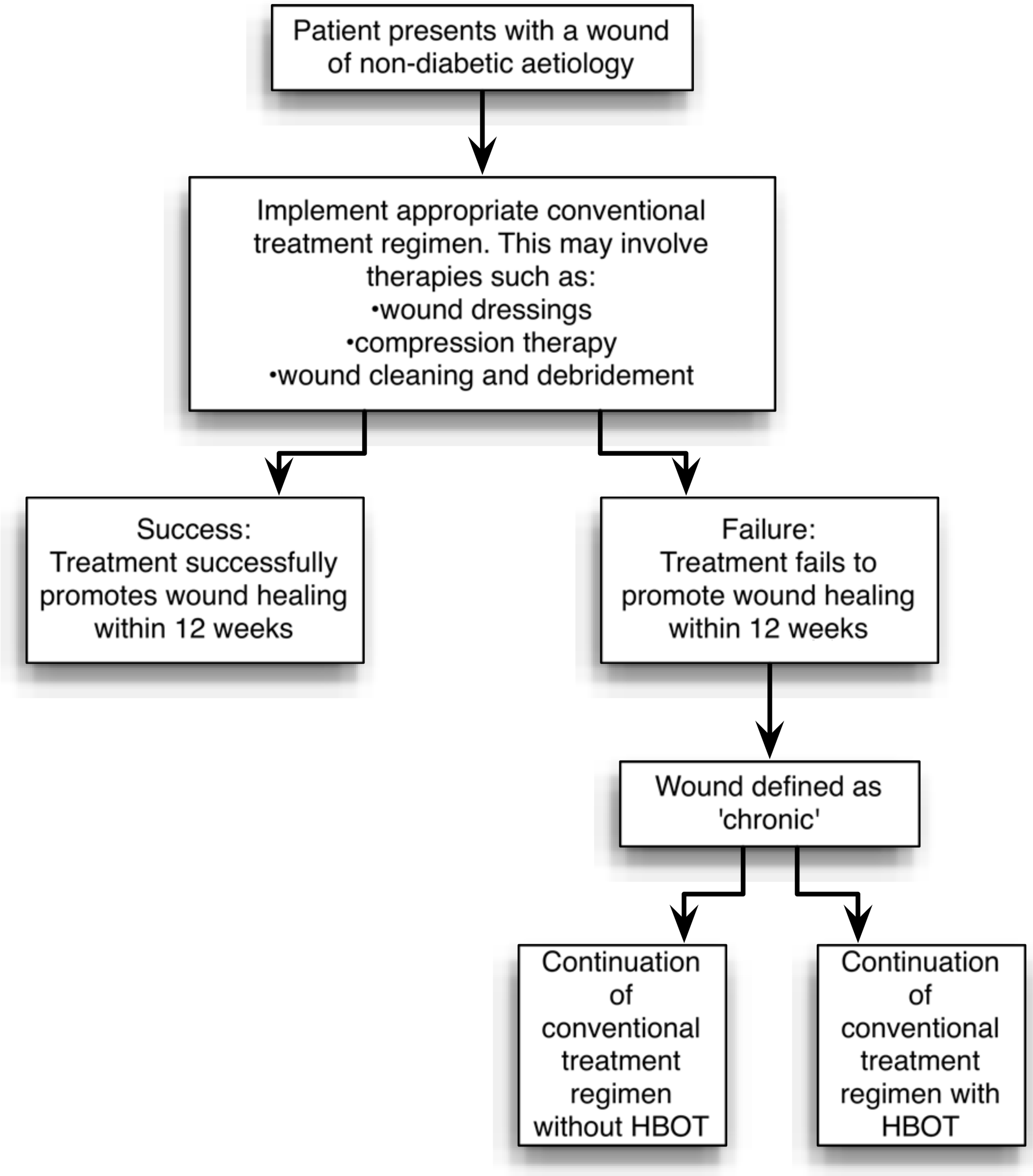
EFFECTIVENESS:

There is very little high level evidence regarding the effectiveness of HBOT vs conventional care in non-diabetic chronic wounds. This is for several reasons:

1) Diabetic wounds make up the bulk of most community based problem wounds that progress rapidly to major surgical interventions. Therefore most studies have been performed on them showing significant improvement with HBOT in several RCTs (and has current public funding under MBS item number 13020). Other wounds have different causes but they all have similar issues with wound hypoxia (low oxygen in the tissues) but because they are divided into smaller 'aetiological groups' no one causative group develops enough numbers to attract funding for an RCT of sufficient power.

2) The end point problem in most of these conditions is the same, hypoxic skin tissue (as is required to be demonstrated for funding) and HBOT has a demonstrable effect on this (as per an oxygen challenge) so there is reasonable circumstantial evidence that the effect is a class effect with virtually all wounds regardless of aetiology.

3) The ANZHMG wound care study has shown that for *ALL* aetiological groups, there is improvement >50% out to a year. This has the starting point of the patient having to have had the wound for *at least 3 months* and the ***average*** time to entry into the study was a wound of greater than 16 months. This is not taken into consideration by the MSAC interpretation as a failure of 'usual treatment' although it is stated on Page 21 of MSAC 1054.1 and is quoted directly in the clinical pathway diagram below.



From MSAC Report 1054.1 Page 7

4) Quality of life assessments are also discounted because there is difficulty in assessing quality of life in a group that has limited lifespans (due to the age group in which these wounds occur). The one study quoted (from data in the ANZHMG wound study) looks specifically at the reduction in pain which greatly enhances quality of life but the economic and lifestyle benefit are not attributed.

5) The ongoing cost of failure of the treatment is also very significant beyond the one year mark. For a lot of patients the end point of the disease is an amputation which has a significant impact both socially and in terms of health economics, that extends well beyond the single year.

COST EFFECTIVENESS:

The biggest issue is that when the cost effectiveness study is performed, there is an assumption that there is no difference in healing between the HBOT group and conventional treatment. A simple comparison between the Gordon et al (2006) paper which looks at two different models of conventional wound care and the Hawkins and Bennett (n.d.) paper both show healing rates at 6 months. This is used in the current MSAC 1054.1 assessment as the source for cost of funding and therefore out to 6 months gives an indication of comparative independent record of healing rates. The MSAC 1054.1 review states healing rates from the Gordon *et al* (2006) paper, with two different care models, of 5/36 patients in both groups (13.9%). On review of the original paper there is no record of the number of patients healed actually contained within the paper itself. Also the total number of patients was 56 (28 in each group randomised). This leads to some concern as to the source and validity of the data.

Personal communications with Dr Gordon actually had the healing rate at 3 months as 20/56 (35.7%) for both groups and 25/50 (50%) at 6 months as points of effectiveness for standard, high level wound care. As the ANZHMG has only the 6-month point of assessment in common, cost calculations can be performed at this point and compared between HBOT and 'usual care' under cost modelling.

Therefore it would be more correct to use this as a cost comparator rather than assuming that the two treatments are equally efficacious.

Using the data from the MSAC review we can do a cost effectiveness study using the real data at 6 months and it generates a table shown below.

Table 1: Cost comparison between "usual care" and HBOT and "usual care" to heal a wound at six months.

ITEM	HBOT+ USUAL CARE		USUAL CARE ONLY		COMMENTS
HBOT Costs	$4,245.65		$0.00		*From MSAC 1054.1 Table 37 Pg 91*
Surgical Costs*	$9,653.00		$9,653.00		*From MSAC 1054.1 Table 39 Pg 93*
Usual Care Costs	$4,610.00		$5,448.39		*From MSAC 1054.1 Table 38 Pg 92*
TOTAL COSTS (Per wound healed at 6 months)		**$18,508.83**		**$15,101.39**	
Documented healing rate	0.689		0.5		*From Hawkins & Bennett (n.d.) and Gordon et al (2006): exact numbers from personal communication with Louisa Gordon*
Failure of treatment cost at 12 months	$42,383.00		$40,232.00		*From MSAC 1054.1 Table 37 Pg 91*
Annual Costs per person per wound healed**		**$25,933.70**		**$27,666.70**	
Annual total costs per annum for service***		**$3,993,789.32**		**$4,260,671.03**	
COST DIFFERENCE (HBOT cost vs Usual Care Cost)	Per person per wound healed	**-$1,733.00**	Per annum cost for all wounds healed	**-$266,881.71**	*Negative number favours HBOT costing less per wound healed than "Usual Care"*

*Calculation from MSAC 1054.1 Table 39, Pg 93 is used as cost calculations in the original paper use the complication cost number in error.
**Annual costs per person per wound healed is: (6 month cost x healing rate) + ((1-healing rate) x failure of treatment cost)
*** Annual total costs per annum for service = Annual costs per person per wound healed x 154 services *(from MSAC 1054.1 Table 42, Pg 96)*
Assumption is made that the wounds that are not healed at 6 months go on to be failure of treatment in both groups at 12 months

The above table using data calculated form the MSAC 1054.1 review shows that in fact, the addition of HBOT after 3 months of standard care saves Medicare **$1733.00** per person per wound healed and **$266,881.71** per annum in total cost savings as compared to usual care. This is a conservative number as we know that the healing rate at 12 months is 85.2% (0.852) from Hawkins and Bennett (n.d.), the difference in cost could be expected to increase in favour of HBOT. This is at odds with the outcome cost of **$331,256.00** per annum in favour of 'usual care' in Table 42 Pg 96 but as noted before this is the accumulating the costs of adding the of HBOT without giving effect credit to the intervention.

The use of the Gordon *et al* (2006) paper as a comparator is valid based on the fact that: 1) both papers looked at rates of healing and provision of costs of service 2) Gordon *et al* (2006) is a standard example of the mixed outpatient/in home care model in Australia and represents the standard of high level wound care available to Australians 3) there are defined outcomes at the same point of treatment (six months) that are directly comparable between the two studies. It is also helpful that the Gordon et al study is independent of the wound care study as it cannot be criticised for potential bias towards HBOT.

The cost effectiveness calculation was done by the Incremental Cost-Effectiveness Ratio (ICER) model, which allows comparative costs to be assessed between different technologies.

DISCUSSION:

MSAC Review 1054.1 did this assessment based on a mixture of hard data (ANZHMG Wound care study) and several assumptions that are not logical and are not supported by the data available. The primary concern is that the outcome was pre-determined as part of the assessment and then the technologies were assessed against this outcome (MSAC 1054.1 Pg 87).

The assumption made is:

> *"However since there is no common comparator it is not possible to undertake a direct comparison of the data from Hawkins and Bennett (n.d) and Gordon et al (2006). **As a result the data from Hawkins and Bennett (n.d) formed the basis of the effectiveness of HBOT and usual care for the economic analysis.***(my emphasis)*"*

This is incorrect as the Hawkins and Bennett paper did not look at the effectiveness of non-hyperbaric wound care and no assumption of efficacy should be made from this paper regarding non-hyperbaric wound care outcomes.

Given that there is an artificial (and incorrect) assumption of equal outcome and both have the same standard care with one having an additional care resource allocated to it, then by definition, it will never be cost effective no matter what the intervention is.

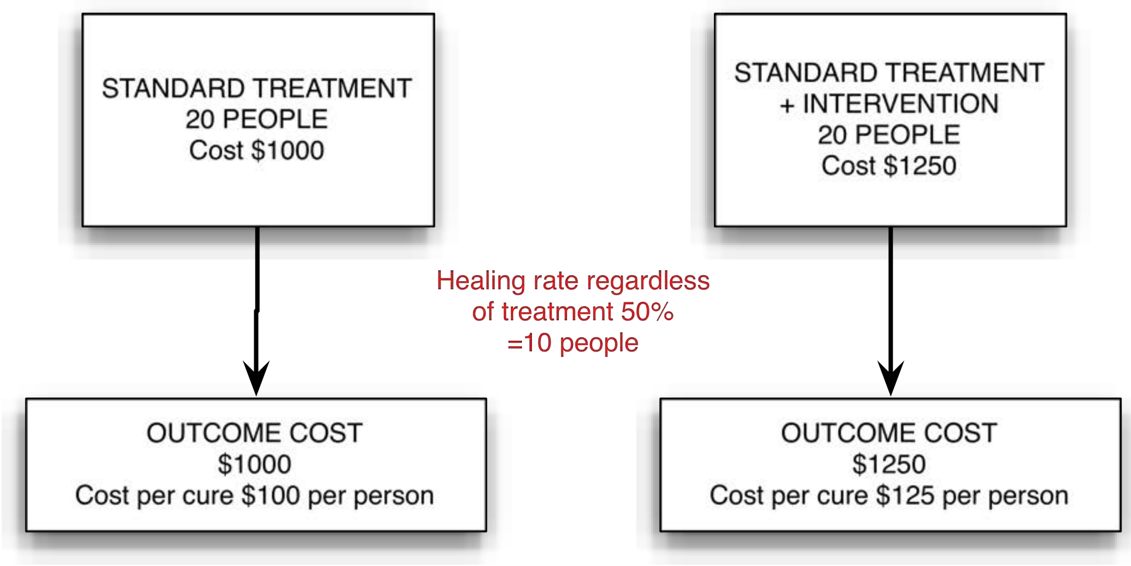
It is stated in the "Objective" under Economic Considerations in MSAC 1054.1 (Pg 84):

> *"For chronic non-diabetic wounds the most appropriate comparator is usual care."*

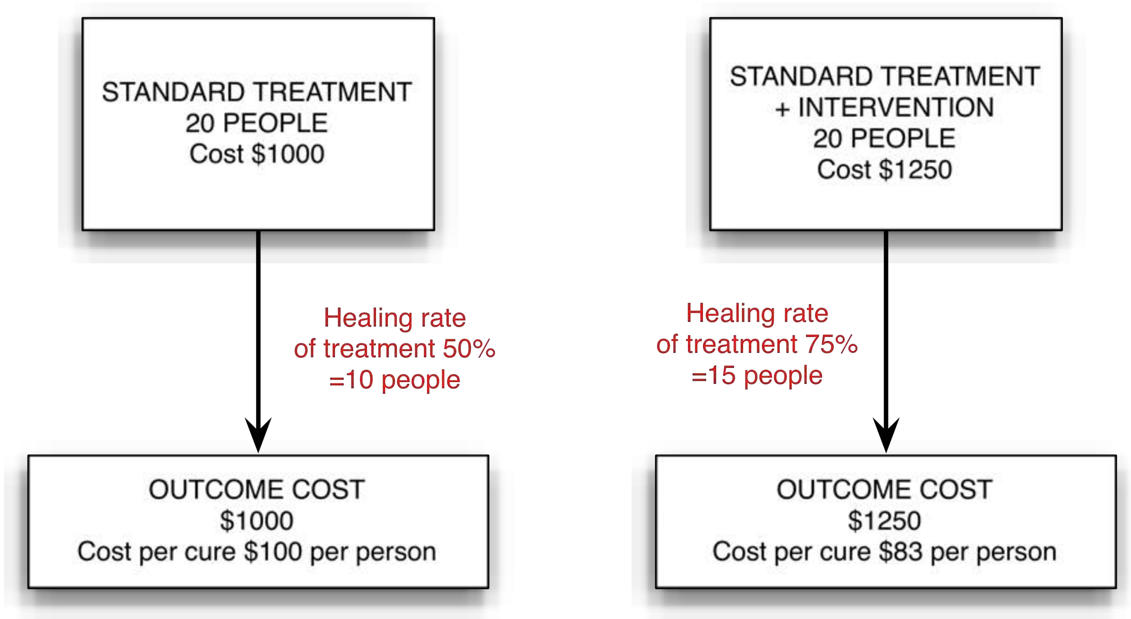
As the Gordon et al (2006) paper is a study of two models of usual care to look at costs effectiveness, the statement on page 87 of the MSAC 1054.1 review that:-

> *"However since there is no common comparator it is not possible to undertake an indirect comparison of the data from Hawkins and Bennett (n.d.) and Gordon et al (2006)"*

-seems illogical as the aetiologies and the reporting dates are identical and they are clearly looking at the two modalities of treatment that we are interested in. It is therefore more appropriate to compare the two papers as benchmarks of best evidence than to make an assumption on a paper that does not cover the results that are used. The model of what has been done and what should have been done is shown in Figure 2.



Predetermined outcome with two treatment modalities



Outcome determined by actual intervention rates

The cost reduction effect is critically dependant on the number of people ‘cured’ so that the artificial equalisation of the outcomes makes the costs effective exercise pointless. The whole basis of the intervention is to reduce either the duration or severity of care and hence saving money it total. In MSAC 1054.1 the cost effectiveness assessment has managed to get the result that is opposite to clinical reality, and in fact will cost the government an incremental differential increase (cost of using more expensive treatments minus loss of cost benefit savings) in costs in excess of $500,000.00 per annum because of this.

CONCLUSION:

So the end conclusion of the MSAC review is incorrect as public funding for this modality of treatment would provide a cost benefit to the public over ‘usual treatment’ alone.

POINTS:

• HBOT is a safe treatment modality and is well tolerated by patients

• it is introduced AFTER conventional wound care has **not** had a significant result for three months and the wound has become “chronic”

• the MSAC requested ANZHMG wound care study shows that patients come to HBOT centres after having a wound for an average of 16 months and of those that are non-diabetic venous ulcers (comparable to Gordon *et al* 2004) at six months 68.9% have healed

• a comparator study of wound care alone in a similar group shows that at six months only 50% have healed

• randomised controlled trials are difficult to perform in this setting because of a) the cost and b) ethical considerations of not treating patients in the control group but current best available data shows a probable benefit in the HBOT group

• a properly funded randomised controlled trial (RCT) to determine wound care cost burden vs potential saving should be performed prior to removing funding for potentially a significant cost saving treatment modality.

OTHER ISSUES OF THE REPORT:

1) The initial sentence in page one is not correct: the application was to retain the MBS number for STRI and HBOT for chronic non-diabetic non-healing wounds. At no stage was this a new treatment and new number. The assessment was aimed at determining whether a 'temporary' number imposed after the 2001 assessment was to be made permanent or not. This is outside the scope of the MSAC system as it was then run (there is now a different system in place).

2) Verbal communications from two expert members of the committee stated that they have dissented from the findings reported based on some of the issues outlined here. This fact is not clear, nor their reasons for dissent. This should have been made clear to the Minister of Health prior to the decision to remove funding.

3) There has been no time for external discussion of the document prior to it being listed as a removal of MBS item number in the May 2012 budget. There was no scrutiny of the decision and the report itself was not available until mid April 2012 prior to a May 8th budget release. In fact the Minister of of Health did not even review the MSAC 1054.1 report until 30th April 2012, eight days before the budget.

4) A number of factual errors are present in the report:

> -there are only three monoplace chambers available on the ARTG at the time of the report. The fourth chamber is a large multiplace chamber (Pg 4)
>
> -the costing of routine treatments surgical component uses the costing of complications (Table 40 Pg 94) not the costing of surgery (Table 39, Pg 93) but as it is incorrect for both sides, only the total number is elevated not the differential.

5) This is the third full review all showing increased evidence that the addition of HBOT to a wound care regimen after 3 months of standard care in all likelihood facilitates

i) a cheaper option than ongoing, 'usual wound care' with treatment already extending beyond a year

ii) the costs of the assessments has probably exceeded any saving that would have been gained in the use of HBOT for wounds

iii) other factors of patient satisfaction and lifestyle are also improved by more rapid healing of the wounds and this component is not factored into the MSAC assessment for wound care unlike it was for STRI.

REFERENCES:

Gordon, L., Edwards, H., et al, 2006. 'A cost-effectiveness analysis of two community models of care for patients with venous leg ulcers', *Journal of Wound Care,* 15 (8), 348–353.

Hawkins, G. C. and Bennett, M. n.d.. 'The outcome of chronic wounds following hyperbaric oxygen therapy: a prospective cohort study – the sixth year report.'

Hawkins, G. C., Bennett, M. H., et al, 2006. 'The outcome of chronic wounds following hyperbaric oxygen therapy: a prospective cohort study - the first year interim report', *Diving and Hyperbaric Medicine,* 36 (2), 94–98.

MSAC 1054.1 REPORT RESPONSE

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Introduction:

The report MSAC 1054.1 was the third review of treatment using hyperbaric oxygen therapy (HBOT) for soft tissue radio-necrosis (STRN) and non-diabetic chronic hypoxic wounds (NDCHW). It was published on the MSAC website in April 2012 and recommended funding for STRN but not for NDCHW.

The report on NDCHW has some significant failures in process and also in fact and interpretation of fact that make its advice to the Minister incorrect and in fact, with respect to the way and manner in which the cost effectiveness modelling has been done, the outcome (when correctly assessed and calculated) is in fact the opposite to what was reported.

MSAC has reviewed the 1054.1 report produced by itself and the responses are inadequate and do not assess the crux of the issue that the cost effectiveness modelling and the interpretation of data is incorrect and this has directly lead to the results that show that HBOT with usual care is less cost effective than usual care alone.

This report is designed to show both the errors in fact and also how the interpretation of some of the studies is incorrect and assumptions made have no basis in fact and cannot be used to calculate data on behalf of the cost effectiveness study that was performed.

There are also significant issues regarding the process of evaluation of treatments by MSAC particularly when the treatment modality is a secondary treatment and how research requested by MSAC has been disregarded when the results are positive but is used selectively when the issues of funding have been assessed. That discussion is beyond the scope of this document however and as the assessment process has changed (MSAC report 1054.1 was the last report done under the old assessment process), most issues that occurred with the 1054.1 report have probably now been rectified for subsequent reports.

This report will break down each point of contention and has background evidence included as part of the document.

Comparator studies:

The original MSAC1054.1 report stated that

> *"For chronic non-diabetic wounds the most appropriate comparator is usual care."*

(MSAC Report 1054.1, Pg 84)

For efficacy and cost effectiveness there needs to be an appropriate comparator for HBOT to determine efficacy rates. There is an Australian based paper by Gordon *et al* (1) that looks specifically at the cost effectiveness of community based venous ulcer wound care in standard form (ie. in home care) vs a 'Leg Club'. The outcome results of this paper were edited out of the final paper but the original manuscript was provided by Dr Gordon with the cure rates in Table 2 of the manuscript of 20 out of 56 at 3 months (35.7%) and using intention to treat, 25 out of 56 at 6 months (44.6%). This study was done independently of any Hyperbaric Oxygen Facility (so no selection bias) and represents the current level of high quality wound care for venous ulcers. This is comparable to the healing rate of venous ulcers for HBOT of 68.3% at the 6 months assessment point(2).

The comparison relevance was acknowledged indirectly by the MSAC assessment process as it is used by the MSAC 1054.1 report for the figures of costing of consumables in 'usual care' in both groups. Therefore there is acknowledgement and use of a comparator in the Gordon *et al* study and therefore the resultant healing rates should also be applicable.

The Gordon *et al* paper also has the additional issue of bias towards benefitting standard 'usual care' as the clinical pathway for HBOT (discussed later) starts by having usual care for three months *prior* to the person being eligible. Therefore the patients have all failed after three months of usual care (rate 0%) as opposed to the Gordon et al study who had already had healing rates of 35.7% by that stage. So by definition the HBOT patient cohort consist of the 64.3% of patients that are not healed by usual care normally.

This does leave a problem where the patients groups are not compatible by date of assessment. HBOT has measurement points at End of HBOT, 1 month post HBOT, 6 months post HBOT and 1 year post HBOT. This is after 3 months of usual care. This is mitigated and the effects can be compared as the average delay for a patient to enter the ANZHMG woundcare study by Hawkins and Bennett (2011)(2) is **19 months** from the time of the wound developing. The six month comparisons can be made as the wound are not going to heal without specialised care provided by a high risk clinic with best available 'usual care' and the intervention of HBOT.

The way that the MSAC process has managed this with its economic model is that it is treating both standard wound care and HBOT as primary modalities (HBOT is a secondary modality after 'usual' wound care has failed) and when calculating healing rates of HBOT has used the paper by Hawkins and Bennett (2011) and used the healing rates from that paper as the healing rates for standard care.

This is not appropriate as the Hawkins and Bennett paper does not have a comparative 'usual' care arm that can be compared to. The people not allocated for HBOT were due to them either 1) not having hypoxic wounds and were therefore ineligible or 2) having wounds that had non reversible disease (eg were already gangrenous) and required immediate surgery. So neither of these groups could be considered appropriate for treatment and therefore did not act as a control comparator for HBOT.

The committee of MSAC 1054.1 stated that:

> *"However since there is no common comparator it is not possible to undertake a direct comparison of the data from Hawkins and Bennett (n.d.) and Gordon et al (2006). As a result the data from Hawkins and Bennett formed the basis of the effectiveness of HBOT and usual care for the economic analysis."*

(MSAC Report 1054.1, Pg 87)

By doing this they have **pre-determined the outcome of the intervention without any evidence** and this makes any intervention that is added to the standard care uneconomic regardless of the nature of the intervention.

An example of this would be the addition of antibiotics to a patient with pneumonia in intensive care. If both groups have intensive care and the outcome measure is predetermined as the same for both groups the addition of antibiotics is going to make the antibiotic group less cost effective. However we know that the addition of antibiotics reduces the stay in ICU and increases the healing rate, which makes the addition of antibiotics a more cost effective treatment in the long term.

This is evident when you look at a comparison between the two systems when reviewed at the 6th month point below.

Using the cost numbers provided in the MSAC 1054.1 document (and these are not correct but we will use them as an example) and only adjusting for the rate of healing you end up with the following two economic charts:

PARAMETER	USUAL CARE	HBOT + USUAL CARE	DIFF*.	USUAL CARE	HBOT + USUAL CARE	DIFF*.
COST OF CARE AT 6M	$11747.00	$17670.00	$5923.00	$11747.00	$17670.00	$5923.00
COST OF CARE AT 12M	$40232.00	$42383.00	$2151.00	$40232.00	$42383.00	$2151.00
NUMBER OF PATIENTS	154	154		154	154	
HEALING RATE @6M	0.683	0.683		0.5	0.683	
TOTAL COST PER HEALED PATIENT**	$20776.74	$25504.02	$4727.28	$25989.50	$25504.02	-$485.48
TOTAL COST OVER ALL***	$3199617.96	$3927616.00	**$727998.04**	$4002383.00	$3927616.00	**-$74766.00**

Table 1: Cost comparison using different healing rates but same cost values.

* Diff. = Difference between HBOT + Usual care vs Usual Care. Positive number favours usual care, negative number favours HBOT + Usual care.

** Total cost per healed patient = (Cost of care at 6m x healing rate at 6m) + (Cost of failed care at 12m x (1-healing rate at 6m)) assumes that all cases not healed at 6m go on and do not heal at all

*** Total cost is Total cost per healed patient x 154 (number of patients billed under 13105)

So when the rates of healing are changed to accurately reflect the documented rates of healing at the different time periods, the cost effectiveness of HBOT is obvious. This does not even take into account the fact the that patients in the HBOT cohort are already selected as non-healing with 'usual care' in the first place and the rates of healing with HBOT continue to increase out to the 12 month assessment point.

Clinical vs Economic Model

The MSAC 1054.1 has used two models in its report 1) the clinical model that shows HBOT as a secondary intervention after failure of usual care and 2) the economic model that uses HBOT as a primary intervention.

Figure 1: Clinical model: (MSAC Report 1054.1 Fig 1, Pg 7)

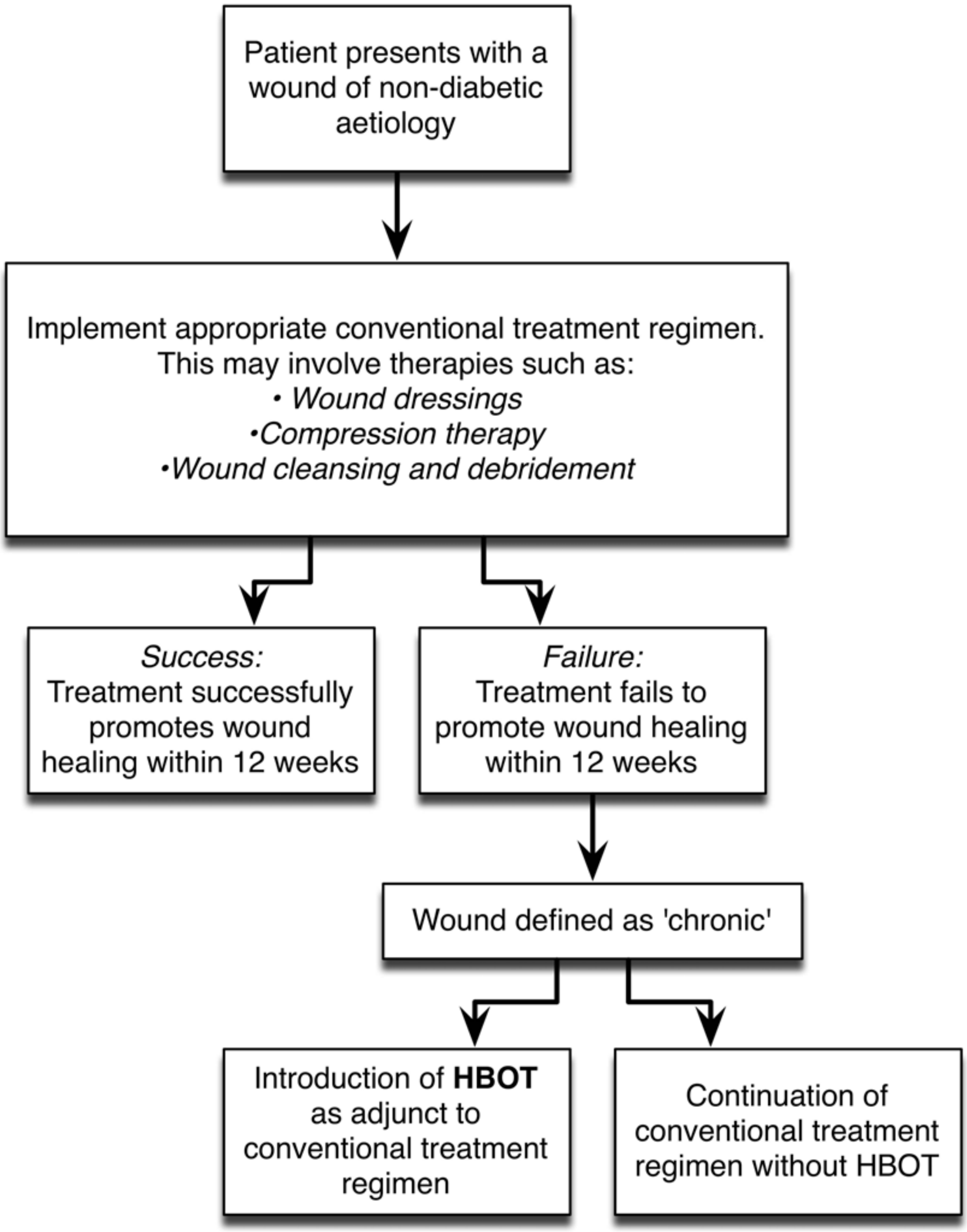
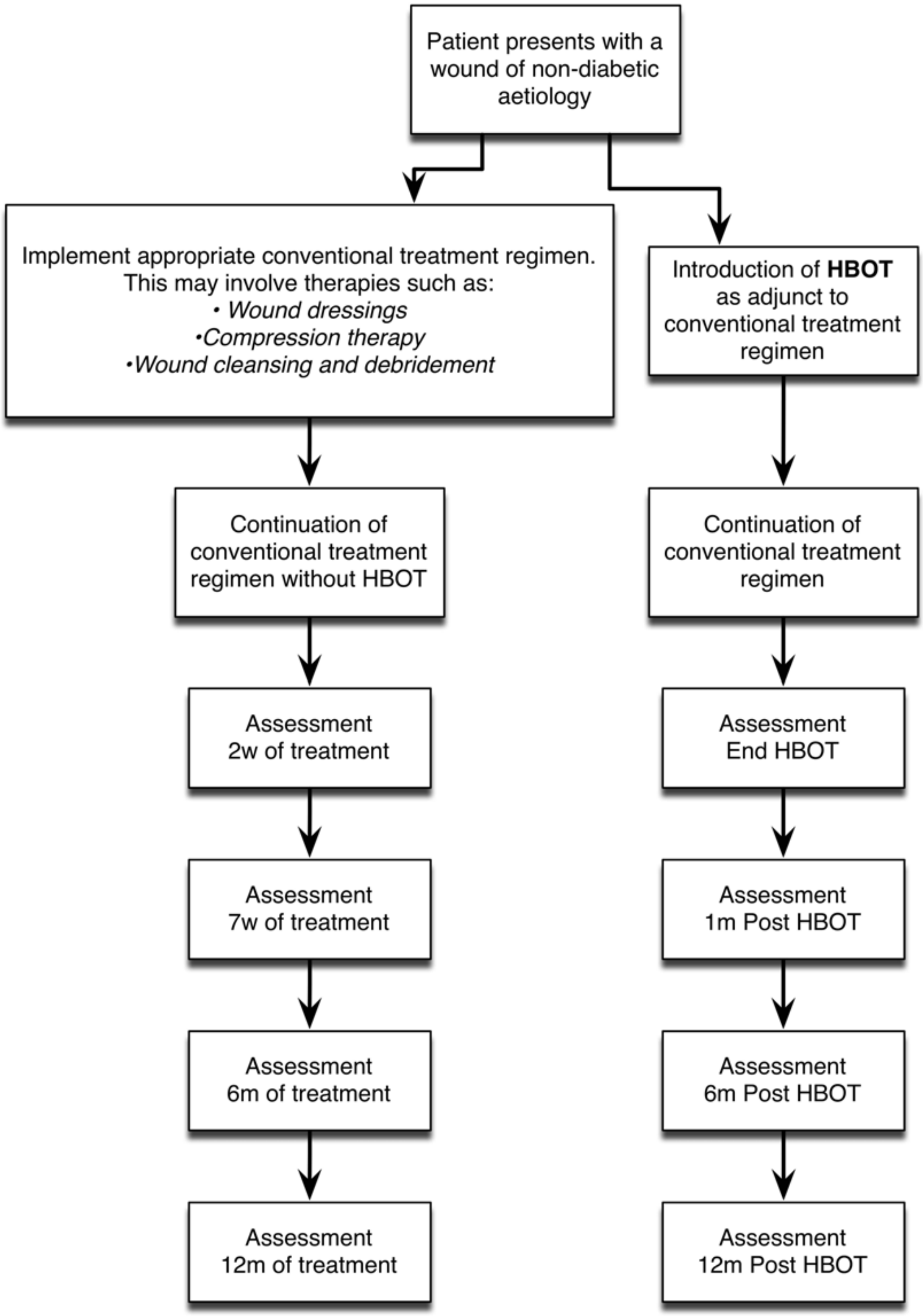


Figure 2: Economic model: Adapted from MSAC 1054.1 Figure 9, Pg 89



What the economic model does not take into account is that 100% of patients that have entered the HBOT stream have already failed conventional treatment (as per study definition with HBOT starting **ONLY** after 3 months of failed conventional treatment) for three months and in fact have failed conventional management for more than 19 months on average.

	RECEIVED HBOT	**NO HBOT**
PATIENTS	355	86
M:F	196:159	46:40
AVERAGE AGE (Range)	69.29y (18-96y)	69.17y (11-94y)
AVERAGE WOUND SIZE (cm^2)	18.20 (s.d. 31.06)	26.90 (s.d. 35.40)
WOUND DURATION (months)	19.94 (s.d. 35.05)	14.32 (s.d. 23.28)

Table 2: Demographics from Hawkins and Bennett (2011)(2)

So the economic model does not take into account the prior 3m which would have a significant impact on outcome as the input is not all patients with wounds BUT all those patients with difficult wounds and the ones that are going to heal with standard treatment are selected out of the group entering the HBOT cohort.

Use of RCT vs Prospective cohort data and interpretation.

After the second MSAC review of HBOT for STRN and NDCHW (MSAC Review 1054 – 2004) an undertaking was made to collate data prospectively and develop a prospective register of patients treated with HBOT and determine their outcome. This was confirmed in a letter from the chairman of the MSAC committee (see Supporting documents) and this was undertaken by the Australian and New Zealand Hyperbaric Medicine Group (ANZHMG) that has published the study in two papers as ongoing research as Hawkins *et al* (2006) (3) and a subsequent follow up paper (2).

This approach was taken because the heterogeneity of the NDCHW is so high that determining the criteria for entry into an RCT would be difficult to establish and the prospective cohort study was thought to be the next best level of evidence and this was agreed by MSAC. When the 3-year review came up, the evidence of the Hawkins *et al* (2006) paper was encouraging but as it was a study that followed people out to a year, the Medicare number was retained under a 3C ruling by the minister so that more data could be gathered. If anything the data from the 6th year of the study (Hawkins and Bennett 2011) is better than the data from the 2006 paper but the results of this were dismissed as they do not reach the level of significance of an RCT.

The only paper that has been determined as an appropriate RCT in the MSAC 1054.1 report was by Hammarlund and Sundberg (1994)(4) which has been interpreted as showing a statistical reduction of wound area at 6 weeks with no difference at 18 weeks.

Surprisingly this is not what the paper itself says. The RCT showed a significant reduction in wound size at week 4 ($p<0.05$) increasing to more significance at week 6 ($p<0.001$) with a large reduction in size of the wound to 64.5% of starting area (vs 97.3% of starting area in the hyperbaric air which in itself is not a placebo). At 18 weeks there was an ongoing reduction in wound size but as stated by Hammarlund and Sundberg:

> *"Although five patients left the study at week 18 (three in the control group and two in the oxygen group), the remaining data indicate a continuing effect on wound healing after the hyperbaric treatment had ceased after week 6.."*

Hammarlund and Sundberg (1994)(5) pg 832.

Statistical analysis was ***not performed*** as the dropout rate did not allow for measurement of the wound area and therefore calculation of size reduction. This is not the same as stating

> *"While the reduction in wound area was greater in HBOT patients at 18 weeks (55.8% compared to 29.6%), this was found to be a statistically non-significant difference.* ***No statistically significant difference was found in the proportion of ulcers healed at 18 weeks in the HBOT group when compared to the placebo treatment, and a pre-planned sensitivity analysis examining the effect of allocation dropouts did not alter the results.****"* [My emphasis]

(MSAC Report 1054.1, Pg 47)

Of those present however all the other oxygen group wounds reduced in size at 18 weeks except for the largest wound, which returned back to pre treatment size.

The MSAC report also states that:

> *'The secondary studies noted that this was a very small RCT in which the randomisation process was inadequately described, concurrent treatments were not reported and only limited patient characteristics were provided.'*

(MSAC Report 1054.1, Pg 46)

Whereas on page 832 of the Hammerlund and Sundberg (1994) paper the randomisation and blinding procedure was spelt out quite clearly including the stratification of patients into age groups <50 years and more than 50 years to remove further confounders.

As these basic facts seem to be incorrectly recorded in the main report, the interpretation of the assessment of the papers must be called into question.

Use of different aetiologies as a pooled result

The calculation of numbers of patients with NDCHW was made off data of Medicare billing of the 13015 item number and percentages of patients treated based on the 2008 Hyperbaric Technicians and Nurses Association (HTNA) reported results of the numbers of NDCHW treated. The problem is that the three aetiological groups that were included in NDCHW in Hawkins and Bennett (2011) have very different treatment regimens and very different healing rates from each other. The rates can be seen in the following graph (with diabetic wounds and the Results from Gordon *et al* (2006)):

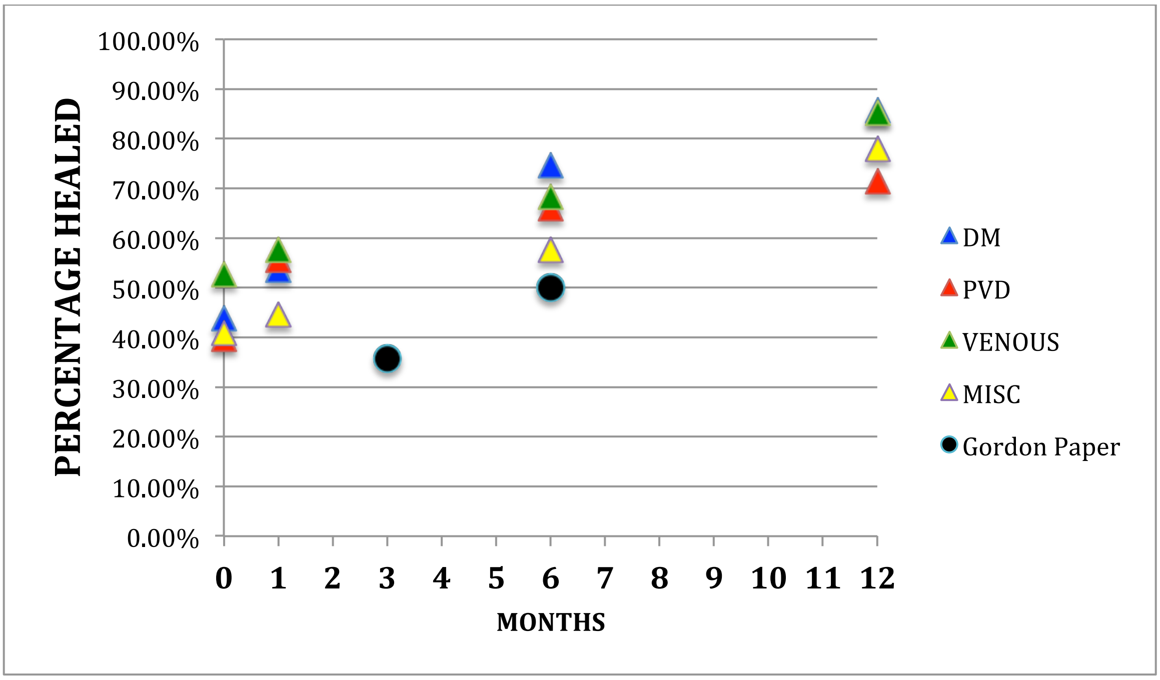


Figure 3: Healing rates from Hawkins and Bennett (2011)(2) and Gordon et al (2006)(1)

DM = Diabetes Mellitus, PVD = Peripheral Vascular Disease (no DM), VENOUS = Venous ulcers, MISC = Miscellaneous ulcers

At 6 months for example the spread of healing rates in the Hawkins and Bennett (2011) paper is approaching 20% difference between aetiologies. They also make up a larger proportion of wounds than venous ulcers (PVD = 25%, MISC =23%, VENOUS = 16%, DM = 36%).

This means that the calculated 154 patients that received HBOT under 13015 only 25% were actually venous ulcers (57/227) and the rest were a variety of aetiologies that may have had differing costs and certainly have different rates of healing. Ultimately, this could have material effect on both the costs and the healing rates.

Miscellaneous

Although the following issues do not have a material impact on the outcome, they do show that there is some concern that things were not checked as thoroughly as would be expected and this may cause a level of concern regarding the calculations that eventually went into the final cost analysis.

1) There are only three **monoplace** chambers available on the ARTG at the time of the report. The fourth chamber is a large **multiplace** chamber **(MSAC 1054.1: Pg 4).**

2) The costing of routine treatments surgical component uses the costing of complications **(MSAC 1054.1: Table 40, Pg 94)** not the costing of surgery **(MSAC 1054.1: Table 39, Pg 93)** but as it is incorrect for both sides, only the total number is elevated not the differential.

3) The statement of potential pathways number 8 is incorrect as it should read:

> *"8. Patients who fail usual care: these patients receive ongoing management + two skin grafts + 12 months community wound care + complications."*

(MSAC 1054.1: Pg 90)

Conclusion

In the MSAC 1054.1 report there are a number of anomalies and errors of fact and interpretation. Also there was a significant lack of clarity regarding what would be considered sufficient evidence which was interpreted by the ANZHMG as a prospective collection of outcome data to 1 year after HBOT (as stated in the 2004 MSAC letter included in Supporting Documents) and which was reinforced in the extension of time to collect further data in 2007 with the extension of the Ministerial 3C ruling to gather sufficient data to be available for analysis in 2010. If it was required in the process to have an RCT, then this would have been performed instead.

Once the data was collected the outcomes of HBOT plus usual care were 'assumed' to be the same as the outcomes of usual care alone with no scientific or evidential basis. All trials to date have shown that the rates of healing of NDCHW have shown a favourable outcome when HBOT is used as a ***secondary*** treatment and this is also verified by the Hammarlund and Sundberg RCT of 1994 which showed a significant effect with only 16 patients randomised into two groups continuing well after the HBOT had finished.

This 'assumption' of equal outcomes as a predetermination means that prior to even assessing the treatment, any additional adjunct treatment cannot be 'cost effective' as it will always cost more than 'usual treatment' alone for the same predetermined outcome. This is not the correct way in assessing any new technology or treatment as a change in outcome rates are what makes a new technology cost effective.

Therefore at worst, HBOT + usual care is as good as usual care alone and is certainly not worse. There is a growing wealth of evidence that when the wound is indolent (in the ANZHMG Study, for 19 months prior to presentation) HBOT can lead to significant healing of the wound, ending the ongoing care and reducing large ongoing costs (not even including severe complications like amputations) into the future while only adding a small initial increased cost (of HBOT) at the beginning.

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Work in progress

The outcome of chronic wounds following hyperbaric oxygen therapy: a prospective cohort study – the first year interim report

Glen C Hawkins, Michael H Bennett, Annelies E van der Hulst

Key words
Chronic wounds, hyperbaric oxygen therapy, research

Abstract

(Hawkins GC, Bennett MH, van der Hulst A. The outcome of chronic wounds following hyperbaric oxygen therapy: a prospective cohort study – the first year interim report. *Diving and Hyperbaric Medicine*. 2006; 36: 94-98.)

Introduction: The treatment of chronic wounds is a major health cost. This study is an ongoing prospective cohort looking at the effects of hyperbaric oxygen therapy (HBOT) on the healing of chronic wounds.

Methods: Data are being collected from patients presenting to hyperbaric facilities in Australia with chronic (>3 months' duration) non-irradiated wounds, including details of aetiology, wound characteristics and possible predictors of wound healing. Participants are being enrolled whether or not a decision was made to treat with HBOT. Assessments are performed at the end of the course of HBOT and at one, six and 12 months post hyperbaric treatment. The aim is to quantify the proportion healed and to identify any significant predictors for wound healing.

Results: There are 110 participants included in this analysis with 88 receiving HBOT. Excluding the miscellaneous aetiologies, at the end of treatment 52.3% of patients had a 'good' outcome to the wound, increasing to 64.1%, 91.7% and 78.2% at one, six and 12 months respectively. Logistic regression for participants with diabetic wounds suggests that wound area, chronicity and transcutaneous oxygen readings on room air combine to produce a statistically significant model for prediction of wound healing at one month after treatment.

Conclusions: This ongoing cohort study suggests that HBOT is highly associated with the healing of chronic wounds in the patients in this study. The wound area at presentation, the duration of the wound and the transcutaneous oxygen pressure on air may predict the likelihood of a chronic wound in diabetic patients healing by one month after treatment.

Introduction

Chronic wounds are defined as an interruption in the continuity of the skin where conventional treatment has not achieved healing within a reasonable time (e.g., 3 months).[1] Such wounds are an increasing burden on healthcare systems throughout the world. Studies have shown a prevalence in hospital patients of up to 24%, and 2% of the general population have some form of chronic wound at any one time.[2–5] This creates a significant financial burden on funding agencies with costs exceeding several billion dollars per year.[6–8] There are compelling reasons to deliver treatment modalities that are cost effective to individuals with such wounds.

Treatment regimens for chronic wounds are multi-modal but have been traditionally of two types: specific treatments designed to reduce the effect of the underlying disease (such as tight glycaemic control in diabetics and compression bandages in venous insufficiency), and wound environment optimisation dressings (e.g., hydrocolloid gels and antibacterial impregnated dressings).

The rationale for adjunctive hyperbaric oxygen therapy (HBOT) in chronic wound care is the premise that the underlying problem in many of these wounds is hypoxia. While acute wounds require low oxygen tensions, low pH and a high lactate load to initiate angiogenesis and wound healing,[9,10] later phases of healing are critically dependent on oxygen, e.g., fibroblastic collagen deposition and macrophage bacteriocidal activity.[11–13] It has been suggested that the stimulus for healing is a rapid drop in the partial pressure of oxygen from surrounding healthy tissue to the wound. In chronic wounds there is a much more gradual drop across the wound margin and this may inhibit healing significantly.[14]

The Medicare Services Advisory Committee (MSAC) was established in 1997 to advise the Australian Minister for Health and Ageing on the safety and cost effectiveness of new medical technologies and procedures, and to make recommendations for funding under the Medicare Benefits Scheme.[15] One such review was initiated into the provision of HBOT, and in 2001 MSAC recommended that a properly conducted prospective trial should be undertaken on the treatment of chronic non-irradiated wounds with HBOT. This report presents the first results of a prospective cohort of patients enrolled since June 2004.

Methods

All hyperbaric facilities in Australia and New Zealand were invited to participate in the study. There are currently 13 such chambers treating patients for chronic wounds. Three facilities (Prince of Wales Hospital, Sydney (POW), The Wesley Hospital, Brisbane (WES) and Royal Hobart Hospital, Hobart (HOB)) have been able to start in the first year and three other facilities are currently awaiting ethics approval or the conditions of their approval have not permitted submission of data in the first year. No enrolments were undertaken prior to obtaining approval from the relevant local ethics committee. Data were collected on each patient by each facility and an identifying number was included in the data collection sheet that allowed each centre to follow individual patients' progress through the four reporting stages. At the collection centre (POW) each individual patient was given a code number to identify the enrolling centre they were from and order of enrolment. Analysis was performed on the POW code numbered datasheets entered into a computer database.

PATIENT SELECTION

All patients referred to a hyperbaric facility for assessment of one or more chronic wounds (present for more than three months) are eligible for inclusion, regardless of prior therapy. Patients considered unsuitable for HBOT due to the presence of a contra-indication, inadequate prior therapy or anticipated lack of response are therefore also eligible for enrolment. Acute (including extensive debridement within three months) wounds and those due to irradiation tissue injury are excluded from the study. The study authors did not determine assessments or impose HBOT treatment schedules on the study centres as there is no definitive treatment schedule that has been shown to be better than any other. We also feel that this allows the study to reflect 'true practice' in the hyperbaric field, with the variety of equipment currently available in each centre also influencing clinical practice.

DATA COLLECTION

A standardised datasheet was developed that recorded demographic data, possible contributing factors to poor wound healing, treatment up to the date of assessment, subsequent hyperbaric treatment (if performed) and outcome immediately following HBOT as well as at one month, six months, and twelve months after HBOT.

Data were collected on a Filemaker Pro™ database (Filemaker Inc, Santa Clara, California). Each patient was given a designated identification number for tracking through the four assessment times. Each facility is responsible for data collection on the subjects enrolled at that facility. Units are being encouraged to use all means at their disposal to locate missing subjects, including direct contact and through their local medical services and family members. Each unit was reminded at the appropriate times when a patient was due for re-assessment.

Table 1
Clinical outcome scores for wounds

Clinical description	Category	Outcome class	Outcome
Deceased	1	No benefit	BAD
Nil benefit ± major amputation	2		
Minimal benefit + minor amputation	3	Some benefit	
Improved + minor amputation	4		
Substantially healed	5	Healed	GOOD
Healed	6		

OUTCOMES

Outcomes are scored on a six-point scale originally developed by Dr Harry Oxer (Davis FM, personal communication, 2003) at Fremantle Hospital Hyperbaric Medicine Unit. However, for this interim assessment we categorised all outcomes as either 'good' or 'bad' as shown in Table 1. We have specifically placed amputations of any sort into the 'bad' outcome category because this seems an appropriately conservative approach to assessing the effectiveness of HBOT. While an amputation may indicate a good outcome (e.g., saved limb but lost toes) or poor outcome (e.g., superficial foot ulcer but lost toe) there may be no clear indication which is the case for any individual patient. In addition, any amputation will alter the location and dynamics of the wound – essentially converting a chronic wound into an acute surgical wound. We planned an annual analysis for reporting back to the contributing units.

WOUND CATEGORIES

Wounds were allocated to one of four main aetiological categories for analysis – diabetic (DM), peripheral vascular disease (PVD), venous disease and miscellaneous (including vasculitic and auto-immune diseases). Because the miscellaneous group contains highly diverse aetiologies in very small numbers, no analysis of the fate of this group has been undertaken in this interim report. Similarly, this report does not compare the chance of a good outcome with and without HBOT because of the small numbers in the non-HBOT group.

STATISTICS

No sample size calculations were performed for this study, as it is an ongoing opportunistic cohort study. We performed a descriptive statistical analysis and a backward stepwise logistic regression analysis on each aetiological group for factors that may predict wound outcome. This was done in order to develop a predictive model for wound healing after HBOT. All calculations were performed using StatsDirect v2.4.5 (StatsDirect Ltd., StatsDirect statistical software. <http://www.statsdirect.com> England: 2002).

Results

There were 110 patients enrolled in the study of whom 88 received hyperbaric oxygen treatment. Sixty-seven (61%) were males and 43 (39%) females. The group receiving hyperbaric oxygen had 54 (61%) males with an average age of 67.2 years. The group that did not receive hyperbaric oxygen had 13 (59%) males with an average age of 70.4 years. The breakdown by aetiology is shown in Table 2.

HYPERBARIC TREATMENT

The average number of treatments for the patients receiving HBOT was 24.4 (range 1–70). The average number of treatments, for each aetiology, is given in Table 3, while the overall frequency distribution is shown in Figure 1.

Table 2
Number of patients and mean ages (with range) of all patients enrolled in the study (whether they had HBOT or not) by aetiology

Aetiology	Number	Average age years (range)	% total wounds
DM	46	66.4 (42–89)	41.8%
PVD	27	73.9 (37–91)	24.5%
Venous	18	69.2 (43–87)	16.4%
Miscellaneous	19	61.7 (11–83)	17.3%
Total	**110**	**67.8 (11–91)**	**100%**

(DM – diabetes mellitus; PVD – peripheral vascular disease; venous – venous insufficiency)

Table 3
Number of patients and treatment averages of those patients who had HBOT by aetiology

Aetiology	Number of patients	Mean number of treatments (SD)
DM	40	23.4 (10.2)
PVD	20	24.7 (8.46)
Venous	13	24.2 (9.49)
Miscellaneous	15	27.0 (14.63)
Total	**88**	**24.4 (10.53)**

(DM – diabetes mellitus; PVD – peripheral vascular disease; venous – venous insufficiency)

OUTCOME DATA

Figure 2 shows the percentage of people in each aetiological group with a 'good' outcome (Scores 5 and 6, Table 1). Overall, immediately after the HBOT course, 52.3% of all aetiological groups combined had a 'good' outcome and this proportion increased to 64.1%, 91.7% and 78.2% at one, six and twelve months respectively. These data suggest that diabetic wounds improve most rapidly following HBOT, with venous wounds catching up at one month and arterial wounds at six months. At the time of the final draft of this interim report, we have follow-up data on 60% of those enrolled, and 43% at one year. Because these data sets are substantially incomplete, they will be reported in future annual analyses.

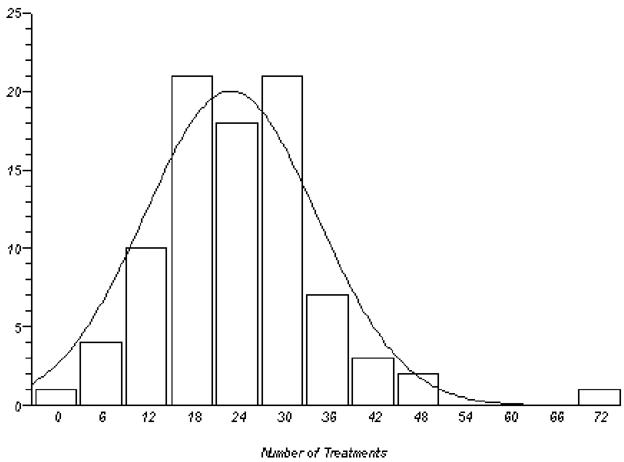
Because of the small numbers enrolled in the study, regression analysis for outcome was possible only for those patients with diabetes mellitus. We performed univariate analysis and a logistic regression for 'good' outcome at the end of HBOT and at one month after HBOT with the potential predictors being gender, duration of wound (months), wound area (cm^2) transcutaneous partial pressure of oxgyen ($P_{tc}O_2$) in air (mmHg) and $P_{tc}O_2$ on 100% oxygen at 1 ATA for 10 minutes (mmHg). Neither at the end of HBOT nor at one month follow up were there any significant predictive factors identified on univariate analysis. Stepwise logistic regression for healing at the end of the HBOT course did not produce a useful model. However, analysis at one month follow up suggested the following model was predictive of healing:

$$\text{Log (OR)} = 2.30 - (0.09*\text{TWA}) - (0.11*\text{DUR}) + (0.06*P_{tc}O_2)$$

where TWA = total wound area in cm^2, DUR = duration of wounds in months and $P_{tc}O_2$ = transcutaneous partial pressure of oxygen on air at 1 ATA in mmHg.

This model suggests that, at presentation, wound healing is negatively impacted by increased wound area, duration of

Figure 1
Frequency distribution (with curve of best fit) of number of treatments for patients receiving HBOT



wound and a lower $P_{tc}O_2$ in air. For example, using this model we would predict that for a wound 7 cm^2 in area and of 10 months' duration with a resting $PtcO_2$ (in air) of 30 mmHg, the odds of healing at one month after completion of a course of HBOT are nearly 11 to one (odds ratio 10.7).

Discussion

This study suggests that we can expect 50% of chronic wounds to heal by the end of a course of HBOT and up to 90% of wounds to be healed at six month follow up. These wounds have all persisted for at least three months at presentation despite comprehensive wound care, and we believe this represents a real and important clinical benefit. Although 50% may not seem a particularly large proportion, given the population of Australia (20,404,617)[16] and an assumed prevalence for chronic wounds of 1%, this represents over 100,000 people who could potentially have a good outcome from HBOT.

Hyperbaric facilities have been treating chronic wounds for several years but there has been very little high-quality clinical research evidence to demonstrate the effectiveness of HBOT. A recent Cochrane meta-analysis on the efficacy of HBOT for chronic wounds included four randomised controlled trials (RCTs).[1] Three of these studies enrolled diabetic foot ulcer patients and one enrolled patients with venous ulcers. There were no RCTs on the effects of HBOT on arterial ulcers. These RCTs suggest that there was a benefit in having HBOT for diabetic and venous ulcers but a larger, multi-centre study is required.

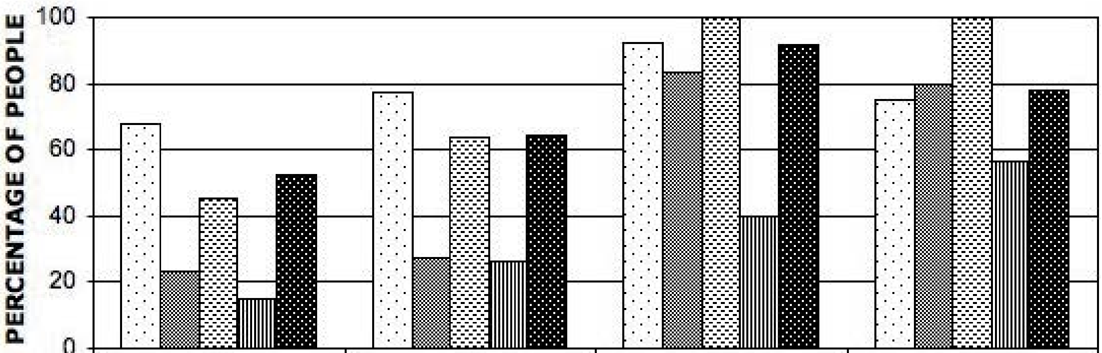
Because of the small number of patients enrolled in this study who did not receive HBOT (n = 22), we have not reported the fate of ulcers in that subgroup of patients in this analysis. While the reasons they were thought unsuitable for HBOT were not always clear, we hypothesise most of them had normoxic $P_{tc}O_2$ levels, failed to adequately respond to oxygen challenge with an increase in $P_{tc}O_2$ or declined to undergo therapy. We intend to more fully address this group in our next report.

There are differences in response to HBOT between aetiologies. Diabetic wounds have a faster resolution (higher percentage of those with a good outcome at the end of treatment) and appear to have a higher chance of a good outcome for the first few months after treatment. The estimated difference narrows rapidly and at six months there is very little between the three main aetiologies.

Logistic regression suggests that even with this small data set, we are able to show that features such as total wound area, duration of wound and $P_{tc}O_2$ at the wound site breathing air at 1 ATA are significant predictors of the proportion of wounds that will heal. We hope that as the data set grows, the regression model will become increasingly predictive of those wounds that can be expected to heal. This would have useful clinical applications for the selection of candidates for HBOT.

There are several limitations to the interpretation and applicability of this study. First among them is the loss of data as the study progresses. This is largely due to inability to contact some patients for follow up, despite considerable efforts to do so. Currently 56.6% of patients' data are lost at the 12-month assessment time reflecting difficulties in following up patients out to this time period. We have attempted to address this with better patient tracking and by

Figure 2
Number of people with 'good' outcome after HBOT as a percentage of total people receiving HBOT



	End HBOT	1 Month	6 Months	12 Months
TES	67.6	77.4	92	75
	23.5	27.3	83.3	80
IS	45.5	63.6	100	100
IISSING	15.1	26.4	40	56.6
OUNDS	52.3	64.1	91.7	78.2

ASSESSMENT TIME

co-ordinating the follow up of patients with active reminders to the collection centres involved. Some apparent loss of data is in fact due to significant numbers of participants who have not yet reached the final assessment time.

Another significant limitation for this cohort study is the relatively small number of participants who had chronic wounds but did not receive HBOT. Financial considerations have made it impractical to improve the methodology of this study by the active recruitment of a comparison cohort of participants for whom hyperbaric referral has not been considered. Such a study is beyond our means at this time but remains highly desirable.

In conclusion, we have reported the first 110 patients of an ongoing prospective study. Our results suggest that a clinically important proportion of patients can expect a good outcome by one month after the completion of hyperbaric therapy. We continue to collect data prospectively and hope to generate a useful predictive model by which to identify those patients in whom HBOT is appropriate. We believe that this study is important in helping to better define the role of hyperbaric oxygen in these patients.

Acknowldegements

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The outcome of chronic wounds following hyperbaric oxygen therapy: a prospective cohort study – the sixth year report

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ABSTRACT:

We report data from the sixth year of the ANZHMG prospective cohort study of wound outcomes after hyperbaric oxygen therapy (HBOT). All patients attending a hyperbaric facility with a wound of greater than three months duration (other than associated with radiotherapy) were eligible for inclusion. Assessment points of the study are; at the end of HBOT, 1 month post HBOT, 6 months post HBOT and 12 months post HBOT. Currently, 441 patients have been enrolled with 355 of them receiving 5 or more hyperbaric oxygen therapy treatments. The people who received HBOT had wounds for an average of 19.9 months and a mean area of 18.2cm^2, while those who did not receive HBOT were of 14.3 months duration and 26.9 cm^2 in size. At each assessment time, all wounds were classified as either 'Good Outcome' or 'Poor Outcome' based on a pre-determined wound score. At the 6 year mark, across all aetiologies, the percentages of patients with a 'Good Outcome' at each assessment period was 43.9%, 54.2%, 68% and 80.4% respectively.

Our study suggests that HBOT has a significant impact in the improvement of chronic indolent wounds with the improvement continuing out to at least 12 months after treatment regardless of the aetiology of the wound.

INTRODUCTION:

This is a report of the results six years into the ongoing Australia and New Zealand Hyperbaric Medicine Group (ANZHMG) Wound Care Study, which was initiated in June 2004. The study methodology has been presented in detail previously.[1]

A chronic wound may be defined as any interruption in the continuity of the body's surface that requires a prolonged time to heal, does not heal, or recurs.[2] These wounds remain a common and expensive health problem. The true incidence and impact are difficult to assess because much care is delivered at home and wound care products are purchased from a variety of sources. The prevalence of wounds is high, and in the UK has been estimated at up to 12% of the aged population and the annual cost to be in excess of £1billion annually.[3,4]

Not surprisingly, there are a very large range of wound care techniques and specialised dressings available to assist with management of these wounds. Strategies include treatment of the underlying pathology (e.g. blood glucose control in diabetes), systemic treatment aimed at improving the local wound environment (e.g. nutrition supplements) and local treatment aimed at improving the wound environment (e.g. dressings). As noted in a Cochrane review of the subject, 'in practice, wound management is often a sequential and fruitless search for a successful combined approach'.[5] In this environment, it is of great importance to accurately assess the success or failure of each treatment strategy.

It is the aim of the current study to examine the fate of chronic wounds referred to hyperbaric facilities in Australia and New Zealand and if possible, develop a predictive model for successful outcome that may assist with future patient selection.

METHODS:

A full description of the methods and statistical approach has been previously published.[1] All hyperbaric facilities in Australia and New Zealand have been invited to participate in the study and currently of the fourteen facilities, ten have returned data collection forms. All locations obtained local ethics committee approval prior to the commencement of collecting data (details available on application to the author).

PATIENT SELECTION:

All patients presenting to a participating hyperbaric unit for assessment of a chronic wound (defined as a wound of greater than three months duration) were eligible to be included in the study regardless of aetiology (with the exception of radiation injury) or prior therapy. Following informed consent, the patients were assessed according to the procedure in place at each facility and data was collected on a standard data collection template developed for this study, which was available in both a paper and electronic format. If multiple wounds were present, a reference wound was chosen for inclusion in the study. All patients presenting for assessment were eligible for inclusion, regardless of any decisions regarding therapy. In particular, there was no requirement for the individual to be suitable for HBOT. Wounds were classified into one of four aetiologic categories for subgroup analysis: diabetic (DM); peripheral vascular disease (PVD); venous disease and miscellaneous.

Specific exclusion criteria included acute wounds (ie less than three months duration), wounds that had surgical intervention within the last three months and wounds associated with exposure to radiation.

Any therapy instituted for patients enrolled in the study was at the discretion of the medical staff responsible in each unit, and no attempt was made to standardise the approach to wound care in general or the HBOT schedule in particular.

Each patient was de-identified before data was transmitted to Prince of Wales Hospital for collation. A unique code was generated to allow backtracking and identification at the enrolling site in order to allow future analysis and comparison of results for different units. All data was transferred to a Filemaker Pro Advanced v11.0 database (Filemaker Inc, Santa Clara, California, 2010).

OUTCOMES:

The primary outcome was the degree of healing assessed by a six-point scale originally developed at Fremantle Hospital (Table 1). For this interim assessment, we have dichotomised the outcome into ‘Good’ (completely or substantially healed) or ‘Bad’ (any other outcome score).

<<INSERT TABLE 1 AROUND HERE>>

This approach is a conservative one that is likely to classify some patients who do functionally well as a poor outcome (for example, any patient requiring a minor amputation but who do eventually heal)

STATISTICAL ANALYSIS:

No sample size calculations were performed for this study, as it is an ongoing opportunistic cohort study. All calculations were performed with StatsDirect v2.7.8 (StatsDirect Ltd, StatsDirect statistical software. <http://www.statsdirect.com> England, 2010). We compared normally distributed continuous data means using Student's t-test and Chi^2 for the comparison of proportions between groups.

RESULTS:

There are currently 441 patients enrolled in the study of whom 355 have received five or more hyperbaric treatments. Other characteristics of the patient populations are listed in Table 2. The reference wounds had been present significantly longer (mean 19.9 months versus 14.3 months, $P = 0.03$) and tended to be smaller in area (mean 18.2 cm^2 versus 26.9 cm^2, $P = 0.08$) in those selected for HBOT than those not thought suitable for HBOT.

Of those who received HBOT, the average number of treatments for all groups was 28.2 with a range of 6-70. The 'Miscellaneous' group was the most variable in this regard.

<< INSERT FIGURE 1 AROUND HERE>>

There are three main treatment peaks around 20, 30 and 40 treatments, indicating the standard treatment regimens in use at most hyperbaric facilities (see Figure 1).

<<INSERT TABLE 2 AROUND HERE>>

The overall outcomes at each time point for the patients who received HBOT are summarised in Table 3. The overall proportion of patients with a good outcome at the one year assessment was 80.4%. Wounds in patients with diabetes mellitus remain the largest aetiological group (36.1%), while those associated with peripheral vascular disease accounted for 25.1%, the miscellaneous group 22.8% and those associated with venous disease 16.1% of the total.

<<INSERT TABLE 3 AROUND HERE>>

All aetiologic groups showed an increasing proportion of patients with a good outcome over the 12 months following treatment with HBOT. Patients with either diabetes or venous disease as their primary aetiology, had healing rates in excess of 85% at twelve months (see Table 4.)

<<INSERT TABLE 4 AROUND HERE>>

DISCUSSION:

This prospective cohort study suggests the majority of patients given HBOT for a chronic wound in Australia and New Zealand will achieve a good outcome at one year, regardless of aetiology. This is consistent with the findings of randomised controlled trials on the subject.[6-11] The inclusion criteria are broad and we have deliberately adopted this position in order that our results might reflect actual clinical practice in the real world. Given the strong evidence base for the treatment of radiation tissue injury, we have specifically excluded such wounds to avoid positive confounding of the overall result by a strongly positive result in this group. Similarly, we have excluded patients with acute wounds that might be expected to heal once adequate perfusion has been established and tissue disruption/infection has been appropriately treated.

The group of chronic wounds included are indolent (averaging almost 20 months in duration for the HBOT group and over 14 months for the non-HBOT group) and almost universally have received competent and intensive therapy including vascular assessment, diabetic control, antisepsis, appropriate debridement and wound dressing prior to referral. Indeed, perhaps because of limited availability, the inconvenience of time-consuming therapy sessions and perceived high short-term costs, many patients have been referred to hyperbaric centres as a treatment modality of 'last resort'. We would expect the predicted chance of achieving a good outcome in these patients to be quite low. In this setting, a 40% chance of a good outcome at the end of HBOT, rising to over 80% at one year, would seem to be very positive.

This ongoing study continues to predict that nearly half of the patients presenting to a hyperbaric facility with a chronic wound can expect to attain a good outcome immediately at the end of a course of hyperbaric treatment. This response rate is clinically significant given the length of time for which these wounds have been present before referral. This observation confirms a number of previous reports and a Cochrane review[8] where HBOT has been associated with good outcomes in chronic wounds.

Outcomes continue to improve for at least 12 months following treatment, and this is consistent with the angioneogenic effects of hyperbaric oxygen seen in a radiotherapy model by Marx et al[12,13] and the positive modifications to the wound milieu demonstrated by Thom, Hunt, Niininkoski and many others.[14-16] Based on our results, at one year after presentation we expect over 80% of all people who present to a hyperbaric facility for wound care assessment and receive more than five HBOT treatments to have a substantially or completely healed wound regardless of aetiology. In the case of people with diabetic ulcers and patients with venous ulcer disease we would expect the rate to exceed 85%.

Not surprisingly, the rate at which wounds heal varies with aetiology. Venous ulcers resolve faster than diabetic wounds for example, and the disparate group of miscellaneous wounds and primary peripheral vascular disease heal most slowly of all on average.

Analysis of the patients that did not have HBOT remains hampered by small numbers and the fact that the assessing centres did not always record why the patients were not offered treatment with HBOT. This shortcoming is being actively addressed for future reports. There are potentially two main reasons that HBOT might not be offered to a particular individual, and the implications for each would lead to opposing conclusions. First, it may be that oxygen supply was not the limiting factor for wound healing (ie. transcutaneous oxygen measurement was normal) and these patients may have a good outcome through the optimisation of other wound therapies. On the other hand, the clinical situation might be so grave as to make HBOT inappropriate – for example when immediate major amputation is indicated. The first subgroup might be expected to do better than the HBOT group, whilst the second would be likely to have worse outcomes. A direct comparison of outcome between groups in this study would not be a valid test of the true impact of HBOT on those patients for whom it is routinely applied.

Table 3 indicates a falling follow-up rate over time. While this is partly due to true loss to follow-up, much is due to patients not yet reaching the time for follow-up and this artefact will be addressed at the conclusion of the study. Some true loss to long-term follow-up is inevitable as many of these patients must travel great distances to reach the State hyperbaric facility. We have tried to reduce this source of data loss by both thorough tracking of patient codes and enrolling local doctors to do the assessment for us under direction. Whilst our confidence in the results for those receiving HBOT increases as we increase the numbers of participants, the same does not necessarily apply to the fate of the group who did not receive HBOT. Perhaps unsurprisingly, a relatively small proportion of patients referred to a hyperbaric facility are unsuitable for HBOT. Whether this is a consequence of careful referral from knowledgeable primary medical teams, or because of a low threshold for therapy is not clear. We continue to collect data on this group and hope to report more meaningfully in the future.

In conclusion, we have reported the first 441 patients at the six-year mark of our ongoing prospective cohort study. Nearly 50% of patients presenting with chronic wounds have a 'Good Outcome' immediately after HBOT regardless of aetiology. At 12 months following HBOT this increases to over 80%, despite the average duration and size of the wounds being 20 months and 18cm^2 respectively. Indeed, it is possible the results following HBOT would be even better if wounds had been referred at an earlier stage. We believe this study strongly suggests a benefit of HBOT for chronic wounds and we continue enrolment in an attempt to identify a useful predictive model to assist with patient selection.

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<table>
<tr><th>CLINICAL DESCRIPTION</th><th>CATEGORY NUMBER</th><th>OUTCOME CLASS</th><th>OUTCOME</th></tr>
<tr><td>Deceased</td><td>1</td><td rowspan="2">No benefit</td><td rowspan="4">BAD OUTCOME</td></tr>
<tr><td>Nil benefit ± major amputation</td><td>2</td></tr>
<tr><td>Minimal benefit ± minor amputation</td><td>3</td><td rowspan="2">Some benefit</td></tr>
<tr><td>Improved ± minor amputation</td><td>4</td></tr>
<tr><td>Substantially healed</td><td>5</td><td rowspan="2">Healed</td><td rowspan="2">GOOD OUTCOME</td></tr>
<tr><td>Completely healed</td><td>6</td></tr>
</table>

Table 1: Clinical outcome scores. Only patients with ‘Good Outcome’ were considered successful

	RECEIVED HBOT	**NO HBOT**
PATIENTS	355	86
M:F	196:159	46:40
AVERAGE AGE (Range)	69.29y (18-96y)	69.17y (11-94y)
AVERAGE WOUND SIZE (cm^2)	18.20 (s.d. 31.06)	26.90 (s.d. 35.40)
WOUND DURATION (months)	19.94 (s.d. 35.05)	14.32 (s.d. 23.28)

Table 2: Patient demographics

"Received HBOT": Has had at least 5 hyperbaric treatments

"No HBOT": Has had less than 5 hyperbaric treatments

s.d. = standard deviation

M:F = Male to Female ratio

	END HBOT		1M POST HBOT		6M POST HBOT		12M POST HBOT	
	HBOT (N=346)	No HBOT (N=30)	HBOT (N=306)	No HBOT (N=55)	HBOT (N=241)	No HBOT (N=43)	HBOT (N=163)	No HBOT (N=29)
GOOD OUTCOME (Scores 5 & 6)	152	11	166	24	164	25	131	17
POOR OUTCOME (Scores 1-4)	194	19	140	31	77	18	32	12
MISSING DATA*	9	56	49	31	114	43	192	57
% GOOD OUTCOME**	43.9%	36.7%	54.2%	43.6%	68.0%	58.1%	80.4%	58.6%

Table 3: Numbers of patients healed by each time period with percentage and missing data points. *Missing data includes those lost to follow up and patients not yet reaching assessment point. **Excludes missing data

AETIOLOGY	NUMBER	RECEIVED HBOT	PERCENTAGE WITH "GOOD OUTCOME"			
	(N)	Mean number of treatments and (s.d.)	END HBOT	1M POST HBOT	6M POST HBOT	12M POST HBOT
DM	128	26.0 (10.0)	43.9	53.7	74.7	85.7
PVD	89	29.1 (10.1)	39.8	55.6	66.0	71.4
VENOUS	57	29.1 (11.7)	52.7	57.7	68.3	85.2
MISC.	81	29.6 (10.2)	40.8	52.3	62.7	78.0
TOTAL	**355**	**28.2 (10.5)**	**43.9**	**54.2**	**68.0**	**80.4**

Table 4: Break down of improvements by aetiology and the mean and standard deviation of number of treatments required.

(N)= absolute number, s.d. = standard deviation

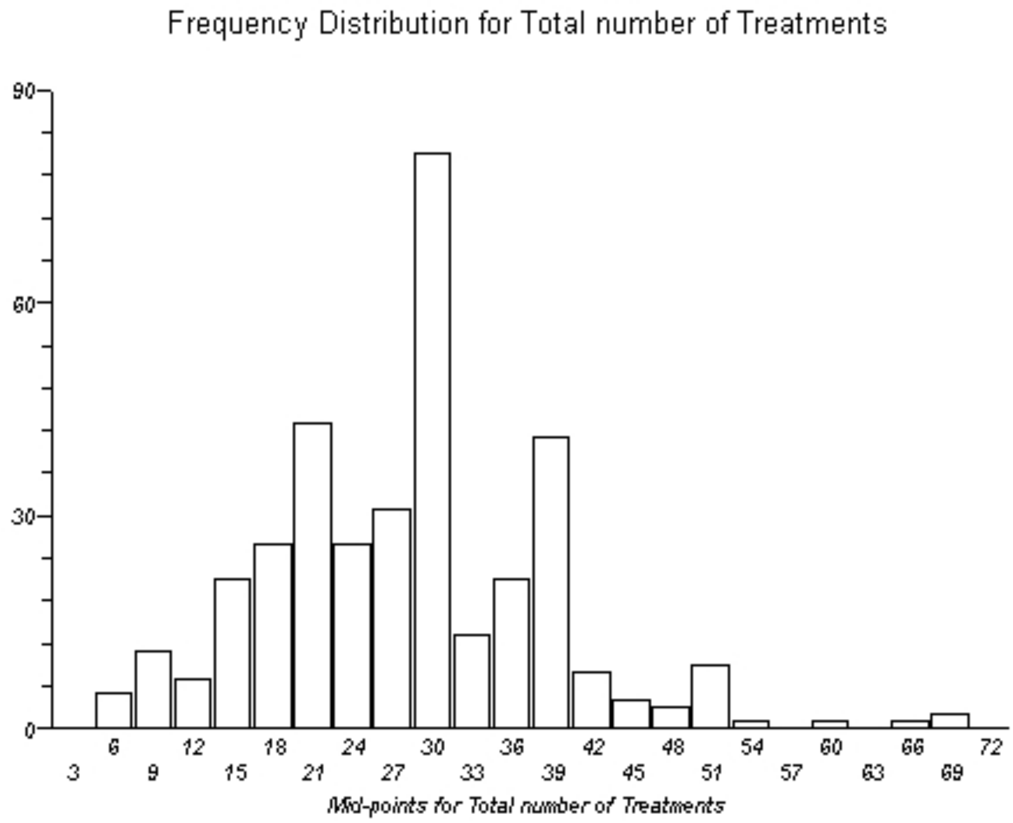

Figure 1: Grouped frequency distribution of treatment numbers.

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A cost-effectiveness analysis of two community models of care for patients with venous leg ulcers

• **Aim:** To conduct a cost-effectiveness analysis based on data from a randomised controlled trial comparing traditional community home nursing with a community Leg Club model for chronic venous leg ulcer management in the south-east metropolitan area of Queensland, Australia.
• **Method:** Participants were randomised to the Leg Club (n=28) or home visits (n=28). Data were obtained on resources/related costs incurred by the service provider, clients and carers, and the community.
• **Results:** From the collective perspective (service provider, clients and carers, and the community), at six months the incremental cost per healed ulcer was $AU515 (€318) and the incremental cost per reduced pain score was $AU322 (€199). For the service provider, Leg Club intervention resulted in cost savings and better health effects when compared with home nursing.
• **Conclusion:** On both clinical and economic grounds, the Leg Club model appears to be more cost-effective than traditional home nursing for the treatment of chronic venous leg ulcers. However, clients and the local community contribute substantial financial and in-kind support to the operation of both services.
• **Declaration of interest:** This project has been supported by a grant from the Queensland Nursing Council, Australia. The views expressed do not necessarily represent the views of the Council or the members, executive officer or staff of the Council.

venous leg ulcers; community management; cost analysis; Leg Club; home nursing

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Community leg ulcer clinics have emerged as a new approach to leg ulcer management. Studies have found that they improved healing rates[1-3] when compared with individual nursing care. Such clinics provide easier access to wound care specialist nurses, increased social interaction and improved information exchange between health-care team members.[4] The Lindsay Leg Club model has extended this concept (Box 1).[4]

Economic studies of leg ulcer management strategies have mainly concentrated on management products rather than modes of delivery or systems of care.[5] However, four studies have investigated the cost-effectiveness of different models of delivery,[6-9] three of which compared new leg ulcer clinic interventions with traditional home nursing.[6,7,9]

Clinic costs were either lower[7,9] or similar,[6] while healing rates were 10–68% better than traditional home nursing.[6,7,9] However, Bosanquet et al.'s[6] use of historical controls for the 'usual care group' may have exaggerated the difference in effects, while in Ellison et al.'s study[7] it is unclear whether healing improvements in the clinic sample were attributable to the clinic model or the different bandaging techniques used: the clinics used specialised high compression techniques whereas 'traditional care' involved alternative products.

Kerstein et al.[8] studied home nursing and physician care services using identical protocols, and found increased costs with home nursing, although both yielded similar levels of effectiveness.

Aim

This study aimed to evaluate the cost-effectiveness of a new model of community nursing care for clients with chronic leg ulcers, compared with traditional home community nursing care. It was undertaken as part of a randomised controlled trial (RCT) comparing effectiveness, in terms of healing, pain and quality-of-life outcomes,[10,11] of the Leg Club model with traditional community nursing.

This paper reports on the cost-effectiveness analysis to assess which model is most economically efficient. Unlike the three UK cost-effectiveness studies,[6,7,9] the analysis includes not only the perspective

Box 1. The Lindsay Leg Club model

The Lindsay Leg Club model is based on the provision of ulcer management and preventive care within an informal, relaxed 'drop-in' centre, promoting social interaction, community involvement and ownership.[4] Collective treatment is provided in an informal environment to de-stigmatise the condition and encourage information exchange and educational opportunities for both clients and staff of the service provider, but also those of clients and the community. These results thus provide economic information on venous leg ulcer services for various provider groups and their consumers.

Ethical approval was received from St Luke's Nursing Service and Queensland University of Technology human research ethics committee.

Method

Sample

The sample consisted of 56 clients — 28 in the intervention (Leg Club) group and 28 in the control (home nursing) group — referred to St Luke's Nursing Service in the south-east metropolitan region of Queensland, Australia.

To be included patients had to have a venous leg ulceration and an ankle brachial pressure index (ABPI) between >0.8 and <1.3 on admission.

Patients with diabetes, ulcers of non-venous aetiology or who were too immobile to be transported to the Leg Club via volunteer transport were excluded.

Participants provided written informed consent and were randomised via a computerised program to receive treatment either at individual home visits from community nurses (the control group) or from the community nurses during a weekly visit to a Leg Club (the intervention group).

Procedure

Study protocols were developed for all participants based on evidence-based assessment and treatment guidelines[12] (primarily short-stretch compression) to promote consistency. Ten community registered nurses were updated and educated on the assessment and treatment guidelines, and research project protocols before starting the trial.

All participants (in both groups) received comprehensive health assessment and treatment including:

- ABPI assessment
- Referral for further circulatory assessment if needed
- Venous ulcer treatment based on above guidelines
- Advice and support about venous leg ulcers
- Follow-up management and preventive care.

Leg Club participants had access to peer support, social interaction and goal-setting to assist in the management of functional and social activities.

Health outcomes

- **Number of healed ulcers** This was a concrete and clear clinical endpoint that took into account the total number of participants receiving each service and the proportion whose ulcers had fully healed. Wound assessments were undertaken on admission and at 12 and 24 weeks.
- **Reduced pain score** Pain improvement rates are the proportion of clients with a clinically important reduction in self-reported pain score. Pain levels were measured using the Rand Medical Outcomes Study Pain Measures.[13] Pain severity ranged from 1 (no pain) to 6 (extreme pain). A score reduction of three or more was considered clinically significant and had implications for conducting normal daily activities such as shopping and doing housework independently.

Further details on the instruments and measures used for other indicators of pain, functional ability and quality of life in the larger study (but not included in this analysis) are available elsewhere.[10,11]

Costs

Types of resources used for both groups included:

- Those borne directly by the service provider, such as health-care personnel, equipment, travel, consumables and operating expenses
- Those borne by clients, such as travel expenses, dressings and bandages
- In-kind resources provided by the community, such as volunteers and equipment.

The timescale for the collection of cost data was three and six months, aligning with the health-outcomes data assessments.

Data on resource quantities were recorded by the project staff. Personnel costs were calculated using award rates of pay,[14] and included estimates of employer on-costs. Operating costs included vehicle leasing, medical consumables, production of resource and educational materials, printing, office administration support, telephone and other incidental items. The cost of medical and office assets used to establish the services, such as Doppler devices and foot stools, was annuitised over the useful life of each asset to obtain its equivalent annual cost.[15,16]

Out-of-pocket expenses incurred by participants as consumers of the services were estimated — these included travelling expenses, dressings, bandages and other expenses. Information on specific brands and quantities of dressings and bandages for each participant was recorded. Out-of-pocket expenses were estimated up to the time taken for ulcers to heal (or not), and so were lower for faster healers. Travelling costs for those who drove to the Leg Club were estimated using each client's residential suburb and mode of transport. Cost per kilometre travelled was obtained from reports on average five-year running costs for cars.[17] Fares for public transport, and other out-of-pocket expenses, such as Leg Club donations, recorded by project staff were included.

Volunteers helped run the Leg Club, and the value of their time was estimated using the market replacement cost method.[18] This is the cost incurred if the volunteer was hired in the marketplace. The value of unpaid work was estimated using national reports from the Australian Bureau of Statistics, which provided hourly costs for volunteer and carer work.[18]

Ulcer-healing and pain data were managed and analysed using a sequential analysis technique;[19] further

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details are available in previous reports.[10,11] Monetary values were rounded up to the nearest dollar and reported in Australian dollars and Euros (2005 exchange rate: $AU1 = €0.6175). Goods and services taxes were included in market estimates as these represent a cost to clients and the health provider. Discounting future costs and benefits was not undertaken due to the short study duration. No assumptions were made on the future benefits or costs of the service.

Analysis
The analyses combined both cost and health outcomes data simultaneously to produce separate cost-effectiveness ratios (cost per healed ulcer and cost per reduced pain score) for both groups. Lower cost-effectiveness ratios indicate greater economic efficiency. However, incremental cost-effectiveness ratios (ICERs) are the key outcomes of interest. With new interventions there is often an efficiency trade-off between increased costs and increased health benefits. The incremental costs and incremental health effects of Leg Clubs over the home nursing service quantify this potential trade-off to produce ICERs, and are expressed algebraically:

$$\text{ICER} = \frac{C_{LC} - C_{HN}}{E_{LC} - E_{HN}}$$

where C is total costs, E is units of effectiveness (healed ulcers and pain improvement scores), LC is Leg Club (intervention) group, and HN is the home nursing (control) group.

All cost-effectiveness ratios were reported from two perspectives: the service provider only and the collective perspective of the service provider, clients and the broader community.

Sensitivity analysis plays an important role in economic evaluations for quantifying the extent of uncertainty often present in data measurement and/or valuation. Using a one-way sensitivity analysis, the results were recalculated over a range of plausible high and low values around the best estimates of cost and health outcome data in the base analysis. Variables where some uncertainty existed included personnel costs, client bandaging and dressings, travelling costs and volunteer inputs. In addition, healing rates were altered to check their influence on the stability of the results. These variables were altered separately using a univariate approach holding all others constant.

Results
Sample profile
Forty-six per cent of participants were female and 54% male, while 68% were aged 71 years or over. Fifty-eight per cent lived alone; 82% received either the aged or military service pension, 14% received disability support pensions and 4% were self-funded.

Costs of Leg Club compared with home nursing
Table 1 summarises the resource unit quantities and costs incurred for each management option. Costs were categorised into those accruing to the service provider, clients and community. Community costs include those estimated from in-kind support.

- **Total costs to the service provider** The Leg Club incurred lower costs than home nursing by $1727 (€1066) over three months through lower personnel and vehicle leasing costs than normally generated by nurses travelling to clients' homes.
- **Total costs to the service provider, community and clients** Compared with resources from the service provider, the financial and in-kind contributions from clients and the community were substantial. Total costs to the community for Leg Club were slightly higher than home nursing over three months: $13,245 (€8179) versus $10,997 (€6790).

Bandages and dressings were bought by clients in both groups and represent the largest cost item overall. Over three months, mean bandage and dressing expenses were $159 (€98) for Leg Club participants and $222 (€137) for those receiving home nursing.

Costs for each model of care over six months show parallel results, with absolute costs approximately doubling from three to six months, with the exception of bandages/dressings and travel costs. These latter expenses incorporated time to healing (the actual need for bandages/dressings and travel, which depended on healing performance). Leg Club participants had shorter healing times, so their out-of-pocket costs over time were lower than those for patients receiving home nursing.

- **Cost per healed ulcer to service provider** The Leg Club cost less and more of its clients' ulcers healed at both time periods. Cost savings were $1727 (€1066) and $3464 (€2139) for 0–3 months and 0–6 months respectively (Table 1). The cost per healed ulcer for home nursing was three times that for Leg Club at 0–3 months and twice that at 0–6 months. These savings are reflected by the negative incremental cost per healed ulcer (-$693 [-€428] at 0–6 months).
- **Cost per healed ulcer to service provider, community and clients** From the collective perspective, the Leg Club cost more than home nursing but produced higher healing rates and had lower costs per healed ulcer at 0–3 months — $1019 (€629) versus $1571 (€970) respectively — and at 0–6 months — $1546 (€955) versus $2061 (€1273). The incremental cost per healed ulcer at 0–6 months was $515 (€318), which represents the extra cost to the collective community to produce more healed ulcers at 0–6 months.
- **Cost per reduced pain score to service provider** More clients attending Leg Clubs experienced clinically meaningful reductions in pain

Table 1. Summary of total costs by each model of care for 0–3 and 0–6 months

	0–3 months				0–6 months			
	Leg Club		Home nursing		Leg Club		Home nursing	
	$AUS	€	$AUS	€	$AUS	€	$AUS	€
Service provider								
Operating expenses:								
• personnel*	2207	1363	3038	1876	4405	2720	6075	3752
• admin. support (follow-up calls, paperwork)	224	138	224	138	448	277	448	277
• consumables (medical, gloves etc)	441	272	441	272	882	545	882	545
• vehicle leasing†	291	180	932	576	582	359	1865	1152
• mobile phones	124	76	247	152	247	152	493	305
Equipment (portable, medical)‡	—	—	132	82	—	—	265	161
Subtotal	3287	2029	5014	3096	6564	4053	10,028	6192
Client/carers								
Travel (self only n=10)§	1860	1148	—	—	2863	1768	—	—
Bandages and other medical supplies§	4610	2846	5983	3694	6785	4190	10,580	6534
Other out-of-pocket expenses/donations	267	166	—	—	535	330	—	—
Catering and club activities	51	32	—	—	103	63	—	—
Subtotal	6788	4192	5983	3694	10,285	6351	10,580	6534
Community (in-kind support)								
Leg Club volunteers	2229	1376	—	—	4458	2753	—	—
Rental and electricity	185	114	—	—	370	229	—	—
Maintenance/cleaning	254	157	—	—	504	311	—	—
Insurance (building)	216	133	—	—	432	267	—	—
Equipment (portable, medical, office, furniture)‖	286	177	—	—	573	354	—	—
Subtotal	3170	1958		—	6337	3913		—
Total	**13,245**	**8179**	**10,997**	**6790**	**23,186**	**14,317**	**20,608**	**12,726**

* Leg Club: based on one experienced registered nurse plus one personal care assistant for three out of every four weeks and two registered nurses plus one personal care assistant for one week out of every four weeks @four hours each per week; home nursing: based on two registered nurses each week @10.3 hours per week. Includes 20% employer on-costs
† Leasing a small four-cylinder vehicle @ 40,000km/year: Leg Club : one vehicle five hours/week; home nursing : two vehicles eight hours/week
‡ Two Dopplers for home nursing; annual equivalent cost pro-rata
§ Travel and bandages/dressings: frequency/quantity account for time to healing for all participants. Many participants lived over 15km from the Leg Club
‖ Purchased with community grant monies

scores at both time periods. From the service provider perspective, costs per reduced pain score ratios were lower for Leg Club than for home nursing at 0–3 months — $299 (€184) versus $2507 (€1548) — and at 0–6 months — $505 (€312) versus $2006 (€1238).

• **Cost per reduced pain score to service provider, clients and community** Similarly, from the collective perspective, the costs per reduced pain score ratios were lower for Leg Club than for home nursing at 0–3 months — $1204 (€743) versus

Table 2. Results of one-way sensitivity analysis on incremental cost per healed ulcer*

	0–3 months Leg Club $AUS	€	Home nursing $AUS	€	0–6 months Leg Club $AUS	€	Home nursing $AUS	€
Base analysis	375	232	375	232	515	318	515	318
Personnel costs (AU$/hr)								
RN level 1 grade 1	346	214	432	267	449	277	652	402
RN level 1 grade 8	409	253	302	187	600	371	341	211
Bandages (AU$)								
0.8	221	136	575	355	244	150	939	580
1.2	528	326	176	109	786	486	93	57
Travel costs (AU$/km)								
Large car	481	297			646	399		
Volunteer costs (AU$/hr)								
0	157	97			324	200		
17	612	378			1415	873		
Healing rates								
x 0.8	749	463	281	173	1289	796	368	227
x 1.2	281	173	449	277	322	199	859	531

* From the collective perspective of the nursing service provider, clients and community

$5499 (€3395) — and at 0–6 months — $1784 (€1101) versus $4121 (€2545). These noticeably lower cost ratios can be attributed to the substantially higher number of clients who experienced clinically meaningful reductions in pain scores, compared with the home-nursing clients. The incremental cost per pain reduction score ratio was $322 (€199) for 0–6 months.

Sensitivity analyses

Results of one-way sensitivity analyses on ICERs, using numbers of healed ulcers and the collective perspective outcome, are provided in Table 2.

The most substantial cost items were tested over a range of low and high estimates around the best estimate used in the base analysis. The base analyses ICERs were $375 (€232) and $515 (€318) over 0–3 and 0–6 months respectively. Personnel costs were tested over the low and high salary grade increments within the level 1 domiciliary nursing state award.[14] Bandages and dressings were tested over 20% variance in actual costs estimated. Variations in annual kilometres estimated for leased vehicles changed leasing costs minimally and were excluded from the sensitivity analysis. Client travel costs were varied according to car size rather than the small car base estimate, and volunteer costs were tested over $0–17 per hour.

For Leg Club, the ICER was smaller than in the base analysis when personnel and bandage costs were at low estimates and if no volunteer expenses were included. Changes in salary increments within the grade 1 staffing level resulted in relatively moderate variations (-$71–169) in the ICER. Smaller changes occurred when client travel expenses varied.

However, if client expenditure on bandages and dressing varied by 20%, a large impact was felt on the ICER for both services, especially home nursing, at 0–6 months. A small change in bandage and dressing costs exerted large price variation for clients as a group. Volunteer in-kind support at the higher estimates substantially increased the ICER to $1415 (€873) at six months.

Small changes in healing rates (±20%) produced large variations in ICERs from $322 (€199) to $1289 (€796) for Leg Club. For example, if Leg Club had 20% fewer healed ulcers (equivalent to 3/28 clients with non-healing ulcers) the ICER increased 2.5- fold from $515 (€318) to $1289 (€796) at six months.

Discussion and limitations

This is the first economic evaluation to compare Leg Clubs with traditional home nursing models of care. Over both time periods, the former produced superior health outcomes to the latter.

Clients and the local community contribute substantial financial and in-kind support integral to the operation of both services; without this, neither model could operate. As a group attending and supporting Leg Clubs, their willingness to pay an additional $515 (€318) over six months for a 20% increase in healing rates needs to be acceptable, affordable and sustainable. Without this mutual cost-sharing of treatment resources (particularly medical equipment, bandages and dressings), expected health gains could not occur.

If a successful partnership is formed between the service provider, potential clients and the community, then the Leg Club represents an excellent public health investment.

From the service provider's perspective, Leg Club is clearly more economically efficient than traditional or usual home nursing practice due to the superior health outcomes and lower costs achieved — the latter largely due to community support.

Other health and social benefits of Leg Club are important for providers to acknowledge.

For clients, improved quality of life, better functional ability, the reduced need for external home-help services, greater socialisation and respite care relief are some of the potential advantages over home nursing that have been omitted from the cost-effectiveness analysis.

As with all economic evaluations, the key goal is economic efficiency, although other decision-making criteria, such as service quality, equity, acceptability and accessibility, are also necessary for comprehensive health service management.

In this study cost and effectiveness data were largely available, credible at the individual level (rather than extrapolated from the research literature) and derived from a RCT.

Nevertheless, sensitivity analyses were undertaken for several variables to check the stability of the base values and associated ICERs and to measure the effect different values may have on the results. They showed that the results are sensitive to changes of ±20% in healing rates achieved by the two services, volunteer costs and, at six months, client bandage and dressing expenses. Therefore, healing rates achieved by Leg Club need to be at least 20% higher than for home nursing to maintain or decrease the incremental cost per healed ulcer of $515 (€318) at six months. Other cost changes have a reasonably stable effect on incremental cost-effectiveness ratios.

This analysis used two important clinical outcomes:

- Completely healed ulcers
- Reduction in pain scores.

While an ulcer with a dramatically reduced area (by at least 50%) is likely to be of value to clients and an indication of successful treatment to service providers, from an economic viewpoint these clients still require full treatment and resources. Thus, for analysis purposes, they were treated the same as clients with non-healing ulcers.

Other measures that may have added value to the analysis, but were unavailable, are wound-free days and ulcer recurrences.

This study has a number of caveats. The sample size is small, limiting the estimation of costs. However, the clinical benefits of Leg Club over home nursing achieved statistically significant differences.[11] Follow-up time was short and data on ulcer recurrences were excluded. This could have underestimated the total costs and overestimated healing outcomes achieved by Leg Club. Indirect community costs that were omitted may include greater health and social service utilisation through opportunistic screening and referrals of clients for further health and social care.

The results are consistent with UK studies comparing the efficiency of leg ulcer clinics with traditional home nursing.[6,7,9]

This project was a RCT using personnel from the same organisation and locality, and delivered a standardised treatment protocol.

However, the Australian health system for the care of older people differs from the UK system: health costs are shifted from the health system towards patients and the community.

Further health services research would be valuable on other components of service delivery, such as client compliance, satisfaction and sustainability. Similarly, a more natural 'real-world' setting than a clinical trial is required, where it is possible that the natural behaviours and motivations of health professionals and patients may have been altered to ensure a successful trial.

Increased partnerships, with mutual benefits, between product companies and health professionals, for affordable and equitable patient outcomes, would improve service delivery of similar Leg Clubs in the future.

This project has shown both clinical and economic evidence in favour of a Leg Club model of care, which should thus be considered a method of treating chronic venous leg ulcers in the community, especially from a service provider viewpoint.

Extensive client and community resources and expenses are required for both models to operate. Measures that promote the affordability, equity and accessibility of these services should therefore be paramount to ensure quality health care reaches those in greatest need. ■

Contributorship statements

Louisa Gordon: developing concepts and design, analysis and interpretation of data, drafting the article, and final approval

Helen Edwards: concept and design of clinical trial, critical review of drafts for intellectual content, interpretation of data, and final approval

Mary Courtney: concept and design of clinical trial, critical review of drafts for intellectual content, and final approval

Kathleen Finlayson: drafting the article, critical review of drafts for intellectual content, interpretation of data, and final approval

Patricia Shuter: drafting the article, and final approval

Ellie Lindsay: critical review of drafts for intellectual content, and final approval

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A cost-effectiveness analysis of two community models of nursing care for managing patients with chronic venous leg ulcers.

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ABSTRACT

Objective: To conduct a cost-effectiveness analysis of traditional community home nursing compared to a community Leg Club model for managing clients with chronic venous leg ulcers. **Design:** A cost-effectiveness analysis was undertaken based on data from a randomised controlled trial. **Setting:** Community nursing focusing on secondary prevention care in the South-east metropolitan area of Queensland, Australia. **Participants:** Clients diagnosed with chronic venous leg ulcers that had an Ankle Brachial Pressure Index >0.8 and <1.3. **Intervention:** Participants were randomised to receive care either via the Leg Club model of care (n=28) or through individual home visits (n=28). Leg Club involved ulcer management and preventative care by registered nurses within an informal community centre that promotes social interaction. Data were obtained on resources and related costs incurred by the service provider, the clients and carers, and the community. **Main outcomes:** The key outcomes were incremental cost per healed ulcer and incremental cost per reduced pain score (using the Rand Medical Outcomes Study Pain Measures). **Results:** From the collective perspective of the service provider, patients and carers and the community, at six months, the incremental cost per healed ulcer was $AU 515 (€ 318) and incremental cost per reduced pain score was $AU 313 (€ 199). Client out-of-pocket expenses for bandages and dressings represent the highest cost item and were twice that of personnel costs paid by the service provider. **Conclusion:** On both clinical and economic grounds, the Leg Club model appears to be the cost-effective option over traditional home nursing for the treatment of chronic venous leg ulcers. However, clients and the local community contribute substantial financial and in-kind support, integral to the operation of both services that should not be overlooked during decision-making.

INTRODUCTION

The prevalence of chronic venous leg ulcers in industrialised nations, including Australia, is approximately 1-3% in the over 60 years population[1-4]. Prevalence increases with age[5] and the burden of this illness is likely to increase given Australia's ageing population. In a recent UK study, the overall incidence rate of venous leg ulcers among the elderly was estimated at 0.76 per 100 person years for men and 1.42 for women. This estimate was based on patients seeking and/or receiving medical care and might therefore underestimate the true extent of the problem[4]. The financial burden of leg ulcers is highlighted when data from recent studies in the UK are combined, indicating that 1.5% of total health expenditure is accounted for by chronic leg ulcer treatment[4 6-8].

The personal and social impact of this condition is substantial and may include continuous pain, restricted mobility, discomfort and embarrassment from wound exudate and odour, significant out-of-pocket expenses, inconvenience and social isolation[1 9-11]. One Australian study found 45% of the study participants were housebound because of their ulcers[1]. Pain associated with chronic leg ulcers can be especially problematic as it has been reported to interrupt sleep and subsequently cause tiredness, lack of energy and difficulty in performing normal daily activities[12].

The mainstay treatment for venous leg ulcers is to apply compression garments (bandages or stockings) to facilitate venous return[5]. High compression multi-layered bandaging techniques represent best clinical practice at present[5], however there is uncertainty over which compression products available on the competitive global market are the most effective. Several barriers plague the successful implementation and maintenance of ongoing venous leg ulcer treatment. These include the need for specialised training of clinicians in assessment and compression bandaging techniques, poor client tolerance and limited understanding of the need for long-term compression treatment[13 14]. As studies have shown between 20% and 50% of community nurses' time is spent on managing leg ulcers, overcoming these barriers has become a priority for service providers[14 15]. Community leg ulcer clinics have emerged as a new approach to addressing this issue.

Since 1992, a number of studies have evaluated the effectiveness of community leg ulcer clinics and found improved ulcer healing rates[14 16 17] compared with individual nursing care. Leg ulcer clinics have advantages over traditional home nursing care for leg ulcer sufferers including easier access to wound care specialist nurses, increased social interaction and improved information exchange between health care team members[18]. The Lindsay Leg Club® model, founded in a rural community in the UK, has extended the idea of a leg ulcer clinic by departing from a formal medical model to one that is social, informal (drop-in rather than appointment-based) and welcoming while simultaneously encouraging community and client ownership[18].

Economic studies of leg ulcer management strategies have mainly concentrated on different compression, dressing and pharmaceutical products rather than different modes of delivery or systems of care[19]. Only four studies have investigated cost-effectiveness of different models of delivering venous leg ulcer care services[20-23]. Three UK studies have assessed cost-effectiveness of new leg clinic interventions compared with traditional home nursing[20 21 23] with efficiencies found generally in favour of leg clinics. Compared to traditional home nursing, costs were either lower[20 21 23] or similar[20] while healing rates were superior by between 10-68%[20 21 23]. However, in one study[20] the use of historical controls used for the usual care group may have exaggerated the difference in effects. In another study[21], it was unclear that ulcer healing improvements in the clinic sample were attributable to the clinic model or the different bandaging techniques used for each participant group, because specialized high compression techniques were used in the clinics but a variety of alternative ulceration products used in traditional care. In the US, Kerstein *et al.* (2000) studied home nursing and physician care services of leg ulcer management using identical protocols across groups and found increased costs with home nursing, while the two services yielded similar levels of effectiveness[22].

Aim

This study aimed to evaluate the cost-effectiveness of a new model of community nursing care for clients with chronic leg ulcers in comparison to traditional individual home community nursing care. The evaluation was undertaken along side a randomised controlled trial investigating the effectiveness of a community Leg Club intervention compared to the traditional community nursing for clients with chronic venous leg ulcers in terms of healing, pain and quality of life outcomes[24 25]. This paper specifically reports on the cost-effectiveness analysis to assess which of the two models provides the economically efficient choice. Unlike the three UK cost-effectiveness studies[20 21 23], the perspective of the analysis included not only that of the service provider, but also the clients and the community. Consequently, these results provide economic information on venous leg ulcer services for various provider groups and consumers of these services.

Prior to commencement, ethical approval for this study was received from St Luke's Nursing Service and Queensland University of Technology Human Research Ethics Committee.

METHODS

Sample

The sample consisted of 56 clients (28 in the intervention group, 28 in the control group) with venous leg ulcers referred for care to St Luke's Nursing Service in the South-east metropolitan region of Queensland, Australia. Clients were eligible for inclusion in the study if they were diagnosed with a venous leg ulcer and recorded an Ankle Brachial Pressure Index >0.8 and <1.3 on admission. Clients were excluded if they had diabetes, ulcers of non-venous aetiology, or were too immobile to be transported to Leg Club via volunteer transport. Participants provided their informed consent and were then randomised via a computerised randomisation program to receive treatment either during individual home visits from community nurses (the home nursing group), or from the community nurses during a weekly visit to a Leg Club (the intervention group).

Procedure

Study protocols were developed for all participants based on evidence-based assessment and treatment guidelines[26] for clients with venous leg ulcers to promote consistency in treatment. These were primarily based on a short-stretch compression bandaging system. A small team of 10 community registered nurses with an interest and skills in wound care were updated and educated (via seminars, learning sessions and assisted practice sessions) on the assessment, treatment guidelines and research project protocols before commencing the trial.

All study participants (in both groups) received comprehensive health assessment including Ankle Brachial Pressure Index assessment and referral for further circulatory assessment, if necessary, venous ulcer treatment based on the above guidelines, advice and support about venous leg ulcers, follow-up management and preventative care. The participants visiting

Leg Club weekly, in addition, were provided with peer support, social interaction and goal setting to assist in the management of functional and social activities. The Lindsay Leg Club® model is based on the provision of ulcer management and preventative care within an informal, relaxed 'drop-in' centre, promoting social interaction, community involvement and ownership[18]. Collective treatment was provided in an informal environment to de-stigmatise the condition and encourage information exchange and educational opportunities for both clients and staff.

Health outcomes

Two health outcomes were used in the cost-effectiveness analysis:

1. Numbers of healed ulcers. The numbers of fully healed ulcers are a concrete and clear clinical endpoint. Healing rates take into account the total participants receiving each service and the proportion of clients whose ulcers are clinically assessed as fully healed. Clinical wound assessments on individual leg ulcer healing were collected on admission to the study, at 12 weeks and 24 weeks from admission.
2. Reduced pain scores. Reductions in pain are believed to be a major influence in improving client quality of life through increased function, mobility and comfort. Pain improvement rates are the proportion of clients with a clinically important reduction in pain score collected on self-reported questionnaires. Pain levels were measured using the Rand Medical Outcomes Study Pain Measures[27]. The severity of pain scale ranged from 1 - 6 on a Likert scale where 1 = no pain to 6 = extreme pain[27]. A score reduction of ≥3 was considered clinically significant by the project staff (ie going from a moderate or severe level of pain to a very mild level or no pain) and had implications for conducting normal daily activities/work (eg shopping and house cleaning, etc) independently.

Further details on the instruments and measures used for other indicators of pain, functional ability and quality of life used in the larger study (but not included in this analysis) are available elsewhere[24,25].

Costs

Types of resources used for both Leg Club and home nursing services included those directly borne by the service provider (eg health care personnel, equipment, travel, consumables and operating expenses etc,) those borne by the clients (eg travel expenses, dressings and bandages, etc) and those in-kind resources provided from the community (volunteers, equipment etc). The time horizon for the collection of cost data was three and six months, aligning with health outcomes data assessments.

Data on resource quantities were recorded by the project staff. Personnel costs were valued using award rates of pay[28] and included estimates of employer on-costs. Operating costs included vehicle leasing, medical consumables, production of resource and educational materials, printing, office administration support, telephone, and other incidentals. The cost of medical and office assets used to establish the services (eg Doppler devices, foot stools) were annuitized over the useful life of the asset to obtain its equivalent annual cost[29,30].

Out-of-pocket expenses incurred by study participants as consumers of the services were estimated and included travelling expenses, dressings and bandages and other expenses. Information on specific brands and quantities of dressings and bandages for each participant was recorded by project staff. Travelling costs for those driving themselves to Leg Club were estimated by using each client's residential suburb and mode of transport. The cost per kilometre travelled was obtained from reports on average five-year running costs for cars[31].

Fares for public transport, and other out-of-pocket expenses (eg Leg Club donations) recorded by project staff were included. The quantities of dressings/bandages and travel incorporated the time taken for ulcers to heal and, consequently after healing, when clients no longer incurred these resources.

Volunteers were involved in running Leg Club and the value of their time was estimated using the market replacement cost method[32]. This is the cost incurred if the volunteer was hired in the marketplace to provide the services concerned. The value of unpaid work was estimated using national reports from the Australian Bureau of Statistics, providing hourly costs for volunteer and carer work[32].

Ulcer healing and pain data were managed and analysed using a sequential analysis technique[33]. Further details on these analyses are available in previous reports[24 25]. Economic cost data were stored and analysed in Microsoft® Excel. Monetary values were rounded up to the nearest dollar, and reported in year 2005 Australian dollars and Euros (exchange rate $AU 1 = € 0.6175). Goods and Services Taxes were included in market estimates as these represent a cost to clients and the health provider. Discounting future costs and benefits was not undertaken due to the short 6-month study duration. No assumptions or judgements were made on the future benefits or costs of the service beyond the study 6-month time frame.

Analysis

The cost-effectiveness analyses combined both cost and health outcomes data simultaneously to produce separate cost-effectiveness ratios (ie cost per healed ulcer and cost per reduced pain score) for both the Leg Club and the home nursing services. Lower cost-effectiveness ratios indicate better economic efficiency. However, the *incremental* cost-effectiveness ratios (ICERs) are the key outcomes of interest for this economic analysis. Often with new interventions there is an efficiency trade-off between increased costs and increased health benefits. The incremental costs and incremental health effects of the Leg Club over the home nursing service quantify this potential trade-off to produce incremental cost-effectiveness ratios (ICERs) and are expressed algebraically as follows:

$$ICER = \frac{C_{LC} - C_{HN}}{E_{LC} - E_{HN}}$$

where C is total costs, E is units of effectiveness (ie healed ulcers and pain improvement scores), LC is the Leg Club group, and HN is the home nursing group. All cost-effectiveness ratios were reported from two perspectives: the service provider only and the collective perspective of the service provider, clients and the broader community.

Sensitivity analysis has an important role in economic evaluations for quantifying the extent of uncertainty often present in data measurement and/or valuation. Using a one-way sensitivity analysis, the results were recalculated over a range of plausible high and low values around the best estimates of cost and health outcome data in the base analysis. Variables where some uncertainty existed included: personnel costs, client bandaging and dressings, travelling costs and volunteer inputs. In addition, healing rates were altered to check their influence on the stability of the results. These variables were altered separately using a univariate approach holding all others constant.

RESULTS

Sample profile

Approximately equal participants in the study sample were of each sex (46% female, 54% male) and 68% were aged 71 years or over. Only one third were married or living in a stable relationship and 58% lived alone. A large majority (82%) of the participants received the aged or military service pension, 14% received disability support pensions, and only 3.6% were self-funded.

Costs of Leg Club versus Home Nursing

A summary of the resource unit quantities and costs incurred for each leg ulcer management option are provided in Table 1. Costs were categorised into those accruing to the service provider, the clients and community. Community costs include those estimated from in-kind support.

Table 1 about here

Total Costs to the Service Provider

From the perspective of the service provider only, the Leg Club incurred lower costs than home nursing by $1,727 (€1,066) over three months. The savings generated from Leg Club arose through lower personnel and vehicle leasing costs normally generated through registered nurses travelling to individual patients homes. These two items comprise the highest operating expenses.

Total Costs to Community and Clients

Compared to the resources provided by the service provider, the financial and in-kind contributions from both clients and the local community were substantial. Taking into account this additional community support and client out-of-pocket expenses (eg volunteer support for transport to Leg Club), the total costs to the community for Leg Club were slightly higher than the home nursing option over three months, $13,245 (€8,179) versus $10,997 (€6,790), respectively.

Bandages and dressings were bought by clients (of both Leg Club and home nursing) and represent the largest cost item overall and was twice that of personnel costs paid by the service provider. Over three months, mean bandage and dressing expenses were $159 (€98) for Leg Club and $222 (€137) for home nursing clients. Costs for each model of care over six months show parallel results with absolute costs approximately doubling from three to six months with the exception of bandages/dressings and travel costs. These latter expenses incorporated time to healing (ie the actual need for bandages/dressings and travel which depended on healing performance). Leg Club participants had quicker healing times and consequently client out-of-pocket costs over time were smaller than for home nursing.

Cost per healed ulcer to Service Provider

From the perspective of the service provider, Leg Club cost less and produced higher numbers of clients with healed ulcers at both time periods (Table 2). Cost savings from Leg Club were $1,727 (€1,066) and $3,464 (€2,139) for 0-3 months and 0-6 months, respectively. The cost per healed ulcer for home nursing was three times that for Leg Club at 0-3 months and twice that for Leg Club at 0-6 months (Table 2). These cost savings are reflected by the negative incremental cost per healed ulcers (eg -$693 (-€428) incremental cost per healed ulcer between 0-6 months).

Cost per healed ulcer to the Service Provider, Clients and Community

From the collective community perspective, the Leg Club service cost more than home nursing but produced higher healing rates (Table 2). Compared to home nursing, Leg Club had smaller costs per healed ulcer at 0-3 months, $1,019 (€629) versus $1,571 (€970) and at 0-6 months, $1,546 (€955) versus $2,061 (€1,273) (Table 2). The incremental cost per healed ulcer was $515 (€318) which represents the extra cost to the collective community to produce more healed ulcers at 0-6 months.

Table 2 about here

Cost per reduced pain scores to the Service Provider

Compared to home nursing, Leg Club produced more clients with clinically meaningful reductions in pain scores at both time periods (Table 3). From the service provider perspective, cost per reduced pain score ratios were smaller for Leg Club than home nursing at 0-3 months, $299 (€184) versus $2,507 (€1,548), respectively, and at 0-6 months $505 (€312) versus $2,006 (€1,238), respectively.

Cost per reduced pain scores to the Service Provider, Clients and Community

Similarly, from the collective perspective, cost per reduced pain score ratios were smaller for Leg Club than home nursing at 0-3 months ($1,204 (€743) versus $5,499 (€3,395), respectively, and at 0-6 months $1,784 (€1,101) versus $4,121 (€2,545), respectively. These noticeably smaller cost ratios of Leg Club are attributable to the substantially greater number of clients with clinically meaningful reduced pain scores, compared to the home nursing clients (Table 3). The incremental cost per pain reduction score ratio was $322 (€199) for 0-6 months.

Table 3 about here

Sensitivity analyses

Results of one-way sensitivity analyses on ICERs, using numbers of healed ulcers and the collective perspective outcome are provided in Table 4. The most substantial cost items were tested over a range of low and high estimates around the best estimate used in the base analysis. The base analyses ICERs were $375 (€231) and $515 (€318) over 0-3 and 0-6 months, respectively. Personnel costs were tested over the low and high salary grade increments within the Level 1 Domiciliary Nursing State Award[28]. Bandages and dressings were tested over 20% variance in actual costs estimated. Variations in annual kilometres estimated for leased vehicles changed leasing cost very minimally and were excluded from the sensitivity analysis. Patient travel costs were varied according to car size rather than the small car base estimate and volunteer costs were tested over $0-17 per hour.

Table 4 about here

For Leg Club, the ICER was smaller than in the base analysis when personnel and bandage costs were at low estimates and if no volunteer expenses were included. Changes in salary increments within the Grade 1 level resulted in relatively moderate variations (-$71 to $169) in the ICER. Smaller changes in the ICER occurred when client travel varied.

However, if client bandage and dressing expenditure varied by 20%, a large impact was felt on the ICER for both services, especially home nursing, at 0-6 months. A small change in bandage and dressing costs exerted large price variation for clients as a group. Volunteer in-kind support at the higher estimates substantially increased the ICER to $1,415 (€873) at six months. Small changes in healing rates (±20%) produced large variations in ICERs from $322 (€199) to $1289 (€796) for Leg Club. For example, if Leg Club had 20% less healed ulcers (equivalent to 3/28 clients with ulcers that did not heal) the ICER increased 2.5-fold from $515 (€318) to $1,289 (€796) at six months.

DISCUSSION AND LIMITATIONS

This cost-effectiveness analysis is the first economic evaluation comparing Leg Clubs with traditional home nursing for venous leg ulcer care. Over both time periods, the Leg Club produced superior health outcomes to those delivered by home nursing. Clients and the local community contribute substantial financial and in-kind support integral to the operation of both services that should not be disregarded during decision-making. Without these contributions, neither Leg Club nor home nursing for treating leg ulcers could operate. As a group attending and supporting Leg Clubs, their willingness to pay an additional $515 (€318) over six months for a 20% increase in healing rates needs to be acceptable, affordable and sustainable. Without this mutual cost-sharing of treatment resources (particularly medical equipment, bandages and dressings), expected health gains could not occur. If a successful partnership is formed between the service provider, potential clients and the community, as is the case here, then Leg Club is an excellent public health investment. From the perspective of the service provider, clearly Leg Club is the economically efficient option over the traditional or usual home nursing practice for treating clients with venous leg ulcers due to superior health outcomes and lower costs, the latter largely due to community support.

Other health and social benefits of Leg Club are important for providers to acknowledge. Potential benefits of Leg Club for clients in terms of improved quality of life, better functional ability, the reduced need of external home help services, greater socialization, respite care relief and other downstream effects are some advantages over home nursing omitted from the cost-effectiveness analysis. These would serve to underestimate the true beneficial impact of Leg Club. The Leg Club model of care also fosters opportunities for nurses' professional development and learning in a group environment that home nursing cannot offer. As with all economic evaluations, the key goal is economic efficiency and other decision-making criteria are necessary for comprehensive health service management, such as considerations of service quality, equity, acceptability or accessibility.

In this study, cost and effectiveness data were largely available, credible at the individual level (rather than extrapolated from the research literature) and derived from a randomised controlled trial. Nevertheless, sensitivity analyses were undertaken for several variables to check the stability of the base values and associated incremental cost-effectiveness ratios and measure the effect different values may have on the results. Consequently, the results are sensitive to changes of ±20% in healing rates achieved by the two services, volunteer costs and at six months, client bandage/dressing expenses. Therefore, healing rates of Leg Club need to be at least 20% higher than home nursing to maintain or decrease the incremental cost per healed ulcer of $515 (€318) at six months. Other cost changes have a reasonably stable effect on incremental cost-effectiveness ratios.

This analysis used numbers of healed ulcers and numbers of clients with clinically meaningful reductions in pain scores as two important clinical outcomes of leg ulcer management. Completely healed ulcers are a concrete and clear clinical endpoint. Partially healed ulcers may have been used to account for those clients with clear improvements in health but fall short of reaching a complete cure. An ulcer with a dramatically reduced ulcer area (by at least 50%) is likely to be of value to clients and an indication of successful treatment to service providers. However, from an economic viewpoint, clients with partially healed ulcers still require full treatment and use of resources and consequently have been treated the same as clients with non-healing ulcers. Other measures that may have added value to the analysis, but were unavailable, are wound-free days and ulcer recurrences.

This study has a number of caveats. The sample size is small and this limits the estimation of costs, however, clinical benefits of Leg Club over home nursing achieved statistically significant differences as documented elsewhere[25]. Other benefits and costs have not been fully captured in this analysis. The study follow-up time was short and data on ulcer recurrences were not included in this project and it is probable that some clients would have ulcers returning at some later time. This could therefore underestimate total costs and overestimate healing outcomes. Indirect community costs that were omitted may include greater health and social service utilization through opportunistic screening/referrals of clients for further health/social care.

The results here are consistent with the UK studies comparing the efficiency of ulcer leg clinics with traditional home nursing[20 21 23]. Unlike two of the UK studies[20 21], this project was a randomised controlled trial using personnel from the same organisation and locality, and delivered a standardized treatment protocol. Also, the Australian health system for aged care differs from the UK system where, as this project illustrates, health costs are shifted from the health system towards patients and the community. Further health services research would be valuable on other components of service delivery (eg client compliance, satisfaction, sustainability) and in a more natural 'real-world' setting rather than within a clinical trial where it is possible that the natural behaviours and motivations of health professionals and patients may have been altered to ensure a successful trial. Increased partnerships with mutual benefits between product companies and health professionals, for affordable and equitable patient outcomes, would improve service delivery of similar Leg Clubs in the future.

Leg Clubs are considered an alternative model of care compared to medical leg ulcer clinics and traditional home nursing care. This project has shown both clinical and economic evidence in favour of a Leg Club model of care and should therefore be given consideration as a method of treating chronic venous leg ulcers in the community, especially from a service provider viewpoint. Extensive client and community resources and expenses are required for both Leg Club and home nursing models to operate. Measures which promote the affordability, equity and accessibility of these services should therefore be paramount to ensure quality health care reaches those of highest need.

What this paper adds

What is already known on this subject

Community leg ulcer clinics and Leg Clubs have demonstrated superior healing rates and social advantages over traditional home nursing care for venous leg ulcer sufferers. No economic evaluation has compared Leg Clubs with home nursing models of nursing care for leg ulcer management.

What this study adds

Our study suggests that the Leg Club model of care for patients with chronic venous leg ulcers is a more economically efficient option than traditional community home nursing. Community nursing administrators should consider adopting this model of care.

Contributorship statements

Louisa Gordon – developing concepts and design, analysis and interpretation of data, drafting the article, final approval **(Guarantor)**

Helen Edwards – critical review of drafts for intellectual content, interpretation of data, final approval

Mary Courtney - critical review of drafts for intellectual content, final approval

Kathleen Finlayson - drafting the article, critical review of drafts for intellectual content, interpretation of data, final approval

Patricia Shuter - drafting the article, final approval

Caroline Lewis - critical review of drafts for intellectual content, final approval

Ellie Lindsay - critical review of drafts for intellectual content, final approval

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Hyperbaric Oxygen Reduced Size of Chronic Leg Ulcers: A Randomized Double-Blind Study

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To evaluate the effect of hyperbaric oxygen therapy on chronic wound healing, 16 otherwise healthy patients who had nondiabetic, chronic leg ulcers with no large vessel disease were included in a double-blind study. Patients were grouped according to age and then randomly assigned to two groups breathing either air or oxygen at 2.5 atmospheres of absolute pressure for 90 minutes 5 days per week for a total of 30 treatments. The wound area was copied onto transparent film covering the wound and then measured using only one matching wound from each patient. The mean decrease of the wound areas at weeks 2, 4, and 6 in the oxygen group were 6 percent (SD ± 14), 22 percent (SD ± 13), and 35.7 percent (SD ± 17), respectively, and in the air group, 2.8 percent (SD ± 11), 3.7 percent (SD ± 11), and 2.7 percent (SD ± 11), respectively, giving a p value less than 0.05 at week 4, and a p value less than 0.001 at week 6 between the groups using the Mann-Whitney U test. These data indicate that hyperbaric oxygen therapy may be used as a valuable adjunct to conventional therapies when nondiabetic wounds do not heal. (*Plast. Reconstr. Surg.* 93: 829, 1994.)

The aim of this study was to evaluate the effect of hyperbaric oxygen therapy on chronic wound healing. Nondiabetic leg ulcers with no signs of large vessel disease were chosen in order to exclude arterial perfusion disturbances as a factor in the pathogenesis of the chronic wound.

BACKGROUND

In 1965, Slack and coworkers[1] demonstrated the effect of hyperbaric oxygen on the healing of chronic venous ulcers. They treated 17 patients at 2.5 atmospheres of absolute pressure (ATA) once a day in a one-person chamber until maximal benefit was achieved. In their series, 65 percent of the ulcers either healed completely or showed marked improvement. In 1970, Bass[2] published similar results using 19 patients. They were treated at 2.0 ATA for 5 days a week. The number of treatments per patient ranged from 16 to 200, with a mean of 60.7. The wounds of 17 patients (89 percent) healed completely. In 1967, Perrins[3] showed a significantly increased surviving area of split thickness skin grafts as an effect of hyperbaric oxygen therapy in a randomized open study.

Kivisaari and Niinikoski[4] concluded, in controlled studies on rats, that hyperbaric oxygen had no effect on the healing rate of full thickness wounds in which the circulation was intact. In devascularized wounds, however, the retarded healing rate approached that of normal healing when hyperbaric oxygen was used.

In 1990, Oriani et al.[5] found a significant decline in amputation rates for diabetic gangrene in the hyperbaric oxygen group (5 percent versus 33 percent) in an open study.

In a search of the literature, no controlled study has been found regarding the effects of hyperbaric oxygen on chronic wound healing, although Marx[6] showed an ingrowth of new capillaries in radiation damaged tissue during 4 to 6 weeks of hyperbaric oxygen treatment, which made these tissues capable of healing a newly opened surgical wound.

The rationale for the use of hyperbaric oxygen is improved healing by elevating tissue oxygen tension intermittently within the wound, resulting in increased collagen forma-

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tion, enhanced fibroblast replication, and improved leukocyte function.[7,8]

Materials and Methods

Patients

Sixteen patients with leg ulcers of more than 1 year's duration were included (nine males and seven females, aged 42 to 75 years, median age 67 years). All patients gave informed consent to take part in the double-blind study as outpatients. The study was accepted by the Ethical Committee of the University of Lund.

Entrance Criteria

The distal blood pressure at the ankle and the first digit had to be within normal ranges (≥100 percent and ≥70 percent, respectively, of the upper arm blood pressure in mmHg) as measured by ultrasound Doppler and blood pressure tourniquet. All patients continued their treatment (elastic stockings, etc.) prescribed by their personal physician and nurse throughout the study.

Exclusion Criteria

Patients with a smoking habit or concomitant chronic conditions (e.g., diabetes mellitus, collagen disease) were not accepted. The ulcers studied were not to have shown any tendency to heal (by visual inspection) during the 2 months before the study.

Methods

A multiplace pressure chamber was used with a double mask breathing system (Scott Masks). Either air or oxygen was used. The gas supply was blinded for all persons involved. The patients were put in two categories according to age and then randomly assigned to two groups with the patients breathing either oxygen or air at 2.5 ATA for 90 minutes 5 days per week for a total of 30 treatments (week 0 to week 6).

Evaluation

The wound area was copied onto transparent film covering the wounds first at 2 weeks before hyperbaric treatment, again when treatment was initiated (week 0), and at 2, 4, 6, and 18 weeks later. The wound area was read into a 386 computer by using a scanning device, and the wound area was then measured by using a specially made program (SAREA®). The calculations were not done until after completion of the study.

Statistics

Because two independent groups were used in the trial, the Mann-Whitney U test, table J, was used, and only the two-tailed results were examined.

Results

All patients went through the 30 treatments. No patient was hospitalized and no patient withdrew.

There were eight patients in each group. The median age in the group treated with oxygen was 71 years (range 75 to 45); in the group treated with air, the median age was 63 years (range 74 to 42). There were five males and three females in the oxygen group and three males and five females in the air group. Only one wound from each patient was included in the measurements (Table I).

The mean decrease of the wound areas at weeks 2, 4, and 6 in the oxygen group were 6.6 percent (SD ± 14), 22 percent (SD ± 13), and 35.7 percent (SD ± 17), respectively, and in the air group, 2.8 percent (SD ± 11), 3.7 percent (SD ± 11), and 2.7 percent (SD ± 11), respectively, giving a p value less than 0.05 at week 4, and a p value less than 0.001 at week 6 between the groups (Table II, Fig. 1).

TABLE I

Wound Area Matching Wounds*

	Patients							
	1	2	3	4	5	6	7	8
Week 0								
Air	221	268	437	500	528	1620	1864	1969
Oxygen	209	366	460	563	585	1587	1624	3070
Week 6								
Air	223	281	370	419	492	1696	1697	2273
Oxygen	77	135	321	433	418	1143	1164	2420

* Values expressed as millimeters squared.

TABLE II
Wound Area (X̄) Expressed in Percentages

	Week −2	Week 0	Week 2	Week 4	Week 6
Air	101	100	97	96	97.3
Oxygen	99.3	100	93.4	78.2	64.3
	NS	NS	NS	$p < 0.05$	$p < 0.001$

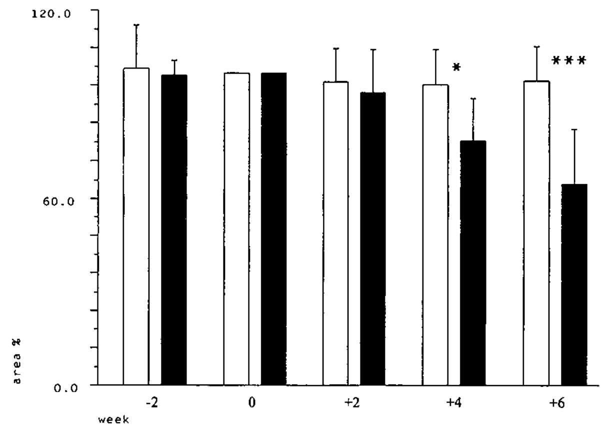

FIG. 1. Wound area (mean ± SD) expressed in percentages. * $p < 0.05$ at week 4, *** $p < 0.001$ at week 6, using the Mann-Whitney U test. □, air group; ■, oxygen group.

DISCUSSION

Hyperbaric oxygen treatment, given for 90 minutes per day at 250 kPa (2.5 ATA) for 5 days a week, had a significant effect on wound healing in the leg ulcers studied. There was a gradual response during the 6 weeks of chamber treatment, with the changes being significant from week 4.

Hunt[8] explained the role of oxygen in wound healing. Lactate synthesized by macrophages is the fundamental trigger stimulating fibroblasts to make collagen. Fibroblasts cannot synthesize collagen without a reasonable amount of oxygen, which is required for the post-translational processing of collagen necessary for its cross-linking space. There is a delicate balance of vessel growth and collagen deposition that is easily upset when host circulatory and nutritional support fail. Because macrophages release lactate, even while well oxygenated, some stimulus to collagen synthesis remains even during hyperoxygenation.

Oxygen breathing causes vasoconstriction and a flow reduction, as shown by Bird and Telfer.[9] They found a 20 percent flow reduction in limb circulation in humans during oxygen breathing but suggested that this vasoconstriction is well compensated for because of the increased amount of oxygen dissolved and transported in the plasma. Lindblom et al.[10] studied the influence of oxygen on perfused capillary density and capillary red cell velocity in rabbit skeletal muscle. They showed that closure of normal capillaries is probably related to the level of oxygen. Whether injured capillaries react in a similar way is unknown, although data from the research done by Perrins[3] suggest a positive effect of hyperbaric oxygen on the survival of split thickness skin grafts.

In a human study, Dooley and Mehm[11] found that hyperbaric oxygen at 2.0 and 3.0 ATA results in an increase in peripheral tissue O_2-delivery, despite vasoconstrictive reductions in peripheral (calf) blood flow.

Using a laser Doppler flowmeter, Hammarlund et al.[12] studied the effects of oxygen breathing on the dermal circulation in healthy volunteers. They found a dose-dependent vasoconstriction in skin in response to oxygen breathing. In a separate experiment, a patient with a chronic venous leg ulcer was tested. He responded to oxygen breathing with the expected vasoconstriction on the fingertip, but flow in the diseased skin near the ulcer remained unchanged. After successful treatment, the dermal vascular response to hyperoxia was normalized in the lower limb. The authors suggested that the dermal flow reduction observed in healthy volunteers is not a general reaction but rather a physiologic response to hyperoxia. Presence of the reaction might thus indicate that the inhaled oxygen has reached the tissues and caused hyperoxia.

Tensile strength of wounds, collagen deposition, and the rate of closure of a dead space are affected by the amount of available oxygen. The decrement due to hypoxia is significant, and so is the increment above normal with clinically obtainable hyperoxia. The increment relates to faster rather than excessive healing. This may seem paradoxical unless one accepts that hypoxic macrophages impel repair. When hypoxia is no longer a feature of the central dead space, healing stops and thus is not allowed to become excessive. Because angiogenesis is accelerated when extra oxygen is supplied by the circulation, healing is completed sooner.[8]

Giving the control group hyperbaric air meant that they were breathing 0.53 ATA oxygen when in the chamber; this was acceptable for the study in order to avoid the risk of the decompression sickness that would have arisen if a nitrox mixture containing 0.21 ATA oxygen had been used. If the rise in oxygen partial pressure affected the wound healing, it would likely be in the same manner as in the oxygen group, with the differences shown between the two groups consequently smaller. There were no significant changes in wound areas in the control group, although minor changes were seen in some wounds (Table I).

Breathing in a closed mask system during hyperbaric treatment required more effort, despite well-functioning masks. However, using the laser Doppler technique, we have previously shown (unpublished data) the dermal microcirculation to be unaffected by breathing in the masks; i.e., there is no evidence of significant carbon dioxide retention due to breathing in the double masks.

Although five patients left the study at week 18 (three patients in the control group and two in the oxygen group), the remaining data indicate a continuing effect on wound healing after the hyperbaric treatment had ceased after week 6 (Table III), except in the largest wound, whose area returned to the initial value. During the period between week 6 and 18, two wounds healed that had initially measured less than 400 mm^2; in addition, a wound that had measured 460 mm^2 initially showed continued healing. In the control group, one wound started to heal after 6 weeks of hyperbaric treatment.

Study Design

Patients. In light of the results published by Slack[1] and Bass,[2] we decided that eight patients in each double-blind group (oxygen or air) would be sufficient to show significant changes in wound healing.

Besides the exclusion of a smoking habit, diabetes mellitus, or a large vessel disease, we assumed that extreme age might be an important factor. When looking at the age distribution of patients with chronic, nondiabetic leg ulcers seen at the department of surgery, Helsingborg Hospital, we found 12 patients with ranging from 45 to 81 years of age. Because of the age distribution, we decided to randomize to age <50 years or >50 but <75 years. The randomization made the two groups similar in age distribution. (One patient was younger than 50 years of age in each group, and the rest of the patients were between 50 and 75 years of age.)

Technical Arrangements. In the chamber room we had arranged two extra gas pipes to penetrate the chamber wall. These pipes were connected to the double mask systems inside the chamber, one marked "gold-gas" and the other marked "silver-gas." The gas supplies were blinded for all, except for a technician, who connected the gas pipes to the ordinary gas supply on the basis of a coin toss. A reduction valve reducing the air pressure to exactly match the oxygen pressure (4.5 bar) had to be included above the ceiling. Because of the double penetrations through the chamber wall we were able to treat "silver-gas" patients and "gold-gas" patients at the same time.

Procedures. We made up 16 envelopes containing instructions to put a patient on either "gold-gas" or "silver-gas" treatment. For two envelopes, marked "<50," we put an instruction of "gold-gas" in one and "silver-gas" in the other. In the remaining 14 envelopes, seven contained instructions for "gold-gas" and seven for "silver-gas." As patients entered the study, an envelope was drawn according to the two age groups and the patient was placed on the coded gas supply given by the instruction.

Entrance Rate. From the start, five patients were accepted after having met the inclusion criteria, and thereafter, two to three patients a year entered the study. Only patients living in Helsingborg who were being regularly treated at the department of surgery, the department of dermatology, or by general practitioners were included.

Conclusion

This double-blind study has shown a significant effect on the wound healing of nonatherosclerotic, nondiabetic chronic leg ulcers. The results indicate that hyperbaric oxygen

TABLE III

Wound Area Matching Wounds in Week 18*

	Patient							
	1	2	3	4	5	6	7	8
Air	292	–	–	42	309	1315	1652	–
Oxygen	0	0	–	103	–	816	1120	3027

* Values expressed as millimeters squared.

therapy might be used as a valuable adjunct to traditional therapy, including the grafting of leg ulcers, when conventional therapies have failed.

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Subject: Discussions with Dr Hammerlund
Date: Monday, 5 November 2012 23:32:27 AET
From: Hyperbaric Health - Dr Glen Hawkins
To: richard.bartlett@health.gov.au
CC: Tim Snowden - Hyperbaric Health

Dear Richard.

I have been in correspondence with Dr Christer Hammarlund (lead author of the RCT) over the weekend and he seems to believe that the paper (which was done as a confirmation paper to two other studies) was highly positive towards HBOT and can't work out why it has been interpreted any other way. He concedes that the 18 week data (which he intended to show the ongoing process of healing) confused the issue as it wasn't statistically analysed but the trend remained. That would place the interpretation in the same way that we discussed that its a positive paper for HBOT and should be interpreted as such from the author. That would imply that the only RCT is in favour of HBOT. Would this be considered as new information considering that the MSAC committee has used a completely different interpretation than the lead author?

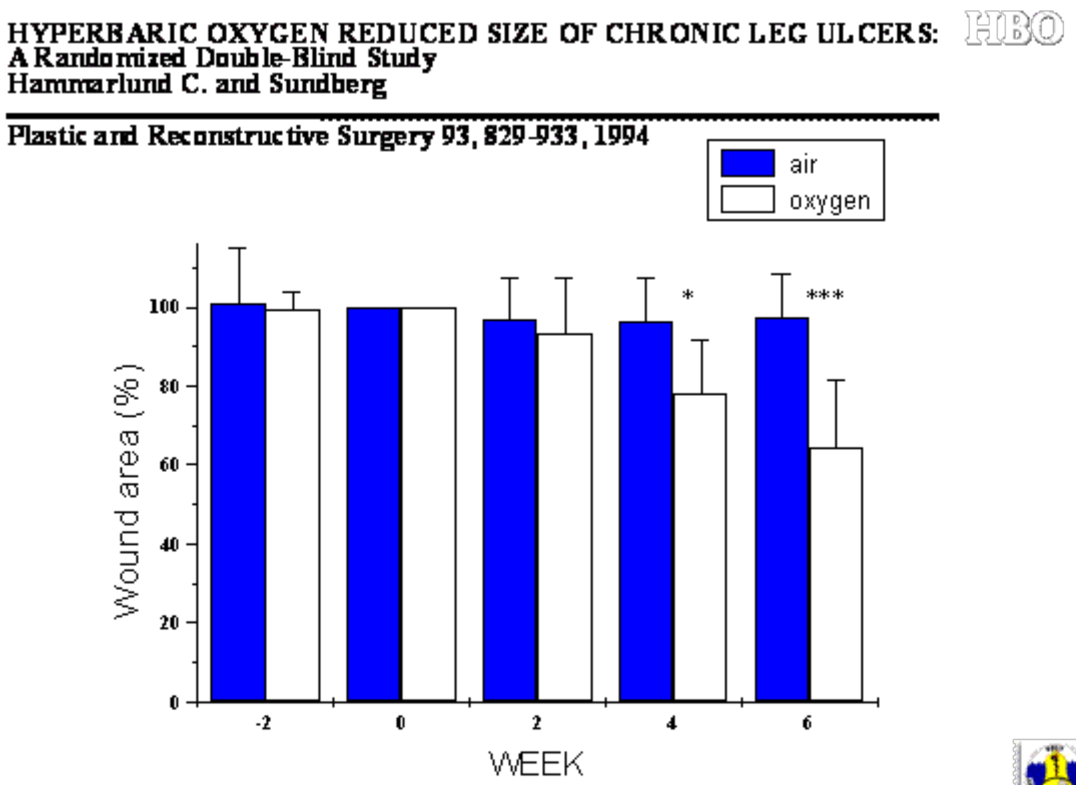
Regards Glen

FROM Christer Hammarlund.

Dear Dr Glen Hawkins

What you find enclosed below is a slide and my introduction during a European conference regarding wound healing in 2006.
I hope this information will help you.

The RCT from 1994 intended to answer if HBO could improve chronic wound healing – and it did!
- as you can see in the slide



Here I give you my introductory comments made during the conference:

Conference on oxygen and tissue repair
27-28 October 2006
Ravenna Italy

My talk had the title:
Role of HBO in the management of limb ulcer

1 2 3	INTRODUCTION Mister chairman, honoured colleagues! Mainly I intend to discuss my paper regarding the effect of HBO on chronic leg ulcers in otherwise healthy patients. I will also try to explain the basic mechanisms "why HBO works" in chronic and hypoxic wounds. This study was done because in 1983 I did not find any randomized controlled double blind study in the literature. As TK Hunt commented the study as a referee: this study has long been overdue.
4	30 HBO sessions in 6 weeks caused significant reduction of the wounds at week 4, and at week 6 in this randomized double-blind study (1).
	STUDY DESIGN The study was not designed to achieve healing of ulcers, just to confirm the effect of hyperbaric oxygenation in a chronic wound model. An earlier and open study by Bass (2) had shown that to heal 89 percent of similar wounds, the number of treatments ranged from 16 and up to 200 treatments, with a mean of 61. We used 30 treatments (90 minutes at 2.5ATA five days a week) in our study because of practical (and economical) reasons.
    5	TYPE OF PATIENTS In light of the results published by Bass we decided that eight persons in each double blinded group (air or oxygen) would be sufficient to show significant changes in wound areas. Thus sixteen, otherwise healthy patients, with chronic leg ulcers with a duration of more than 1 year were included. Patients with a smoking habit or concomitant chronic condition were excluded. The patients had no signs of large vessel disease in order to exclude arterial perfusion disturbances as a factor in the pathogenesis of the chronic wound. This was confirmed by measuring the distal blood pressure at the ankle and the first digit to be within normal limits - That leaves the pathology of the wounds mainly to consist of venous insufficiency.
 6	RANDOMIZATION Because age itself might be a factor in problem wound healing we made the two groups similar in age distribution by randomize to age less than50 years or over50 but not over75 years. -

7	DOUBLE BLIND DESIGN The blinding of the treatment was arranged by two extra gas pipes to penetrate the chamber wall and were connected to the double mask system inside the chamber as "gold gas" and "silver-gas". These gas supplies were blinded to all but a technician, who connected the gas pipes to the ordinary gas supply above the ceiling on the basis of a coin toss. A reduction valve had to be inserted to reduce the air pressure to exactly match the oxygen pressure. As patients entered the study an envelope was drawn according to the two age groups and placed on the coded gas supply given by the instruction.
	WOUND MEASUREMENTS The patient's ordinary doctor and nurse were contracted to copy the wound area onto transparent film covering the wounds. This was done 2 weeks before the start of the hyperbaric treatment and 2, 4, 6 and 18 weeks later. The wound areas were then scanned into a computer. No calculations were made until after completion of the study. A specially made program that counted pixels was used to measure the wound areas.
	RESULTS IN DETAIL In the oxygen group there was an overall reduction in wound area after 30 HBO-treatments of 36% compared with 3% in the control group. Being carefully selected and otherwise healthy patients it is tempting to look at the matching wound areas. Just looking at the smaller wounds (up to 366 mm^2) the effect of HBO was a reduction of 63% because of 30 hyperbaric tretments. At follow up 3 months later these wounds had completely healed The larger wound areas showed less, but nonetheless significant effect with a reduction of 21-30%. Remember that a reduction in wound area of 10 to 15 percent a week represents normal healing as Attinger and coworkers stated this year, and this is how the smallest wounds reacted. Regarding the small number of treatments it is not a surprise that the larger wounds -did not heal.

Looking forward to your comments

Best regards
Christer Hammarlund

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Dear Glen!

The study was **not** designed to achieve healing of ulcers, just to **confirm** the effect of hyperbaric oxygenation in a chronic wound model. All our patients just got 30 treatments !!

- Of course you can not do statistics at the follow up – and that was never my intention either

Remember that in 1983 there were no controlled studies at all showing benefit of HBO on chronic wound healing.
Our study just confirmed the results of former open studies (Slack 1966, Bass 1970) – i.e. "they did not lie about their results".
The open study by Bass in 1970 had shown that to heal 89 percent of similar wounds, the number of treatments ranged from 16 and up to 200 treatments, with a mean of 61.

Thus: to heal small wounds demands less (effort) and larger wounds demands more effort to heal.
Nothing strange to that.
That is my comment to the follow-up at 18 weeks.
It might have been better I never had the follow-up. It seems to confuse people…

Keep up your work
Regards
Chris

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Från: Dr. Glen Hawkins - Hyperbaric Health [mailto:glen@hyperbarichealth.com]
Skickat: den 12 oktober 2012 09:24
Till: Hammarlund Christer
Kopia: Mike Bennett
Ämne: Re: SV: Some advice about your 1994 RCT

Thank you for your very rapid reply Dr Hammarlund,

That's the interpretation I had that the wound significantly improved much more in the HBOT group (to be that highly significant in only 8 persons per arm shows a large effect as far as I can see).

The main issue they have is the 18 week data where they say there is no difference between the groups.

My interpretation of the paper is that you could't perform the statistical analysis due to drop out but the effect continued. Would that be a correct interpretation or was a significance value generated at 18 weeks?

As stated they are interpreting the effect as being present at 6 weeks but no difference at 18 weeks (and therefore subsequently). Any suggestions as to the interpretation of that point?

Regards Glen

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hyperbarichealth

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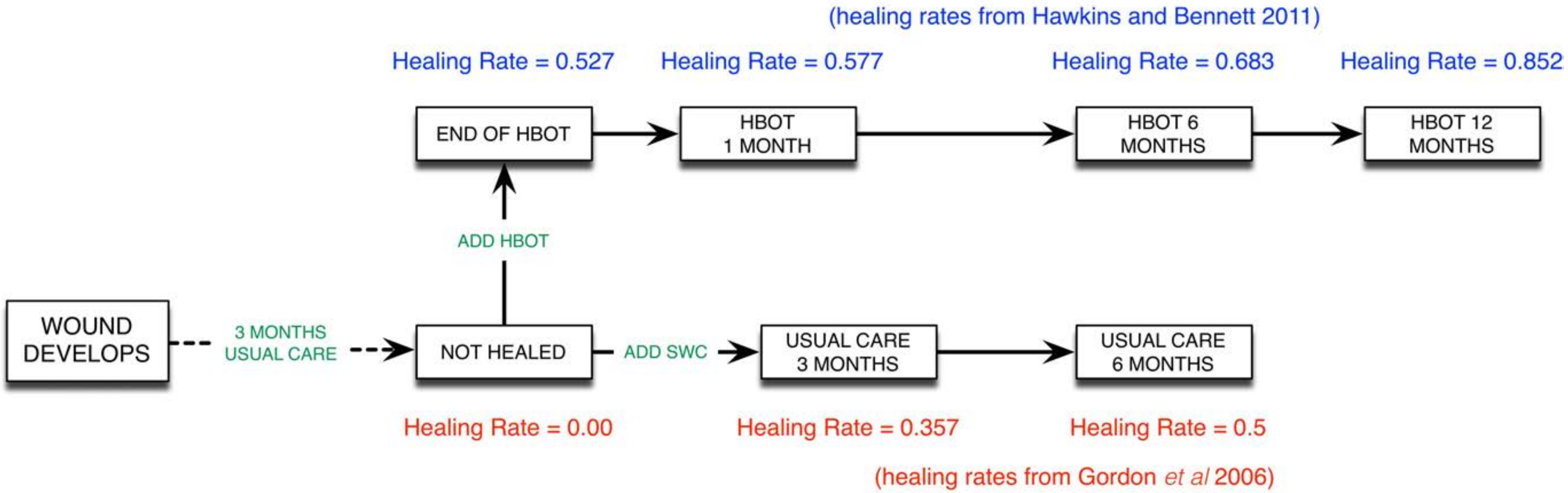
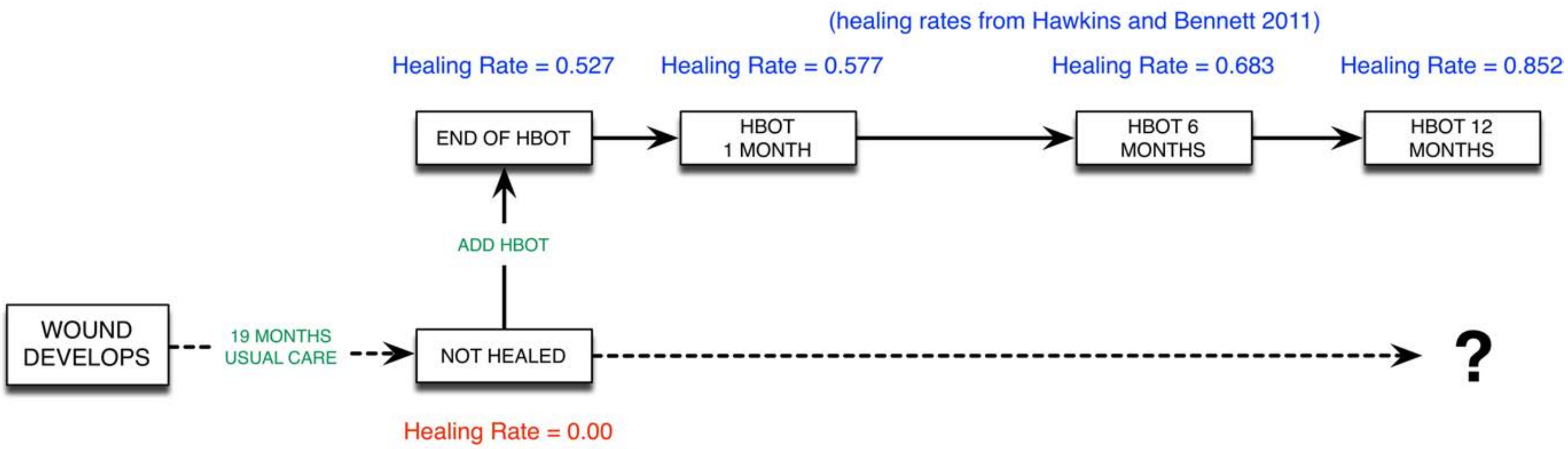
CLINICAL PATHWAY FOR NON-DIABETIC CHRONIC HYPOXIC WOUNDS IN HAWKINS AND BENNETT 2011



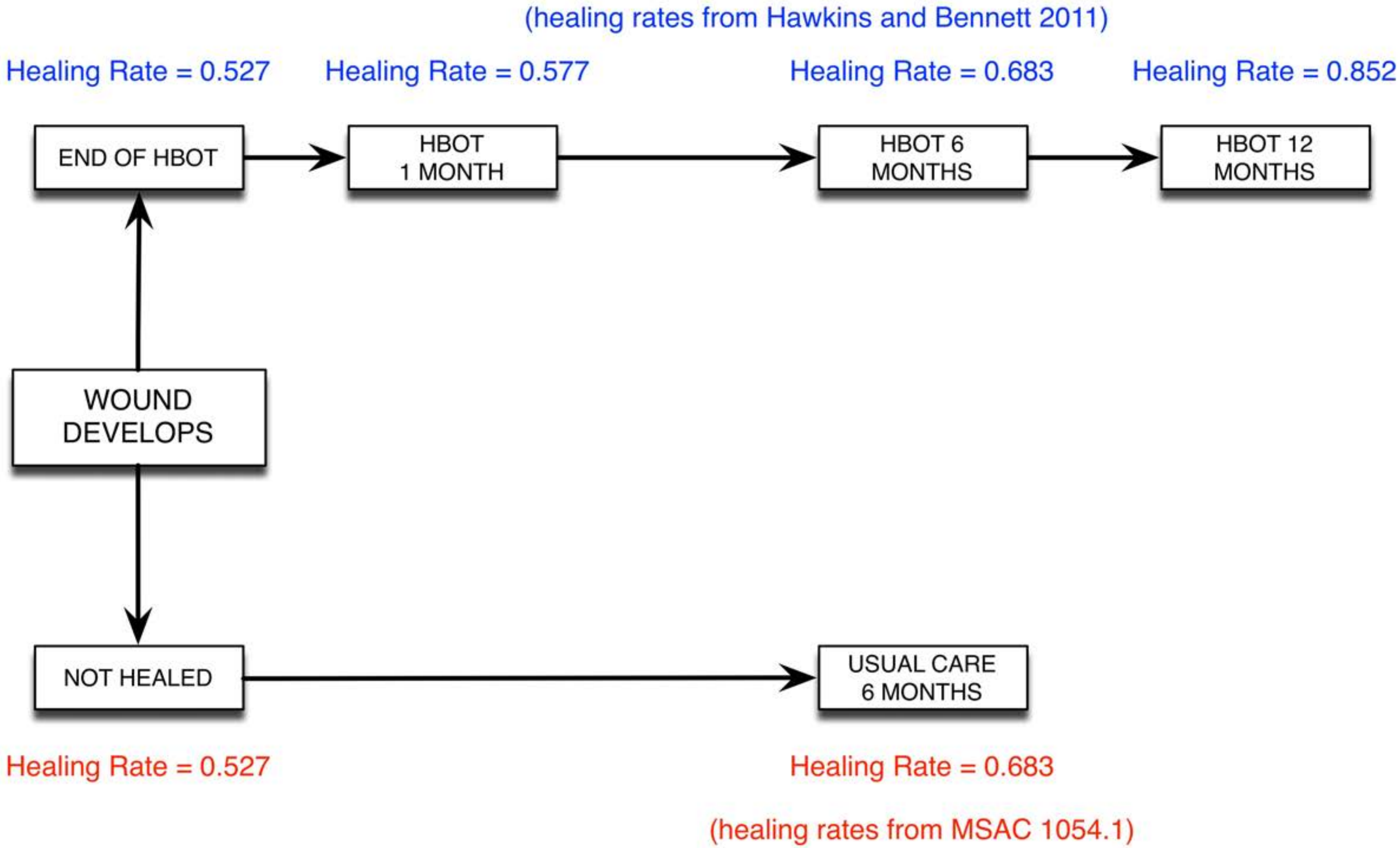
HBOT = HYPERBARIC OXYGEN THERAPY
SWC = SPECIALISED WOUND CARE

ACTUAL PATHWAY FOR NON-DIABETIC CHRONIC HYPOXIC WOUNDS IN HAWKINS AND BENNETT 2011



HBOT = HYPERBARIC OXYGEN THERAPY

CLINICAL PATHWAY FOR ECONOMIC CALCULATIONS MSAC 1054.1



HBOT = HYPERBARIC OXYGEN THERAPY