

APPENDIX 1: Literature Search Strategies

In Dialog®

- de = descriptor, ie. Medical Subject Heading (a controlled vocabulary, or thesaurus term)
- ti = title (i.e. word has to occur in title field of the bibliographic record)
- ab = abstract (i.e. word has to occur in abstract field of bibliographic record)
- ! = explode; picks up narrower terms as well, i.e. terms which are conceptually subsets of a broader term
- F1\$ = a large MeSH category, e.g. Behavior and behavior mechanisms, which is exploded to pick up all terms related to behavior and behavior mechanisms, as defined by the National Library of Medicine, i.e. about 400 MeSH terms
- () = words must be adjacent
- (2n) = words a maximum of two words apart in either direction
- ? = truncation symbol
- dt = publication type
- Set 22: Set 23 = Set 22 OR Set 23

In PubMed

- [MeSH] = Medical Subject Headings (a controlled vocabulary, or thesaurus term)
- [Title/Abstract] = word must appear in title or abstract of record
- [All Fields] = word must appear in any field

DATABASE	LIMITS	KEYWORDS
Dialog® OneSearch® (including MEDLINE® (1966-present) (File 155), TOXFILE, EMBASE® (1974-present), BIOSIS Previews® (1969-present), PASCAL	Human Date: (up to 23 June 2005	Economic Search: <ol style="list-style-type: none"> 1. s Hyperbaric Oxygenation/de from 155, 156 2. s Oxygen therapy!/de from 73 3. s Hyperbaric oxygen therapy/de OR Hyperbaric oxygen/de OR Oxygen therapy/de from 5, 144 4. s hyperbaric oxygenotherapy/de OR hyperbaric oxygen/de OR hyperbaric chamber/de from 144 5. s hyperbaric(1n)oxygen?/ti,ab OR HBOT/ti,ab OR HBO2T/ti,ab OR (high())pressure(1n)(oxygen? OR 02)/ti,ab OR hyperbaric(1n)chamber?/ti,ab 6. s s1:s5 7. s Wound healing/de OR Wounds and Injuries!/de OR Skin Ulcer/de OR Ulcer/de from 155, 156 8. s Skin injury!/de OR Wound!/de OR Wound healing!/de OR Wound infection/de OR Wound care!/de from 73 9. s Foot ulcer/de OR Foot ulcer/de OR Skin abscess/de OR Skin ulcer!/de OR Ulcer/de OR Ulcer healing/de from 73 10. s Skin infection/de OR Skin lesion/de OR Skin ulcer/de OR Skin wound/de OR wound/de OR wound healing/de OR wound infection/de OR wound repair/de from 5 11. s Foot ulcer/de OR Foot ulcer/de OR Ulcer/de OR Ulcer healing/de OR Ulceration/de from 5 12. s Wound/de OR Wound healing/de OR Ulcer/de OR Foot ulcer/de OR Foot ulcers/de from 144 13. s wound?/ti,ab OR ulcer/ti,ab OR ulcers/ti,ab OR ulceration?/ti,ab

		<p>14. s s7:s13</p> <p>15. s Diabetes Mellitus!/de OR Diabetes Insipidus!/de from 155, 156, 73</p> <p>16. s Diabetes/de OR Diabetes Insipidus/de OR Diabetes Mellitus/de OR non-insulin-dependent diabetes mellitus/de OR insulin-dependent diabetes/de OR insulin-dependent diabetes mellitus/de OR type 1 diabetes/de OR type 2 diabetes/de OR type 1 diabetes mellitus/de OR type 2 diabetes mellitus/de Or maturity-onset diabetes of the young/de from 5</p> <p>17. s diabetes/de OR insulin dependent diabetes/de OR non insulin dependent diabetes/de OR type 2 diabetes/de OR type 1 diabetes/de from 144</p> <p>18. s diabetes/ti,ab OR diabetic?/ti,ab OR MODY/ti,ab OR IDDM/ti,ab OR NIDDM/ti,ab</p> <p>19. s s15:s18</p> <p>20. s s14 AND s19</p> <p>21. s Diabetic Foot/de from 155, 156, 73, 5</p> <p>22. s Diabetic Foot Ulcer/de from 5</p> <p>23. s diabetic(1n)foot/ti,ab OR diabetic(1n)ulcer?/ti,ab OR diabetic(1n)foot?/ti,ab</p> <p>24. s s21:s23</p> <p>25. s s20 OR s24</p> <p>26. s Budget/de OR Cost/de OR Cost Analysis/de OR Costs and Cost Analysis!/de OR Cost Effectiveness/de OR Cost Savings/de OR Cost Benefit Analysis/de OR Costs/de</p> <p>27. s cost efficiency analysis/de OR cost estimation/de OR cost lowering/de OR cost minimization/de OR cost price/de OR cost savings/de OR cost utility analysis/de from 144</p> <p>28. s Economic Analysis/de OR Economic Aspect!/de OR Economic Factors/de OR Economic Impact/de</p> <p>29. s economic importance/de OR economic information/de OR economic market/de OR economic model/de OR economic policy/de OR economic study/de OR health economics/de OR health economy/de OR medical cost/de from 144</p> <p>30. s Economic Value of Life/de OR Economic Value/de OR Economics/de OR Economics!/de</p> <p>31. s Health Care Cost/de OR Health Care Utilization/de OR Hospital Costs/de</p> <p>32. s Medical Costs/de OR Models, Economic!/de OR Patient Satisfaction/de OR Pharmacoeconomics/de OR Quality Adjusted Life Year/de</p> <p>33. s Quality adjusted Life Years/de OR Quality of Life/de OR Quality of Life!/de OR Value(2n)Life/de</p> <p>34. s afford?/ti,ab OR budget?/ti,ab OR cost/ti,ab OR costs/ti,ab OR costly/ti,ab OR costing/ti,ab OR costed/ti,ab OR cost()analy?/ti,ab OR cost()benefit?/ti,ab</p> <p>35. s cost()effect?/ti,ab OR cost()efficacy/ti,ab OR cost()utilit?/ti,ab OR discount?/ti,ab OR economic?/ti,ab OR econometric?/ti,ab</p>
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		<p>36. s expenditure?/ti,ab OR pharmacoeconomic?/ti,ab OR price?/ti,ab OR pricing/ti,ab</p> <p>37. s QALY/ti,ab OR QALYS/ti,ab OR QOL/ti,ab OR QOLY/ti,ab OR QOLYs/ti,ab OR quality(adjusted)life(year?/ti,ab</p> <p>38. s quality()”of”(Life/ti,ab OR willingness()”to”(pay/ti,ab OR (value or values OR valuation)(2N)(life OR lives)/ti,ab OR patient()satisfaction/ti,ab</p> <p>39. s s26:s38</p> <p>40. s s6 AND s25 AND s39</p> <p>Non-filtered Search:</p> <p>41. s (s6 AND s25) NOT s40</p>
PubMed	Human Date: (up to 23 June 2005	<p>Results will be imported into temporary Reference Manager database; duplicates are automatically detected by Reference Manager duplicate detection program.</p> <p>Economic Search:</p> <p>1. Hyperbaric Oxygenation[MESH] OR Oxygen/therapeutic use[MeSH Terms] OR hyperbaric oxygen*[title/abstract] OR HBOT[title/abstract] OR HBO2T[title/abstract] OR high pressure oxygen[title/abstract] OR high pressure O2[title/abstract] OR hyperbaric chamber*[title/abstract]</p> <p>2. ((wound healing[MeSH] OR Wounds and Injuries[MeSH] OR Skin Ulcer[MeSH] OR Ulcer[MeSH] OR wound*[title/abstract] OR ulcer[title/abstract] OR ulcers[title/abstract] OR ulceration*[title/abstract]) AND (diabetes mellitus[MeSH] OR diabetes[title/abstract] OR diabetic*[title/abstract] OR MODY[title/abstract] OR IDDM[title/abstract] OR NIDDM[title/abstract])) OR (Diabetic Foot[MeSH] OR diabetic foot[title/abstract] OR diabetic ulcer*[title/abstract] OR diabetic foot*[title/abstract])</p> <p>3. economics[MeSH] OR economic*[Title/Abstract] OR econometric*[Title/Abstract] OR economics[MeSH subheading] OR value of life[MeSH] OR models, Economic[MeSH] OR quality-adjusted life years[MeSH] OR "quality adjusted life years"[Title/Abstract] OR "quality adjusted life year"[Title/Abstract] OR Health Care Economics and Organizations[mesh:noexp]</p> <p>4. price[Title/Abstract] OR prices[Title/Abstract] OR priced[Title/Abstract] OR pricing[Title/Abstract] OR discount[Title/Abstract] OR discounts[Title/Abstract] OR discounting[Title/Abstract] OR discounted[Title/Abstract] OR cost[Title/Abstract] OR costs[Title/Abstract] OR costing[Title/Abstract] OR costly[Title/Abstract] OR costed[Title/Abstract] OR expenditure[Title/Abstract] OR expenditures[Title/Abstract]</p>

		<p>5. Budgets[MeSH] OR budget[Title/Abstract] OR budgets[Title/Abstract] OR budgeting[Title/Abstract] OR affords[Title/Abstract] OR afford[Title/Abstract] OR affordability[Title/Abstract] OR qol[Title/Abstract] OR qaly[Title/Abstract] OR qalys[Title/Abstract] OR qoly[Title/Abstract] OR qolys[Title/Abstract] OR quality adjusted life year*[Title/Abstract]</p> <p>6. pharmacoeconomic*[Title/Abstract] OR willingness to pay[Title/Abstract]</p> <p>7. Quality of Life[MeSH] OR quality of life[Title/Abstract] OR Patient Satisfaction[MeSH] OR patient satisfaction[Title/Abstract]</p> <p>8. Set 1 AND Set 2 AND Set 3:Set 7</p> <p>Non-filtered Search:</p> <p>9. (Set 1 AND Set 2) NOT Set 8</p>
CINAHL	Human Date: (up to 23 June 2005	<p>1. Hyperbaric Oxygenation/de</p> <p>2. Oxygen therapy/de</p> <p>3. hyperbaric(1n)oxygen?/ti,ab OR HBOT/ti,ab OR HBO2T/ti,ab OR (high())pressure(1n)(oxygen? OR O2)/ti,ab OR hyperbaric(1n)chamber?/ti,ab</p> <p>4. Set 1:Set 3</p> <p>5. Wound healing/de OR Wounds and Injuries/de Wound infection/de OR Wound care/de OR Foot ulcer/de OR Foot ulcer/de OR Skin ulcer/de OR Ulcer/de</p> <p>6. wound?/ti,ab OR ulcer/ti,ab OR ulcers/ti,ab OR ulceration?/ti,ab</p> <p>7. Set 5:Set 6</p> <p>8. Diabetes Mellitus!/de</p> <p>9. diabetes/ti,ab OR diabetic?/ti,ab OR MODY/ti,ab OR IDDM/ti,ab OR NIDDM/ti,ab</p> <p>10. Set 8:Set 9</p> <p>11. Set 7 AND s10</p> <p>12. Diabetic Foot/de</p> <p>13. diabetic(1n)foot/ti,ab OR diabetic(1n)ulcer?/ti,ab OR diabetic(1n)foot?/ti,ab</p> <p>14. Set 12:Set 13</p> <p>15. Set 4 AND (Set 11 OR Set 14)</p>
The Cochrane Library via Internet		<p>Same strategy as for PubMed i.e. Medical Subject Headings and textwords, using the syntax and system features specific to The Cochrane Library. Results will be imported into temporary Reference Manager database; duplicates are automatically detected by Reference Manager duplicate detection program.</p>
CADTH HTA Checklist		<p>Includes HTA agencies, near-HTA agencies, trial registries, clinical practice guidelines, etc.-Grey literature search, to determine if other projects planned or ongoing, or if there are reviews in this area which have been produced by agencies.</p>
Internet searching		<p>Google™ search engine and others, as appropriate.</p>
Specialized databases		<p>As appropriate.</p>
Appropriate societies/association websites		<p>For conference abstracts.</p>

APPENDIX 2: Data Collection Form

HBOT Diabetic Ulcer Treatment Studies		
Authors		
Reference journal (language)		
Source of funding		
Statement of conflict of interest		
Study specification		
Study design		
Patient selection criteria		
Patient recruitment methods		
Number of treatments per HBOT patient		
Minutes per treatment; pressure		
Type of HBO chamber		
Standard treatment, non-HBOT		
Length of follow-up		
Patient characteristics		
Age		
Gender		
Previous history of diabetes		
Ulcer severity		
Other		
Patient numbers and outcomes		
	HBOT	non-HBOT
Number eligible or recruited		
Number enrolled		
Number discontinued treatment (reasons)		
Number analyzed		
Minor LEA		
Major LEA		
Wounds healed		
Non-healed at end follow-up		
Ulcer recurrence		
Other		
Hospital stay (days)		
Treatment-related adverse effects		

NR=not reported.

APPENDIX 3: Appraisal of Study Quality

In the approach used, scores are given for study design and for study performance.¹²

Table 1: Scores for study design

Design	Score
large RCT*	5
small RCT	3
prospective, non-randomized comparative	2
retrospective comparative	1

*Large RCTs are defined as those with at least 50 subjects in each arm.

Table 2: Assessment of study performance

Area of Interest	Points to Consider
patient selection	methods of randomization or selection, equivalence of intervention and control groups, dropouts before commencement of intervention
description or specification of the interventions	adequate description of intervention, control groups adequately specified
specification and analysis of study	sample size, statistical methods used, clear specification of outcome measures
patient disposal	length of follow-up, dropouts, compliance failures
outcomes reported	fullness and clarity of reporting, missing results, statistical summary, whether conclusions were consistent with data

Each of the five areas is given a score of 0, 1, or 2, based on the following judgements:

0=relevant information was missing or provided with minimal detail

1=reasonable detail was provided, but there were some significant limitations

2=information was satisfactory, there were no significant limitations.

Judgements take into account what was done (or omitted) in a study, and how the study was reported.

Reviewers independently assigned scores to each study. If there was disagreement on the study design classification, or if individual scores for any performance item differed from each other by more than one, the discrepancies were resolved by consensus.

As some selected studies partly addressed issues that were not considered in this assessment, the evaluation of their quality was based on components that were relevant to the outcomes of interest in the economic analysis.

Based on the combined performance and design scores (possible maximum score is 15, 10 for performance plus five for design) each study was assigned to one of five categories, to give an indication of the reliability of the findings that they reported.

Table 3: Study quality and reliability scores

Overall Quality Score	Reliability	Implications for Decision Makers
11.5 to 15	A	high quality; high degree of confidence in study findings
9.5 to 11.0	B	good quality; some uncertainty regarding the study findings
7.5 to 9.0	C	fair quality; some limitations that should be considered in any implementation of study findings
5.5 to 7.0	D	poor to fair quality; substantial limitations in the study, findings should be used cautiously
5.0	E	poor quality; study findings have unacceptable uncertainty

Quality and reliability scores for the seven studies selected for the assessment are shown in Table 4.

Table 4: Quality and reliability scores for reviewed studies

Study	Quality Score	Reliability Score	Patient Numbers	Weighted Quality Score
Baroni ¹⁵	8.5	C	28	0.78
Doctor ¹¹	6	D	30	0.59
Faglia ¹³	11.0	B	68	2.45
Zamboni ¹⁶	8.5	C	10	0.28
Faglia ¹⁷	7	D	115	2.64
Kalani ¹⁸	9	C	38	1.12
Abidia ¹⁴	10.5	B	16	0.55
Mean	8.6	NA	NA	NA
Total	NA	NA	305	8.4

NA=not applicable.

APPENDIX 4: Wagner Grading System for DFU Classification

- Grade 1: superficial diabetic ulcer
- Grade 2: ulcer extension; involves ligament, tendon, joint capsule, or fascia;
no abscess or osteomyelitis
- Grade 3: deep ulcer with abscess or osteomyelitis
- Grade 4: gangrene to portion of forefoot
- Grade 5: extensive gangrene of foot

Source: Wagner FW. The diabetic foot. *Orthopedics* 1987;10(1):163-72.

APPENDIX 5: HBOT Procedures in Selected Studies

Table 1: Details of HBOT procedures				
Study	Type of HBOT Chamber (monoplace or multiplace)	Treatments per Patient	Minutes per Treatment	Pressure
Baroni ¹⁵	multiplace	34	90	2.8 ATA antibacterial, then 2.5 ATA reparative effect
Doctor ¹¹	monoplace	4	45	3.0 ATA
Faglia ¹³	multiplace	38	90	2.5 ATA
Zamboni ¹⁶	monoplace	30	120	2.0 ATA
Faglia ¹⁷	multiplace	32	90	2.5 ATA for 90 minutes daily; 2.2 to 2.4 ATA for 90 minutes, five days a week
Kalani ¹⁸	monoplace	55 (40 for n=4, 60 for n=13)	90	250 kPa (~15 m H ₂ O)
Abidia ¹⁴	multiplace	30	90	2.4 ATA, five days a week

ATA=one atmosphere absolute.