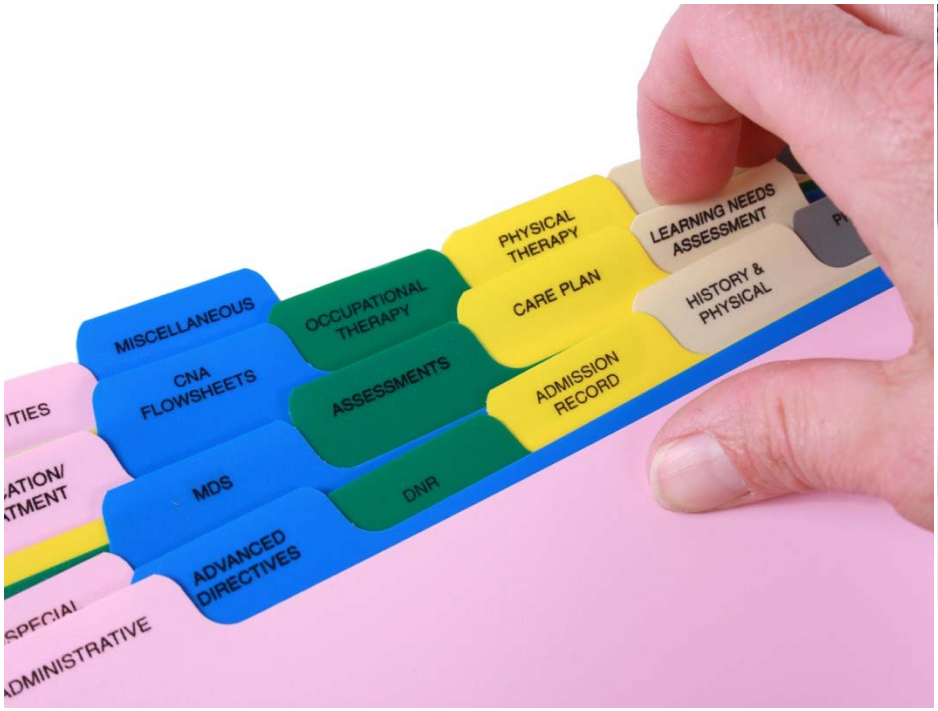
KCE REPORT 203S4

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

A NATIONAL GUIDELINE FOR THE TREATMENT OF PRESSURE ULCERS

APPENDIX VOLUME IV



KCE REPORT 203S4
GOOD CLINICAL PRACTICE

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

A NATIONAL GUIDELINE FOR THE TREATMENT OF PRESSURE ULCERS

APPENDIX VOLUME IV (APPENDICES 6-15)

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COLOPHON

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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
- **Finally, this report has been approved by common assent by the Executive Board.**
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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ABPI	Ankle Brachial Pressure Index
ACA	Available case analysis
ESTR	Electrical stimulation for tissue repair
FDA	Food and Drug Administration
HBOT	Hyperbaric Oxygen Therapy
HP	Health point
HVPC	High voltage pulsed direct current
ICU	Intensive care unit
ITT	Intention-to-treat analysis
LLLT	Low level light therapy
MD	Mean difference
MID	Minimal important difference
MRI	Magnetic resonance imaging
NPUAP	National Pressure Ulcer Advisory Panel
NPWT	Negative pressure wound therapy
NR	Not reported
OR	Odds ratio
PSST	Pressure sore status tool
PU	Pressure ulcer
PUSH	Pressure ulcer scaling for healing
PWAT	Photographic wound assessment tool
RR	Relative risk
SATA	Spatial average temporal average
SD	Standard deviation

SEM	Standard error of the mean
TNPT	Transcutaneous electrical nerve stimulation
UVC	Topical negative pressure therapy
VAC	Ultraviolet C
WAD	Vacuum assisted closure

6. INDICATIONS FOR SURGERY

6.1. Review protocol

Table 1 – Review protocol

Protocol	Indications for surgery
Review question	What are the indications for surgery for the treatment of pressure ulcers?
Population	Individuals of all ages, with at least one pressure ulcer of any category/grade.
Intervention	• Surgery (flap reconstruction)
Comparison	• No surgery
Outcomes	Critical outcomes for decision-making • Time to complete healing (time to event data) • Rate of complete healing • Rate of reduction in size and volume of pressure ulcer • Reduction in size and volume of pressure ulcer • Proportion of patients completely healed within trial period Important outcomes • Wound related pain • Health-related quality of life • Acceptability of treatment (e.g. compliance, tolerance) • Time in hospital • Side effects (treatment related pain, bleeding, healthy tissue damage, surgical complications)
Study design	• High quality systematic reviews of RCTs and/or RCTs only. • Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.

Exclusion	• Studies with another population, intervention, comparison or outcome. • Non-English, non-French, non-Dutch language papers
Search strategy	**The electronic databases to be searched are:** • Medline (OVID interface), Cinahl (EBSCO-interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	**How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews)** • Population – any population will be combined for meta-analysis except combination of children and adults. Must have active pressure ulcers at time of enrolment. • Intervention – any type of systemic antifungal will be combined for meta-analysis.; any type of systemic antibiotic will be combined for meta-analysis. • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – same outcomes will be combined for meta-analysis. • Blinding – Blinded and unblinded studies will be meta-analysed together. • Unit of analysis – patients, individual pressure ulcers • Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum. Use available case analysis for dealing with missing data if there is a 10% differential or higher between the groups or if the missing data is higher than the event rate, if cannot work out the available case analysis will take the author's data.
Analysis	**The following groups will be considered separately if data are present:** • Children and adults (neonates, infants, children); **Subgroups:** The following groups will be considered separately as subgroups if data are present: • Different categories of pressure ulcers (from category 2 upwards where outcomes are reported separately) • Different locations of pressure ulcers: sacral, heel and others
Other terms	
Notes	

6.2. Search strategy

6.2.1. Search filters for RCT's

Table 2 – Search filters Medline (OVID)

Date	29/11/2012	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	1. Pressure ulcer.sh	9 281
	2. decubit*.ti,ab.	4 056
	3. (pressure adj (sore* or ulcer* or damage)).ti,ab.	6 424
	4. (bedsore* or bed-sore*).ti,ab.	522
	5. ((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	678
	6. OR/1 – 5	
	7. reconstructive surgical procedures.sh	14 157
	8. surgical flaps.sh	25 694
	9. skin, artificial.sh	43 373
	10. skin transplantation.sh	1 736
	11. skin surg*.ti,ab	30 364
	12. flap surg*.ti,ab	211
	13. flap reconstruct*.ti,ab	1 213
	14. skin reconstruct*.ti,ab	2 043
	15. skin substitute*.ti,ab	133
	16. apligraf.ti,ab	755
	17. skin graft*.ti,ab	98
	18. skin transplant*.ti,ab	13 264
	19. dermagraft*.ti,ab	1 182
	20. dermatoplasty.ti,ab	55
	21. OR/7 – 20	147
	22. randomized controlled trial.pt.	92 486
	23. controlled clinical trial.pt.	342 800
	24. randomi#ed.ab.	85 716
	25. placebo.ab.	310 460
	26. randomly.ab.	141 976
	27. Clinical Trials as topic.sh	188 807
	28. trial.ti	163 816
	29. OR/22 – 28	111 485
	30. AND/6, 21, 29	841 265

	31. Limit language: 'English, Dutch, Flemish, French'	7 6
Note		

Table 3 – Search filters EMBASE

Date	29/11/2012	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp	13 605
	2. decubit*:ti,ab	5 545
	3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti	7 623
	4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ti,ab	746
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab	829
	6. OR/1 – 5	
	7. 'skin surgery'/exp	18 588
	8. (skin NEAR/1 surg*):ti,ab	75 952
	9. (flap NEAR/1 surg*):ti,ab	657
	10. (flap NEAR/1 reconstruct*):ti,ab	1 391
	11. (skin NEAR/1 reconstruct*):ti,ab	2 454
	12. (skin NEAR/1 substitute*):ti,ab	442
	13. apligraf:ti,ab	947
	14. (skin NEAR/1 graft*):ti,ab	117
	15. (skin NEAR/1 transplant*):ti,ab	16 147
	16. dermagraft*:ti,ab	1 675
	17. dermatoplasty:ti,ab	70
	18. OR/7 – 17	156
	19. 'clinical trial'/exp	82 562
	20. 'clinical trial (topic)'/exp	929 638
	21. random*:ti,ab	50 600
	22. factorial*:ti,ab	770 828
	23. crossover*:ti,ab OR (cross NEXT/1 over*):ti,ab	20 284
	24. ((doubl* or singl*) NEAR/2 blind*):ti,ab	65 147
	25. (assign* or allocat* or volunteer* or placebo*):ti,ab	148 667
	26. 'crossover procedure'/exp	594 032
	27. 'single blind procedure'/exp	34 622
	28. 'double blind procedure'/exp	16 053
	29. OR/19 - 28	110 973

	30. AND/6, 18, 29	1 798 709
	31. Limit language: 'English, Dutch, French' exclude medline	76
		64
Note		

Table 4 – Search filters Cochrane library

Date	29/11/2012	
Database	The Library of the Cochrane Collaboration	
Search Strategy (attention, for PubMed, check « Details »):ti,ab,kw	1. MeSH descriptor "Pressure ulcer" explode all trees	490
	2. Decubit*:ti,ab,kw	353
	3. (pressure near/2 (sore* or ulcer* or damage*)):ti,ab,kw	872
	4. (bedsore* or bed-sore*):ti,ab,kw	34
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur*or lesion*)):ti,ab,kw	64
	6. OR/1 – 5	1209
	7. MeSH descriptor "reconstructive surgical procedures" explode all trees	1561
	8. MeSH descriptor "surgical flaps" explode all trees	
	9. MeSH descriptor "skin, artificial" explode all trees	833
	10. MeSH descriptor "skin transplantation" explode all trees	106
	11. (skin surg*):ti,ab,kw	339
	12. (flap surg*):ti,ab,kw	3 053
	13. (flap reconstruct*):ti,ab,kw	1 491
	14. (skin reconstruct*):ti,ab,kw	250
	15. (skin substitute*):ti,ab,kw	188
	16. (apligraf*):ti,ab,kw	120
	17. (skin graft*):ti,ab,kw	30
	18. (skin transplant*):ti,ab,kw	683
	19. (dermagraft*):ti,ab,kw	582
	20. (dermatoplasty):ti,ab,kw	19
	21. OR/7 – 20	0
	22. "Clinical Trial":pt	6 211
	23. "Randomized Controlled Trial":pt	335 772
	24. MeSH descriptor "clinical trial as topic" explode all trees	316 373
	25. (trial*):ti,ab,kw	51 713
	26. (randomized or randomised):ti,ab,kw	249 993
	27. (randomly):ti,ab,kw	266 659

	28. (group*):ti,ab,kw	86 342
	29. OR/22 – 28	275 267
	30. AND/6, 21, 29	536 015
		51
Note		

Table 5 – Search filters CINAHL

Date	29/11/2012	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	1. MH “Pressure Ulcer”	7 915
	2. Decubit*	495
	3. Pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8 698
	4. Bedsore* OR bed-sore*	160
	5. ((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1 448
	6. OR/1 – 5	
	7. MH "surgical flaps"	10 060
	8. MH “skin transplantation”	2 289
	9. MH “skin, artificial”	1 476
	10. skin n1 surg*	535
	11. flap n1 surg*	1 158
	12. flap n1 reconstruct*	137
	13. skin n1 reconstruct*	266
	14. skin n1 substitute*	35
	15. flap n1 substitute*	163
	16. apligraf	1
	17. skin n1 graft*	52
	18. skin n1 transplant*	938
	19. dermagraft*	1 496
	20. dermatoplasty	33
	21. OR/7 – 19	1
	22. MH "Clinical Trials+"	5 520
	23. “trial*”	110 112
	24. “randomi#ed”	141 368
	25. “randomly”	68 721
	26. “randomized controlled trial”	25 836
	27. PT “randomized controlled trial”	9 412

	28. PT "clinical trial"	12 301
	29. OR/22 - 28	51 982
	30. AND/6, 21, 29	172 918
	31. Limit language='English, Dutch, French' and exclude medline records	30
		12
Note		

6.2.2. Search filters for cohort studies

Table 6 – Search filters Medline (OVID)

Date	29/11/2012	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	1. Pressure ulcer.sh	9 281
	2. decubit*.ti,ab.	4 056
	3. (pressure adj (sore* or ulcer* or damage)).ti,ab.	6 424
	4. (bedsore* or bed-sore*).ti,ab.	522
	5. ((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	678
	6. OR/1 – 5	
	7. reconstructive surgical procedures.sh	14 157
	8. surgical flaps.sh	25 694
	9. skin, artificial.sh	43 373
	10. skin transplantation.sh	1 736
	11. skin surg*.ti,ab	30 364
	12. flap surg*.ti,ab	211
	13. flap reconstruct*.ti,ab	1 213
	14. skin reconstruct*.ti,ab	2 043
	15. skin substitute*.ti,ab	133
	16. apligraf.ti,ab	755
	17. skin graft*.ti,ab	98
	18. skin transplant*.ti,ab	13 264
	19. dermagraft*.ti,ab	1 182
	20. dermatoplasty.ti,ab	55
	21. OR/7 – 20	147
	22. AND/6, 21	92 486
	23. Limit language: 'English, Dutch, Flemish, French'	47
		38

Note		

Table 7 – Search filters EMBASE

Date	29/11/2012	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp 2. decubit*:ti,ab 3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti 4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ti,ab 5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab 6. OR/1 – 5 7. 'skin surgery'/exp 8. (skin NEAR/1 surg*):ti,ab 9. (flap NEAR/1 surg*):ti,ab 10. (flap NEAR/1 reconstruct*):ti,ab 11. (skin NEAR/1 reconstruct*):ti,ab 12. (skin NEAR/1 substitute*):ti,ab 13. apligraf:ti,ab 14. (skin NEAR/1 graft*):ti,ab 15. (skin NEAR/1 transplant*):ti,ab 16. dermagraft*:ti,ab 17. dermatoplasty:ti,ab 18. OR/7 – 17 19. AND/6, 18, 29 20. Limit language: 'English, Dutch, French' exclude medline	13 605 5 545 7 623 746 829 18 588 75 952 657 1 391 2 454 442 947 117 16 147 1 675 70 156 82 562 974 650
Note		

Table 8 – Search filters Cochrane Library

Date	29/11/2012	
Database	The Library of the Cochrane Collaboration	
Search Strategy (attention, for PubMed, check « Details »):ti,ab,kw	1. MeSH descriptor "Pressure ulcer" explode all trees 2. Decubit*:ti,ab,kw 3. (pressure near/2 (sore* or ulcer* or damage*)):ti,ab,kw 4. (bedsore* or bed-sore*):ti,ab,kw 5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur*or lesion*)):ti,ab,kw	490 353 872 34 64

	6. OR/1 – 5 7. MeSH descriptor “reconstructive surgical procedures” explode all trees 8. MeSH descriptor “surgical flaps” explode all trees 9. MeSH descriptor “skin, artificial” explode all trees 10. MeSH descriptor “skin transplantation” explode all trees 11. (skin surg*):ti,ab,kw 12. (flap surg*):ti,ab,kw 13. (flap reconstruct*):ti,ab,kw 14. (skin reconstruct*):ti,ab,kw 15. (skin substitute*):ti,ab,kw 16. (apligraf*):ti,ab,kw 17. (skin graft*):ti,ab,kw 18. (skin transplant*):ti,ab,kw 19. (dermagraft*):ti,ab,kw 20. (dermatoplasty):ti,ab,kw 21. OR/7 – 20 22. AND/6, 21, 29	1209 1561 833 106 339 3 053 1 491 250 188 120 30 683 582 19 0 6 211 57
Note		

Table 9 – Search filters CINAHL

Date	29/11/2012	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	32. MH “Pressure Ulcer” 33. Decubit* 34. Pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage* 35. Bedsore* OR bed-sore* 36. ((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*)) 37. OR/1 – 5 38. MH "surgical flaps" 39. MH “skin transplantation” 40. MH “skin, artificial” 41. skin n1 surg* 42. flap n1 surg* 43. flap n1 reconstruct* 44. skin n1 reconstruct* 45. skin n1 substitute*	7 915 495 8 698 160 1 448 10 060 2 289 1 476 535 1 158 137 266 35

	46. flap n1 substitute* 47. apligraf 48. skin n1 graft* 49. skin n1 transplant* 50. dermagraft* 51. dermatoplasty 52. OR/7 – 19 53. AND/6, 21 54. Limit language='English, Dutch, French' and exclude medline records	163 1 52 938 1 496 33 1 5 520 184 72
Note		

6.2.3. Flow chart

Figure 1 – Flow chart RCT's

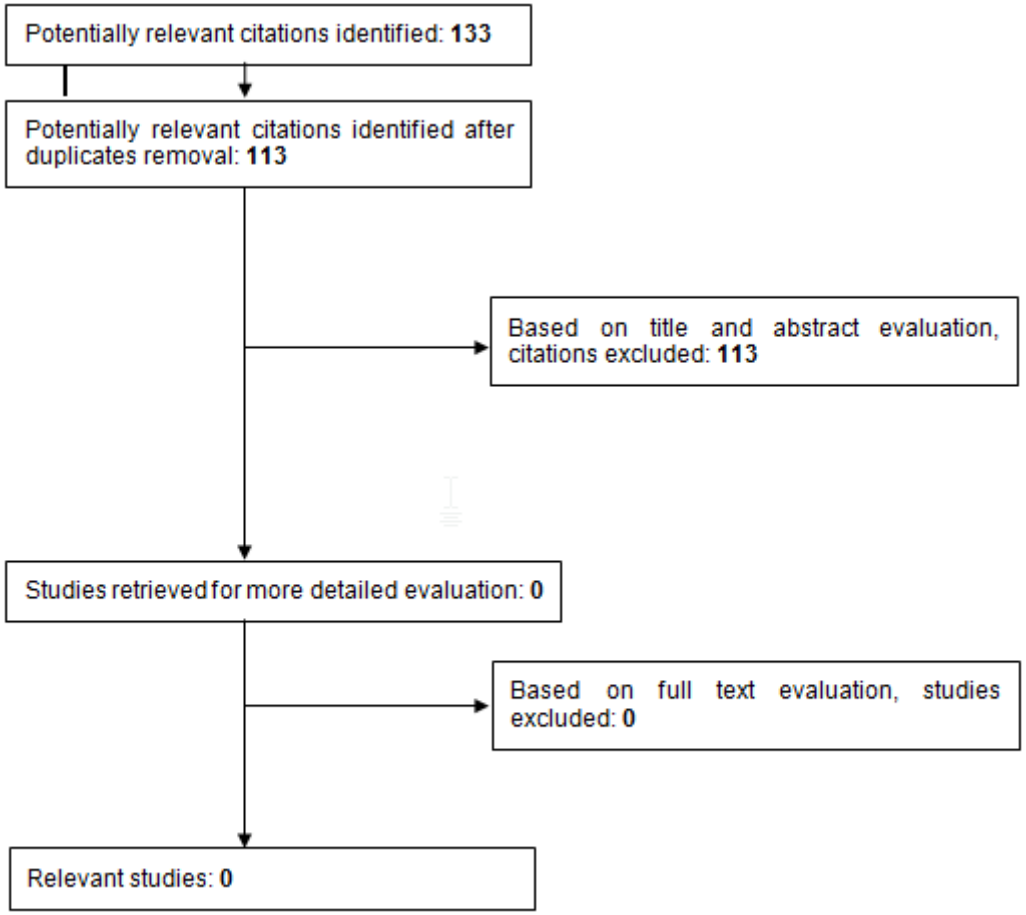
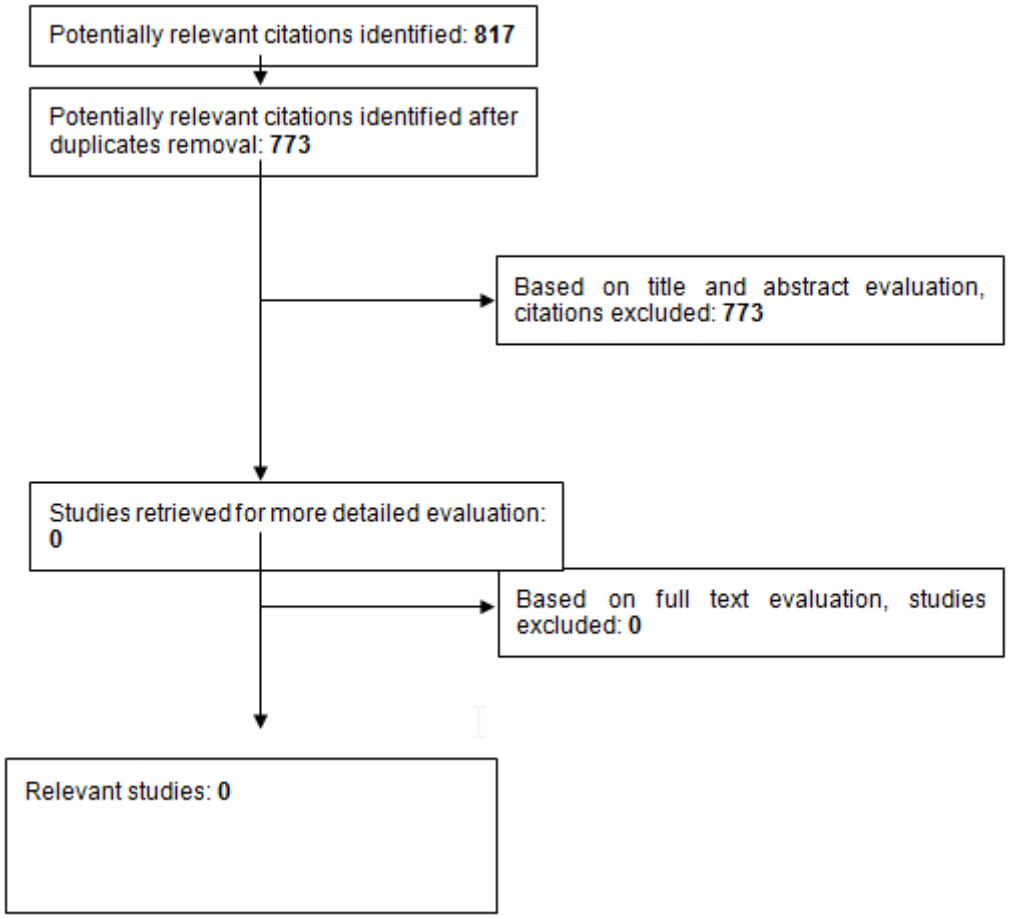


Figure 2 – flow Chart cohort studies



6.2.4. List of excluded studies (RCTs)

Not applicable

6.2.5. List of excluded studies (cohort studies)

Not applicable

6.3. Clinical evidence

The systematic search through multiple electronic databases resulted in 133 records: 6 in Medline (Ovid), 12 in Cinahl (EBSCO interface), 64 in Embase, and 51 in the Library of the Cochrane Collaboration. Duplicate records were excluded, which resulted in 113 records. Based on the screening of title and abstract 113 records were excluded.

Secondly, a systematic search for cohort studies through multiple electronic databases resulted in 817 records: 38 in Medline (Ovid), 72 in Cinahl (EBSCO interface), 650 in Embase, and 57 in the Library of the Cochrane Collaboration. Duplicate records were excluded, which resulted in 773 records. Based on the screening of title and abstract 773 records were excluded.

7. SYSTEMIC AGENTS

7.1. Review protocol

Table 10 – Review protocol

Protocol	Systemic antimicrobials
Review question	What are the most clinically effective systemic agents for the treatment of pressure ulcers?
Population	Individuals of all ages, with at least one pressure ulcer of any category/grade.
Intervention	• Systemic antimicrobials: systemic antibiotics, systemic antifungals.
Comparison	• No systemic antimicrobials • Placebo • Comparison between types of systemic antimicrobials • Other type of therapy for pressure ulcer treatment
Outcomes	**Critical outcomes for decision-making** • Time to complete healing (time to event data) • Rate of healing • Rate of reduction in size and volume of pressure ulcer • Reduction in size and volume of pressure ulcer • Proportion of patients completely healed within trial period **Important outcomes** • Wound related pain • Health-related quality of life • Acceptability of treatment (e.g. compliance, tolerance) • Time in hospital • Side effects (irritation skin, rash, itching, allergic reaction, normal flora disruption, toxicity, treatment related pain)
Study design	• High quality systematic reviews of RCTs and/or RCTs only.

	• Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.
Exclusion	• Studies with another population, intervention, comparison or outcome. • Non-English, non-French, non-Dutch language papers
Search strategy	**The electronic databases to be searched are:** • Medline (OVID interface), Cinahl (EBSCO-interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	**How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews)** • Population – any population will be combined for meta-analysis except combination of children and adults. Must have active pressure ulcers at time of enrolment. • Intervention – any type of systemic antifungal will be combined for meta-analysis.; any type of systemic antibiotic will be combined for meta-analysis. • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – same outcomes will be combined for meta-analysis. • Blinding – Blinded and unblinded studies will be meta-analysed together. • Unit of analysis – patients, individual pressure ulcers • Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum. Use available case analysis for dealing with missing data if there is a 10% differential or higher between the groups or if the missing data is higher than the event rate, if cannot work out the available case analysis will take the author's data.
Analysis	**The following groups will be considered separately if data are present:** • Children and adults (neonates, infants, children); **Subgroups:** The following groups will be considered separately as subgroups if data are present: • Different categories of pressure ulcers (from category 2 upwards where outcomes are reported separately) • Different locations of pressure ulcers: sacral, heel and others

Other terms
Notes

7.2. Search strategy

7.2.1. Search filters for RCT's

Table 11 – Search filters Ovid medline

Date	22/10/2012	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	1. Pressure ulcer.sh	**9 203**
	2. decubit*.ti,ab.	**3 982**
	3. (pressure adj (sore* or ulcer* or damage)).ti,ab.	**6 350**
	4. (bedsore* or bed-sore*).ti,ab.	**508**
	5. ((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	**662**
	6. OR/1 – 5	
	7. anti-bacterial agents.sh	**13976**
	8. antibiotic prophylaxis.sh	**219 140**
	9. anti-infective agents.sh	**7 803**
	10. antifungal agents.sh	**35 831**
	11. penicillins.sh	**39 454**
	12. penicillin*.ti,ab	**33 259**
	13. cephalosporins.sh	**43 096**
	14. cephalosporin*.ti,ab	**16 631**
	15. aminoglycosides.sh	**16 221**
	16. aminoglycoside*.ti,ab	**8 752**
	17. quinolones.sh	**14 070**
	18. quinolone*.ti,ab	**8 032**
	19. clindamycin.sh	**9 644**
	20. clindamycin*.ti,ab	**4 708**
	21. lincosamides.sh	**7 406**
	22. lyncomycin*.ti,ab	**305**
	23. metronidazole.sh	**12**
	24. metronidazole*.ti,ab	**10 343**
	25. trimethoprim.sh	**11 068**

	26. trimethoprim*.ti,ab	**6 037**
	27. trimethoprim-Sulfamethoxazole Combination.sh	**11 841**
	28. (trimethoprim-sulfamethoxazole* or trimethoprim-sulfamethoxazole*).ti,ab	**5 476**
	29. (systemic and (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)).tw	**5 172**
	30. OR/7 – 29	**13 219**
	31. randomized controlled trial.pt.	
	32. controlled clinical trial.pt.	
	33. randomi#ed.ab.	**383 565**
	34. placebo.ab.	**339 721**
	35. randomly.ab.	**85 426**
	36. Clinical Trials as topic.sh	**305 580**
	37. trial.ti	**140 618**
	38. OR/31 – 37	**186 455**
	39. AND/6, 30, 38	**163 072**
	40. Limit language: 'English, Dutch, Flemish, French'	**109 653**
		832 123
		22
		20
Note		

Table 12 – Search filters EMBASE

Date	29/10/2012	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp	**13 535**
	2. decubit*:ti,ab	**5 523**
	3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti	**7 580**
	4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ti,ab	**743**
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab	**825**
	6. OR/1 – 5	
	7. 'antibiotic agent'/exp	**18 491**
	8. 'antiinfective agent'/exp	**913 440**
	9. 'antifungal agent'/exp	**2 034 701**
	10. 'Penicillin g'/exp	**245 527**
	11. Penicillin*:ti,ab	**75 730**

12.	‘cephalosporin’/exp	**51 597**
13.	Cephalosporin*:ti,ab	**17 434**
14.	‘aminoglycoside’/exp	**21 771**
15.	Aminoglycoside*:ti,ab	**10 832**
16.	‘quinoline’/exp	**17 689**
17.	Quinolone*:ti,ab	**2 952**
18.	‘clindamycin’/exp	**13 143**
19.	Clindamycin*:ti,ab	**35 301**
20.	‘lincosamide’/exp	**9 321**
21.	Lyncomycin*:ti,ab	**1 412**
22.	‘metronidazole’/exp	**15**
23.	Metronidazole*:ti,ab	**47 051**
24.	‘trimethoprim’/exp	**14 305**
25.	Trimethoprim*:ti,ab	**21 733**
26.	‘cotrimoxazole’/exp	**14 556**
27.	(Systemic NEAR/1 (antibiotic or anti-biotic or antimicrobial or anti-microbial or antifungal or anti-fungal or antiinfective or anti-infective)): ti,ab	**55 330** **2 599**
28.	OR/7 – 27	
29.	‘clinical trial’/exp	
30.	‘clinical trial (topic)’/exp	**2 048 647**
31.	random*:ti,ab	**926 100**
32.	factorial*:ti,ab	**47 689**
33.	crossover*:ti,ab OR (cross NEXT/1 over*):ti,ab	**764 273**
34.	((doubl* or singl*) NEAR/2 blind*):ti,ab	**20 125**
35.	(assign* or allocat* or volunteer* or placebo*):ti,ab	**64 802**
36.	‘crossover procedure’/exp	**147 910**
37.	‘single blind procedure’/exp	**590 118**
38.	‘double blind procedure’/exp	**34 377**
39.	OR/29-38	**15 931**
40.	AND/6, 28, 39	**110 516**
41.	Limit language: ’English, Dutch, French’ exclude medline	**1 786 470** **253** **189**

Note

Table 13 – Search filters Cochrane Library

Date	23/10/2012	
Database	The Library of the Cochrane Collaboration	
Search Strategy	1. MeSH descriptor "Pressure ulcer" explode all trees	**492**
	2. Decubit*:ti,ab,kw	**353**
	3. (pressure near/2 (sore* or ulcer* or damage*)):ti,ab,kw	**872**
	4. (bedsore* or bed-sore*):ti,ab,kw	**34**
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur*or lesion*)):ti,ab,kw	**63**
	6. OR/1 – 5	
	7. MeSH descriptor "anti-bacterial agents" explode all trees	**1 208**
	8. MeSH descriptor "antibiotic prophylaxis" explode all trees	**8 133**
	9. MeSH descriptor "anti-infective agents" explode all trees	**1 053**
	10. MeSH descriptor "antifungal agents" explode all trees	**20 602**
	11. MeSH descriptor "penicillins" explode all trees	**1 495**
	12. Penicillin*:ti,ab,kw	**4 457**
	13. MeSH descriptor "cephalosporins" explode all trees	**2 862**
	14. Cephalosporin*:ti,ab,kw	**3 629**
	15. MeSH descriptor "aminoclycosides" explode all trees	**1 934**
	16. Aminoclycoside*:ti,ab,kw	**6 334**
	17. MeSH descriptor "quinolines" explode all trees	**0**
	18. Quinolon*:ti,ab,kw	**5 653**
	19. MeSH descriptor "clindamycin" explode all trees	**906**
	20. Clindamycin*:ti,ab,kw	**630**
	21. MeSH descriptor "lincosamides" explode all trees	**1 033**
	22. Lyncomycin*:ti,ab,kw	**667**
	23. MeSH descriptor "metronidazole" explode all trees	**0**
	24. Metronidazole*:ti,ab,kw	**1 603**
	25. MeSH descriptor "trimethoprim" explode all trees	**2 586**
	26. Trimethoprim*:ti,ab,kw	**1 058**
	27. MeSH descriptor "trimethoprim-sulfamethoxazole combination" explode all trees	**1 447**
	28. (trimethoprim-sulfamethoxazole* or trimethoprim sulfamethoxazole*):ti,ab,kw	**651**
	29. Systemic near/1 (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*):ti,ab,kw	**1 178**
	30. OR/7 – 29	
	31. "Clinical Trial":pt	**485**
	32. "Randomized Controlled Trial":pt	

	33. MeSH descriptor “clinical trial as topic” explode all trees	
	34. (trial*):ti,ab,kw	**198 940**
	35. (randomized or randomised):ti,ab,kw	**335 464**
	36. (randomly):ti,ab,kw	**315 781**
	37. (group*):ti,ab,kw	**51 720**
	38. OR/31 – 37	**249 914**
	39. AND/6, 30, 38	**266 474**
		86 236
		274 998
		535 710
		271
Note		

Table 14 – Search filters CINAHL

Date	22/10/2012	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	55. MH “Pressure Ulcer”	**7 825**
	56. Decubit*	**488**
	57. Pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	**8 619**
	58. Bedsore* OR bed-sore*	**158**
	59. ((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	**1 439**
	60. OR/1 – 5	
	61. MH "antibiotics"	**9 969**
	62. Systemic n1 (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)	**15 148**
	63. MH “penicillins”	**388**
	64. Penicillin*	
	65. Cephalosporin*	**896**
	66. Aminoglycoside*	**1 764**
	67. Quinolone*	**1 103**
	68. MH “clindamycin”	**1 001**
	69. Clindamycin*	**401**
	70. Lyncomycin*	**390**
	71. Metronidazole*	**613**
	72. MH “trimethoprim”	**0**

	73. Trimethoprim*	**990**
	74. Trimethoprim-sulfamethoxazole or trimethoprim sulfamethoxazole	**124**
	75. OR/7 – 15	**849**
	76. MH "Clinical Trials+"	**1**
	77. "trial*"	**19 561**
	78. "randomi#ed"	**109 039**
	79. "randomly"	**139 916**
	80. "randomized controlled trial"	**67 808**
	81. PT "randomized controlled trial"	**25 614**
	82. PT "clinical trial"	**9 270**
	83. OR/17 - 23	**11 680**
	84. AND/6, 16, 24	**51 716**
	85. Limit language='English, Dutch, French' and exclude medline records	**171 300**
		8
		1
Note		

7.2.2. Search filters for cohort studies

Table 15 – Search filters Ovid Medline

Date	22/10/2012	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	1. Pressure ulcer.sh	**9 203**
	2. decubit*.ti,ab.	**3 982**
	3. (pressure adj (sore* or ulcer* or damage)).ti,ab.	**6 350**
	4. (bedsore* or bed-sore*).ti,ab.	**508**
	5. ((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	**662**
	6. OR/1 – 5	
	7. anti-bacterial agents.sh	**13976**
	8. antibiotic prophylaxis.sh	**219 140**
	9. anti-infective agents.sh	**7 803**
	10. antifungal agents.sh	**35 831**
	11. penicillins.sh	**39 454**
	12. penicillin*.ti,ab	**33 259**
	13. cephalosporins.sh	**43 096**

	14. cephalosporin*.ti,ab	**16 631**
	15. aminoglycosides.sh	**16 221**
	16. aminoglycoside*.ti,ab	**8 752**
	17. quinolones.sh	**14 070**
	18. quinolone*.ti,ab	**8 032**
	19. clindamycin.sh	**9 644**
	20. clindamycin*.ti,ab	**4 708**
	21. lincosamides.sh	**7 406**
	22. lyncomycin*.ti,ab	**305**
	23. metronidazole.sh	**12**
	24. metronidazole*.ti,ab	**10 343**
	25. trimethoprim.sh	**11 068**
	26. trimethoprim*.ti,ab	**6 037**
	27. trimethoprim-Sulfamethoxazole Combination.sh	**11 841**
	28. (trimethoprim-sulfamethoxazole* or trimethoprim-sulfamethoxazole*).ti,ab	**5 476**
	29. (systemic and (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)).tw	**5 172**
	30. OR/7 – 29	**13 219**
	31. AND/6, 30	
	32. Limit language: 'English, Dutch, Flemish, French'	
		383 565
		308
		255
Note		

Table 16 – Search filters EMBASE

Date	29/10/2012	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp	**13 535**
	2. decubit*:ti,ab	**5 523**
	3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti	**7 580**
	4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ti,ab	**743**
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab	**825**
	6. OR/1 – 5	
	7. 'antibiotic agent'/exp	**18 491**

	8. ‘antiinfective agent’/exp	**913 440**
	9. ‘antifungal agent’/exp	**2 034 701**
	10. ‘Penicillin g’/exp	**245 527**
	11. Penicillin*:ti,ab	**75 730**
	12. ‘cephalosporin’/exp	**51 597**
	13. Cephalosporin*:ti,ab	**17 434**
	14. ‘aminoglycoside’/exp	**21 771**
	15. Aminoglycoside*:ti,ab	**10 832**
	16. ‘quinoline’/exp	**17 689**
	17. Quinolone*:ti,ab	**2 952**
	18. ‘clindamycin’/exp	**13 143**
	19. Clindamycin*:ti,ab	**35 301**
	20. ‘lincosamide’/exp	**9 321**
	21. Lyncomycin*:ti,ab	**1 412**
	22. ‘metronidazole’/exp	**15**
	23. Metronidazole*:ti,ab	**47 051**
	24. ‘trimethoprim’/exp	**14 305**
	25. Trimethoprim*:ti,ab	**21 733**
	26. ‘cotrimoxazole’/exp	**14 556**
	27. (Systemic NEAR/1 (antibiotic or anti-biotic or antimicrobial or anti-microbial or antifungal or anti-fungal or antiinfective or anti-infective)): ti,ab	**55 330** **2 599**
	28. OR/7 – 27	
	29. AND/6, 28	
	30. Limit language: ’English, Dutch, French’ exclude medline	**2 048 647** **1 549** **1 147**
Note		

Table 17 – Search Filters Cochrane Library

Date	23/10/2012	
Database	The Library of the Cochrane Collaboration	
Search Strategy	1. MeSH descriptor “Pressure ulcer” explode all trees	**492**
	2. Decubit*:ti,ab,kw	**353**
	3. (pressure near/2 (sore* or ulcer* or damage*)):ti,ab,kw	**872**
	4. (bedsore* or bed-sore*):ti,ab,kw	**34**

5.	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur*or lesion*)):ti,ab,kw	**63**
6.	OR/1 – 5	
7.	MeSH descriptor “anti-bacterial agents” explode all trees	**1 208**
8.	MeSH descriptor “antibiotic prophylaxis” explode all trees	**8 133**
9.	MeSH descriptor “anti-infective agents” explode all trees	**1 053**
10.	MeSH descriptor “antifungal agents” explode all trees	**20 602**
11.	MeSH descriptor “penicillins” explode all trees	**1 495**
12.	Penicillin*:ti,ab,kw	**4 457**
13.	MeSH descriptor “cephalosporins” explode all trees	**2 862**
14.	Cephalosporin*:ti,ab,kw	**3 629**
15.	MeSH descriptor “aminoclycosides” explode all trees	**1 934**
16.	Aminoclycoside*:ti,ab,kw	**6 334**
17.	MeSH descriptor “quinolines” explode all trees	**0**
18.	Quinolon*:ti,ab,kw	**5 653**
19.	MeSH descriptor “clindamycin” explode all trees	**906**
20.	Clindamycin*:ti,ab,kw	**630**
21.	MeSH descriptor “lincosamides” explode all trees	**1 033**
22.	Lyncomycin*:ti,ab,kw	**667**
23.	MeSH descriptor “metronidazole” explode all trees	**0**
24.	Metronidazole*:ti,ab,kw	**1 603**
25.	MeSH descriptor “trimethoprim” explode all trees	**2 586**
26.	Trimethoprim*:ti,ab,kw	**1 058**
27.	MeSH descriptor “trimethoprim-sulfamethoxazole combination” explode all trees	**1 447**
28.	(trimethoprim-sulfamethoxazole* or trimethoprim sulfamethoxazole*):ti,ab,kw	**651**
29.	Systemic near/1 (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*):ti,ab,kw	**1 178**
30.	OR/7 – 29	**485**
31.	AND/6, 30	**198 940**
		327

Note

Table 18 – Search filters CINAHL

Date	22/10/2012	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	86. MH “Pressure Ulcer”	**7 825**
	87. Decubit*	**488**
	88. Pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	**8 619**
	89. Bedsore* OR bed-sore*	**158**
	90. ((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	**1 439**
	91. OR/1 – 5	
	92. MH "antibiotics"	**9 969**
	93. Systemic n1 (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)	**15 148** **388**
	94. MH “penicillins”	
	95. Penicillin*	
	96. Cephalosporin*	**896**
	97. Aminoglycoside*	**1 764**
	98. Quinolone*	**1 103**
	99. MH “clindamycin”	**1 001**
	100. Clindamycin*	**401**
	101. Lyncomycin*	**390**
	102. Metronidazole*	**613**
	103. MH “trimethoprim”	**0**
	104. Trimethoprim*	**990**
	105. Trimethoprim-sulfamethoxazole or trimethoprim sulfamethoxazole	**124**
	106. OR/7 – 15	**849**
	107. AND/6, 21	**1**
	108. Limit language=’English, Dutch, French’ and exclude medline records	**19 561** **108** **31**
Note		

7.2.3. Search filters for additional search

Table 19 – Search Filters Ovid Medline

Date	21/12/2012	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	1. Pressure ulcer.sh	**9 309**
	2. decubit*.ti,ab.	**4 065**
	3. (pressure adj (sore* or ulcer* or damage)).ti,ab.	**6 454**
	4. (bedsore* or bed-sore*).ti,ab.	**522**
	5. ((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	**680**
	6. OR/1 – 5	
	7. Exp anti-bacterial agents/	**14 200**
	8. Exp antibiotic prophylaxis/	**499 809**
	9. Exp anti-infective agents/	**7 923**
	10. Exp antifungal agents/	**1 204 302**
	11. Exp penicillins/	**137 399**
	12. Exp cephalosporins/	**67 214**
	13. Exp aminoglycosides/	**35 418**
	14. Exp quinolones/	**122 967**
	15. Exp clindamycin/	**33 422**
	16. Exp lincosamides/	**4 738**
	17. Exp metronidazole/	**6 667**
	18. Exp trimethoprim/	**10 425**
	19. Exp trimethoprim-Sulfamethoxazole Combination/	**10 135**
	20. (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*).tw	**5 506** **296 999**
	21. (anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid* or fungicid*).ti,ab	
	22. OR/7 – 21	**31 383**
	23. AND/6, 22	
	24. Limit language: ‘English, Dutch, Flemish, French’	**1 394 442** **711** **568**
Note		

Table 20 – Search filters EMBASE

Date	21/12/2012	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp	**13 660**
	2. decubit*:ti,ab	**5 666**
	3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti	**7 647**
	4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ti,ab	**752**
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab	**835**
	6. OR/1 – 5	
	7. (antibiotic or anti-biotic or antimicrobial or anti-microbial or antifungal or anti-fungal or antiinfective or anti-infective):ti,ab	**18 654**
	8. (anti-mycobacterial or antimycobacterial or bacteriocid or bactericid or fungicid):ti,ab	**276 164**
	9. OR/7 – 8	**3 462**
	10. AND/6, 9	
	11. Limit language: 'English, Dutch, French' exclude medline	**279 090**
		389
		272
Note		

Table 21 – Search filters Cochrane

Date	21/12/2012	
Database	The Library of the Cochrane Collaboration	
Search Strategy	1. MeSH descriptor "Pressure ulcer" explode all trees	**490**
	2. Decubit*:ti,ab,kw	**357**
	3. (pressure near/2 (sore* or ulcer* or damage*)):ti,ab,kw	**879**
	4. (bedsore* or bed-sore*):ti,ab,kw	**34**
	5. ((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur*or lesion*)):ti,ab,kw	**64**
	6. OR/1 – 5	
	7. (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*):ti,ab,kw	**1 220**
	8. (anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid* or fungicid*):ti,ab,kw	**20 041**
	9. OR/7 – 8	
	10. AND/6, 9	**901**

		20 584
		41
Note		

Table 22 – Search filters CINAHL

Date	21/12/2012	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	1. MH “Pressure Ulcer”	**7 928**
	2. Decubit*	**498**
	3. Pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	**8 718**
	4. Bedsore* OR bed-sore*	
	5. ((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	**160**
	6. OR/1 – 5	**1 452**
	7. (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)	**10 086**
	8. (anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid* or fungicid*)	**34 281**
	9. MH "antibiotics+"	
	10. MH “antibiotic prophylaxis+”	**662**
	11. MH “antiinfective agents+”	
	12. MH “antifungal agents+”	**24 731**
	13. MH “penicillins+”	**2472**
	14. MH “cephalosporins+”	**51 735**
	15. MH “aminoglycosides+”	**2 876**
	16. MH “clindamycin+”	**1 948**
	17. MH “metronidazole+”	**1 443**
	18. MH “trimethoprim+”	**4 042**
	19. OR/7 – 18	**393**
	20. AND/6, 19	**739**
	21. Limit language=’English, Dutch, French’ and exclude medline records	**569**
		60 978
		372
		114
Note		

7.2.4. Flow charts

Figure 3 – Flow chart RCTs

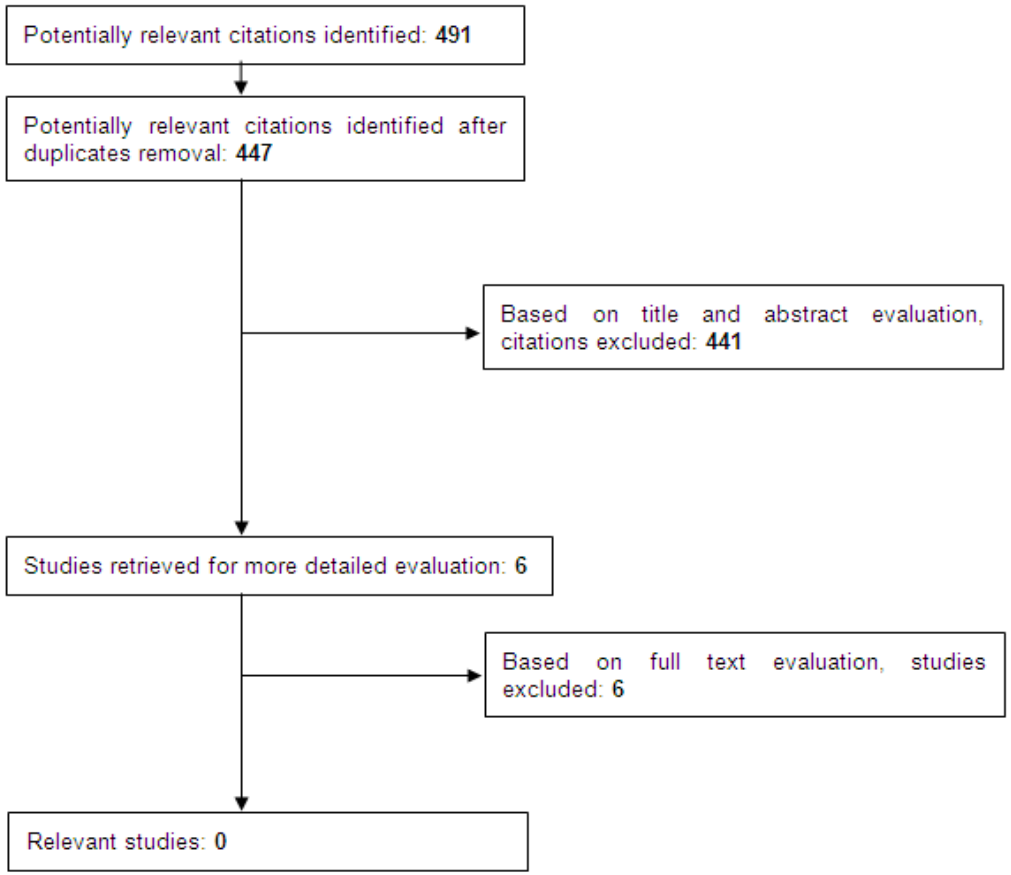


Figure 4 – Flow chart cohort studies

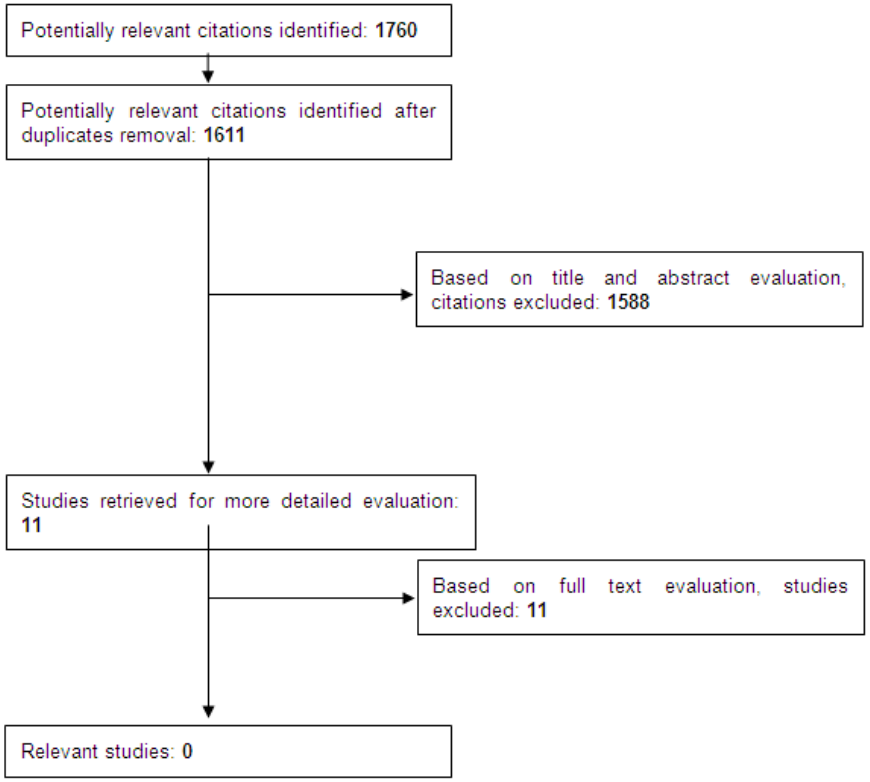
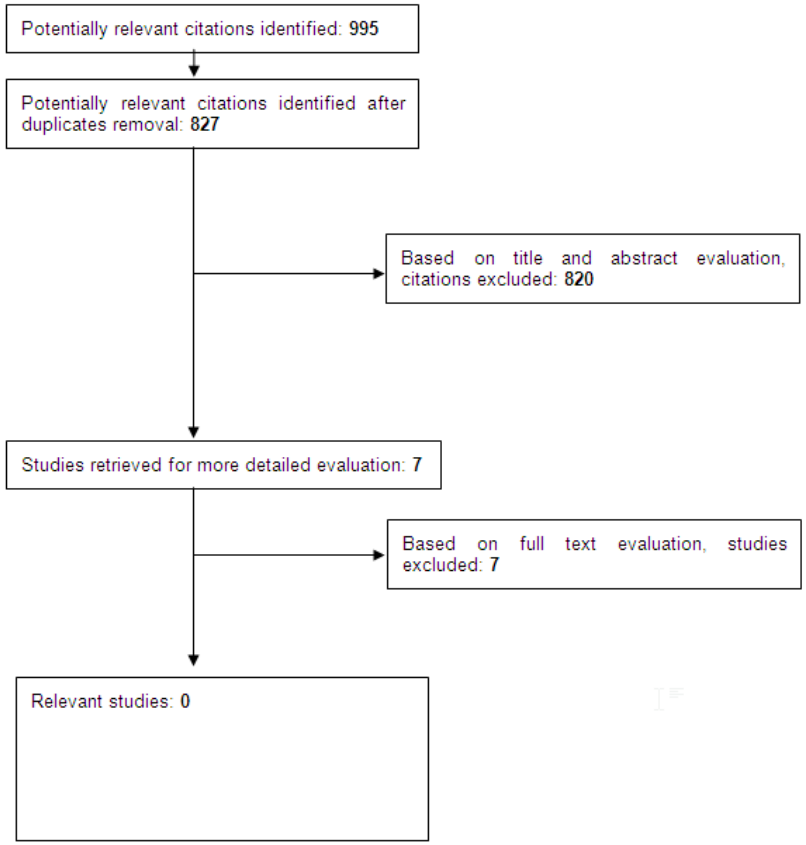


Figure 5 – Flow chart additional search



7.2.5. List of excluded studies (RCTs)

Reference	Reason of exclusion
Baker 1981	Design (no RCT)
Culter 1994	Design (no RCT, no comparison)
O'Meara 2000	Design (systematic review). No eligible trials of systemic antimicrobial agents used with pressure ulcers were identified'.
O'Meara 2001	Design (systematic review) No eligible trials of systemic antimicrobial agents used with pressure ulcers were identified'.
Parish 1984	Outcome: data for patients with decubitus could not be extracted
Parish 1984	Outcome: absence of outcome measures as defined in the protocol

7.2.6. List of excluded studies (cohort studies)

Reference	Reason of exclusion
Does metronidazole help leg ulcers and pressure sores? 1982	Design (opinion letter)
Bacteria & pressure ulcers: the role of silver versus traditional antimicrobials... 2002	Paper could not be retrieved
Baker 1981	Design:inadequate study design: cross-over study
Burkhardt 2006	Design (no comparison)
Cutler 1994	Design (no comparison)
D'Silva 1983	Outcome (impossible to extract data for pressure ulcers)
Mookhoek 1994	Design (no comparison)
Parish 1984	Outcome: absence of outcome measures as defined in the protocol
Parish 1984a	Outcome (impossible to extract data for pressure ulcers)
Parish 1989	Design: narrative review No eligible trials of systemic antimicrobial agents used with pressure ulcers were identified'.

Romanelli 2003	Design: narrative review. No eligible trials of systemic antimicrobial agents used with pressure ulcers were identified'.

7.2.7. List of excluded studies, additional search (RCTs)

Reference	Reason of exclusion
Baker 1981	Design:inadequate study design: cross-over study
Berger 2011	Outcome (no separate data for PU)
Culter 1994	Design (no RCT, no comparison)
Jones 2007	Design (retrospective chart review review).
Jones 2007	Design (retrospective chart review review)
Parish 1984	Outcome: data for patients with decubitus could not be extracted
Parish 1984	Outcome: absence of outcome measures as defined in the protocol

7.3. Clinical evidence

The systematic search through multiple electronic databases resulted in 481 records: 20 in Medline (Ovid), 1 in Cinahl (EBSCO interface), 189 in Embase, and 271 in the Library of the Cochrane Collaboration. Duplicate records were excluded, which resulted in 447 records. Based on the screening of title and abstract 441 records were excluded. Reasons for exclusion were listed. The full text of the remaining 6 records was reviewed in detail. Based on this review, all 6 records were excluded.

Secondly, a systematic search for cohort studies through multiple electronic databases resulted in 1760 records: 255 in Medline (Ovid), 31 in Cinahl (EBSCO interface), 1147 in Embase, and 327 in the Library of the Cochrane Collaboration. Duplicate records were excluded, which resulted in 1588 records. Based on the screening of title and abstract 1577 records were excluded. Reasons for exclusion were listed. The full text of the remaining 11 records was reviewed in detail. Based on this review, all 11 records were excluded.

Third, given the low retrieval an additional search was performed. In this search "(antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*).tw" was used instead of "(systemic and (antibiotic* or anti-biotic* or antimicrobial* or anti-microbial* or antifungal* or anti-fungal* or antiinfective* or anti-infective*)).tw." and the terms" (anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid* or fungicid*).ti,ab" and "(anti-mycobacterial* or antimycobacterial* or bacteriocid* or bactericid* or fungicid*).ti,ab" were added. Furthermore, the index terms in the Medline and CINAHL searches were exploded.

8. ELECTROTHERAPY

8.1. Review protocol

Table 23 – Review protocol

Protocol	Electrotherapy
Review question	What is the clinical effectiveness of electrotherapy for the treatment of pressure ulcers?
Population	People of any age with existing pressure ulcers in any care setting
Intervention	• Electrotherapy as treatment for people with pressure ulcers
Comparison	Other type of therapy for pressure ulcer treatment. Standard wound care
Outcomes	**Critical outcomes for decision-making** (what are the outcomes important to patients): • Time to complete healing (time to event data) • Rate of complete healing (continuous data) • Rate in change of size of ulcer (absolute and relative) (continuous data) – reduction in size of ulcer and volume of ulcer. • Proportion of patients completely healed within trial period **Important outcomes:** • Pain (wound-related) • Time in hospital or NHS care (continuous data) • Patient acceptability eg measured by compliance and tolerance • Side effects • Health-related quality of life (continuous data) (although unlikely to be sensitive enough to detect changes in

	pressure ulcer patients, therefore may have to be narratively summarised • Short-form health survey (SF36) • Manchester Short Assessment of Quality of Life • EQ-5D • WHO-Quality of life BREF • Cardiff HRQoL tool • HUI • Pressure ulcer quality of life (Gorecki)
Study design	• High quality systematic reviews of RCTs and/or RCTs only. • Crossover trials will be meta-analysed together with parallel trials • Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions)
Exclusion	• Studies of patients who do not have active pressure ulcers at time of enrolment • Studies with outcomes that do not involve pressure ulcers • Abstracts unless no RCTs are found • Non-English language papers
Search strategy	**The electronic databases to be searched are:** • Medline (OVID interface), Cinahl (EBSCO-interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	**How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews)** • Population - any population will be combined for meta-analysis except children and adults. Must have active pressure ulcers at time of enrolment. • Intervention - any type of electrotherapy • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – single side effects will be meta-analysed separately from other side effects • Study design – randomised and quasi-randomised studies will be meta-analysed together. Blinded and unblinded studies will be meta-analysed together. • Unit of analysis – patients, clusters (hospital wards), individual pressure ulcers. We will not meta-analyse studies where patients have multiple ulcers and the unit of analysis is pressure ulcer with studies where the unit of analysis is patients.

	• Minimal important difference: default of 0.75 to 1.25 for dichotomous variables and 0.5 x standard deviation for continuous variables. • Minimum duration of treatment = no minimum. • Minimum follow up = no minimum. • Minimum total sample size = no minimum. • Use available case analysis for dealing with missing data if there is a 10% differential or higher between the groups or if the missing data is higher than the event rate, if cannot work out the available case analysis will take the author's data.
Analysis	**The following groups will be considered separately if data are present:** • Children and adults (neonates, infants, children); **Subgroups:** The following groups will be considered separately as subgroups if data are present: • Different categories of pressure ulcer (from category 2 upwards where outcomes are reported separately) • Different ulcer locations
Other terms	Electrical stimulation
Notes	

8.2. Search strategy

8.2.1. Search Filters

Table 24 – Search filters in OVID Medline

Search strategy	Electrotherapy		Results
Date	April 2013		
Database	Medline-Ovid		
Search strategy	1	pressure ulcer/	8808
	2	decubit*.ti,ab.	3835
	3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	5981

Search strategy	Electrotherapy		Results
	4	(bedsore* or bed-sore*).ti,ab.	494
	5	(incontinen* adj2 dermatitis).ti,ab.	49
	6	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	617
	7	or/1-6	13355
	8	limit 7 to english language	10638
	9	Electric Stimulation Therapy/	15097
	10	(electrotherap* or electro-therap*).ti,ab.	998
	11	(electric* adj3 (stimulat* or current*)).ti,ab.	53340
	12	((frequenc* or intensity) adj3 (current* or pulsed)).ti,ab.	4855
	13	((pulse or pulsed) adj3 current*).ti,ab.	1626
	14	(interferential adj3 therap*).ti,ab.	67
	15	((direct or monophas* or galvan* or alternating) adj3 (pulse or pulsed or current*)).ti,ab.	6697
	16	high voltage.ti,ab.	5744
	17	or/9-16	79744
	18	8 and 17	110
	19	letter/	746344
	20	editorial/	298172
	21	news/	142693
	22	exp historical article/	300542
	23	Anecdotes as Topic/	4107
	24	comment/	485995
	25	case report/	1547550
	26	(letter or comment*).ti.	82174

Search strategy	Electrotherapy		Results
	27	or/19-26	2999509
	28	randomized controlled trial/ or random*.ti,ab.	663062
	29	27 not 28	2984714
	30	animals/ not humans/	3555421
	31	exp Animals, Laboratory/	656437
	32	exp Animal Experimentation/	5136
	33	exp Models, Animal/	358711
	34	exp Rodentia/	2424947
	35	(rat or rats or mouse or mice).ti.	1020925
	36	or/29-35	7051075
	37	18 not 36	87
Notes			

Table 3 – Search filters in Embase

Search strategy	Electrotherapy		
Date	April 2013		
Database	Embase-OVID		
Search strategy	1	decubitus/	12153
	2	decubit*.ti,ab.	4622
	3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6840
	4	(bedsore* or bed-sore*).ti,ab.	631
	5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	737

Search strategy	Electrotherapy		
	6	(incontinen* adj2 dermatitis).ti,ab.	53
	7	or/1-6	16442
	8	limit 7 to english language	12672
	9	electrostimulation therapy/	9979
	10	(electrotherap* or electro-therap*).ti,ab.	1296
	11	(electric* adj3 (stimulat* or current*)).ti,ab.	56255
	12	((frequenc* or intensity) adj3 (current* or pulsed)).ti,ab.	5209
	13	((pulse or pulsed) adj3 current*).ti,ab.	1686
	14	(interferential adj3 therap*).ti,ab.	96
	15	((direct or monophas* or galvan* or alternating) adj3 (pulse or pulsed or current*)).ti,ab.	6975
	16	high voltage.ti,ab.	5991
	17	or/9-16	80385
	18	8 and 17	148
	19	letter.pt. or letter/	755980
	20	note.pt.	462893
	21	editorial.pt.	389767
	22	case report/ or case study/	1773737
	23	(letter or comment*).ti.	132642
	24	or/19-23	3259271
	25	randomized controlled trial/ or random*.ti,ab.	753909
	26	24 not 25	3235493
	27	animal/ not human/	1268427
	28	nonhuman/	3776367

Search strategy	Electrotherapy		
	29	exp Animal Experiment/	1487854
	30	exp experimental animal/	366838
	31	animal model/	620584
	32	exp Rodent/	2424924
	33	(rat or rats or mouse or mice).ti.	1074023
	34	or/26-33	8606171
	35	18 not 34	117
Notes			

Table 4 – Search filters in CINAHL

Search strategy	Electrotherapy		Results	
Date	April 2013			
Database	CINAHL			
Search strategy	S18	S7 and S16 Limiters - English Language; Exclude MEDLINE records	63	63
	S17	S7 and S16	149	149
	S16	S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15	16725	16725
	S15	high voltage	244	244
	S14	((direct or monophas* or galvan* or alternating) and (pulse or pulsed or current*))	3295	3295
	S13	(interferential and therap*)	109	109
	S12	((pulse or pulsed) and current*)	674	674
	S11	((frequenc* or intensity) and (current* or pulsed))	5218	5218
	S10	(electric* and (stimulat* or current*))	7818	7818
	S9	electrotherap* or electro-therap*	952	952
	S8	exp Animal Experiment/	804	804
	S7	exp experimental animal/	9497	9497
	S6	animal model/	1349	1349
	S5	exp Rodent/	66	66

Search strategy	Electrotherapy		Results	
	S8	(MH "Electrotherapy")	152 8192	804
	S7	S1 or S2 or S3 or S4 or S5 or S6	468 7470	9497
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))		1349
	S5	incontinen* n2 dermatitis		66
	S4	bedsore* OR bed-sore*		152
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*		8192
	S2	decubit*		468
	S1	(MH "Pressure Ulcer")		7470
Notes				

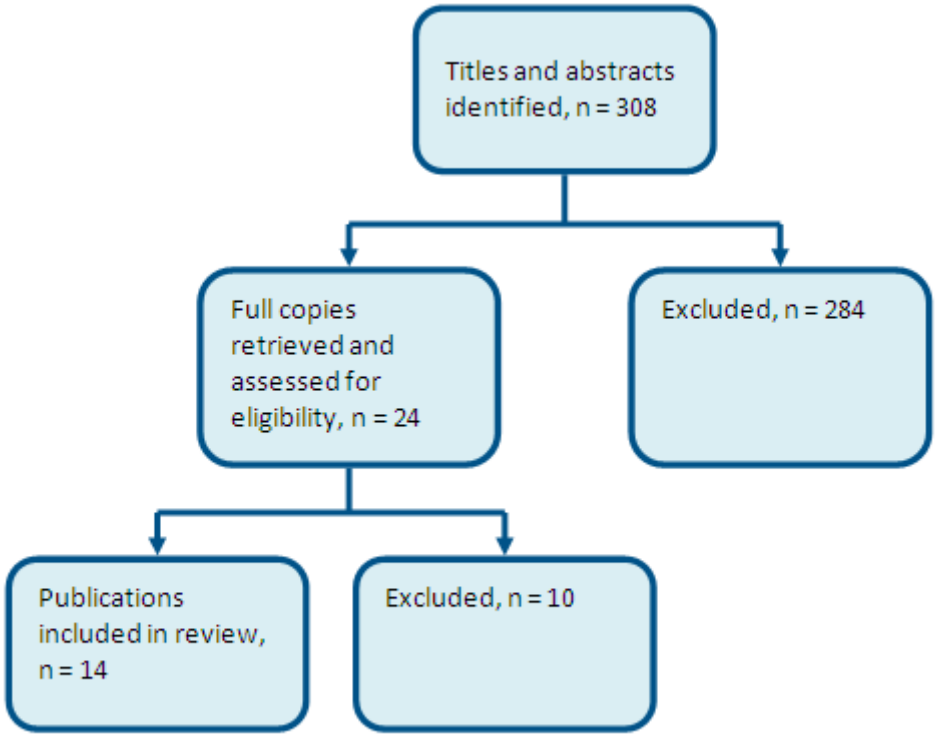
Table 5 – Search filters in Cochrane

Search strategy	Electrotherapy		
Date	April 2013		
Database	Cochrane (- CDSR [3/2012]; DARE; Central [3/2012]; NHS EED; HTA)		
Search strategy	#1	MeSH descriptor Pressure Ulcer explode all trees	480
	#2	decubit*:ti,ab,kw	341
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	818
	#4	(bedsore* or bed-sore*):ti,ab,kw	32
	#5	(incontinen* near/2 dermatitis):ti,ab,kw	10
	#6	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	62
	#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	1151
	#8	MeSH descriptor Electric Stimulation Therapy, this term only	1274
	#9	(electrotherap* or electro-therap*):ti,ab,kw	173
	#10	(electric* near/3 (stimulat* or current*)):ti,ab,kw	4483
	#11	((frequenc* or intensity) near/3 (current* or pulsed)):ti,ab,kw	500
	#12	((pulse or pulsed) near/3 current*):ti,ab,kw	94

Search strategy	Electrotherapy		
	#13	(interferential near/3 therap*):ti,ab,kw	57
	#14	((direct or monophas* or galvan* or alternating) near/3 (pulse or pulsed or current*)):ti,ab,kw	406
	#15	high voltage:ti,ab,kw	225
	#16	(#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15)	5412
	#17	(#7 AND #16)	38
Notes			

8.2.2. Flow chart

Figure 6 – Flow chart



8.2.3. Excluded Studies

Table 24 – Studies excluded from the clinical review

Reference	Reason for exclusion
SHEFFET2000 Applying electric and electromagnetic energy as adjuvant treatment for pressure ulcers: a critical review	Not a systematic review
KARBA1997 Electrical stimulation for chronic wound healing enhancement	Wounds not pressure ulcers
GUPTA2009 Efficacy of pulsed electromagnetic field therapy in healing of pressure ulcers	Electromagnetic not electrotherapy
SCHUBERT2001 Effects of phototherapy on pressure ulcer healing in elderly patients after a falling trauma	Phototherapy not electrotherapy
GENTZKOW1993 Healing of refractory stage III and IV pressure ulcers by a new electrical stimulation device	Not an RCT
GARDNER1999 Effect of electrical stimulation on chronic wound healing: a meta-analysis	Meta-analysis which included RCTs and non-RCTs and other wound types
ULLAH2007 A study to detect the efficacy of Micro-current Electrical Therapy on decubitus wounds	Errors in publication
FEEDAR1991 Chronic Dermal Ulcer Healing Enhanced with Monophasic Pulsed Electrical Stimulation	Mixed ulcer types
CARLEY1985 Electrotherapy for acceleration of wound healing: low intensity direct current	Mixed ulcer types
GAULT1976 Use of low intensity direct current in management of ischemic skin ulcers	Mixed ulcer types

8.3. Clinical Evidence

We searched for randomized trials comparing the effectiveness of electrotherapy versus placebo or usual care for treatment of patients with pressure ulcers. Fourteen randomized trials were identified.[1-14]

Various types of electrical stimulation were included as were different populations. We included one study which compared different types of electrical stimulation (which also compared these to a control group).[5] Another trial looked at different durations of electrotherapy compared to placebo.[3] We separated studies that reported ulcers (where one patient could have more than one ulcer) from those who reported patients. One study included a mixed population of children and adults (aged 14 to 88) but did not report the results separately.[7] The studies had varying time periods (4 weeks to 5 months), we meta-analyzed them together and no significant heterogeneity was found. We used change from baseline scores rather than final values to get the reduction in ulcer size. We reported outcomes such as size of ulcer separately from other outcomes, as the data was continuous and there was a probability that the data was skewed but this was not counter-acted with log transformation within the studies. It should be emphasized that this data should be interpreted with caution. It should also be noted that many of the studies had very small sample sizes.

8.3.1. Summary table

Table 25 – Summaries of studies

Study	Intervention/comparison	Population	Outcomes	Length of study
Adegoke 2001[1]	Interrupted direct current vs sham interrupted direct current. Both groups: routine nursing care.	Spinal cord injury patients with grade IV pressure ulcers in the pelvic region	% reduction in surface area	4 weeks treatment
Adunsky 2005[2]	Direct current vs sham direct current. Both groups received conservative treatment of wounds.	Geriatric rehabilitation patients with stage 3 degree ulcers.	Proportion with complete healing; speed of wound closure; reduction in absolute ulcer area; reduction in % ulcer size	Treatment lasted 8 weeks (57 days) and followed up at day 147 Results given for 45 days also
Ahmad 2008[3]	High-voltage pulsed galvanic stimulation (50usec, 120 Hz, 100-175 v) (45, 60 and 120 minutes) vs sham treatment and conventional wound therapy, wet dressing and whirlpool therapy Both groups: debridement before admission to study.	Patients with an indolent pressure ulcer of grade II (Yarkony-Kirk classification) chronic pressure ulcers	Reduction in wound surface area (cm2)	5 weeks treatment
Asbjornsen 1990[4]	Transcutaneous electrical nerve stimulation (3Hz, 85 ms, 100Hz, 20-30mA) vs placebo transcutaneous electrical nerve stimulation Both groups: conventional pressure sore treatment including measures to improve general condition, adequate local care and avoidance of pressure.	Geriatric patients with pressure sores on the heels or the sacral region	Proportion with complete haling; proportion of ulcers reduced; proportion of ulcers increased.	6 weeks treatment
Baker 1996[5]	Asymmetric biphasic (100usec, 50 pulses/sec) versus symmetric biphasic (300Usec, 50 pulses/sec) vs microcurrent (4mA, 10 usec, 1 pulse/sec vs sham	Spinal cord injury patients with one or more pressure ulcers	Rate of healing;	4 weeks treatment

	electrical stimulation			
Franek 2011 [7]	High voltage monophasic stimulation (100us, 100Hz, 100v) vs no stimulation Both groups received pharmacological agents, including wound cleansing with potassium permanganate. The ulcer base was covered with compresses of fibrolan, colistin, and iruxol and wet dressings of 10% sodium chloride.	Surgical inpatients with stage I, II and III pressure ulcers	Proportion of ulcers completely healed; relative change of total surface area; relative change in length, relative change in width, relative change in volume, relative change in Gilman Index.	6 weeks treatment
Franek 2012[6]	Standard care plus **h**igh voltage electrical stimulation (Voltage exceeded 100V, twin monophasic pulses lasting 100us in total and frequency of 100HZ applied). Five 50-minute procedures per week (one procedure per day) vs no stimulation Both groups standard care. Pressure redistribution surfaces and devices and pillows as needed; repositioning; standard topical care including cleansing with potassium permanganate followed by dressings; sharp debridement in small number; cleansing; immobilised patients received low-molecular-weight heparin (enoxaparin). Antibiotics for those requiring.	Surgical inpatients with stage II and III ulcers	Change in wound surface area (%); change in longest length (%); change in longest width (%); change in cavity volume (%); change in granulation tissue area (%); Gilman parameter.	6 weeks treatment
Gentzkow 1991[8]	Low voltage pulsed direct current (2pps/250 usec to 128pps/150 usec) d vs placebo low voltage pulsed direct current	Patients with stage II, III or IV pressure ulcers	Proportion of ulcers healed, rate of healing, mean healing , withdrawals due to adverse events, acceptability of treatment	4 weeks treatment
Griffin 1991[9]	High-voltage pulsed direct current (100pps, 200v) vs placebo high-voltage pulsed	Patients with spinal cord injury and grade II to IV	Change in wound surface area; proportion of ulcers	20 days treatment

	direct current Both groups received equivalent nursing care - cleansing and application of gel and a dry dressing; wound mechanically debrided. 2 hourly turning.	pressure ulcers in the pelvic region	completed healed	
Houghton 2010[10]	Twin peaked high-voltage monophasic pulsed current (50 usec, 50-150v). vs no stimulation Both groups received a community-based interdisciplinary wound care program	People in the community with spinal cord injuries with pressure ulcers stage II to IV	% reduction in wound surface area; proportion of wounds reduced by at least 50%; changes in wound appearance (PWAT scores); improved PWAT scores; proportion with increased wounds; proportion with improved PSST scores; proportion of stage II completely healed; proportion of stage III, IV, X ulcers healed; proportion of stage III, IV, X ulcers at reduced by at least 50%; EST compliance; adverse reactions.	3 months treatment, 4 months follow-up
Jercinovic 1994[11]	Low frequency pulsed current (biphasic, asymmetric, charge-balanced pusses 40pps, 205us, 35mA) vs no Stimulation Both groups: standard wound care. Debridement; standard dressings; antibiotics in cases of infection; dry-floatation mattresses; repositioning; standard rehabilitation program.	Spinal cord injured patients with pressure ulcers	Rate of healing.	4 weeks treatment
Karba 1995[12]	4-second trains of biphasic, charge-balanced asymmetrical current stimuli, which alternated with pauses of the same	Spinal cord injured male patients with pressure ulcers	Rate of healing	98 days

	duration (4 seconds) vs sham treatment. Both groups: cleansing; covered with semi-occlusive foam gel dressings			
Kloth 1988[13]	High voltage pulsed current (105Hz, 50 usec, 100-175v) versus sham treatments Both groups: pressure-relieving device that reduced exogenous cutaneous pressure; High-protein dietary supplement; manual debridement and with enzymes.	Patients with stage IV pressure ulcers	Proportion completely healed; healing rate;	16 weeks treatment
Wood 1993[14]	Pulsed low-intensity direct current (600uA, 0.8Hz) vs placebo pulsed low-intensity direct current + standard treatment. Standard treatment: wound cleansing, simple moist dressing, whirlpool baths.	Patients with stage II and stage III chronic pressure ulcers	Proportion of ulcers completely healed; reduction in ulcer area; reduction in ulcer area over 80%, ulcer depth	8 weeks treatment

8.3.2. Clinical GRADE evidence tables

Table 26 – Clinical evidence profile: Electrotherapy versus control (placebo or usual treatment)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Electrotherapy	Control	Relative (95% CI)	Absolute		
Proportion of participant's completely healed - end of study - patients - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005);. geriatric patients, pressure ulcer stage not reported (Asbjornsen 1990); Surgical inpatients, stage I, II and III pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); Patients with spinal cord injury, grade II to IV pressure ulcers (DeLisa classication system) (Griffin 1991); Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP) (Houghton 2010)												
5 Adunsky (2005); Asbjornsen (1990); Franek (2011); Griffin	randomised trials	very serious[a]	serious inconsistency[b]	no serious indirectness	serious imprecision	none	26/95 (27.4%)	23/93 (24.7%)	RR 1.09 (0.68 to 1.75)	22 more per 1000 (from 79 fewer to 167 more)	⊕OOO VERY LOW	Critical
								22.2%		20 more per 1000 (from 71 fewer to 167		

(1991); Houghton (2010);										more)		
Proportion of ulcers completely healed - end of study – ulcers - patients with chronic pressure ulcers, stage II and III (classification system not reported)												
1 Wood (1993)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[e]	none	25/43 (58.1%)	1/31 (3.2%)	RR 18.02 (2.58 to 126.01)	549 more per 1000 (from 51 more to 1000 more)	⊕OOO VERY LOW	Critical
								3.2%		545 more per 1000 (from 51 more to 1000 more)		
>80% decrease in ulcer area - ulcers- patients with chronic pressure ulcers, stage II and III (classification system not reported)												
1 Wood (1993)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31/43 (72.1%)	4/31 (12.9%)	RR 5.59 (2.2 to 14.21)	592 more per 1000 (from 155 more to 1000 more)	⊕⊕OO LOW	Important
								12.9%		592 more per 1000 (from 155 more to 1000 more)		
Proportion of pressure ulcers that reduced by at least 50% at 3 months – patients - Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
1 Houghton (2010)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[c]	none	12/15 (80%)	5/14 (35.7%)	RR 2.24 (1.06 to 4.73)	443 more per 1000 (from 21 more to 1000 more)	⊕⊕OO LOW	Important
								35.7%		443 more per 1000 (from 21 more to 1000 more)		
Proportion with improved PWAT scores - patients - Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
1 Houghton (2010)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Serious imprecision[c]	none	12/16 (75%)	8/18 (44.4%)	RR 1.69 (0.94 to 3.04)	307 more per 1000 (from 27 fewer to 907 more)	⊕⊕OO LOW	Important
								44.4%		306 more per 1000 (from 27 fewer to 906 more)		
Proportion with improved PSST scores – patients - Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
1 Houghton (2010)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[c]	none	8/16 (50%)	9/18 (50%)	RR 1.00 (0.51 to 1.96)	0 fewer per 1000 (from 245 fewer to 480 more)	⊕⊕OO LOW	Important

								50%		0 fewer per 1000 (from 245 fewer to 480 more)		
Proportion of patients with decreased ulcers - geriatric patients, pressure ulcer stage not reported												
1 Asbjornsen (1990)	randomised trials	very serious[a]	no serious	no serious indirectness	very serious[c,e]	none	3/7 (42.9%)	0/9 (0%)	Peto OR 13.98 (1.21 to 162.00)	430 more per 1000 (from 60 fewer to 800 more)	⊕OOO VERY LOW	Important
Proportion of patients with increased ulcers - geriatric patients, pressure ulcer stage not reported (Asbjornsen 1990); community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP) (Houghton 2010)												
2 Asbjornsen (1990); Houghton (2010)	randomised trials	very serious[a]	very serious[g]	no serious indirectness	very serious[d,e]	none	3/23 (13%)	4/27 (14.8%)	RR 1.05 (0.02 to 68.36)	7 more per 1000 (from 145 fewer to 1000 more)	⊕OOO VERY LOW	Important
								11.1%		6 more per 1000 (from 109 fewer to 1000 more)		
Proportion of patients with increased ulcers – geriatric patients, pressure ulcer stage not reported												
1 Asbjornsen (1990)	Randomised trials	Very serious[a]	No serious inconsistency	No serious indirectness	Very serious[c,e]	None	3/7 (42.9%)	0/9 (0%)	Peto OR 13.98 (1.21 to 162.00)	430 more per 1000 (from 60 fewer to 800 more)	⊕OOO VERY LOW	Important
								0%		430 more per 1000 (from 60 fewer to 800 more)		
Proportion of patients with increased ulcers – community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
Houghton (2010)	Randomised trials	serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	none	0/16 (0%)	4/18 (22.2%)	RR 0.12 (0.01 to 2.14)	196 fewer (from 220 fewer to 253 more)	⊕OOO VERY LOW	Important
								22.2%				
Proportion of ulcers which increased in size - patients with chronic pressure ulcers, stage II and III (classification system not reported)												
1 Wood (1993)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious	none	0/43 (0%)	10/31 (32.3%)	Peto OR 0.02 (0 to 0.42)[6]	313 fewer per 1000 (156 fewer to 323 fewer)	⊕OOO VERY LOW	Important
								32.3%		314 fewer per 1000 (from 156 fewer to 323 fewer)		

Mortality - geriatric patients, pressure ulcer stage not reported (Asbjornsen 1990); Surgical inpatients, stage I, II and III pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); Surgical inpatients with stage II and III pressure ulcers (Franek 2012); Patients with spinal cord injury, grade II to IV pressure ulcers (DeLisa classication system)(Griffin 1991); patients with stage IV pressure ulcers (Kloth 1988); patients with chronic pressure ulcers, stage II and III (classification system not reported) (Wood 1993)												
6 Asbjornsen (1990); Franek (2011); Franek (2012); Griffin (1991); Kloth (1988); Wood (1993);	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[d]	none	3/120 (2.5%)	5/108 (4.6%)	RR 0.58 (0.18 to 1.88)	19 fewer per 1000 (from 38 fewer to 41 more)	⊕OOO VERY LOW	Important

a Adunsky (2005) No details of allocation concealment. High drop-out, per protocol was used but was unclear about number analysed in the control group. No details of whether outcome assessors were blinded. Asbjornsen (1990) No details of sequence generation or allocation concealment or baseline differences. Higher drop-out in the treatment group. No statistical tests mentioned. Franek (2011) No blinding (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Griffin (1991) No details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. No blinding of outcome assessors. Houghton (2010) No blinding of caregiver and participant. Outcome assessor was blinded. Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. No details of blinding of outcome assessor. Unclear number randomised but 49 were entered into study, and 34 completed, no detail of withdrawals; measured pressure ulcer by using length and width. Wood (1993) No details of sequence generation method. More participants in treatment than control group. High drop-out in control group arm.

b Wide variations in follow-up times.

c Confidence interval crossed one MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes)

d Confidence interval crossed both MID points (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes)

e Very wide confidence interval.

f Peto odds ratio was used as one arm had zero events.

g I^2 = 77%, p=0.04. Asbjornsen, 1990 was a study which included a majority of heel ulcers.

Table 27 – Clinical evidence profile: Electrotherapy versus control (placebo or usual treatment)

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Electrotherapy	Control	Relative (95% CI)	Absolute		
% mean reduction in wound surface area - patients - Surgical inpatients with stage II and III pressure ulcers (Franek 2012); community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP) (Houghton 2010)												
2 Franek (2012); Houghton (2010);	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	N=42	N=42	-	MD 40.16 higher (20.39 to 59.92 higher)	⊕⊕OO LOW	Important
% mean reduction in wound surface area - ulcers - patients with pressure ulcers stage II, III or IV (classification system not reported but details given – see evidence table)												
1 Gentzkow (1991)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[f]	49.8 (SD 30.9) n=21	23.4 (SD 47.4) n=19	-	MD 26.4 higher (1.32 to 51.48 higher)	⊕OOO VERY LOW	Important
% median reduction in wound surface area (at 20 days) – patients - Patients with spinal cord injury, grade II to IV pressure ulcers (DeLisa classication system)												
1 Griffin (1991)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious imprecision[e]	Serious[f]	Median 80% (range 52 to 100%)	Median 52% (range 14% to 100%	p=0.05	MD 28%	⊕OOO VERY LOW	Important
Healing rate (%/week) - patients - Patients with stage IV pressure ulcers (classification system not reported)												
1 Kloth (1988)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	44.8 (SD 22.6) N=9	-11.59 (SD 18.6) N=7	-	MD 56.39 higher (36.19 to 76.59 higher)	⊕OOO VERY LOW	Important
Healing rate (%/week) - ulcers - spinal cord injury patients (classification system not reported (BAKER 1996); patients with pressure ulcers stage II, III or IV (classification system not reported but details given – see evidence table) (Gentzkow 1991												
2 Baker (1996); Gentzkow (1991)	randomised trials	very serious[a]	no serious inconsistency[l]	no serious indirectness	serious imprecision[b]	Serious[f]	N=79	N=44	-	MD 2.99 lower (6.03 lower to 0.05 higher)	⊕OOO VERY LOW	Important

Healing rate (%/day)- participants - patients with spinal cord injuries (classification system not reported)												
1 Karba (1995)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	7.13 (SD 1.46) N=6	-0.66 (SD 1.16) N=6	-	MD 7.79 higher (6.30 to 9.28 higher)	⊕⊕OO LOW	Important
Healing rate (%/day) - exponential fitting – ulcers - patients with spinal cord injuries (classification system not reported)												
1 Jercinovic (1994)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[f]	5.7 (SD 7.1) N=61	2.7 (SD 3.6) N=48	-	MD 3 higher (0.95 to 5.05 higher)	⊕OOO VERY LOW	Important
Healing rate (%/day) - linear fitting – ulcers - patients with spinal cord injuries (classification system not reported)												
1 Jercinovic (1994)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[f]	2.2 (SD 2.1) N=61	1.5 (SD 1.7) N=48	-	MD 0.7 higher (0.01 lower to 1.41 higher)	⊕OOO VERY LOW	Important
Healing rate (%/day) - exponential fitting - crossover group – ulcers - patients with spinal cord injuries (classification system not reported)												
1 Jercinovic (1994)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[f]	5 (SD 4.2) N=20	1.2 (SD 2.1) N=20	-	MD 3.8 higher (1.74 to 5.86 higher)	⊕OOO VERY LOW	Important
Healing rate (%/day) - linear fitting - crossover group – ulcers - patients with spinal cord injuries (classification system not reported)												
1 Jercinovic (1994)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	2.4 (SD 1.4) N=20	0.6 (SD 1.5) N=20	-	MD 1.8 higher (0.9 to 2.7 higher)	⊕OOO VERY LOW	Important
Time to complete healing – patients - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	serious indirectness[e]	no serious imprecision	Serious[f]	63.4 (SD 15.1) N=9	89.7 (9.2) N=10	-	MD 26.3 lower (32.35 to 20.25 lower)	⊕OOO VERY LOW	Important
Speed of healing (% change from baseline – days) – patients - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[f]	-0.24 (SD 0.14) N=35	- 0.25 (SD 0.14) N=28	-	MD 0.01 higher (0.06 lower to 0.08 higher)	⊕OOO VERY LOW	Important

Acceptability of treatment – compliance to electrotherapy (hours per day) – patients - Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
1 Houghton (2010)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	N/A	None	Mean 3.0 (SD 1.5) h/day[g]	-	-	-	⊕OOO VERY LOW	Important
Acceptability of treatment – uncomfortable sensation in the ulcer when current was turned on - ulcers- patients with pressure ulcers stage II, III or IV (classification system not reported but details given – see evidence table)												
1 Gentzkow (1991)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious imprecision[k]	Serious[f]	13.6% N=21	4.2% N= 18	-	MD 9.4%	⊕OOO VERY LOW	Important
Side effects – patients - Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP)												
1 Houghton (2010)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	N/A	Serious[f]	See footnote[h]	-	-	-	-	Important
Mean reduction in length (%) - Surgical inpatients with stage II and III pressure ulcers												
1 Franek (2012)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	74 (SD 29.6) N=26	36.1 (SD 33.9) N=24	-	MD 37.9 higher (20.2 to 55.6 higher)	⊕⊕OO LOW	Important
Mean reduction in longest width (%) - Surgical inpatients with stage II and III pressure ulcers												
1 Franek (2012)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	79 (SD 25.1) N=26	36.3 (41.9) N=24	-	MD 42.7 higher (23.36 to 62.04 higher)	⊕⊕OO LOW	Important
Mean reduction in cavity volume (%) - Surgical inpatients with stage II and III pressure ulcers												
1 Franek (2012)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[f]	100 (SD 0.0001) N=26	54 (SD 39.4) N=24	-	46 higher (30.24 to 61.76 higher)[j]	⊕⊕OO LOW	Important

Mean reduction in granulation tissue area (%) - Surgical inpatients with stage II and III pressure ulcers												
1 Franek (2012)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Very serious imprecision[c]	Serious[f]	37.66 (SD 76.17) N=26	10.36 (SD 43.46) N=24	-	MD 27.3 higher (6.75 lower to 61.35 higher)	⊕OOO VERY LOW	Important
Gillman parameter - Surgical inpatients, stage I, II and III pressure ulcers (classification system not reported, see criteria in evidence table) (Franek 2011); surgical inpatients with stage II and III pressure ulcers (Franek 2012)												
2 Franek (2011); Franek (2012)	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Serious imprecision[b]	Serious[f]	N=26	N=24	-	MD 0.41 higher (0.28 to 0.54 higher)	⊕OOO VERY LOW	Important

a Adunsky (2005) No details of allocation concealment. High drop-out, per protocol was used but was unclear about number analysed in the control group. No details of whether outcome assessor's were blinded. Non-parametric tests used so possibly skewed data but no log transformations. Adegoke (2001) No details of sequence generation. Unclear allocation concealment. No details of blinding of outcome assessors. 1 drop-out but no details of which arm. Difference at baseline. No statistical tests mentioned. Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data. Franek (2011) No blinding (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Non-parametric test used so possibly skewed data but no log-transformations. Franek (2012) No sham treatment, no blinding of patients, caregivers or outcome assessors. Gentzkow (1991) no details of sequence generation method; difference at baseline in ulcer size; measured pressure ulcer by using length and width. Griffin (1991) No details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. No blinding of outcome assessors. Non-parametric tests used so possibly skewed data but no log transformations. Houghton (2010) No blinding of caregiver and participant. Outcome assessor was blinded. Jercinovic (1994) No details of sequence generation or allocation concealment. No blinding. Unclear number randomised and missing outcome data. Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned.

b Confidence interval crossed one MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes)

c Confidence interval crossed both MID points (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes)

d Confidence interval crossed one MID point (0.5 x standard deviation for continuous outcomes and 0.75 to 1.25 for dichotomous outcomes) and limited number of events.

e Medians given, no standard deviations given.

f Skewed data and no log transformations were done. ; g Recommended treatment time 8 hours per day. Proportion using the recommended time: 4/16. Those who healed used the electrotherapy the longest (539 total hours; 2.54h/day); those who did not heal 331 total hours; 2.24h/day; Average for those who healed: 136.4 days (4.5 months).

h Red area or burn under the active electrode after EST treatment, area resolved within 48 hours and remedied by turning down the intensity of subsequent electrotherapy treatments. One patient complained of dizziness and delusions while receiving electrotherapy but was evaluated as withdrawal from narcotics after a lapse in prescription.

i Baker (1996) included 3 treatments and treatment B (symmetric biphasic 200usec, 50 pulses/sec) was the most similar to Gentzkow (1991) which was pulsed electrical current (2pulses/sec/350usec to 128pulses/sec/150usec).; j We had to use standard deviation of 0.001 in Revman as the standard deviation of zero showed no result.

k No numerator or denominator given so unable to analyse in Revman.

Table 28 – Clinical evidence profile: Asymmetric biphasic electrostimulation at 100us versus control for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Asymmetric biphasic electrostimulation at 100us	Control	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) - spinal cord injury patients (classification system not reported)												
1Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[c]	36.40 (SD 6.2) N=67	32.7 (SD 7) N=25	-	MD 3.7 higher (0.58 to 6.82 higher)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Confidence interval crossed one MID point (0.5 x standard deviation for continuous variables).

c Possibly skewed data but no log transformation.

Table 29 – Clinical evidence profile: Symmetric biphasic electrostimulation 300 usec versus control for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Symmetric biphasic electrostimulation 300 usec	Control	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) - spinal cord injury patients (classification system not reported)												
1 Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[c]	N=58	N=25	-	MD 3 lower (6.04 lower to 0.04 higher)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Confidence interval crossed one MID point (0.5 x standard deviation for continuous variables).

c Possibly skewed data but no log transformation.

Table 30 – Clinical evidence profile: Microcurrent versus control for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Microcurrent	Control	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) - spinal cord injury patients (classification system not reported)												
1 Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	serious imprecision[b]	Serious[c]	N=42	N=25	-	MD 9.4 lower (12.5 to 6.3 lower)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Confidence interval crossed one MID point (0.5 x standard deviation for continuous variables).

c Possibly skewed data but no log transformation.

Table 31 – Clinical evidence profile: Asymmetric biphasic electrostimulation 100usec vs 300usec for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Asymmetric biphasic electrostimulation 100usec	300usec	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) - spinal cord injury patients (classification system not reported)												
1 Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	No serious imprecision	Serious[b]	36.4 (SD 6.2) N=67	29.7 (SD 5.1) N=58	-	MD 6.7 higher (4.72 to 8.68 higher)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Possibly skewed data but no log transformation.

Table 32 – Clinical evidence profile: Asymmetric biphasic electrostimulation 100usec vs microcurrent for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Asymmetric biphasic electrostimulation 100usec	Microcurrent	Relative (95% CI)	Absolute		
Mean reduction in wound surface area (% per week) - spinal cord injury patients (classification system not reported)												
1 Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[b]	36.4 (SD 6.2) N=67	23.3 (SD 4.8) N=42	-	MD 13.1 higher (11.02 to 15.18 higher)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Possibly skewed data but no log transformation.

Table 33 – Clinical evidence profile: Asymmetric biphasic electrostimulation 300usec vs microcurrent for treatment of pressure ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Asymmetric biphasic electrostimulation 300usec	Microcurrent	Relative (95% CI)	Absolute		
Mean reduction in wound surface area % per week) - spinal cord injury patients (classification system not reported)												
1 Baker (1996)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	Serious[b]	29.7 (SD 5.1) N=58	23.3 (SD 4.8) N=42	-	MD 6.4 higher (4.44 to 8.36 higher)	⊕OOO VERY LOW	Important

a Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data.

b Possibly skewed data but no log transformation.

Table 34 – Hard to heal ulcers (grades 3 and four) – electrotherapy versus control group

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Electrotherapy	Control	Relative (95% CI)	Absolute		
Proportion of participants completely healed - at end of study - patients - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005); patients with spinal cord injury, grade II to IV pressure ulcers (DeLisa classication system)(Griffin 1991); Community patients with spinal cord injuries, pressure ulcers stage II to IV (NPUAP) (Houghton 2010)												
3 Adunsky (2005); Griffin (1991); Houghton (2010);	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[b]	none	15/56 (26.8%)	11/49 (22.4%)	RR 1.14 (0.6 to 2.2)	31 more per 1000 (from 90 fewer to 269 more)	⊕OOO VERY LOW	Critical
								7.1%		10 more per 1000 (from 28 fewer to 85 more)		
Mortality - patients with stage IV pressure ulcers (classification system not reported) (Kloth 1988)												
1 Kloth (1998)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	None	0/9 (0%)	0/7 (0%)	not pooled	not pooled	⊕⊕OO LOW	Important
								0%		not pooled		
Absolute reduction in size of pressure ulcer (cm) at end of treatment (Better indicated by higher values) - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision[b]	none	11.15 (SD 1.1) N=21	16.7 (SD 1) N=25	-	MD 5.55 lower (6.16 to 4.94 lower)	⊕⊕OO LOW	Critical
Absolute reduction in size of pressure ulcer (cm) at end of follow-up (Better indicated by higher values) - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[c]	none	2.53 (SD 2.11) N=21	2.88 (SD 1.92) N=25	-	MD 0.35 lower (1.53 lower to 0.83 higher)	⊕OOO VERY LOW	Critical
Healing rate (%/week) (participants) - Patients (Better indicated by higher values) - patients with stage IV pressure ulcers (Kloth 1988)												
1 Kloth (1988)	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	no serious imprecision	none	44.8 (SD 22.6) N=9	-11.59 (SD 18.6) N=7	-	MD 56.39 higher (36.19 to 76.59 higher)	⊕⊕OO LOW	Critical

Time to complete healing (days) (Better indicated by lower values) - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	serious indirectness[e]	no serious imprecision	none	63.4 (SD 15.1) N=9	89.7 (SD 9.2) N=10	-	MD 26.3 lower (37.69 to 14.91 lower)	⊕OOO VERY LOW	Critical
Speed of healing (% change from baseline - days) (Better indicated by lower values) - Geriatric rehabilitation patients, stage III pressure ulcers (classification system not reported) (Adunsky 2005)												
1 Adunsky (2005)	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[c]	none	-0.24 (SD 0.14) N=35	-0.25 (SD 0.14) N=28	-	MD 0.01 higher (0.06 lower to 0.08 higher)	⊕OOO VERY LOW	Critical

a Adunsky (2005) No details of allocation concealment. High drop-out, per protocol was used but was unclear about number analysed in the control group. No details of whether outcome assessor's were blinded. Non-parametric tests used so possibly skewed data but no log transformations. Adegoke (2001) No details of sequence generation. Unclear allocation concealment. No details of blinding of outcome assessors. 1 drop-out but no details of which arm. Difference at baseline. No statistical tests mentioned. Baker (1996) No details of sequence generation or allocation concealment. No blinding except of outcome assessor. Unclear missing outcome data. Franek (2011) No blinding (although the authors say it was not possible for EST), but the outcome assessors were not blinded either. Non-parametric test used so possibly skewed data but no log-transformations. Franek (2012) No sham treatment, no blinding of patients, caregivers or outcome assessors. Gentzkow (1991) no details of sequence generation method; difference at baseline in ulcer size; measured pressure ulcer by using length and width. Griffin (1991) No details of sequence generation method or allocation concealment. There was a significant difference in groups for duration of spinal cord injury, which was longer in the treatment group. No blinding of outcome assessors. Non-parametric tests used so possibly skewed data but no log transformations. Houghton (2010) No blinding of caregiver and participant. Outcome assessor was blinded. Jercinovic (1994) No details of sequence generation or allocation concealment. No blinding. Unclear number randomised and missing outcome data. Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. Ullah (2007) No details of sequence generation or allocation concealment. No details of missing data, how they measured ulcer size, baseline differences or whether outcome assessors were blinded.

b Confidence interval crossed both MID points.

c Confidence interval crossed one MID point.

d Kloth (1988) No details of allocation concealment, baseline differences, blinding of outcome assessors. No statistical tests mentioned. No details of blinding of outcome assessor. Unclear number randomised but 49 were entered into study, and 34 completed, no detail of withdrawals; measured pressure ulcer by using length and width.

e Time to event data not given as hazard ratio, high risk of bias from mean values.

8.3.3. Forrest plots

8.3.3.1. Electrotherapy versus placebo or no stimulation

Figure 7 – Electrotherapy vs control; Proportion of participants completely healed – end of study

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 patients						
Adunsky, 2005	9	35	10	28	46.4%	0.72 [0.34, 1.53]
Asbjornsen, 1990	0	7	2	9	9.3%	0.25 [0.01, 4.50]
Franek, 2011	8	29	4	29	16.7%	2.00 [0.68, 5.91]
Griffin, 1991	3	8	2	9	7.9%	1.69 [0.37, 7.67]
Houghton, 2010	6	16	5	18	19.7%	1.35 [0.51, 3.59]
Subtotal (95% CI)		**95**		**93**	**100.0%**	**1.09 [0.68, 1.75]**
Total events	26		23			

Heterogeneity: Chi² = 3.88, df = 4 (P = 0.42); I² = 0%

Test for overall effect: Z = 0.36 (P = 0.72)

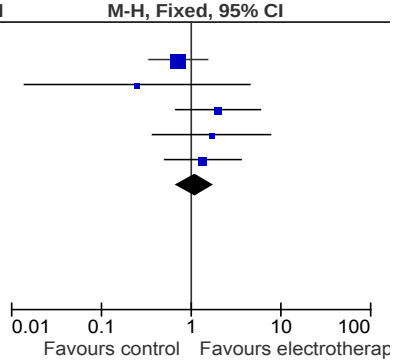


Figure 8 – Electrotherapy vs control; Proportion of ulcers completely healed – end of study

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
1.2.2 Ulcers						
Wood, 1993	25	43	1	31	100.0%	18.02 [2.58, 126.01]
Subtotal (95% CI)		**43**		**31**	**100.0%**	**18.02 [2.58, 126.01]**
Total events	25		1			

Heterogeneity: Not applicable

Test for overall effect: Z = 2.91 (P = 0.004)

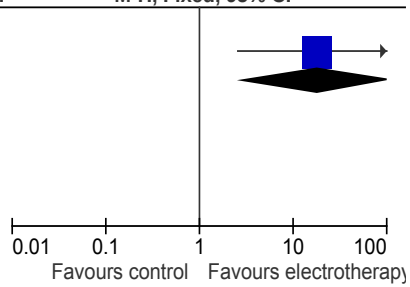


Figure 6 – Electrotherapy vs control; Proportion with improved PSST scores

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Houghton, 2010	8	16	9	18	100.0%	1.00 [0.51, 1.96]
Total (95% CI)		**16**		**18**	**100.0%**	**1.00 [0.51, 1.96]**
Total events	8		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

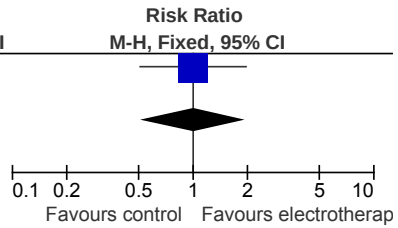


Figure 7 – Electrotherapy vs control; >80% decrease in ulcer area

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Wood, 1993	31	43	4	31	100.0%	5.59 [2.20, 14.21]
Total (95% CI)		**43**		**31**	**100.0%**	**5.59 [2.20, 14.21]**
Total events	31		4			

Heterogeneity: Not applicable
Test for overall effect: Z = 3.61 (P = 0.0003)

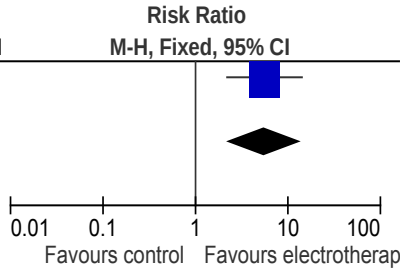


Figure 8 – Electrotherapy vs control; % ulcers reduced by at least 50% at 3 months

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Houghton, 2010	12	15	5	14	100.0%	2.24 [1.06, 4.73]
Total (95% CI)		**15**		**14**	**100.0%**	**2.24 [1.06, 4.73]**
Total events	12		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.12 (P = 0.03)

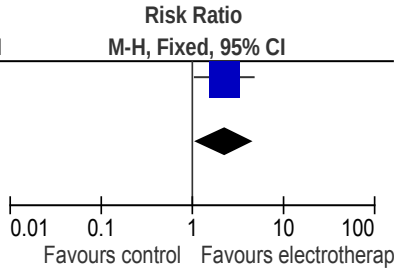


Figure 9 – Electrotherapy vs control; proportion of patients with decreased ulcers

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Asbjornsen, 1990	3	7	0	9	100.0%	13.98 [1.21, 162.00]
Total (95% CI)		**7**		**9**	**100.0%**	**13.98 [1.21, 162.00]**
Total events	3		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.11 (P = 0.03)

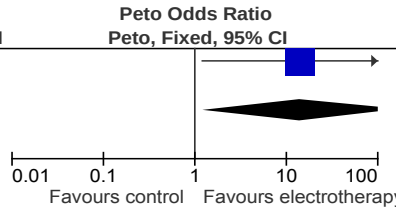


Figure 10 – Electrotherapy vs control; proportion of patients with increased ulcers

Study or Subgroup	Electrotherapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Asbjornsen, 1990	3	7	0	9	50.1%	8.75 [0.52, 145.86]
Houghton, 2010	0	16	4	18	49.9%	0.12 [0.01, 2.14]
Total (95% CI)		**23**		**27**	**100.0%**	**1.05 [0.02, 68.36]**
Total events	3		4			

Heterogeneity: Tau² = 7.00; Chi² = 4.36, df = 1 (P = 0.04); I² = 77%
Test for overall effect: Z = 0.02 (P = 0.98)

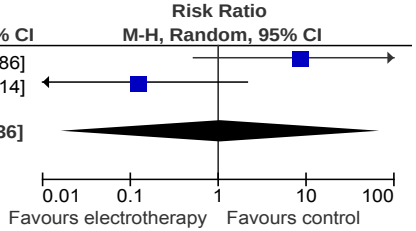


Figure 11 – Electrotherapy vs control; % mean reduction in wound surface area (participants)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.11.1 patients								
Franek, 2012	88.9	14	26	44.4	63.1	24	58.6%	44.50 [18.69, 70.31]
Houghton, 2010	70	25	16	36	61	18	41.4%	34.00 [3.27, 64.73]
Subtotal (95% CI)			**42**			**42**	**100.0%**	**40.16 [20.39, 59.92]**

Heterogeneity: Chi² = 0.26, df = 1 (P = 0.61); I² = 0%
Test for overall effect: Z = 3.98 (P < 0.0001)

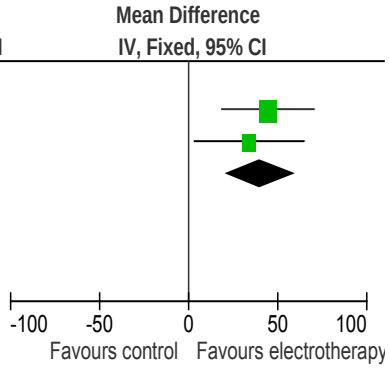


Figure 12 – Electrotherapy vs control; Healing rate (%/week) (participants)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
1.15.1 Patients								
Kloth, 1988	44.8	22.6	9	-11.59	18.6	7	100.0%	56.39 [36.19, 76.59]
Subtotal (95% CI)			**9**			**7**	**100.0%**	**56.39 [36.19, 76.59]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.47 (P < 0.00001)

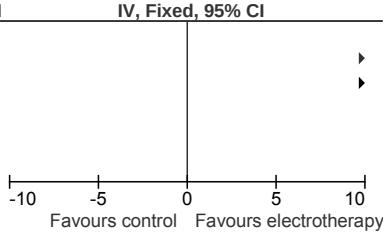


Figure 13 – Electrotherapy vs control; Healing rate (%/day) (exponential fitting) – crossover group

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Jercinovic, 1994	5	4.2	20	1.2	2.1	20	100.0%	3.80 [1.74, 5.86]
Total (95% CI)			**20**			**20**	**100.0%**	**3.80 [1.74, 5.86]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.62 (P = 0.0003)

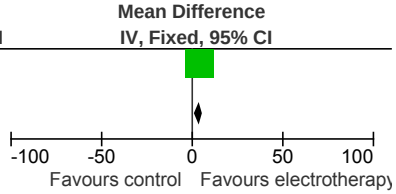


Figure 14 – Electrotherapy vs control; Healing rate (%/day) (linear fitting) – crossover group

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Jercinovic, 1994	2.4	1.4	20	0.6	1.5	20	100.0%	1.80 [0.90, 2.70]
Total (95% CI)			**20**			**20**	**100.0%**	**1.80 [0.90, 2.70]**

Heterogeneity: Not applicable
Test for overall effect: Z = 3.92 (P < 0.0001)

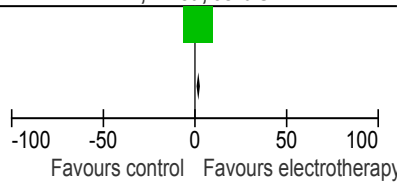


Figure 15 – Electrotherapy vs control; Time to complete healing

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adunsky, 2005	63.4	15.1	9	89.7	9.2	10	100.0%	-26.30 [-37.69, -14.91]
Total (95% CI)			**9**			**10**	**100.0%**	**-26.30 [-37.69, -14.91]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.52 (P < 0.00001)

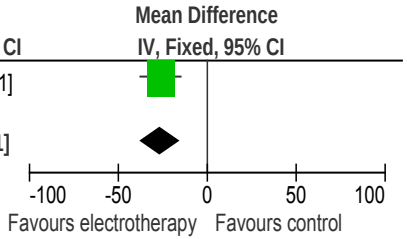


Figure 16 – Electrotherapy vs control; speed of healing (% change from baseline – days)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adunsky, 2005	-0.24	0.14	35	-0.25	0.14	28	100.0%	0.01 [-0.06, 0.08]
Total (95% CI)			**35**			**28**	**100.0%**	**0.01 [-0.06, 0.08]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)

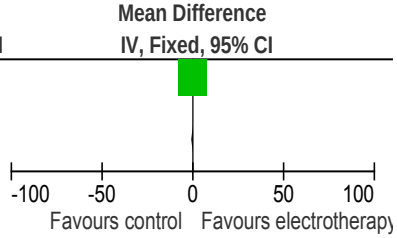


Figure 17 – Electrotherapy vs control; mean reduction in length (%)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Franek, 2012	74	29.6	26	36.1	33.9	24	100.0%	37.90 [20.20, 55.60]
Total (95% CI)			**26**			**24**	**100.0%**	**37.90 [20.20, 55.60]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.20 (P < 0.0001)

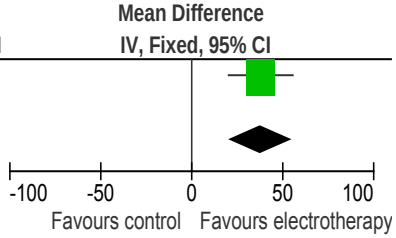


Figure 18 – Electrotherapy vs control; mean reduction in the longest width (%)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Franek, 2012	79	25.1	26	36.3	41.9	24	100.0%	42.70 [23.36, 62.04]
Total (95% CI)			**26**			**24**	**100.0%**	**42.70 [23.36, 62.04]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.33 (P < 0.0001)

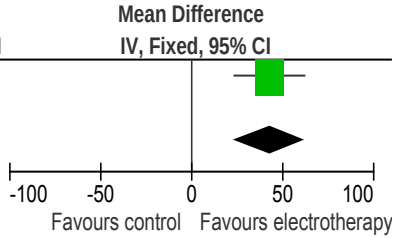


Figure 19 – Electrotherapy vs control; mean reduction in cavity volume (%)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Franek, 2012	100	0.0001	26	54	39.4	24	100.0%	46.00 [30.24, 61.76]
Total (95% CI)			**26**			**24**	**100.0%**	**46.00 [30.24, 61.76]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.72 (P < 0.00001)

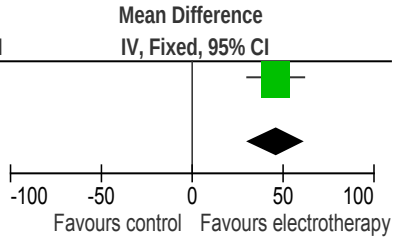


Figure 20 – Electrotherapy vs control; mean reduction in granulation tissue area (%)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Franek, 2012	37.66	76.17	26	10.36	43.46	24	100.0%	27.30 [-6.75, 61.35]
Total (95% CI)			**26**			**24**	**100.0%**	**27.30 [-6.75, 61.35]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.57 (P = 0.12)

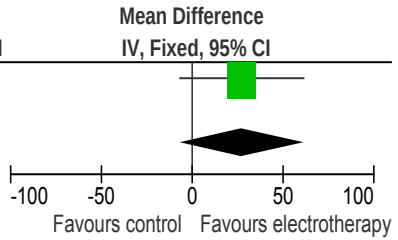
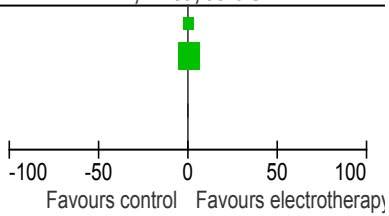


Figure 21 – Electrotherapy vs control; Gilman parameter

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Franek, 2011	0.86	0.45	29	0.42	0.51	29	27.2%	0.44 [0.19, 0.69]
Franek, 2012	0.66	0.24	26	0.26	0.3	24	72.8%	0.40 [0.25, 0.55]
Total (95% CI)			**55**			**53**	**100.0%**	**0.41 [0.28, 0.54]**

Heterogeneity: Chi² = 0.07, df = 1 (P = 0.79); I² = 0%
Test for overall effect: Z = 6.24 (P < 0.00001)

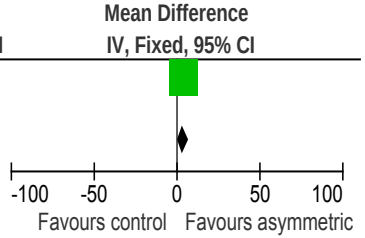


8.3.3.2. Asymmetric biphasic electrostimulation at 100usec versus control

Figure 22 – Asymmetric biphasic electrostimulation at 100usec vs control; mean reduction in wound surface area (%/week)

Study or Subgroup	Asymmetric biphasic Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Baker, 1996	36.4	6.2	67	32.7	7	25	100.0%	3.70 [0.58, 6.82]
Total (95% CI)			**67**			**25**	**100.0%**	**3.70 [0.58, 6.82]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.32 (P = 0.02)

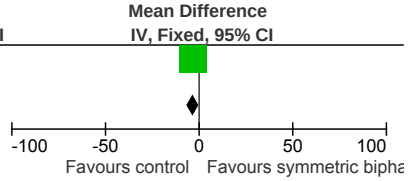


8.3.3.3. Symmetric biphasic electrostimulation at 300usec versus control

Figure 23 – Symmetric biphasic electrostimulation at 300usec vs control; mean reduction in wound surface area (%/week)

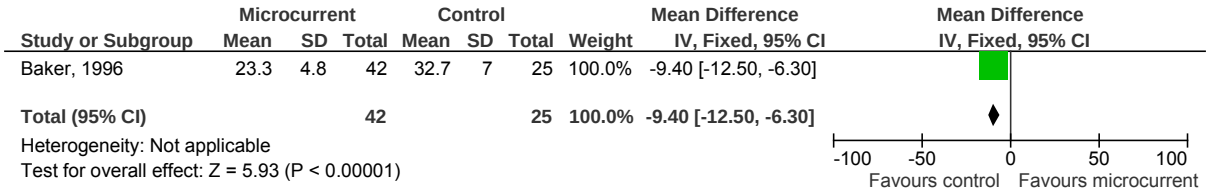
Study or Subgroup	Symmetric biphasic Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Baker, 1996	29.7	5.1	58	32.7	7	25	100.0%	-3.00 [-6.04, 0.04]
Total (95% CI)			**58**			**25**	**100.0%**	**-3.00 [-6.04, 0.04]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.93 (P = 0.05)



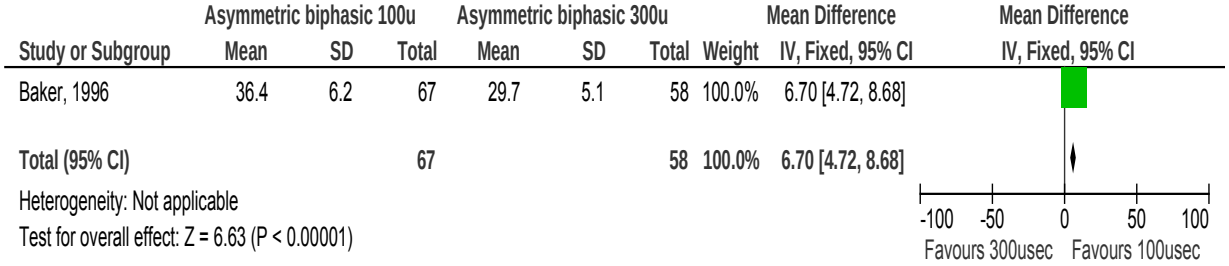
8.3.3.4. Microcurrent versus control

Figure 24 – Microcurrent vs control; mean reduction in wound surface area (%/week)



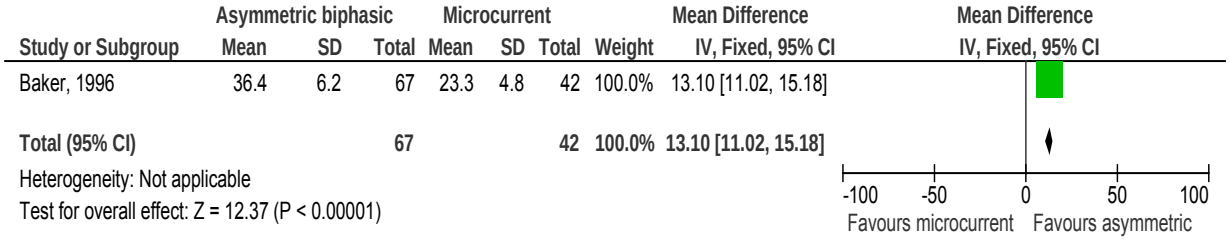
8.3.3.5. Asymmetric biphasic electrostimulation at 100usec versus 300usec

Figure 25 – Asymmetric biphasic electrostimulation at 100usec vs symmetric biphasic electrostimulation at 300usec vs control; mean reduction in wound surface area (%/week)



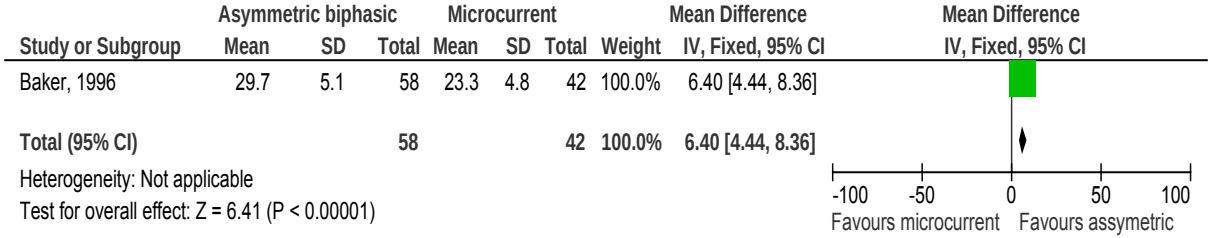
8.3.3.6. Asymmetric biphasic electrostimulation at 100usec versus microcurrent

Figure 26 – Asymmetric biphasic electrostimulation at 100usec versus microcurrent; mean reduction in wound surface area (%/week)



8.3.3.7. Asymmetric biphasic electrostimulation at 300usec versus microcurrent

Figure 27 – Asymmetric biphasic electrostimulation at 300usec versus microcurrent; mean reduction in wound surface area (%/week)



8.3.3.8. Hard to heal ulcers (grade 3 and 4) electrotherapy vs control

Figure 28 – proportion of participants completely healed

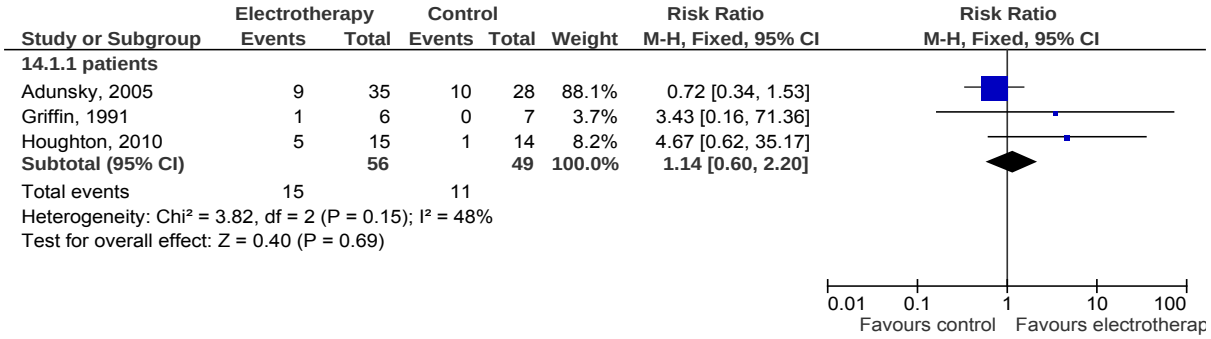


Figure 29 – Absolute reduction in size of pressure ulcer at end of treatment (cm)

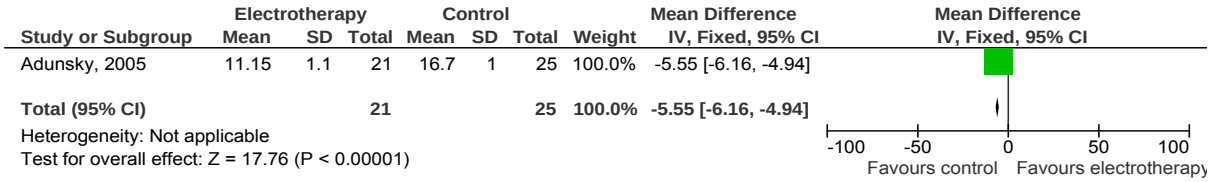


Figure 30 – Absolute reduction in size of pressure ulcer at end of follow-up (cm)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adunsky, 2005	2.53	2.11	21	2.88	1.92	25	100.0%	-0.35 [-1.53, 0.83]
Total (95% CI)			**21**			**25**	**100.0%**	**-0.35 [-1.53, 0.83]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.58 (P = 0.56)

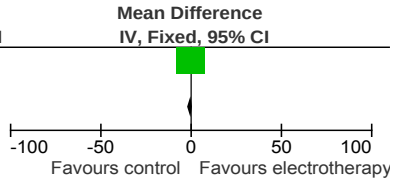


Figure 31 – Healing rate (%/week)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
14.15.1 Patients								
Kloth, 1988	44.8	22.6	9	-11.59	18.6	7	100.0%	56.39 [36.19, 76.59]
Subtotal (95% CI)			**9**			**7**	**100.0%**	**56.39 [36.19, 76.59]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.47 (P < 0.00001)

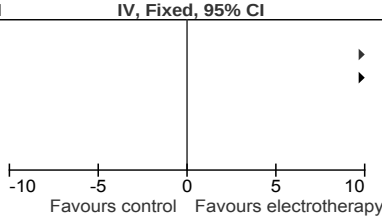


Figure 32 – Time to complete healing (days)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adunsky, 2005	63.4	15.1	9	89.7	9.2	10	100.0%	-26.30 [-37.69, -14.91]
Total (95% CI)			**9**			**10**	**100.0%**	**-26.30 [-37.69, -14.91]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.52 (P < 0.00001)

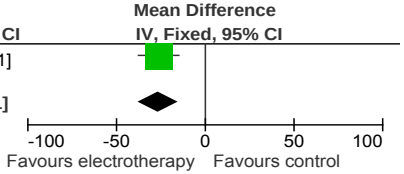
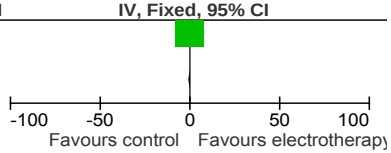


Figure 33 – Speed of healing (% change from baseline – days)

Study or Subgroup	Electrotherapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Adunsky, 2005	-0.24	0.14	35	-0.25	0.14	28	100.0%	0.01 [-0.06, 0.08]
Total (95% CI)			**35**			**28**	**100.0%**	**0.01 [-0.06, 0.08]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.28 (P = 0.78)



8.3.4. Evidence tables

Table 35 – GENTZKOW1991

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Gentzkow (1991) **Title:** Improved healing of pressure ulcers using Dermapulse, a new electrical stimulation device. **Journal:** Wounds: Compend Clin. Res. Pract.3, 5, 158-170 **Study type:** RCT **Sequence generation:** not stated **Allocation concealment:** adequate **Blinding:** double-blind **Addressing incomplete outcome data:** gives details of what happened to drop outs and uses patients available. **Statistical analysis:** continuous variables two sample t-tests used. For categorical variables chi square	**Patient group:** patients with pressure ulcers that were open and stage II, III or IV (Stage II – full thickness skin defect extending into subcutaneous tissue; stage III, defect extending into muscle; stage IV, defect extending to bone or joint structure). 80% were inpatients, 50% were bedbound, 42% wheelchair bound or ambulatory (8%). **All patients** **Randomised N:** 49 ulcers **Completed N:** 40 ulcers (37 patients) **Drop-outs:** 6 (< 4 weeks treatment), 3 (protocol violation) **Group 1** **Randomised N:** 25 ulcers **Completed N:** 21 ulcers	**Group 1:** Stimulation (25): negative polarity unit, wound debrided and serosanguinous drainage appeared, then polarity alternated every 3 days; 128 pps, 35mA, 0.89 C per 30-minute treatment, twice daily for 4 weeks; when ulcer healed to stage 2, treatment at 64pps and polarity changed daily **Group 2:** Sham stimulation (24) identical procedures. Both groups: 100% received wound cleansing with normal saline and dressing; 10% received surgical or whirlpool debridement; 100% received turning to relieve pressure; 55% received bed rest and elevation of an extremity	**Outcome 1:** Mean+/-SD percentage of ulcers healed at 4 weeks	**Group 1:** 49.8+/-30.9% **Group 2:** 23.4+/-47.4% P=0.042	**Funding:** grant from Staodyn, Inc. **Limitations:** no details of randomisation method. Difference at baseline but likely to be in favour of sham group. Used length x width to estimate wound size. **Additional outcomes:** mean % wound healed as a possible function of various factors: metabolic condition, treatment group, tunnels, sex and stage. Patients who were crossed over from the sham to the unblended active therapy after the
			Outcome 2: Rate of healing	**Group 1:** 12.5%/week **Group 2:** 5.8%/week	
			Outcome 3: Mean +/-SD healing at 1 week	**Group 1:** 18+/-19.6% **Group 2:** 3.7%+/-25.7% P=0.053	
			Outcome 4: Mean +/-SD healing at 2 weeks	**Group 1:** 33.2+/-29% **Group 2:** 10.2+/-38.1% P=0.037	
			Outcome 5: Mean +/-SD healing at 3 weeks	**Group 1:** 35.1+/-36.1% **Group 2:** 23.1+/-40.3% P=0.325	
			Outcome 6: withdrawal due to adverse event:	**Group 1:** 0/21 ulcers **Group 2:** 0/19 ulcers	
			Outcome 7: acceptability of treatment (uncomfortable sensations in the ulcer when current turned	**Group 1:** 13.6% of ulcers **Group 2:** 4.2% of ulcers	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
test used. Yate's correction for continuity was used for dichotomous variables. Stepwise multiple regression and three-way ANOVA for separate effects on % healed. **Baseline differences:** Ulcers in group 1 were larger, and therefore measures of percentage healing favours sham group. Ulcers were slightly deeper in the sham group. There were also a higher proportion of females in the sham group (favours sham according to multivariate analysis). **Study power/sample size:** A priori sample-size calculation required 23 patients to detect a 15% difference in healing at 4 weeks, error of 0.05 and 80% power an estimated variance of 18%. **Setting:** 9 site multi-	**Dropouts:** 2 (< 4 weeks treatment), 2 (protocol violation) **Age mean +/- SD (range):** 63.3 +/-17.8 years (29-91 years) **Gender (m/f):** 61.9%/38.1% **Mean+/-SD ulcer depth at week 0:** 1.1+/-2.1cm **Mean+/-SD ulcer area at week 0:** 19.2+/-23.2cm^2 **Number of stage 2 ulcers:** 0 **Number of stage 3 ulcers:** 16 **Number of stage 4 ulcers:** 5 **Duration of ulcer </=12 months:** 85% **Duration of ulcer >12 months:** 15% **Group 2** **Randomised N:** 24 ulcers **Completed N:** 19 ulcers **Dropouts:** 4 (< 4 weeks treatment), 1 (protocol		**on)**		four week trial (n=15). They had healed an average of 13.4% in the sham group but after active stimulation had an average of 47.9% reduction in size for the 4 weeks of electrotherapy, (p=0.012) By last week of treatment had healed an average of 63.9%. 17 of the original electrotherapy group received additional treatment (average 10.7 weeks in total, range 5-2 weeks) had healed an average of 45% by end of therapy and by last week of therapy had healed an average of 74.6% Stage 2: full-thickness skin defect to subcutaneous

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
centre trial in hospital and community, USA. **Length of study:** 4 weeks treatment period. Crossed over at 4 weeks and continued until average 9.8 weeks (range 5-10 weeks). **Assessment of PUs:** Ulcer length and width measured at 0,1,2,3 and 4 weeks. Size measured by longest diameter and widest width **Multiple ulcers:** Patients could have more than one ulcer entered into the study (had to be opposite sides of the body) in which case each ulcer was randomised separately.	violation) **Age mean +/-SD (range):** 62.2+/-18.4 years (31-90 years) **Gender (m/f):** 47.4%/52.6% **Mean+/-SD ulcer depth at week 0:** 1.4+/-2.3cm **Mean+/-SD ulcer area at week 0:** 12.5+/-11.9cm^2 **Number of stage 2 ulcers:** 1 **Number of stage 3 ulcers:** 14 **Number of stage 4 ulcers:** 4 **Duration of ulcer </=12 months:** 66.7% **Duration of ulcer >12 months:** 33.3% **Inclusion criteria:** stage 2, 3 or 4 pressure ulcer **Exclusion criteria:** ulcer totally excluded by eschar, had bleeding or involved major blood vessels; located in pre-sternal, peri-orbital, laryngeal/pharyngeal				tissue; stage 3 defect to muscle; stage 4 defect to bone joint. .

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	regions; pregnant; cardiac pacemaker; osteomyelitis; peripheral vascular disease; malignancy; long-term steroids; chemotherapy; radio-therapy; very obese.				

Table 36 – GRIFFIN1991

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Griffin (1991) **Title:** Efficacy of high voltage pulsed current for healing of pressure ulcers in patients with spinal cord injury. **Journal:** Phys Ther, 71, 433-42 **Study type:** RCT **Sequence generation:** no details on method of sequence generation, randomisation was stratified by grade of ulcer and smoking status **Allocation concealment:** no	**Patient group:** patients with spinal cord injury with pressure ulcers in the pelvic region **All patients** **Randomised N:** 20 **Completed N:** 17 **Drop-outs:** 2 medical complications, 1 surgical repair of ulcer. **Group 1** **Randomised N:** 10 **Completed N:** 8 **Dropouts:** 2 **Median (range) age:** 32.5 years (17-54 years) **Median (range ulcer duration:** 4.5 weeks (2-	**Group 1:** Stimulation and routine dressings: frequency 100pps, 200V, negative polarity, 1 h/day for 20 consecutive days; pressure sore cleansed using Cara-Klenz, application of Carrington gel and a dry dressing; wound mechanically debrided as necessary. **Group 2:** Sham stimulation + routine dressing. All patients: 2 hourly turning; no change of mattress during the study. Patients received equivalent nursing care. Cleansing of	**Outcome 1:** median (range) change in wound surface area - day 5	**Group 1:** -32% (-12% to -100%) **Group 2:** -14% (+17% to -74%) P=0.03	**Funding:** funded in part by a grant from the foundation for Physical Therapy Inc. **Limitations:** Very small sample size. No details of sequence generation method or allocation concealment. No blinding of outcome assessors. The authors had designed the study with the assumption that
			Outcome 2: median (range) change in wound surface area - day 10	**Group 1:** -47% (-23% to -100%) **Group 2:** -42% (+42% to -41%) P=0.14	
			Outcome 3: median (range) change in wound surface area - day 15	**Group 1:** -66% (-42% to -100%) **Group 2:** -44% (+22% to -100%) P=0.05	
			Outcome 4: median (range) change in wound surface area - day 20	**Group 1:** -80% (-52% to -100%) **Group 2:** -52% (-14% to -100%) P=0.05	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
details **Blinding:** double blinded. No blinding of outcome assessors. **Addressing incomplete outcome data:** the authors state why patients dropped out and they were similar reasons in the two groups. **Statistical analysis:** for difference between groups for continuous variables the Mann-Whitney U test was used. For nominal data the Fisher's Exact Test was used. **Baseline differences:** significant difference between groups for duration of spinal cord injury, longer in the HVPC group. **Study power/sample size:** very small n=20, a sample size calculation was given of 10 in each group for 80% power to detect a 20% improvement between groups using a one-sided test; given	116 weeks) **Mean (range) ulcer size at day 0:** 234.1mm^2 (126-1027mm^2) **Ulcer grade 2:** 2 **Ulcer grade 3:** 5 **Ulcer grade 4:** 1 **Group 2** **Randomised N:** 10 **Completed N:** 9 **Dropouts:** 1 **Median (range) age:** 26 years (10-74 years) **Median (range ulcer duration:** 3.0 weeks (1-30 weeks) **Mean (range ulcer size at day 0):** 2771.8mm^2 (41-4067mm^2) **Ulcer grade 2:** 2 **Ulcer grade 3:** 6 **Ulcer grade 4:** 1 **Inclusion criteria:** male; spinal cord injury; pressure sore grade 2-4, Delisa system, on sacral/coccygeal or gluteal/ischial region	ulcers twice a day, followed by gel and a dry dressing. Wounds were mechanically debrided, as necessary; enzymatic debridement was not used. All ulcers were cultured before treatment began. All possible efforts were made to keep pressure off the ulcer. A routine 2-hour turning schedule was followed when patients were in bed.			ischial and sacral ulcers would occur equally in each group, but the placebo group had a higher amount than the treatment group. The authors also state that both patient who were older than 70 years were in the placebo group, although they had appropriate healing or similar to another patient aged 26 years. **Additional outcomes:**
			Outcome 5: Number of grade 2 ulcers completely healed at 20 days	**Group 1:** 2/2 **Group 2:** 2/2	
			Outcome 5: Number of grade 3 ulcers completely healed at 20 days	**Group 1:** 1/5 **Group 2:** 0/6	
			Outcome 5: Number of grade 4 ulcers completely healed at 20 days	**Group 1:** 0/1 **Group 2:** 0/1	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
a standard deviation of 15% **Setting:** inpatients, specialist spinal injuries unit, USA. **Length of study:** 20 days treatment. **Assessment of PUs:** measured at 0,5,10,15 and 20 days by computerised planimetry from projected transparencies. **Multiple ulcers:** if multiple ulcers, the larges in wound surface area was used.	**Exclusion criteria:** severe cardiac disease; cardiac arrhythmia; uncontrolled autonomic dyreflexia; cardiac pacemaker				

Table 37 – WOOD1993

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Wood (1993) **Title:** A multicentre study on the use of pulsed low-intensity direct current for healing chronic stage II and stage III	**Patient group:** patients with stage II and stage III chronic pressure ulcers. **All patients** **Randomised N:** 71	**Group 1:** pulsed low-intensity direct current + standard treatment. 600UA, pulse frequency 0.8Hz, three applications around each ulcer, alternate days, three times weekly; for larger ulcers, on e or more	**Outcome 1:** Number of ulcers completely healed at 8 weeks	**Group 1:** 25/43 (58%) **Group 2:** 1/31 (3%)	**Funding:** support from Veterans Administration Hospitals, the universities of Minnesota and Hambur, and by Harbor Medical
			Outcome 2: Decrease in ulcer area>80% at 8 weeks	**Group 1:** 31/43 (72.9%) **Group 2:** 4/31 (12.9%) P<0.0001 (Fisher t-test)	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
decubitus ulcers. **Journal:** Arch Dermatol, 129, 999-1009. **Study type:** multicentre RCT **Sequence generation:** method of randomisation not stated. **Allocation concealment:** instruments were labelled either A or B by an independent investigator before study began. Multicentre study. **Blinding:** double-blinded. **Addressing incomplete outcome data:** details of drop-outs and how many followed-up. **Statistical analysis:** Fisher Exact Test (two tailed) **Baseline differences:** no significant differences **Study power/sample size:** small n=41	patients, 74 ulcers **Completed N:** 63 patients **Drop-outs:** 6 died, 2 lost to follow-up. **Group 1** **Randomised N:** 41 patients, 43 ulcers **Completed N:** 39 patients **Dropouts:** 2 died, 0 lost to follow-up Mean age: 75.6 years Gender (m/f): 26/15 Mean duration of ulcer: 5.5 months Mean ulcer area: 2.61 cm^2 Mean ulcer depth: 2.81cm **Group 2** **Randomised N:** 30 patients, 31 ulcers **Completed N:** 24 **Dropouts:** 4 died, 2 lost to follow-up Mean age: 74.9 years Gender (m/f): 15/15 Mean duration of ulcer: 4.9 months	additional electrode placements. **Group 2:** Sham pulsed low-intensity direct current + standard treatment. Standard treatment: wound cleansing, simple moist dressing whirlpool baths; no hydrocolloids, films or foam dressings were used.	**Outcome 3:** Mean +/-SD ulcer area at 8 weeks (number of ulcers) **Outcome 4:** Mean+/-SD ulcer depth at 8 weeks	**Group 1:** 0.41+/-0.99cm^2 (41) **Group 2:** 1.66+/-2.14cm^2 (25) **Group 1:** 1.0+/-1.1cm **Group 2:** 2.6+/-1.0cm	Inc. **Limitations:** No details of sequence generation; unclear allocation concealment. Difference in number of participants in group 1 and group 2. High drop-out in control group. **Additional outcomes:**

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Setting: 4 centres, USA **Length of study:** 8 weeks treatment. **Assessment of PUs:** diameter, perimeter and photograph of ulcer taken weekly over weeks 0-8. **Multiple ulcers:** data presented by ulcers rather than by patients	Mean ulcer area: 1.91 cm^2, p<0.05 (between groups) Mean ulcer depth: 2.84cm **Inclusion criteria:** stage 2 or 3 chronic pressure sores showing no improvement with standard nursing care over preceding 5 weeks **Exclusion criteria:** patients receiving steroids or other drugs that influence wound healing				

Table 38 – ADUNSKY2005

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Adunsky (2005) **Title:** Decubitus direct current treatment (DDCT) of pressure ulcers: results of a randomised double-blinded placebo controlled study. **Journal:** Archives of Gerontology and Geriatrics 41, 261-269.	**Patient group:** post-acute care in-patients from geriatric and rehabilitation medicine departments with stage 3 degree non-diabetic pressure ulcers lasting >/= 30 days (defined by NPUAP scoring system). **All patients**	**Group 1:** decubitus direct current treatment (DDCT) – the DDCT is a mains-powered stand-alone device, connected to a computer with a software to file such information as patient database and photographs of the ulcer at different points of time. During the trial the device provided wound size measurement and recorded the electrical activity around	**Outcome 1:** Closure (complete healing) of ulcers at end of follow-up (147 days)	**Group 1:** 9/35 (25.7%) ITT **Group 2:** 10/28 (35.7%) ITT P=0.28	**Funding:** supported by the Lifewave Medical Devices Company. **Limitations: no details of allocation concealment. High drop-out, per protocol was used but control**
			Outcome 2: Closure by end of treatment (57 days)	**Group 1:** 5/35 **Group 2:** 3/28 P=0.39 **Per protocol** **Group 1:** 5/25 (20%) **Group 2**: 1/?	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Study type: multicentre, double-blind randomised placebo-controlled trial **Sequence generation:** randomisation in each department using a block design of size 4, to assure a ratio of 50:50 in the two groups **Allocation concealment:** no details **Blinding:** double-blinded and placebo used. **Addressing incomplete outcome data:** ITT and per protocol - although 38 completed trial (54% of treatment group and 64% of placebo group = 37). Details drop-outs from which arms but unclear. **Analysis:** primary objective ITT. **Statistical analysis:** two-sample t-test and non-parametric tests for testing differences	**Randomised N:** 63 (54 elderly patients and 9 spinal cord injured patients). **Completed N:** 38 **Drop-outs:** 25 (ten elderly patients due to a variety of reasons. Other 15 patients (but none of the paraplegic patients) were withdrawn during this study owing to adverse events such as a need for limb amputation (n=3), deterioration of ulcer status (n=1), acute clinical deterioration (n=8: massive pneumonia, urosepsis, ischemic colitis, installation of a cardiac pacemaker), patient's consent withdrawal (n=2), technical difficulty (n=1). **Mean age (years):** 71.1 (18.8) **Males/females:** 13/22 **Ulcer area (cm^2):** 7.4 (1.8) **Ulcer depth (cm^2):** 1.5 (1.4) **Ulcer width (cm^2):** 3.2	the wound before and after each treatment. During DDCT treatment, electrical currents are transferred to the healthy skin surrounding the necrotic wound area, through the use of soft external electrodes placed on the healthy skin surrounding the wound. The treatment consisted initially of three such 20-min sessions daily, reduced to two daily sessions after 14 days. **Group 2:** placebo (sham). Both groups received conservative treatment of wounds (eg surgical debridement, if deemed necessary, followed by the application of hydrocolloid or collagen dressings) and placebo- DDCT	**Outcome 3: Speed of wound closure (mean time to complete closure)**	**Group 1:** 63.4 (15.1) days **Group 2:** 89.7 (9.2) days P=0.16 Model of logistic regression applied for calculating odds ratio between groups OR 1.6 (95% CI 0.4-4.73)	**arm denominator was unclear.** **Additional outcomes:**
			Outcome 4: absolute ulcer area reduction at day 147	**Group 1: 13.56** **Group 2: 14.54** **MD -0.98**	
			Outcome 5: speed of healing: (standardised estimate for trend of healing speed): (rate of wound area reduction reflected by change from baseline of ulcer area, percentage). Using model of linear regression (standardised estimate of healing speed)	**Group 1: -0.44** **Group 2: -0.14** **Group 1:** -0.24 **Group 2:** -0.25 P=0.78	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
between groups for quantitative parameters. Chi-square and Fisher's exact tests for testing difference between groups for the categorical parameters. A multiple linear regression was applied to compare the effect of change in the wound area along the weeks. **Baseline differences:** no **Study power/sample size:** 31 patients were required in each group. **Setting:** 11 departments of geriatric and rehabilitation medicine. **Length of study:** 8 weeks treatment; followed up for 12 weeks (90 days) from DDCT treatment termination. **Assessment of PUs:** measurements of the surface area using a specific software	(1.3) **Ulcer length (cm^2):** 4.4 (1.6) **Ulcer duration (days):** 3.8 (1.5) 63 patients with 63 Pus with 25 located over the sacrum, 13 on the trochanters, 13 on the calves and ankles, 6 on the heels, 4 on the buttocks and 2 on the ischium. The distribution of these was similar in both groups. **Group 1** **Randomised N:** 35 **Completed N:** 19 **Dropouts:** 16 (5 elderly due to a variety of medical reasons) **Mean age (years): 71.4 (18.9)** **Males/females: 26/37** **Ulcer area (cm^2): 7.5 (2.1)** **Ulcer depth (cm^2): 1.5 (1.3)** **Ulcer width (cm^2): 3.2 (1.4)**				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
program to assure accuracy of method of measuring the wounds size. **Multiple ulcers:** no	**Ulcer length (cm^2): 4.4 (1.8)** **Ulcer duration (days): 4.2 (1.0)** **Group 2** **Randomised N:** 28 **Completed N:** 18 **Dropouts:** 10 (5 elderly due to a variety of medical reasons) **Mean age (years): 71.8 (19.5)** **Males/females: 13/15** **Ulcer area (cm^2): 7.6 (1.1)** **Ulcer depth (cm^2): 1.5 (1.3)** **Ulcer width (cm^2): 3.3 (1.5)** **Ulcer length (cm^2): 4.4 (2.0)** **Ulcer duration (days): 5.0 (1.2)** **Inclusion criteria:** age >18 years, informed consent, ulcer duration less than 24 months, ulcer size greater than 1cm^2 but smaller than 50cm^2, no recent history				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	(minimum of 30 days) of growth factors or vacuum-assisted treatment. **Exclusion criteria:** stages other than 3 degree, liver function enzymes higher than twice the upper limit of normal values, renal failure with creatinine >2mg%, anaemia (haemoglobin <10g%), albumin <2.6g%, and patients having a pacemaker. Also those with significant medical disorder that might interfere with treatment results, patients with recent (2 months) use of steroids, chemotherapy or other immuno-compromising drugs. Withdrawal criteria were applied to remove patients from the study whenever considered necessary for their well-being.				

Table 39 – HOUGHTON 2010

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Houghton (2010) **Title:** Electrical stimulation therapy increases rate of healing of pressure ulcers in community-dwelling people with spinal cord injury **Journal:** Arch Phys Med Rehabil, 91, 669-678. **Study type:** single-blind, parallel-group RCT **Sequence generation:** stratified into 4 groups according to ulcer duration and severity before randomisation. Randomised using a concealed random process by an independent person with random number generation. **Allocation concealment:** used an opaque envelope prepared by an independent person **Blinding:** single-	**Patient group:** people in the community with spinal cord injuries with pressure ulcers (stage II to IV) **All patients** **Randomised N:** 34 **Completed N:** 34 **Drop-outs:** 0 at 3 months Mean age (SD): 51 (14) **Group 1** **Randomised N:** 16 **Completed N:** 16 (at 3 months, n=14 at 6 months) **Dropouts:** treatment discontinued n=1, those who used EST <100 hrs n=3. Age: 50.3 (SD 17, range 23-74) Males/females: 8/8 Quadriplegia: 7 Paraplegia; 6 Spina bifida: 3 Wound location (no of subjects):	**Group 1:** Electric stimulation therapy (EST) (self-guided) as part of a community-based interdisciplinary wound care program in addition to a standard wound care program. Patients, family, and/or community nurses were trained to apply daily treatments of EST – included a 1 hour general inservice followed by 2 to 3 half-hour sessions in which specific instructions were provided by experienced study personnel to 2 to 3 caregivers at the bedside. Wounds were loosely packed with silver nylon dressing premoistened in sterile water or coated in hydrogel (in order to conduct electric current throughout the wound bed and to the base of deep wounds). Additional inactive packing materials (silver, zinc, hypertonic saline) or petrolatum-based products were added in order to manage the wound moisture properly for each subject. In	**Outcome 1 (study's primary outcome):** % decrease in wound surface area at the end of 3 months - mean (sd)	**Group 1:** 70% (25%) **Group 2:** 36% (61%) P=0.048	**Funding:** Ontario Neurotrauma foundation grant. **Limitations:** small sample size. No blinding of caregiver and participant but the authors say it is not possible for EST. **Additional outcomes:** Notes: for ethical reasons, those who did not have EST were offered after the 3 month intervention period. And those with reduction on EST were offered to continue after the 3-month intervention period. Wound surface area (cm2) was
			Outcome 2: proportion of wounds that improved (by at least 50% reduction) at end of 3 months	**Group 1:** 12/15 (80%) **Group 2:** 5/14 (36%) OR: 7.2 (95% CI 1.4-38.3), p=0.02	
			Outcome 3: changes in wound appearance at end of 3 months - mean PWAT scores (sd):	**Group 1:** 9 (5.1) - previously 13.38 (3.0), p=0.031 **Group 2:** not reported.	
			Outcome 4: Proportion with improved PWAT scores:	**Group 1:** 12/16 (75%) **Group 2:** 8/18 (44%) P=0.070	
			Outcome 5: Proportion with wounds that increased (worsened):	**Group 1:** 0/16 (0%) **Group 2:** 4/18 (22%) P=0.01	
			Outcome 6: Proportion with	**Group 1: 8/16 (50%)** **Group 2: 9/18 (50%)**	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
blinded. Outcome assessor was blinded. **Addressing incomplete outcome data:** Clear flow diagram of patients completing treatment. The EST treatment and regular wound dressing changes continued during the 3 month intervention or until the ulcer healed. Once healed the subject was discharged from wound care services, however monthly evaluations continued for at least 6 months when possible. **Baseline differences:** no statistically significant differences found. **Study power/sample size:** small **Statistical analysis:** student tests for continuous variables and chi-square analysis for categorical data. **Setting:** Community-	Buttock region -ischial tuberosity:8 - sacrum, coccyx, hip:4 Leg: foot, ankle, knee: 4 Wound duration (years): 1.2 (SD 1.0, range 0.3-4.1) No of subjects with duration of ulcer > 2 years: 3 Wound severity (no of subjects) NPUAP stages: Stage II: 1 Stage III: 6 Stage IV: 7 Stage X=2 Initial wound surface area (cm2): 3.38 (sd 3.44, range 1.2 s.d 12.0) No. of subjects with multiple wounds: 8 No of subjects with previous or recurrent problems with pressure ulcers: 10 **Group 2** **Randomised N:** 18 **Completed N:** 18 **Dropouts:** 0 at 3	most cases (11/16 subjects) a single electrode (4.8x10.2cm) was placed directly over the wound and a larger (12.7x20.3cm) dispersive electrode was placed on intact skin at least 20cm from the wound. A small portable, programmable device (micro Z) was used to deliver a twin –peaked monophasic pulsed current (high-voltage pulsed current) with 50us pulse duration, intensity of the machine 50 -150v at a level that was below the level of muscle contraction and based on sensory level on intact skin. Provided 20 minutes at a pulse frequency of 100Hz followed by 20 minutes at 10Hz and then 20 minutes off cycle each hour for 8 hours each day for a period of at least 3 months. The polarity of the active electrode used in monopolar set-up was initially negative (cathode) and alternated each week.. EST protocol was incorporated into regular wound dressing changes scheduled every 1 to 3 days.	improved PSST scores:	**P=0.560**	determined at initial assessment before treatment and was measured at monthly intervals for 3 months.
			Outcome 7: Proportion of stage II ulcers healed	**Group 1:** 1/1 (100%) **Group 2:** 4/4 (100%) P=0.620	
			Outcome 8: Proportion of stage III, IV, X ulcers healed:	**Group 1:** 5/15 (33.3%) **Group 2:** 1/14 (7.1%) 0.550	
			Outcome 9: Proportion of stage III, IV, X ulcers at least 50% smaller:	**Group 1:** 12/15 (8**0%)** **Group 2:** 5/14 (36%) P=0.020	
			Outcome 10: EST compliance - mean (s.d) and proportion using the recommended time:	**Group 1:** 3.0 (1.5)h/d (recommended treatment time 8h/d) 4/16 Those who healed used the EST longest (539 total hours; 3.54h/d); those who did not heal (331 total hours; 2.24h/d).Average for those who healed: 136.4 days (4.5 months)	
			Outcome 11: Adverse reactions:	**Group 1:** Red area or burn under the active electrode after EST treatment, area resolved within 48 hours and remedied by turning down	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
based home care setting, Ontario, Canada. **Length of study:** evaluated on a monthly basis for at least 3 months and thereafter followed up for an average of 4 months **Assessment of Pus:** Wound surface area (cm2) was determined at initial assessment before treatment and was measured at monthly intervals for 3 months. **Assessment of Outcomes:**. wound surface area determined using Visitrak system – previously validated, which involves tracing the wound perimeter onto acetate film and digitising using a calibrated tablet. Change in wound appearance evaluated using the PWAT and PSST. EST compliance - a meter tracked the total no. of	months, 1 at 6 months. Age: 50.3 (SD 17, range 23-74) Males/females: 8/8 Quadriplegia: 8 Paraplegia; 8 Spina bifida: 2 Wound location (no of subjects): Buttock region -ischial tuberosity: 11 - sacrum, coccyx, hip: 4 Leg: foot, ankle, knee: 3 Wound duration (years): 3.0 (s.d 5.6, range 0.3-15.20) No. of subjects with duration of ulcer > 2 years: 4 Wound severity (no of subjects) NPUAP stages: Stage II: 4 Stage III: 4 Stage IV: 10 Stage X: 0 Initial wound surface area (cm^2): 2.73 (s.d 2.89, range 1.1 -10.9) No. of subjects with multiple wounds: 5 No of subjects with	**Group 2:** Standard wound care program. Both groups received standard wound care. Standard wound care program: evaluated in their homes and in clinic setting by nurses, occupational therapists, physical therapist or dieticians with experience of treating SCI and/or pressure ulcers. Medical and wound histories collected. Patient activity schedule completed to identify all surfaces encountered and the type of transfers performed daily. If wheelchair seating a concern an assessment conducted. A review of nutritional issues conducted. Blood analysis performed. A wound assessment was performed to assess wound dressing required. Tailored program of needs of each subject for nutritional intervention, optimisation of wound		the intensity of subsequent EST treatments. One patient complained of dizziness and delusions while receiving EST but was evaluated as withdrawal from narcotics after lapse in prescription.	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
hours the machine was used to determine amount of time EST applied for each subject. **Categorisation of Pus: stratified into 4 groups using NPUAP definitions for stages:** stage II or III ulcers present for more than 2 years, stage II or III ulcers present for less than 2 years, stage IV or unstageable (stage X) ulcers present for more than 2 years, and stage IV or X ulcers present for less than 2 years. **Multiple ulcers:** no	previous or recurrent problems with pressure ulcers: 11 **Inclusion criteria:** people with paraplegia or quadriplegia caused by congenital, medical or traumatic SCI, over the age of 18 years, living in the community, had a stage II to IV pressure ulcer between 1 and 20cm^2 present for at least 3 months in standard wound care program that included appropriate pressure redistribution **Exclusion criteria:** Serious or multiple medical conditions that would limit healing; any condition that was contraindicated for EST (cardiac pacemaker, osteomyelitis, pregnancy, cancer).	dressing protocol and continence management. Subjects did nor receive same wound dressing protocol and had a customised program. A comprehensive pressure management program was also included. The program was described to patients prior to randomisation so they could decide if they wished to participate in the study.			

Table 40 – FRANEK2011

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Franek 2011 **Title:** Effect of high voltage monophasic stimulation on pressure ulcer healing: results from a randomised controlled trial **Journal:** Wounds 2011, 23(1), 15-23 **Study type:** RCT **Sequence generation:** computer-generated randomised numbers **Allocation concealment:** the generated random numbers were sealed in sequentially numbered envelopes and group allocation was independent of place and person delivering the treatment. **Blinding:** no blinding. **Addressing incomplete outcome data:** no mention of drop-outs. **Baseline differences:**	**Patient group: patients with stage I, II and III pressure ulcers** **All patients** **Randomised N:** 58 **Completed N:** 58 **Drop-outs:** 0 **Group 1** **Randomised N:** 29 **Completed N:** 29 **Dropouts:** 0 **Females/males:** 10/19 **Age (years):** 59.90 (s.d 8.8, range 19-87) 3 patients had ulcers from poorly fitting footwear, 3 from poorly fitted artificial limbs (prosthesis), 6 from plaster cast usage after a bone fracture, and 2 due to complication of unhealed post-operative wounds, 3 from internal pressure from surgical metal plates and screws following orthopaedic operation, 4 from prolonged immobilisation, other	**Group 1:** high voltage monophasic stimulation (double-peaked monophasic impulses of 100us and frequency 100Hz were applied at 100v. Treatment performed with a current amplitude, which produced sub-motor stimulation that caused a mild tingling sensation. Electrodes were made of silver or conductive carbon rubber. The active electrode size was matched to the wound size and placed on saline soaked gauze directly into the wound. The return electrode was positioned on intact periwound skin. Each procedure lasted 50 minutes. Stimulation was repeated once daily for 5 days a week. Treatment always began with cathode stimulation to clean the wounds of nonviable tissue. Cathode stimulation time lasted for 2 weeks. This was followed by anode stimulation, performed for 4 weeks. **Group 2:** pharmacologic agents, administered identically as in group 1.	**Outcome 1:** Proportion of patients with ulcers healed	**Group 1:** 8/29 (27.6%) **Group 2:** 4/29 (13.8%)	**Funding:** no details **Limitations:** small study, no blinding (although authors say not possible for EST but no mention of outcome assessors **Additional outcomes:**
			Outcome 2: relative change of total surface area	**Group 1:** 85.38% **Group 2:** 40.08%	
			Outcome 3: relative change in length	**Group 1:** 71.22% **Group 2:** 30.38%	
			Outcome 4: relative change in width	**Group 1:** 76.09% **Group 2:** 32.48%	
			Outcome 5: relative change in volume	**Group 1:** 20.69% **Group 2:** 9.39%	
			Outcome 6: relative change in Gilman Index	**Group 1:** 0.64cm **Group 2:** 0.28cm P</=0.001 in favour of group A	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
no statistically significant differences **Study power/sample size:** small, no power calculation **Statistical analysis:** chi-square independence test used for analysis of the indicators. Mean values of the Gilman Index, total area, length, width and volume of the ulcers before and after therapy were compared in both groups by Wilcoxon matched-pairs signed-rank test and the Mann-whitney U-test was used to evaluate differences in relative changes between the groups. To define relationships between the change of wound are and volume with changes of linear dimensions the Spearman correlation index was used. **Setting:** the Traumatic Surgery Hospital, Piekary Skaskie,	patient's ulcers were from mechanical soft tissue injuries (abrasion, scratch etc) **Ulcer stage (no. of patients):** **Stage I:** 7 **Stage II:** 13 **Stage III:** 9 **Ulcer location:** Lower leg: 16 Foot: 8 Gluteal/ischial: 2 Ankle: 2 Hand: 1 **Duration of disorder (months):** mean 3.17 (s.d 2.33, range 1-6) **Initial wound area (cm2):** mean 4.45 (s.d 3.39, range 1.11-15.81) **Initial wound volume (cm2):** mean 0.04 (s.d 0.12, range 0.01-1.24) **Group 2** **Randomised N:** 29 **Completed N:** 29 **Dropouts:** 0 **Age (years):** 60 (s.d 9.97, range 14-88) Females/males: 18/11 1 patient had pressure	Both groups: pharmacological agents, including wound cleansing with potassium permanganate. The ulcer base was covered with compresses of fibrolan, colistin, and iruxol and wet dressings of 10% sodium chloride. Dressings were changed daily (in experimental group local bath, compresses, and wet dressings were provided after HVMS procedures).			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Poland. **Length of study:** 6 weeks treatment. **Assessment of PUs:** measured by planimetry of congruent projections of the wounds onto transparency paper then using a digitzing pallet. The depth was measured at various point by precision micrometry. Measurements of area (total and isolated areas covered with pus or granulation) and volume were performed in each person before therapy and every week during treatment. Length and perpendicular width dimension measurements were also recorded. Observation of healing process supported by precisely calculated parameters such as the Gilman index and relative changes. **Multiple ulcers:** no	ulcers from poorly fitting footwear, 3 from a poorly fitted artificial limb (prosthesis), 2 from plaster cast usage after a bone fracture and three as a result of complications of unhealed postoperative wounds, 3 had ulcers related to internal pressure from surgical metal plates and screws after an orthopaedic operation, 7 had ulcers from prolonged immobilisation, the rest had ulcers from mechanical soft tissue injuries. p>0.05 **Ulcer stage (no. of patients):** **Stage I:** 8 **Stage II:** 13 **Stage III:** 8 p>0.05 **Ulcer location:** Lower leg: 13 Foot: 6 Gluteal/ischial: 4 Ankle: 2 Hand: 4 **Duration of disorder**				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	(months): mean 2.80 (s.d 2.32, range 1-6) **Initial wound area (cm2):** 4.93 (s.d 4.95, range 1.14-15.09) **Initial wound volume (cm2):** 0.04 (s.d 0.11, range 0.01-1.29) **Inclusion criteria:** Stage I (erythema of intact skin - darker skin, discoloration of the skin, warmth, edema, hardness); Stage II (partial-thickness, skin loss, involving the epidermis, dermis or both; the injury is superficial and clinically presents as an abrasion, blister or shallow crater); or Stage III (total-thickness skin loss, involving damage to or necrosis of subcutaneous tissue that may extend down to fascia or muscle; pressure ulcer appears clinically as a deep crater). **Exclusion criteria:**				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	spinal cord injuries or other loss of sensitivity (paresis or paralysis), chronic venous insufficiency, arteriosclerosis (ABPI <0.9), diabetes, ventricular arrhythmia, cardiac pacemakers, metal implants, pregnancy, and post-steroid therapy.				

Table 41 – KLOTH1988

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Kloth 1988 **Title:** Acceleration of wound healing with high voltage, monophasic, pulsed current **Journal:** Physical therapy, 68 (4), 503-508 **Study type:** RCT **Sequence generation:** coin tossed by person not involved in the study **Allocation concealment:** no	**Patient group:** patients with stage IV decubitus ulcers **All patients** **Randomised N:** 16 **Completed N:** 16 **Drop-outs:** 0 Age range: 20-89 years of age **Group 1** **Randomised N:** 9 **Completed N:** 9 **Dropouts:** 0 Age (mean): 71 (s.d 21)	**Group 1:** high voltage, monophasic, pulsed current (daily electrical stimulation from a commercial high voltage generator - Dyna Wave model 12 high voltage, monphasic twin-pulsed generator) The frequency was 105Hz, an intraphase interval of 50usec, and a voltage just below that capable of producing a visible muscle contraction (100-175 V). At 100 V with an intraphase interval f 100usec, the single-phase charge was calculated at about 1.6uC with a total-	**Outcome 1:** proportion with ulcers healed completely healed (total ulcer surface area change (%)) **Outcome 2:** healing rate (%/week) Wound surface area reduction per week	**Group 1:** 9/9 (100%) over mean period 7.3 weeks **Group 2:** 0/7 (0%) (increased by 28.93% s.d 89.8%) over mean period of 7.4 weeks **Group 1:** 44.80% (s.d 22.6) **Group 2:** -11.59% (s.d 18.6)	**Funding:** no details **Limitations:** very small sample size**.** No allocation concealment. No mention of outcome assessor blinding. **Additional outcomes:** three patients who were crossed over from control to treatment group

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
details **Blinding:** sham placebo used. **Addressing incomplete outcome data:** no missing data. **Analysis:** no details **Statistical analysis:** none **Baseline differences:** no details **Study power/sample size:** very small study/no sample calculation given **Setting:** no details , assume hospital **Length of study:** 16 weeks treatment. **Assessment of PUs:** the same physical therapist recorded surface area wound dimensions before and after treatment at weekly treatment intervals. Plastic wrap was placed over the wound and traced (three times) round the wound's perimeter with a fine-tipped transparency marker. Metric graph paper	years **Group 2** **Randomised N:** 7 **Completed N:** 7 **Dropouts:** 0 3 patients whose ulcers did not heal were re-assigned arbitrarily to the treatment group to assess whether their ulcers would respond to the HVS treatment. Age (mean): 66 (s.d 21) years **Inclusion criteria: (not strictly listed as inclusion criteria but common to all participants:** intact peripheral nervous systems; stage IV ulcers that had eroded into or through a muscle; ulcers had been unresponsive to previous treatments administered by other health care personnel. **Exclusion criteria:** no details	pulse charge accumulation of 342uC/sec. Patients received 45 minutes of ESTR once a day, five days a week. **Group 2:** had the electrodes applied daily but received no stimulation. Sham treatments were given for periods of 4,5 and 16 weeks to three patients in the control group - the wound dimensions either increased or did not change in size and they were then reassigned to the treatment group. Both groups: all patients who had ulcers caused by pressure against the skin used a pressure-relieving device that reduced exogenous cutaneous pressure. All patients took a high-protein dietary supplement to help offset nitrogen loss from wound protein breakdown. Wounds were debrided manually and with enzymes. Thick eschar and the outermost necrotic tissue were debrided manually. A proteolytic enzyme ointment Elase was			had a healing rate of 38.1%per week after being reassigned and had 100% healing over 8.3 weeks.

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
used to determine the wound area to nearest hundredth of a square centimetre. Analysed wound area weekly from % change in wound dimensions. Additionally 35mm macro slides at weekly intervals to further document wound dimensions. **Multiple ulcers:** no		applied twice daily for the first 3 days of treatment to selectively digest the necrotic protein. Any remaining necrotic collagen was debrided on the 4th treatment day with a collagenase enzyme ointment, Biozyme-C. The wound was packed with saline-moistened gauze during enzymatic debridement to absorb slough and was covered with plastic wrap to retain moisture until the healing was complete. Enzyme residues were flushed from the wound with a saline solution before electrode placement and the wound was packed loosely and covered with sterile, saline-saturated gauze sponges to enhance electrical conductivity. The positive electrode was placed over the wound and the edge-to-edge distance between the anode and the cathode was maintained at 15cm with the anode cephalad to the cathode and close to the nueraxis, this was maintained unless the patient			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
		reached a plateau in wound healing. 4 patients in the treatment group reached an initial healing plateau, then the cathode was moved over the wound, and the anode repositioned 15cm cephalad. When the same patients reached a second healing plateau, electrode polarity on the wound was alternated daily.			

Table 42 – AHMAD 2008

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Ahmad 2008 **Title:** High-voltage pulsed galvanic stimulation: effect of treatment on healing of chronic pressure ulcers **Journal:** Journal of Burns and Fire Disasters, vol XXI, 3, 124-128 **Study type:** multicentre RCT **Sequence generation:** no details **Allocation**	**Patient group:** patients with an indolent pressure ulcer of grade II (Yarkony-Kirk classification) chronic pressure ulcers **All patients** **Randomised N:** 60 (60 wounds) **Completed N:** unclear **Drop-outs:** unclear Number of wounds: 60 Age: 30 to 50 years. **Group 1**	**Group 1:** high-voltage pulsed galvanic current (HVPC) for 45 minutes seven days a week **Group 2:** HVPC for 60 minutes seven days a week **Group 3:** HVPC for 120 minutes seven days a week **Group 4:** control group - sham HVPC for 45 minutes seven days per week in addition to conventional wound therapy wet dressing and whirlpool therapy four or five times per week) All wounds were debrided	**Outcome 1:** reduction in wound surface area (cm2)	**Group 1 (45 min):** MD 2.02 **Group 2 (60 min):** MD 6.52 **Group 3 (120 min):** MD 6.3 **Group 4 (control):** MD 1.82	**Funding:** No details **Limitations:** no details of sequence generation, allocation concealment. No blinding between treatments as duration. No details of withdrawals. Small sample size in each group and no sample size calculation.

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
concealment: no details **Blinding:** control group was sham treatment but other groups differed on duration of HVPC so not blinded between these groups. **Addressing incomplete outcome data:** no details of withdrawals. **Statistical analysis:** paired t-test to compare wound areas at baseline and after 3 and 5 weeks. An unpaired t-test was used to compare the three treatment groups with the control group. **Baseline differences:** no **Study power/sample size:** no sample size calculation. Small sample in each group. **Setting:** 4 sites. **Length of study:** 5 weeks treatment. **Assessment of PUs:** wound surface area was measured by	**Randomised N:** 15 **Completed N:** unclear **Dropouts:** unclear Male/female: 6/9 Mean age (sd): 38.40 (6.82) Mean wound duration months (sd): 4.41 (0.9) **Group 2** **Randomised N:** 15 **Completed N:** unclear **Dropouts:** unclear Male/female: 7/8 Mean age (sd): 38.47 (1.68) Mean wound duration months (sd): 4.40 (0.9) **Group 3** **Randomised N:** 15 **Completed N:** unclear **Dropouts:** unclear Male/female: 8/7 Mean age (sd): 39.40 (1.74) Mean wound duration months (sd): 4.41 (0.9) **Group 4** **Randomised N:** 15	before admission to the study Equipment: small, portable high-voltage monophase twin-pulsed generator. Frequency of 120Hz, an interphase interval of 50usec, and a voltage just below that capable of producing a visible muscle contraction (100-175 V). Patients in the treatment groups received 45, 60 and 120 minutes of HVPC applied to the ulcer site once daily seven days per week. A piece of heavy-duty aluminium foil, slightly wet and larger than the perimeter of the ulcer, was attached with an alligator clip to the negative lead of the HVPC unit. The foil electrode was placed over the ulcer on top of saline-soaked gauze. A sandbag or elastic wrap was used if needed to hold the wound electrode in place. The dispersive electrode was strapped over the patient's medial thigh with wet gauze placed between the electrode and the patient's skin. The			**Additional outcomes:**

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
tracing the wound perimeter (Kloth and Feedar). A sterilised transparency film was placed over ulcer and the perimeter was traced by using the film-tipped transparency marker (three time). This was then traced onto metric graph paper and the number of square millimetres counted. **Multiple ulcers:** no	**Completed N:** unclear **Dropouts:** unclear Male/female: 9/6 Mean age (sd): 39.40 (1.69) Mean wound duration months (sd): 4.48 (0.9) **Inclusion criteria:** pressure ulcer of grade II (Yarkony-Kirk classification) **Exclusion criteria:** cardiac pacemaker, peripheral vascular diseases disposing them to thrombosis, or active ostemyelitis and if they were pregnant or receiving long-term radiation therapy, steroid therapy, or chemotherapy.	active electrode was of negative polarity for the first three days of HVPC application, while the dispersive electrode was positive. After this 3-day period, positive polarity was in the active electrode and negative polarity was in the dispersive electrode. Positive polarity was maintained in the active electrode until the wound healed or a healing plateau was noted. If such a plateau was reached, the protocol of negative polarity in the wound site for a 3-day period was restarted. Patients in the control group had electrodes applied in the same manner as patients in the treatment groups, except that voltage was maintained at zero.			

Table 43 – ADEGOKE2001

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Adegoke 2001 **Title:** Acceleration of pressure ulcer healing in spinal cord injured	**Patient group:** spinal cord injured patients with grade IV pressure ulcers located in the pelvic region	**Group 1:** routine nursing care plus interrupted direct current	**Outcome 1: %** reduction in surface area	**Group 1:** 22.2% (week 0 - mean 15.8, sd 14.3, end of week 2 - mean 13.3, sd 14.1 (15% change), end of week 4 - mean 12.3,	**Funding:** no details **Limitations:** very

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
patients using interrupted direct current **Journal:** African journal of Medicine and Medical Sciences, 30, 195-197. **Study type:** RCT **Sequence generation:** no details about how sequence was generated. **Allocation concealment:** randomly assigned by an individual with no knowledge of the treatment modality. **Blinding:** placebo but no details of blinding of outcome assessors. **Addressing incomplete outcome data:** 1 drop out but unsure which arm and discounted as they requested to be discharged from the hospital before the end of the study **Statistical analysis:** no statistical tests used. **Baseline differences:**	**All patients** **Randomised N:** 7 **Completed N:** 6 **Drop-outs:** 1 Age: 21-60 years (mean 43.8, s.d 13.9) **Group 1** **Randomised N:** 3 (there was one other patient but they were discharged from the hospital before the end of the study but does not say which arm this patient was in). **Completed N:** 3 **Dropouts:** 0/1 Age: median 54.0 years (mean 52.7, sd 8.1) Ulcer duration (weeks): 12.0 , s.d 2.0. Ulcer surface area 15.8 (s.d 14.3) Ulcer location at baseline: Greater throcanter: 2 Sacrum: 1 Diagnosis: Quadriplegia: 3 Paraplegia: 0	**Group 2:** routine nursing care plus placebo interrupted direct current. Both groups: After cleaning, treatment group were covered with sterilised gauze soaked in 0.9% saline. Two pieces of aluminium plate electrodes cut to sizes slightly larger that the ulcers' perimeters were then attached to the leads of the IDC machine. The electrodes were wrapped in 6 layers of lint soaked in 0.9% saline; the active electrode was placed directly over the ulcer and the inactive electrode on any suitable part of the body. The IDC unit was then turned on and the intensity gradually increased until a 'minimal perceptible contraction' was produced. The intensity was then turned down to a level just below that capable of producing muscle contractions. The rest to surge ratio was 2:1 at a frequency of 30Hz and the wave form was rectangular. Each treatment session		s.d 14.1 (7.5% change) **Group 2:** 2.6% (week 0 - mean 15.4, sd 3.6, end of week 2 - mean 15.1, sd 3.6 (1.9% change), end of week 4 - mean 15.0, s.d 0.7 (2.6% change)	small sample size. No details of sequence generation. Unclear allocation concealment. No details of blinding of outcome assessors. 1 drop-out but no details of which arm. Difference at baseline. **Additional outcomes:** *

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
difference in age, although the authors say there was no statistically significant differences for age or other physical characteristics. **Study power/sample size:** very small, no sample size calculation given. **Setting:** neurology wards of the University College Hospital, Ibadan, Nigeria. **Length of study:** 4 weeks treatment. **Assessment of PUs:** measured for surface area on day 0, 2 weeks and 4 weeks. The surface of a double sheet of tracing paper that was in contact with the ulcer was first cleaned with methylated spirit. The ulcer's perimeter was then traced with a fine-tipped marker, the surface of the tracing paper in contact with ulcer cut off and the ulcer's impression	**Group 2** **Randomised N:** 3 **Completed N:** 3 **Dropouts:** 0/1 Age: median 36.9 years (mean 35.0, s.d 13.5) Ulcer duration (weeks): 8.0 (s.d 2.0) t value 1.94 Ulcer surface area 15.4 (s.d 3.2, t value 0.05). Ulcer location at baseline: Greater throcanter: 1 Sacrum: 2 Diagnosis: Quadriplegia: 2 Paraplegia: 1 **Inclusion criteria:** not stated **Exclusion criteria:** not stated	lasted 45 minutes.			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
transferred onto a metric graph paper from where the surface area of the ulcer was measured. The number of square millimetres on the metric graph paper which fell within the ulcer tracing were counted to determine the ulcer area to the nearest tenth of a square centimetre. **Multiple ulcers:** no					

Table 44 – BAKER 1996

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Baker 1996 **Title:** Effect of electrical stimulation waveform on healing of ulcers in human beings with spinal cord injury **Journal:** wound repair and regeneration **Study type:** RCT **Sequence generation:** no details	**Patient group:** spinal cord injury patients with one or more pressure ulcers **All patients** **Randomised N:** 80 (Ulcers N: 192) **Completed N:** unclear **Drop-outs:** unclear Number of pressure ulcers: 192 (all of which received one of four	**Group 1:** asymmetric biphasic electrostimulation Amplitude: below contraction Phase duration (usec): 100 Frequency (pulses/sec): 50 On/off time (sec) 7:7 **Group 2:** symmetric biphasic electrostimulation Amplitude: below contraction Phase duration (usec): 300 Frequency (pulses/sec): 50	**Outcome 1:** Healing rates - mean % reduction per week (sd) **Outcome 2:** Healing rates - mean cm^2 (taken from initial area to final area)	**Group 1:** 36.4 (6.2) **Group 2:** 29.7 (5.1) **Group 3:** 23.3 (4.8) **Group 4:** 32.7 (7.0) **Group 1:** 2.2 cm^2 **Group 2:** 1.3 cm^2 **Group 3:** 5.1 cm^2 **Group 4:** 3.1 cm^2	**Funding:** grant from the National Institute on Disability Research and Rehabilitation, department of Education. **Limitations:** no details of sequence generation or

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Allocation concealment: no details **Blinding:** blinded outcome assessor. **Addressing incomplete outcome data:** unclear **Statistical analysis:** comparison of mean healing rates was done with a one-way analysis of variance. An ANOVA with repeated measures design and covariate was used when comparing ulcers which were treated with both control and stimulation protocols. Multiple and stepwise regression analyses were also used. **Baseline differences:** no significant differences. **Study power/sample size:** n=80 patients, 192 ulcers **Setting:** hospital **Length of study:** 4 weeks treatment. Crossed over if	treatment protocols) **Group 1** **Randomised N:** 20 (Ulcers N: 67) **Completed N:** unclear **Dropouts:** unclear Males/females: 17/3 Age (mean, sd, range): 34 (sd, 19-64) No. of wounds: 67 Duration of ulcer (range, days): 183 (42), 2-454 Ulcer location: Foot:9 Thigh: 10 Ischial: 20 Sacral: 24 Other: 3 Ulcer source: Surgery: 31 Pressure: 36 Infected (yes/no): 47/19 Duration of stimulation therapy (days): 34 (5) Stimulation time (hr/day): 1.4 (0.1) **Group 2** **Randomised N:** 21	On/off time (sec) 7:7 Group 3: microcurrent (was to be control group but preliminary data showed some therapeutic effect) Amplitude: 4mA Phase duration (usec): 10 Frequency (pulses/sec): 1 On/off time (sec) 7:7 Group 4: control group - received same stimulation procedures as the microcurrent treatment groups but special leads interrupted the passage of current so the patient received no electrical stimulation. All inpatients were seen 5 days a week by a physical therapist working on the research project. Three treatment sessions of 30 minutes duration were provided with a short break between sessions. After each break the stimulator was programmed to automatically restart the			allocation concealment **Additional outcomes:** stratified mean healing rates according to good response and poor response.

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
required. **Assessment of PUs:** tracing of the wound edge onto a clear acetate sheet. Measured every week for inpatients and every 2 to 4 weeks for outpatients. In addition a calibrated photograph was used to assist in the later interpretation of the tracing. The surface area of the wound was digitized from the tracing by a technician who was not knowledgeable about the treatment received by the patient. When there was a significant depth to an ulcer several techniques were used. The volume of sterile saline solution which filled the wound but was not possible for patients due to not being able to position the ulcer perpendicular to gravity. **Multiple ulcers:** patients could be used	Ulcers N: 58 **Completed N:** unclear **Dropouts:** unclear Males/females: 16/5 Age (mean, sd, range): 40 (sd 2, 21-64) No. of wounds: 58 Duration of ulcer (range, days): 231 (38), 2-1095 Ulcer location: Foot: 5 Thigh: 13 Ischial: 18 Sacral: 19 Other: 3 Ulcer source: Surgery: 41 Pressure: 17 Infected (yes/no): 24/34 Duration of stimulation therapy (days): 42 (5) Stimulation time (hr/day): 1.6 (0.1) **Group 3** **Randomised N:** 20 Ulcers N: 42 **Completed N:** unclear **Dropouts:** unclear Males/females: 17/3	treatment session. The patient was instructed to remove the stimulator after three sessions. Compliant stimulation time was considered to be 1.5 hours per day, with half that amount (45 minutes) defined as semicompliant stimulation. If patients chose to remain on stimulation for longer periods of time this was monitored by the therapist each day through the compliance feature of the stimulation unit. Subjects treated as outpatients were monitored regularly through clinic appointments, home visits and frequent phone calls. Compliance to the stimulation treatment was monitored through the compliance meter on the stimulator whenever the patient was seen by the research therapist. Follow-up was done every 2 to 4 weeks. Electrical stimulation was given through surface electrodes mad of carbon-rubber. The sizes of the			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
with more than one ulcer. Reported data by ulcer.	Age (mean, sd, range): 36 (sd 2, 17-64) No. of wounds: 42 Duration of ulcer (range, days): 154 (39), 5-961 Ulcer location: Foot: 3 Thigh: 11 Ischial: 12 Sacral: 10 Other: 6 Ulcer source: Surgery: 17 Pressure: 25 Infected (yes/no): 21/21 Duration of stimulation therapy (days): 38 (5) Stimulation time (hr/day): 1.9 (0.2) **Group 4** **Randomised N:** 19 Ulcers N: 25 **Completed N:** unclear **Dropouts:** unclear Males/females: 16/3 Age (mean, sd, range): 33 (sd 4, 19-76) No. of wounds: 25 Duration of ulcer (range, days): 86 (24), 5-415	electrodes varied, depending on the size and location of the ulcer, but ranged from 2.5 x 2.5 to 5x10cm. Electrodes were placed proximal and distal to the treated ulcers, but medical and lateral placements were used in some regions (coxygeal ulcers). The electrodes of patients in group 1 had the negative electrode during the leading phase of the waveform proximal to the wound, with the more positive electrode placed distally. Stimulation amplitude was set for each subject and each wound by increasing the intensity until a minimal muscle contraction was observed. The intensity was then decreased until the contraction was no longer present. This procedure was followed for patients treated in group 1 and 2 only. Stimulation amplitude was fixed at 4mA for the microcurrent and control groups, the minimal intensity necessary to allow the stimulator's compliance monitor to function.			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	Ulcer location: Foot: 2 Thigh: 4 Ischial: 10 Sacral: 9 Other: 0 Ulcer source: Surgery: 16 Pressure: 9 Infected (yes/no): 12/13 Duration of stimulation therapy (days): 20 2) Stimulation time (hr/day): 0.2) **Inclusion criteria:** patients with spinal cord injuries **Exclusion criteria:** no details				

Table 45 – ASBJORNSEN1990

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Asbjornsen 1990 **Title:** the effect of transcutaneous electrical nerve stimulation on pressure sores in	**Patient group:** geriatric patients with pressure sores on the heels or the sacral region **All patients**	**Group 1:** low frequency transcutaneous electrical nerve stimulation (TENS) 30 minutes twice daily for 4-6 weeks (5 days per week). The stimulator delivered pulses at rate of 3Hz,	**Outcome 1:** Proportion of ulcers completely healed	**Group 1:** 0/7 **Group 2:** 2/9	**Funding:** no details **Limitations:** very small sample. No details of sequence
			Outcome 2: proportion of ulcers reduced	**Group 1:** 4/7 **Group 2:** 9/9	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
geriatric patients **Journal:** Journal of clinical and experimental gerontology, 12 (4), 209-214 **Study type:** RCT **Sequence generation:** no details **Allocation concealment:** no details **Blinding:** placebo used. blinded outcome assessor **Addressing incomplete outcome data:** 4 did not participate for a minimum of 4 weeks. Used numbers available at 4 weeks. **Statistical analysis:** no statistical tests **Baseline differences:** only baseline values mentioned are similar age and distribution of ulcer size. No statistical significance given. **Study power/sample size:** very small.	**Randomised N:** 20 **Completed N:** 16 **Drop-outs:** 4 did not participate for minimum of 4 weeks, in the treatment group one had early discharge, one had leg amputation and one got tired of treatment. One patient in the control group's disease progressed and he died. **Group 1** **Randomised N:** 10 **Completed N:** 7 **Dropouts:** 3 (one had an early discharge, one had a leg amputation and one got tired of the treatment). **Age (mean, range):** 83 years(73-94) Ulcer region: Sacral: 3 Heel: 4 **Group 2** **Randomised N:** 10 **Completed N:** 9 **Dropouts:** 1 (one patient's disease	stimulus had duration of 85 ms and consisted of a train of square wave pulses with an internal frequency of 100Hz. The electrodes were placed one between the first and second metacarpal bones and one at the ulcer edge of the same hand. The intensity was increased until contractions of adjacent muscles occurred without producing pain (usually 20-30mA) **Group 2:** placebo TENS (similar manner) - same procedure as treatment group except no electrical output to the electrodes. Both groups: conventional pressure sore treatment including measures to improve their general condition, adequate local care and avoidance of pressure by staff members not involved in the study.	**Outcome 3:** proportion of ulcers increased	**Group 1:** 3/7 **Group 2:** 0/9	generation or allocation concealment or baseline differences. Higher drop-out in the treatment group. **Additional outcomes:**

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Setting: assume a hospital. **Length of study:** 6 weeks treatment. **Assessment of PUs:** one of the researchers who did not know the patients allocation to treatment or control group measured the ulcers. Measurement of perpendicular diameters. **Multiple ulcers:** no	progressed and he died). Age (mean, range): 83 years (73-91) Ulcer region: Sacral: 2 Heel: 7 **Inclusion criteria:** pressure ulcers of the heels or sacral region. **Exclusion criteria:** no details				

Table 46 – JERCINOVIC 1994

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Jercinovic 1994 **Title:** Low frequency pulsed current and pressure ulcer healing **Journal:** ICEEE transactions on rehabilitation engineering, 2 (4), 225-233 **Study type:** RCT	**Patient group:** spinal cord injured patients with 109 pressure ulcers **All patients** **Randomised N:** 73 **Completed N:** unclear **Drop-outs:** unclear Age: 18 to 68 years (mean 36 years, s.d 15 years)	**Group 1:** electrical stimulation with low frequency pulsed current and standard wound care. The patients received two hours of electro stimulation daily, five times per week. The electrostimulation was delivered by two flexible self-adhering electrodes measuring 75 or 50mm in diameter, which were placed	**Outcome 1:** mean healing rate (s.d)	**Group 1:** 2.2% (2.1) per day (linear fitting method) 5.7% (7.1) per day (exponential fitting method) **Group 2:** 1.5% (1.7) per day (linear) 2.7% (3.6) per day (exponential)	**Funding:** supported by the Ministry of Science and Technology of the Republic of Slovenia and the National Institute for Disability and Rehabilitation Research Department of

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Sequence generation: no details **Allocation concealment:** no details **Blinding:** The authors state that because of visible muscle contractions, it was not possible to conduct a double-blind clinical trial. **Addressing incomplete outcome data:** unclear number randomised and completing. **Statistical analysis:** wound area values evaluated using exponential and linear fitting. For parallel groups two sample t-tests were used; for crossover group paired t-test was used. **Baseline differences:** ulcers in the control group were more complex regarding their initial size, and ulcers in the electrostimulation group were more	Patients had been disabled from one month to several years (mean 32 s.d 60 months). **Group 1** **Randomised N:** unclear **Completed N:** unclear **Dropouts:** unclear Number of ulcers: 61 Mean initial area (s.d) cm^2: 10.6 (13.3) Mean initial depth (s.d) mm: 3.0 (8.5) Number of ulcers with initial depth <5mm: 51 (83%) Number of ulcers with granulation: 27 (44%) Mean ulcer duration (s.d) days: 158 (284) n=60 Number of ulcers on - sacral: 14 - trochanter: 16 - legs: 18 - gluteal: 5 - other: 8 **Group 2** **Randomised N:**	on healthy skin approximately 3cm from the edge of the ulcer. Biphasic, asymmetric, charge-balanced pulses having a repetition frequency of 40pps and a pulse duration of 205us were used. Pulses were delivered repeatedly in trains lasting 4s, followed by a 4-s pause. The amplitude was adjusted (up to 35mA) for each patient individually to achieve minimal muscle contraction, when feasible. **Group 2:** standard wound care The standard treatment included initial selective debridement, the application of a new standard dressing to the ulcer two or more times per day, as needed, and a broad spectrum antibiotic in cases of infection, which were rare. The patients were lying on dry-floatation mattresses and were turned to a new position every four hours during the night. They were included in the standard rehabilitation			Education, Washington, USA. **Limitations:** no details of sequence generation or allocation concealment. No blinding. Unclear number randomised and missing outcome data. **Additional outcomes:**

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
complex regarding their tissue characteristics (appearance of granulation or necrotic tissue). **Study power/sample size:** n=73 **Setting:** no details **Length of study:** four weeks treatment then crossed over if required. **Assessment of PUs:** weekly measurements of wound area and changes in wound depth, appearance of granulation were recorded. **Multiple ulcers:** patients with 109 pressure ulcers were included and reported by ulcers.	unclear **Completed N:** unclear **Dropouts:** unclear Number of ulcers: 48 Mean initial area (s.d) cm2: 17.2 (20) Mean initial depth (s.d) mm: 4.0 (8.2) Number of ulcers with initial depth <5mm: 36 (75%) Number of ulcers with granulation: 25 (52%) Mean ulcer duration (s.d) days: 125 (129) n=41 Number of ulcers on - sacral: 20 - trochanter: 11 - legs: 10 - gluteal: 4 - other: 3 **Inclusion criteria:** not explicitly states as inclusion criteria but all participants had pressure ulcers that had developed in decentralised skin below the spinal cord lesion level and before the	program one to two hours per day, depending on their conditions. **Crossover group -** patients were offered to crossover to electrostimulation after the four week trial period.			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	study they were only treated with standard wound care. twenty four patients had more than one pressure ulcer at a time. The duration of pressure ulcers prior to study varied from one month to several years. Total 109 ulcers: - sacral area: 34 - critical areas of the legs (heel, foot, knee) - trochanter area: 27 - gluteal area: 9 - other locations: 11 **Exclusion criteria:** no details				

Table 27 – FRANEK2012

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Franek 2012 **Title:** using high-voltage electrical stimulation in the treatment of recalcitrant pressure ulcers: results of a randomised, controlled clinical study **Journal:** Ostomy	**Patient group:** stage 2 and 3 lower extremity pressure ulcers (legs, feed, lateral and medial ankles, and greater femoral trochanter. Had pressure ulcers for 1 to 6 months before the study. **All patients** **Randomised** N: 50	**Group 1:** Standard care plus HVES procedures (Ionoson device). Voltage exceeded 100V, twin monophasic pulses lasting 100us in total and frequency of 100HZ applied. Five 50-minute procedures per week (one procedure per day). Treated until healed or for maximum of 6 weeks. The first 1 to 2	**Outcome 1:** Change in surface area (%)(s.d)	**Group 1:** 88.90 (14.00) **Group 2:** 44.40 (63.10 P=0.00003	**Funding:** no details **Limitations:** the study length (4 years) could have introduced some variability in methods and procedures. No blinding and no
			Outcome 2: Change in the longest length (%)(s.d)	**Group 1:** 74.00 (29.60) **Group 2:** 36.10 (33.90) P=0.0003	
			Outcome 3: change in the longest width (%)	**Group 1:** 79.00 (25.10) **Group 2:** 36.30 (41.90) P=0.00008	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
wound management (2012), 58 (3), 30-44. **Study type: RCT** **Sequence generation:** randomly allocated but no details of sequence generation method **Allocation concealment:** Adequate. The physician allocating patients to groups had 60 envelopes, each containing a piece of paper marked with either A or B. The physician would draw and open an envelope in the presence of a physiotherapist to see the symbol and direct the patient to one of the groups. **Blinding:** no blinding **Addressing incomplete outcome data:** **Statistical analysis:** Wilxoxon matched pairs test used to compare average wound areas, volumes, lengths and	**Completed** N: 45 **Drop-outs:** 5 (author says 5 dropped out but no details of other 2 randomised). **Group 1** **Randomised N: 26** **Completed N:** **Dropouts:** 3 (2 complications unrelated to treatment and directed to other hospital, 1 withdrew for personal reasons) **Age mean (range):** 59 (19 to 87 years) **Gender (f/m):** 8/18 **Body mass mean (range):** 75.4kg (55 to 112 kg). **BMI > 30:** 7 **Stage II ulcers: 17 (5 were IIA)** **Group 2** **Randomised N:** 24 **Completed N:** **Dropouts:** 2 (1 complications unrelated to treatment and directed to other	weeks cathodic stimulation was used to facilitate granulation tissue formation, followed by anode stimulation for the rest of the treatment period. **Group 2:** standard care (see below) Both groups: measures to prevent the development of additional pressure ulcers were implemented for all patients. Pressure-redistribution surfaces and devices and pillows were used as needed. Patients were also instructed to change their positions frequently and to relieve pressure on the ulcer area as much as possible. Patients who were unable to move were repositioned by the physical therapist at least every 2 hours. All wounds received standard topical care, including cleansing with potassium permanganate followed by covering the ulcer base with dressing. Dressings were tailored to meets the patient's needs and to promote moist	(s.d)		placebo in the control group. **Additional outcomes:** no adverse events observed. The amperage evoked a tingling sensation in the patients, but no motor effects were induced.
			Outcome 4: Change in cavity volume (%) (s.d)	**Group 1:** 100 (0) **Group 2:** 54.0 (39.40) P=0.008	
			Outcome 5: change in granulation tissue area (%) (s.d)	**Group 1:** 37.66 (76.17) **Group 2:** 10.36 (43.46) P=0.18	
			Outcome 6: Gilmann parameter (s.d)	**Group 1:** 0.66 (0.24) **Group 2:** 0.26 (0.30) P=0.000003	
			Outcome 7:	**Group 1:** **Group 2:**	
			Outcome 8:	**Group 1:** **Group 2:**	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
widths as well as average relative granulation tissue areas before and after treatment within each group. The Mann-Whitney U test compared average percentage change in relative granulation tissue areas. ANOVA and Tukey's post-hoc test for unequal sample sizes to compare average wound areas and average relative granulation tissue areas. Correlations from the Spearman test. **Baseline differences:** distribution of men and women only significant difference (p=0.03). **Study power/sample size:** no sample size calculation. Small study. **Setting:** Janusz Daab Surgery Hospital, Poland **Length of study:** treated until healed,	hospital, 1 died) Age mean (range): 56.2 (14 to 88) years Gender (f/m): 14/10 Body mass mean (range): 69.4kg (45 to 96kg) **Inclusion criteria:** lower extremity pressure ulcers Exclusion criteria: ankle-brachial pressure index (ABPI <0.9, diabetes mellitus, systemic sclerosis, a cancer diagnosis, pareses, and paralysis caused by injuries to the central or peripheral nervous system; patients whose pressure ulcers required surgical intervention.	interactive healing. Wound dressings included nonadherent gauze pads, dressings moistened with 0.9% sodium chloride, hydrogel, propolis extractum and solcoseryl. If wound infection was suspected, desoxyribonucleasum plus fibrinolysinum, ethacridine lactate and colistinum were additionally applied. Dressings suspected of adversely interacting with electrical stimulation, such as topical agents with metal ions and petrolatum-based products, were not prescribed in electrical stimulation group. Sharp debridement was performed in a relatively small number of subjects (four in HVES group and six in control group). Before electrical stimulation was applied, pressure ulcers were thoroughly cleansed with 0.9% sodium chloride solution. As soon as procedure complete, dressings were applied. All immobilised patients received low-molecular-weight heparin (enoxaparin)			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
until maximum of 6 weeks. **Assessment of PUs:** change in wound area, volume, longest length and width and granulation tissue calculated. Gilman method estimates wounds size based on surface area and length of perimeter used. **Multiple ulcers:** no		as a standard therapy. Patients with elevated leukocyte levels were administered antibiotics based on culture and sensitivity testing of microbiological swabs taken from pressure ulcers.			

Table 28 – KARBA1995

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Karba (1995) **Title:** Combination of occlusive dressings and electrical stimulation in pressure ulcer treatment **Journal:** Med. Sci Res (1995), 23, 671-673. **Study type: RCT** **Sequence generation:** 'randomly assigned' but no further details	**Patient group: male patients with spinal cord injuries who had developed pressure ulcers** **All patients** **Randomised N: 12** **Completed N: 6** **Drop-outs:** 6 from control group switched to electrical stimulation **Age (range): 29-42**	**Group 1:** electrical stimulation (ES) group. 4 second trains of biphasic, charge-balanced asymmetrical current stimuli, which alternated with pauses of the same duration (4 seconds). The stimulation intensity was set in the active stimulators so that a slight, scarcely visible contraction of the muscles in the wound area was achieved.	**Outcome 1:** proportion of ulcers completely healed (from graphs)	**Group 1:** 6/6 **Group 2:** 0/6 – see comments, this group were stopped, when crossed over 2 were completely healed in this group.	**Funding:** supported by the Ministry of Science and Technology of the Republic of Slovenia. **Limitations:** no details of sequence generation or allocation concealment or
			Outcome 2: relative healing rate (mean)	**Group 1:** 7.13 (s.d 1.46)% per day **Group 2:** -0.66 (s.d 1.16)% per day	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Allocation concealment: no details **Blinding:** sham treatment as placebo **Addressing incomplete outcome data:** describes patients in control group who had to be stopped but unclear which reason for which patient. **Statistical analysis:** student's t-test used to test the hypothesis regarding the equality of mean relative healing rate. **Baseline differences:** no details **Study power/sample size:** no sample size calculation but very small sample size **Setting:** hospitalised at the Rehabilitation Institute, Slovenia **Length of study:** 98 days. Not stated but graph showed some patients at 98 days. **Assessment of PUs:** measured at dressing	**years** **Group 1** **Randomised N: 6** **Completed N: 6** **Dropouts:** 0 **Group 2** **Randomised N:** 6 **Completed N: 0** **Dropouts:** 6 (switched to electrical stimulation) **Inclusion criteria: no details** **Exclusion criteria: no details**	**Group 2:** sham treatment control group (CO) **All patients:** self-adhesive stimulation electrodes placed on healthy skin at the dressing edge for two hours daily and connected to the stimulators. Half of the devices actually delivered electrical stimulation (ES group), while other half were inactive (CO group). Cleaning given with a physiological solution and covering with semiocclusive foam gel dressings. The dressings were changed as necessary or at the latest after one week.			whether outcome assessors were blinded. Very small sample size. No details of baseline differences or inclusion /exclusion criteria. **Additional outcomes:** **Notes:** Treatment had to be stopped in the control group after an unpleasant odour, unhealthy exudate, non-healing and in some cases also pain observed. These patients were crossed over to a combination of conventional treatment with standard gauze dressing and electrical stimulation and all six cases

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
changes and photographs taken. **Multiple ulcers:** no					improved and healed with an average relative healing rate of 2.93 (s.d 1.01)% per day.

9. HYPERBARIC OXYGEN THERAPY

9.1. Review protocol

Table 47 – Review protocol

	HBOT
Review question	• What is the clinical and cost-effectiveness of hyperbaric oxygen therapy for the treatment of pressure ulcers?
Population	• People of any age with existing pressure ulcers in any care setting
Intervention	• Hyperbaric oxygen therapy as treatment for people with pressure ulcers.
Comparison	• Other type of therapy for pressure ulcer treatment • Standard wound care
Outcomes	Critical outcomes for decision-making (what are the outcomes important to patients): • Time to complete healing (time to event data) • Rate of healing (continuous data) • Rate of change in size of ulcer (absolute and relative) (continuous data) – reduction in size of ulcer and volume of ulcer. • Proportion of patients completely healed within trial period Important outcomes: • Pain (wound-related) • Time in hospital or NHS care (continuous data) • Patient acceptability eg measured by compliance and tolerance • Side effects • Health-related quality of life (continuous data) (although unlikely to be sensitive enough to detect changes in pressure ulcer patients, therefore may have to be narratively summarised o Short-form health survey (SF36) o Manchester Short Assessment of Quality of Life o EQ-5D

	o WHO-Quality of life BREF o Cardiff HRQoL tool o HUI o Pressure ulcer quality of life (Gorecki)
Study design	• High quality systematic reviews of RCTs and/or RCTs only. • Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.
Exclusion	• Studies of patients who do not have active pressure ulcers at time of enrolment • Studies with outcomes that do not involve pressure ulcers • Abstracts unless no RCTs are found • Non-English language papers
The search strategy	The databases to be searched are: • Medline, Embase, Cinahl, the Cochrane Library. • All years. • Studies will be restricted to English language only
Review strategy	How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews) • Population - any population will be combined for meta-analysis except for different strata. Must have active pressure ulcers at time of enrolment. • Intervention - any type of hyperbaric oxygen therapy • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – single side effects will be meta-analysed separately from other side effects • Study design – randomised and quasi-randomised studies will be meta-analysed together. Blinded and unblinded studies will be meta-analysed together. Crossover trials will be meta-analysed together with parallel trials • Unit of analysis – patients, clusters (hospital wards), individual pressure ulcers. We will not meta-analyse studies where patients have multiple ulcer and the unit of analysis is pressure ulcer with studies where the unit of analysis is patients. • Minimum duration of treatment = no minimum.

	• Minimum follow up = no minimum. • Minimum total sample size = no minimum. • Use authors data. If there is a 10% differential or higher between the groups or if the missing data is higher than the event rate downgrade on risk of bias. If authors use ACA and ITT, ACA is preferable over ITT. • MIDs: 0.75 to 1.25 for dichotomous variables and 0.5 x standard deviation for continuous variables.
Analysis	Strata: The following groups will be considered separately as strata if data are present: • Children (neonates, infants, children) and adults Subgroups: The following groups will be considered separately as subgroups if data are present and there is inconsistency: • Different categories of pressure ulcer (from category 2 upwards where outcomes are reported separately • Different ulcer locations
Other terms	HBOT

9.2. Search strategy

9.2.1. Search Filters

Table 48 – Search filters in OVID Medline

Search strategy	HBOT			Results
Date	April 2013			
Database	Medline-Ovid			
Search strategy		1	pressure ulcer/	8806
		2	decubit*.ti,ab.	3834
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	5978

Search strategy	HBOT			Results
		4	(bedsore* or bed-sore*).ti,ab.	494
		5	(incontinen* adj2 dermatitis).ti,ab.	49
		6	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	615
		7	or/1-6	13348
		8	limit 7 to english language	10631
		9	exp hyperbaric oxygenation/	9435
		10	Atmosphere Exposure Chambers/	2333
		11	oxygen inhalation therapy/	10641
		12	hyperbar*.ti,ab.	10004
		13	(HBO or HBOT).ti,ab.	2139
		14	100% oxygen.ti,ab.	2582
		15	pure oxygen.ti,ab.	782
		16	(pressur* adj5 oxygen).ti,ab.	12605
		17	((multiplace or monoplace or oxygen* or hyperbar*) adj5 chamber*).ti,ab.	1186
		18	or/9-17	39476
		19	8 and 18	136
		20	letter/	745664
		21	editorial/	297746
		22	news/	142587
		23	exp historical article/	300477
		24	Anecdotes as Topic/	4103
		25	comment/	485339

Search strategy	HBOT			Results
		26	case report/	1546965
		27	(letter or comment*).ti.	82083
		28	or/20-27	2997528
		29	randomized controlled trial/ or random*.ti,ab.	662142
		30	28 not 29	2982754
		31	animals/ not humans/	3554274
		32	exp Animals, Laboratory/	656077
		33	exp Animal Experimentation/	5133
		34	exp Models, Animal/	358451
		35	exp Rodentia/	2423863
		36	(rat or rats or mouse or mice).ti.	1020260
		37	or/30-36	7047236
		38	19 not 37	117
	Extra:			
		1	pressure ulcer/	8951
		2	decubit*.ti,ab.	3877
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6106
		4	(bedsore* or bed-sore*).ti,ab.	502
		5	(incontinen* adj2 dermatitis).ti,ab.	51
		6	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	630
		7	or/1-6	13566
		8	limit 7 to english language	10829

Search strategy	HBOT			Results
		9	exp hyperbaric oxygenation/	9513
		10	Atmosphere Exposure Chambers/	2354
		11	oxygen inhalation therapy/	10799
		12	hyperbar*.ti,ab.	10122
		13	(HBO or HBOT).ti,ab.	2197
		14	100% oxygen.ti,ab.	2628
		15	pure oxygen.ti,ab.	803
		16	(pressur* adj5 oxygen).ti,ab.	12818
		17	((multiplace or monoplace or oxygen* or hyperbar*) adj5 chamber*).ti,ab.	1209
		18	or/9-17	40053
		19	8 and 18	139
		20	letter/	761331
		21	editorial/	307397
		22	news/	150574
		23	exp historical article/	303523
		24	Anecdotes as Topic/	4269
		25	comment/	501891
		26	case report/	1566069
		27	(letter or comment*).ti.	83649
		28	or/20-27	3054854
		29	randomized controlled trial/ or random*.ti,ab.	680637
		30	28 not 29	3039713
		31	animals/ not humans/	3611730

Search strategy	HBOT			Results
		32	exp Animals, Laboratory/	669805
		33	exp Animal Experimentation/	5300
		34	exp Models, Animal/	368368
		35	exp Rodentia/	2474141
		36	(rat or rats or mouse or mice).ti.	1037341
		37	or/30-36	7178396
		38	19 not 37	120
		39	((topical or local or portable) adj5 oxygen).ti,ab.	1376
		40	(oxygen adj2 (therap* or treat*)).ti,ab.	9072
		41	39 or 40	10290
		42	8 and 41	32
		43	42 not 37	26
Notes				

Table 49 – Search filters in Embase

Search strategy	HBOT			Results
Date	April 2013			
Database	Embase-OVID			
Search strategy		1	decubitus/	12153
		2	decubit*.ti,ab.	4622
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6840
		4	(bedsore* or bed-sore*).ti,ab.	631

Search strategy	HBOT			Results
		5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	737
		6	(incontinen* adj2 dermatitis).ti,ab.	53
		7	or/1-6	16442
		8	limit 7 to english language	12672
		9	hyperbaric oxygen/	11880
		10	oxygen therapy/	17226
		11	hyperbar*.ti,ab.	11324
		12	(HBO or HBOT).ti,ab.	2338
		13	100% oxygen.ti,ab.	2888
		14	pure oxygen.ti,ab.	968
		15	(pressur* adj5 oxygen).ti,ab.	14079
		16	((multiplace or monoplace or oxygen* or hyperbar*) adj5 chamber*).ti,ab.	1368
		17	or/9-16	48185
		18	8 and 17	210
		19	letter.pt. or letter/	755980
		20	note.pt.	462893
		21	editorial.pt.	389767
		22	case report/ or case study/	1773737
		23	(letter or comment*).ti.	132642
		24	or/19-23	3259271
		25	randomized controlled trial/ or random*.ti,ab.	753909
		26	24 not 25	3235493
		27	animal/ not human/	1268427

Search strategy	HBOT			Results
		28	nonhuman/	3776367
		29	exp Animal Experiment/	1487854
		30	exp experimental animal/	366838
		31	animal model/	620584
		32	exp Rodent/	2424924
		33	(rat or rats or mouse or mice).ti.	1074023
		34	or/26-33	8606171
		35	18 not 34	161
	Extra:			
		1	decubitus/	12517
		2	decubit*.ti,ab.	4766
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	7117
		4	(bedsore* or bed-sore*).ti,ab.	659
		5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	767
		6	(incontinen* adj2 dermatitis).ti,ab.	56
		7	or/1-6	17007
		8	limit 7 to english language	13126
		9	hyperbaric oxygen/	12189
		10	oxygen therapy/	17862
		11	hyperbar*.ti,ab.	11685
		12	(HBO or HBOT).ti,ab.	2447

Search strategy	HBOT		Results
	13	100% oxygen.ti,ab.	3012
	14	pure oxygen.ti,ab.	1004
	15	(pressur* adj5 oxygen).ti,ab.	14688
	16	((multiplace or monoplace or oxygen* or hyperbar*) adj5 chamber*).ti,ab.	1424
	17	or/9-16	49967
	18	8 and 17	217
	19	letter.pt. or letter/	778574
	20	note.pt.	514042
	21	editorial.pt.	401605
	22	case report/ or case study/	1831335
	23	(letter or comment*).ti.	135434
	24	or/19-23	3393890
	25	randomized controlled trial/ or random*.ti,ab.	801083
	26	24 not 25	3367763
	27	animal/ not human/	1323451
	28	nonhuman/	3824666
	29	exp Animal Experiment/	1504918
	30	exp experimental animal/	410580
	31	animal model/	633405
	32	exp Rodent/	2532293
	33	(rat or rats or mouse or mice).ti.	1107552
	34	or/26-33	8891638
	35	18 not 34	165

Search strategy	HBOT		Results
	36	((topical or local or portable) adj5 oxygen).ti,ab.	1531
	37	(oxygen adj2 (therap* or treat*)).ti,ab.	10863
	38	36 or 37	12192
	39	8 and 38	44
	40	39 not 34	35
Notes			

Table 50 – Search filters in CINAHL

Search strategy	HBOT		Results
Date	April 2013		
Database	CINAHL		
Search strategy	S17	S7 and S15 Limiters - English Language; Exclude MEDLINE records	38
	S16	S7 and S15	74
	S15	S8 or S9 or S10 or S11 or S12 or S13 or S14	5024
	S14	((multiplace or monoplace or oxygen*) and chamber*)	224
	S13	pressur* N5 oxygen	961
	S12	100% oxygen or pure oxygen	199
	S11	HBO or HBOT	254
	S10	hyperbar*	1228
	S9	(MH "Oxygen Therapy")	2718
	S8	(MH "Hyperbaric Oxygenation")	1049
	S7	S1 or S2 or S3 or S4 or S5 or S6	9473
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1345
	S5	incontinen* n2 dermatitis	66
	S4	bedsore* OR bed-sore*	152
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8173
	S2	decubit*	467

Search strategy	HBOT		Results
	S1	(MH "Pressure Ulcer")	7443
	Extra		
	S21	S7 and S19 Limiters - English Language; Exclude MEDLINE records	22
	S20	S7 and S19	37
	S19	S17 or S18	4159
	S18	oxygen N2 therap* OR oxygen N2 treat*	4101
	S17	topical N5 oxygen OR portable N5 oxygen OR local N5 oxygen	126
	S16	S7 and S15	74
	S15	S8 or S9 or S10 or S11 or S12 or S13 or S14	5085
	S14	((multiplace or monoplace or oxygen*) and chamber*)	227
	S13	pressur* N5 oxygen	974
	S12	100% oxygen or pure oxygen	201
	S11	HBO or HBOT	255
	S10	hyperbar*	1235
	S9	(MH "Oxygen Therapy")	2760
	S8	(MH "Hyperbaric Oxygenation")	1057
	S7	S1 or S2 or S3 or S4 or S5 or S6	9631
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1374
	S5	incontinen* n2 dermatitis	69
	S4	bedsore* OR bed-sore*	155
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8295
	S2	decubit*	476
	S1	(MH "Pressure Ulcer")	7535
Notes			

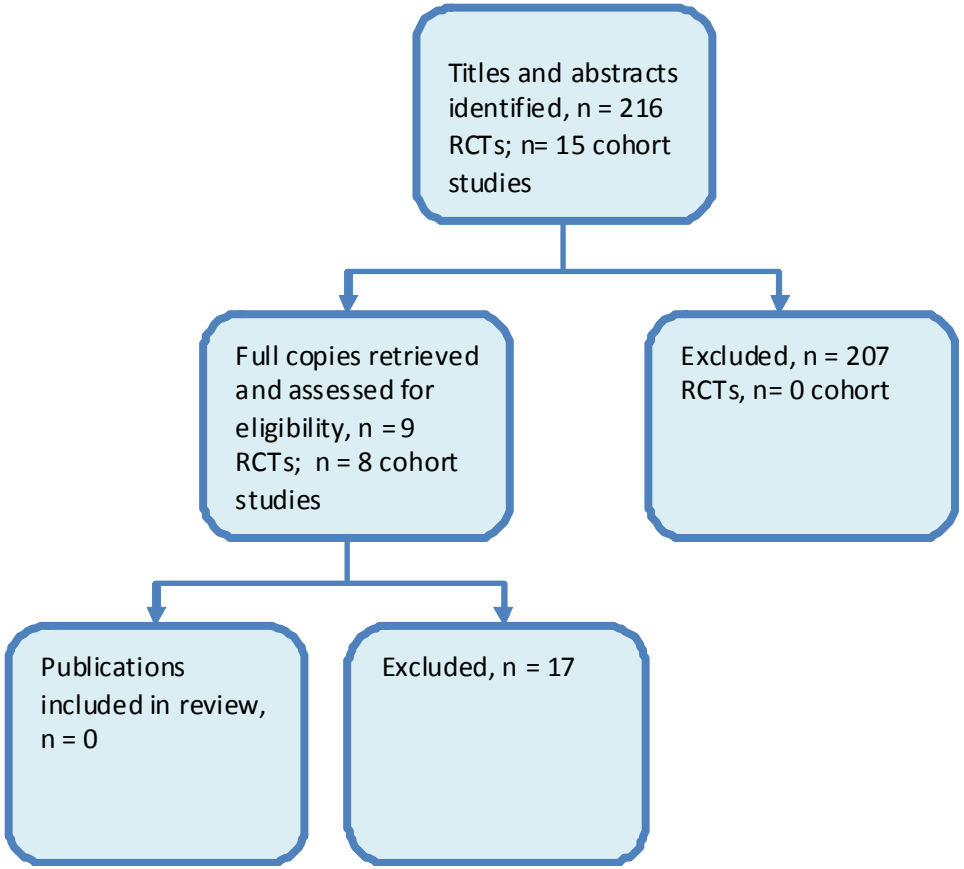
Table 51 – Search filters in Cochrane

Search strategy	HBOT		Results
Date	April 2013		
Database	Cochrane (- CDSR [3/2012]; DARE; Central [3/2012]; NHS EED; HTA)		
Search strategy	#1	MeSH descriptor Pressure Ulcer explode all trees	480
	#2	decubit*:ti,ab,kw	341
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	818
	#4	(bedsore* or bed-sore*):ti,ab,kw	32
	#5	(incontinen* near/2 dermatitis):ti,ab,kw	10
	#6	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	62
	#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	1151
	#8	MeSH descriptor Hyperbaric Oxygenation explode all trees	326
	#9	MeSH descriptor Oxygen Inhalation Therapy, this term only	748
	#10	MeSH descriptor Atmosphere Exposure Chambers, this term only	64
	#11	(hyperbar* or HBO or HBOT):ti,ab,kw	1405
	#12	(100% oxygen or pure oxygen):ti,ab,kw	717
	#13	(pressur* near/5 oxygen):ti,ab,kw	2173
	#14	((multiplace or monoplace or oxygen* or hyperbar*) near/5 chamber*):ti,ab,kw	84
	#15	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)	4666
	#16	(#7 AND #15)	79
	Extra		
	#1	MeSH descriptor Pressure Ulcer explode all trees	487
	#2	decubit*:ti,ab,kw	349
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	829
	#4	(bedsore* or bed-sore*):ti,ab,kw	33
	#5	(incontinen* near/2 dermatitis):ti,ab,kw	10
	#6	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	63
	#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	1171
	#8	MeSH descriptor Hyperbaric Oxygenation explode all trees	330
	#9	MeSH descriptor Oxygen Inhalation Therapy, this term only	756

Search strategy	HBOT		Results
	#10	MeSH descriptor Atmosphere Exposure Chambers, this term only	66
	#11	(hyperbar* or HBO or HBOT):ti,ab,kw	1425
	#12	(100% oxygen or pure oxygen):ti,ab,kw	727
	#13	(pressur* near/5 oxygen):ti,ab,kw	2220
	#14	((multiplace or monoplace or oxygen* or hyperbar*) near/5 chamber*):ti,ab,kw	88
	#15	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)	4749
	#16	(#7 AND #15)	81
	#17	((topical or local or portable) near/5 oxygen):ti,ab,kw	115
	#18	(oxygen near/2 (therap* or treat*)):ti,ab,kw	2445
	#19	(#17 OR #18)	2507
	#20	(#7 AND #19)	6
	#21	(#16 OR #20)	82
Notes			

9.2.2. Flow Chart

Figure 34 – Flow diagram of clinical article selection for what is the clinical effectiveness of hyperbaric oxygen therapy for the treatment of pressure ulcers review



9.2.3. Excluded Studies

Table 52 – Studies excluded from the clinical review

Reference	Reason for exclusion
ROSENTHAL1971	Not an RCT or cohort study
EDSBERG2002	Not an RCT or cohort study
FISCHER1969	Not an RCT or cohort study
BLACK2000	Not an RCT or cohort study
NIINIKOSKI2004	Not an RCT or cohort study
CHIU2006	Not pressure ulcer outcomes.
ELTORAI1981	Literature review
GRAY2006	Systematic review of wounds, not pressure ulcers. Study included for pressure ulcers was Rosenthal 1971.
ROECKL2005	Systematic review of wounds, not pressure ulcers
THACKHAM2008	Systematic review of wounds, not pressure ulcers
SAHNI2003	Literature review
FISCHER1970	Not an RCT or cohort study
COURVILLE1998	Not an RCT or cohort study
DEPENBUSCH1972	Not an RCT or cohort study
TORELLI1973	Not an RCT or cohort study
FISCHER1966	Conference abstract from 1966
VILLANUEVA2000	No hyperbaric oxygen therapy evidence

9.3. Clinical Evidence

We conducted a search for randomized controlled trials of hyperbaric oxygen therapy for the treatment of pressure ulcers but none were found. We then conducted a search for hyperbaric oxygen cohort studies but none relating to pressure ulcers were found. Therefore, no studies were included in this review. One Cochrane Review was found (Kranke 2012)[15] but no randomized controlled trials were identified.

10. NEGATIVE PRESSURE WOUND THERAPY

10.1. Review protocol

Table 53 – Review protocol

	NPWT
Review question	What is the clinical and cost-effectiveness of negative pressure wound therapy for the treatment of pressure ulcers?
Population	• People of any age with existing pressure ulcers in any care setting
Intervention	• Negative pressure wound therapy as treatment for people with pressure ulcers.
Comparison	• Other type of therapy for pressure ulcer treatment.
Outcomes	Critical outcomes for decision-making (what are the outcomes important to patients): • Time to complete healing (time to event data) • Rate of healing (continuous data) • Rate of change in size of ulcer (absolute and relative) (continuous data) – reduction in size of ulcer and volume of ulcer. • Proportion of patients completely healed within trial period Important outcomes: • Pain (wound-related) • Time in hospital or NHS care (continuous data) • Patient acceptability eg measured by compliance and tolerance • Side effects (pain, problems with vacuum sealing, reaction of foam) • Health-related quality of life (continuous data) (although unlikely to be sensitive enough to detect changes in pressure ulcer patients, therefore may have to be narratively summarised o Short-form health survey (SF36) o Manchester Short Assessment of Quality of Life o EQ-5D

	o WHO-Quality of life BREF o Cardiff HRQoL tool o HUI o Pressure ulcer quality of life (Gorecki)
Study design	• High quality systematic reviews of RCTs and/or RCTs only. • Cochrane reviews will be included if they match our inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.
Exclusion	• Studies of patients who do not have active pressure ulcers at time of enrolment • Studies with outcomes that do not involve pressure ulcers • Abstracts unless no RCTs are foundNon-English language papers
The search strategy	The databases to be searched are: • Medline, Embase, Cinahl, the Cochrane Library. • All years. • Studies will be restricted to English language only
Review strategy	How will individual PICO characteristics be combined across studies in a meta-analysis (for intervention reviews) • Population - any population will be combined for meta-analysis except for different strata. Must have active pressure ulcers at time of enrolment. • Intervention - any type of negative pressure wound therapy • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – single side effects will be meta-analysed separately from other side effects • Study design – randomised and quasi-randomised studies will be meta-analysed together. Blinded and unblinded studies will be meta-analysed together. Crossover trials will be meta-analysed together with parallel trials • Unit of analysis – patients, clusters (hospital wards), individual pressure ulcers. We will not meta-analyse studies where patients have multiple ulcer and the unit of analysis is pressure ulcer with studies where the unit of analysis is patients. • Minimum duration of treatment = no minimum.

	• Minimum follow up = no minimum. • Minimum total sample size = no minimum. • Use authors data. If there is a 10% differential or higher between the groups or if the missing data is higher than the event rate downgrade on risk of bias. If authors use ACA and ITT, ACA is preferable over ITT. • MIDs: 0.75 to 1.25 for dichotomous variables and 0.5 x standard deviation for continuous variables.
Analysis	Strata: The following groups will be considered separately as strata if data are present: • Children (neonates, infants, children) and adults Subgroups: The following groups will be considered separately as subgroups if data are present and there is inconsistency: • Different categories of pressure ulcer (from category 2 upwards where outcomes are reported separately • Different ulcer locations
Other terms	Vacuum-assisted wound closure; topical negative pressure therapy
Notes	

10.2. Search strategy

10.2.1. Search Filters

Table 54 – Search filters in OVID Medline

Search strategy	NPWT			Results
Date	April 2013			
Database	Medline-Ovid			
Search strategy		1	pressure ulcer/	8806
		2	decubit*.ti,ab.	3835
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	5979

Search strategy	NPWT			Results
		4	(bedsore* or bed-sore*).ti,ab.	494
		5	(incontinen* adj2 dermatitis).ti,ab.	49
		6	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	615
		7	or/1-6	13350
		8	limit 7 to english language	10633
		9	Negative-Pressure Wound Therapy/	759
		10	negative pressure.ti,ab.	4763
		11	vacuum/	3148
		12	suction/	9586
		13	(sub-atmospheric or subatmospheric).ti,ab.	410
		14	(vacuum adj2 (therapy or dressing* or closure or seal* or compression or pack or drainage)).ti,ab.	1329
		15	((suction or drainage) adj2 (dressing* or wound* or therapy or closure)).ti,ab.	1159
		16	or/9-15	18972
		17	8 and 16	144
		18	letter/	745880
		19	editorial/	297880
		20	news/	142634
		21	exp historical article/	300508
		22	Anecdotes as Topic/	4103
		23	comment/	485577
		24	case report/	1547128
		25	(letter or comment*).ti.	82104
		26	or/18-25	2998167

Search strategy	NPWT			Results
		27	randomized controlled trial/ or random*.ti,ab.	662482
		28	26 not 27	2983388
		29	animals/ not humans/	3554513
		30	exp Animals, Laboratory/	656163
		31	exp Animal Experimentation/	5133
		32	exp Models, Animal/	358527
		33	exp Rodentia/	2424128
		34	(rat or rats or mouse or mice).ti.	1020470
		35	or/28-34	7048347
		36	17 not 35	100
Notes				

Table 55 – Search filters in Embase

Search strategy	NPWT			Results
Date	April 2013			
Database	Embase-OVID			
Search strategy		1	decubitus/	12153
		2	decubit*.ti,ab.	4622
		3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6840
		4	(bedsore* or bed-sore*).ti,ab.	631
		5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	737
		6	(incontinen* adj2 dermatitis).ti,ab.	53

Search strategy	NPWT			Results
		7	or/1-6	16442
		8	limit 7 to english language	12672
		9	vacuum assisted closure/	1767
		10	negative pressure.ti,ab.	5182
		11	(sub-atmospheric or subatmospheric).ti,ab.	430
		12	(vacuum adj2 (therapy or dressing* or closure or seal* or compression or pack or drainage)).ti,ab.	1577
		13	((suction or drainage) adj2 (dressing* or wound* or therapy or closure)).ti,ab.	1339
		14	vacuum/	5049
		15	suction drainage/	1248
		16	suction/	6062
		17	or/9-16	19951
		18	8 and 17	197
		19	letter.pt. or letter/	755980
		20	note.pt.	462893
		21	editorial.pt.	389767
		22	case report/ or case study/	1773737
		23	(letter or comment*).ti.	132642
		24	or/19-23	3259271
		25	randomized controlled trial/ or random*.ti,ab.	753909
		26	24 not 25	3235493
		27	animal/ not human/	1268427
		28	nonhuman/	3776367
		29	exp Animal Experiment/	1487854

Search strategy	NPWT			Results
		30	exp experimental animal/	366838
		31	animal model/	620584
		32	exp Rodent/	2424924
		33	(rat or rats or mouse or mice).ti.	1074023
		34	or/26-33	8606171
		35	18 not 34	140
Notes				

Table 56 – Search filters in CINAHL

Search strategy	NPWT		Results
Date	April 2013		
Database	CINAHL		
Search strategy	S17	S16 Limiters - English Language; Exclude MEDLINE records	73
	S16	S7 and S15	193
	S15	S8 or S9 or S10 or S11 or S12 or S13 or S14	6345
	S14	((suction or drainage) and (dressing* or wound* or therapy or closure))	2598
	S13	(vacuum and (therapy or dressing* or closure or seal* or compression or pack or drainage))	531
	S12	sub-atmospheric or subatmospheric	38
	S11	negative pressure	1205
	S10	(MH "Suction")	1
	S9	(MH "Vacuum")	2352
	S8	(MH "Negative Pressure Wound Therapy")	28
	S7	S1 or S2 or S3 or S4 or S5 or S6	10210
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1347
	S5	incontinen* n2 dermatitis	66
	S4	bedsore* OR bed-sore*	152
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8180

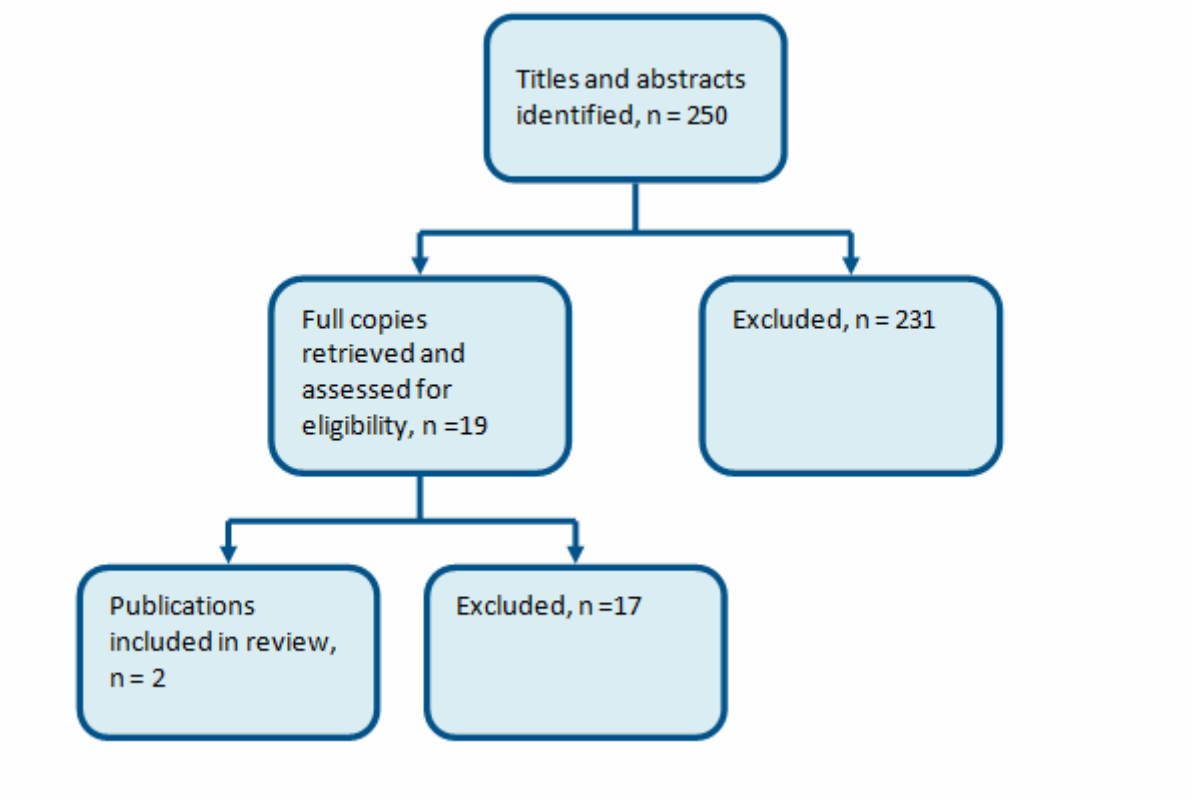
Search strategy	NPWT		Results
	S2	decubit*	468
	S1	(MH "Pressure Ulcer")	727
Notes			

Table 57 – Search filters in Cochrane

Search strategy	NPWT		Results
Date	April 2013		
Database	Cochrane (- CDSR [3/2012]; DARE; Central [3/2012]; NHS EED; HTA)		
Search strategy	#1	MeSH descriptor Pressure Ulcer explode all trees	480
	#2	decubit*:ti,ab,kw	341
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	818
	#4	(bedsore* or bed-sore*):ti,ab,kw	32
	#5	(incontinen* near/2 dermatitis):ti,ab,kw	10
	#6	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	62
	#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	1151
	#8	MeSH descriptor Negative-Pressure Wound Therapy explode all trees	56
	#9	MeSH descriptor Vacuum explode all trees	110
	#10	MeSH descriptor Suction explode all trees	701
	#11	negative pressure:ti,ab,kw	2034
	#12	(sub-atmospheric or subatmospheric):ti,ab,kw	19
	#13	(vacuum near/2 (therapy or dressing* or closure or seal* or compression or pack or drainage)):ti,ab,kw	110
	#14	((suction or drainage) near/2 (dressing* or wound* or therapy or closure)):ti,ab,kw	422
	#15	(#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14)	3141
	#16	(#7 AND #15)	56
Notes			

10.2.2. Flow chart

Figure 35 – Flow chart



10.2.3. Excluded Studies

Table 58 – Studies excluded from the clinical review

Reference	Reason for exclusion
JOSEPH2000	Wounds, not just pressure ulcers
VIKATMAA2008	Systematic review, which did not add any more details to review
BAHARETSTANI2008	Not an RCT
ALFADHLI2009	Not an RCT
APELQVIST2008	Diabetic foot wounds, not pressure ulcers
MODY2008	Wounds, not just pressure ulcers
XIE2010	Systematic review, which did not add any more details to review
ASHBY2010	Abstract of pilot RCT.
GREER1999	Abstract of an RCT in progress.
DELAAT2011	Wounds, not just pressure ulcers
GREGOR2008	Systematic review, which did not add any more details to review
PHAM2003	Systematic review, which did not add any more details to review
ASHBY2011	Abstract
SUISSA2011	Meta-analysis of TNPT for wounds, not just pressure ulcers
WILD2008	2 different methods of vacuum sealing

10.3. Clinical Evidence

One Cochrane review was identified (Ubbink 2008)[16] for negative pressure wound therapy for treating chronic wounds. We used this as a basis for the review, focusing only on the pressure ulcer studies included in the Cochrane review. No further studies were identified since the 2008 Cochrane review.

Two studies with pressure ulcers were included in the Cochrane review[17, 18]. Ford 2002[17] included 28 patients with stage III or IV ulcers and compared NPWT to modern wound dressings (wound gel products) and followed up for 3- 10 weeks. Wanner 2003 [18] included 22 paraplegic or tetraplegic patients with grade 2 or above pressure ulcers of the pelvic region and compared NPWT to wet-to-dry/wet-to-wet gauze dressings with Ringer's solution.

10.3.1. Summary table

Table 59 – Summary of studies included in the review

Study	Study type	Intervention/comparison	Population	Outcomes	Length of study/follow-up
FORD 2002[17]	RCT	Vacuum-assisted wound closure vs modern wound dressings	Patients with one to three full-thickness decubitus ulcers (Grade II &/or IV) present for a minimum of 4 weeks	Proportion of ulcers healed; mean % reduction in wound volume.	6 weeks treatment/3-10 weeks follow-up
WANNER 2003[18]	RCT	Ulcer debridement followed by: Vacuum-assisted wound closure vs wet-to-dry/wet-to wet technique with gauze soaked in Ringer's solution	Spinal injury patients (paraplegic or tetraplegic patients) with higher than grade 2 ulcers in the pelvic region	Time to reach 50% of the initial volume; mean wound volume (%).	56 days

10.3.2. Clinical GRADE evidence tables

Table 60 – Clinical evidence profile: NPWT versus wet-to-dry/wet-to-wet gauze

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NPWT	Wet-to-dry/wet-to-wet	Relative (95% CI)	Absolute		
Time to 50% of initial wound volume (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic patients												
1Wanner 2003[3]	randomised trials	Very serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	27 (SD10) days N=11	28 (SD7) days N=11	-	MD 1 lower (8.21 lower to 6.21 higher)	⊕OOO VERY LOW	Critical
Mean reduction in volume (% change) (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic patients												
1Wanner 2003[3]	randomised trials	Very serious[a]	no serious inconsistency	no serious indirectness	Very serious[c]	none	53%	65%	p=0.9[d]	MD 12% larger in control group	⊕OOO VERY LOW	Critical
Mean reduction in volume (actual change) (follow-up 42 days; measured with: photograph of wound and plaster wound impression) – paraplegic or tetraplegic patients												
1Wanner 2003[3]	randomised trials	Very serious[a]	no serious inconsistency	no serious indirectness	Very serious[c]	none	26.5ml	27.3ml	-p=0.2?	MD 0.8ml larger in control group	⊕OOO VERY LOW	Critical

a No details of sequence generation, allocation concealment or blinding. The mean wound size was larger in the vacuum-assisted than the wet-to-dry/wet-to-wet group.
b The confidence interval crossed one MID point.
c Data taken from graph, no standard deviations given. Very small sample size.
d Wilcoxon rank-sum test result.

Table 61 – Clinical evidence profile: NPWT versus modern dressings: wound gel products

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NPWT	Modern dressings: wound gel products	Relative (95% CI)	Absolute		
Ulcers healed within 6 weeks (follow-up 3-10 months)												
1Ford 2002[2]	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Very serious[b]	none	2/20 (10%)	2/15 (13.3%)	RR 0.75 (0.12 to 4.73)	33 fewer per 1000 (from 117 fewer to 497 more)	⊕OOO VERY LOW	Critical
							-	13.3%		33 fewer per 1000 (from 117 fewer to 496 more)		
Mean reduction in pressure ulcer volume (% change)[d]												
1Ford 2002[2]	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Very serious[c]	none	51.8%	42.1%	P=0.46	MD 9.7% larger in intervention group	⊕OOO VERY LOW	Critical

a No details of allocation concealment. Difference in age at baseline.
b Confidence interval crossed both MID points.
c No standard deviations given. Very small sample size.
d There were details of reduction in length, width and depth of pressure ulcer (cm). The Cochrane Review (Ubbink 2008) found the figures to be surprisingly large and contacted the author for verification but received no response. No standard deviations were available for this data.

10.3.3. Forrest plots

Figure 36 – Time to 50% of initial wound volume

Study or Subgroup	NPWT Mean	NPWT SD	NPWT Total	Wet-to-dry/wet-to-wet Mean	Wet-to-dry/wet-to-wet SD	Wet-to-dry/wet-to-wet Total	Weight	Mean Difference IV, Fixed, 95% CI
Wanner, 2003	27	10	11	28	7	11	100.0%	-1.00 [-8.21, 6.21]
Total (95% CI)			**11**			**11**	**100.0%**	**-1.00 [-8.21, 6.21]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.27 (P = 0.79)

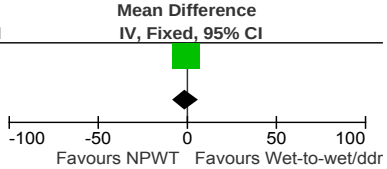
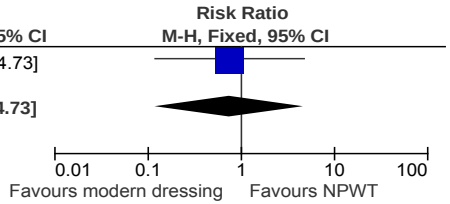


Figure 37 – Pressure ulcers healed within 6 weeks

Study or Subgroup	NPWT Events	NPWT Total	Modern dressings Events	Modern dressings Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Ford, 2002	2	20	2	15	100.0%	0.75 [0.12, 4.73]
Total (95% CI)		**20**		**15**	**100.0%**	**0.75 [0.12, 4.73]**
Total events	2		2			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.31 (P = 0.76)



10.3.4. Evidence tables

Table 62 – WANNER2003

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author: Wanner (2003). **Title:** Vacuum-assisted wound closure for cheaper and more comfortable healing of pressure sores: a prospective study **Journal:** Scand J Plast Reconstr Surg Hand Surg, 37, 28-33 **Study type:** randomised controlled trial **Study quality:** **Sequence generation:** no details **Allocation concealment:** no details **Blinding:** No blinding of healthcarers or patients. Outcome assessors were not blinded. **Unit of analysis:** patient **Addressing incomplete outcome**	**Patient group:** spinal injury patients - paraplegic or tetraplegic patients with higher than grade 2 ulcers in the pelvic region **All patients** **Randomised** N=22/24? Study numbers show that it was n=24 patients and 2 dropped out after randomisation (1 due to lack of data and 1 from severe diahorrea) but authors specify n=22 randomised. **Completed N=**22 **Drop-outs:** 2 **Group 1** **Randomised N: 12** **Completed N:11** **Dropouts: 1** **Age (mean): 49 (25-73 years)** **Wound size (mean, SD, range): 50 (33), 3-132**	**Group 1:** vacuum-assisted wound closure **Group 2:** wet-to-dry/wet-to-wet technique with gauze soaked in Ringer's solution three times per day	**Outcome 1:** time to reach 50% of the initial volume (at that point all ulcers were then closed with a flap) mean (SD)	**Group 1:** 27 (10) days **Group 2:** 28 (7) days **WMD:** -1.00 day; 95% CI -8.21 to 6.21 P=0.79	**Funding:** no financial support received. **Limitations:** very small sample size, no details of sequence generation, allocation concealment or blinding. The mean wound size was larger in the vacuum-assisted than the wet-to-dry/wet-to-wet group. **Additional outcomes**: there was no significant difference between the two groups (T50 variable, Wilcoxon rank-sum test, p=0.9) or when the mean values of the two groups were adjusted
			Outcome 2: actual reduction in mean wound volume at 42 days(read from graph)	**Group 1:** 26.5ml **Group 2:** 27.3ml **MD:** 0.8ml [there is a p-value of 0.2 but unsure if this is correct for this value]	
			Outcome 3: % reduction in mean wound volume at 42 days(read from graph)	**Group 1: 53%** **Group 2: 65%** **MD:** 12% larger	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
data: not ITT, withdrawals are described. **Baseline differences:** The mean wound size was larger in the vacuum-assisted than the wet-to-dry/wet-to-wet group. **Study power/sample size:** small (n=22), no sample size calculation. **Statistical analysis:** Wilcoxon rank-sum test used. Equivalence test set at 20% of the mean for adjusted and non-adjusted values. **Setting:** hospital in Switzerland. **Length of follow-up:** 42 days **Assessment of PUs:** Measurement of wound healing: reduction in wound volume calculated by wound impressions **Outcome measurement:** volume calculated by covering the ulcer with	**Group 2** **Randomised N: 12** **Completed N:11** **Dropouts:1** **Age (mean): 53 (34-77) years** **Wound size (mean, SD, range): 42 (16), 5-68.** **Inclusion criteria:** pressure sore in the pelvic region, deeper than grade 2 (described by Daniel et al, which means at least a penetration in the subcutaneous fat). **Exclusion criteria:** not stated explicitly but excluded 7 patients because pressure sore not in the pelvic region, three because depth of pressure sore less than grade 3; one patient could not be analysed because of lack of data and one excluded because he developed severe diarrhoea which				with the absolute initial volume (p=0.2).

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
a transparent, elastic polymer. The sheet was punctured at the highest point and 0.9% saline solution was injected through a second puncture with a hypodermic needle until no air was left in the cavity. The injected volume was measured. Repeated measurements the same day on the same wound gave satisfactory reproducible results. **Study length:** endpoint defined as when wound volume decreased by 50% because all ulcers were then closed by a flap	made it impossible to fix the vacuum dressing properly.				

Table 63 – FORD 2002

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author: Ford (2002)[2] **Title:** Interim analysis of a prospective, randomised trial of	**Patient group:** patients with one to three full-thickness decubitus ulcers which were	Group 1: ulcer debridement followed by 6 weeks treatment with Vacuum-Assisted Closure device	**Outcome 1: proportion of ulcers healed**	**Group 1:**2/20 (10%) NR **Group 2:** 2/15 (13%) NR **Relative risk:** 0.75 **95% CI:** 0.12, 4.73	**Funding:** Alpha Omega Alpha Student Research fellowship, plastic

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
vacuum-assisted closure versus the healthpoint system in the management of pressure ulcers **Journal:** Ann Plast . Surg, 49, 55-61. **Study type:** randomised controlled trial **Study quality:** **Sequence generation:** randomisation by table of random letters, V or H, generated before trial began. **Allocation concealment:** no details **Blinding:** blinded clinic staff (nurses, medical students and interns) measured wounds and took plaster impressions. Plaster impressions, soft-tissue biopsies and bone biopsies were coded. Volume displacements of plaster impressions were determined by a medical student. No	present for a minimum of 4 weeks **All patients** **Randomised N=28 patients with 41 pressure ulcers** **Completed N= 22 (with 35 pressure ulcers)** **Drop-outs: 6** in total: 3 patients lost to follow-up, 1 patient noncompliant with treatment and removed, 1 patient died of coronary artery disease and 1 patient died of respiratory arrest secondary to Guillain-Barre syndrome **Age:** 18-80 years **Group 1** **Randomised** N: 20 **Completed N:** not sure which group drop-outs were from **Dropouts:** not sure which group drop-outs were from **Age (mean): 41.7 years** **Group 2**	(VAC) Group 2: ulcer debridement followed by 6 weeks treatment with Healthpoint system (HP) – three FDA – approved gel products – accuzzyme, iodosorb, and panafil. Patients randomised to HP and whose wounds showed substantial exudate received Iodosrot or Iodoflex; those whose ulcers were clean and granulating received Panafil. Because all wounds were debrided surgically as appropriate, Accuzyme was not used. VAC dressings were changed Mondays, Wednesdays and Fridays. HP dressings were changed once or twice daily, depnding on the degree of wound drainage.	**Outcome 2: mean % reduction in wound volume over 6 weeks**	**Group 1:** 51.8% **Group 2:** 42.1% **MD:** 9.7% P=0.46	surgery education foundation scientific essay award winner, grants from the plastic surgery education foundation and Kinetic Concepts. **Limitations:** difference in age at baseline, no details of allocation concealment. No patient blinding. Inclusion criteria was for patients aged 18-80 but enrolled patients aged 18 -80 years. 3 patients lost to follow-up. **Additional outcomes:** One lateral malleolar ulcer in a patient with diabetes, hypertension and vascular insufficiency was

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
patient blinding. **Unit of allocation:** patient **Addressing incomplete outcome data:** not ITT. 3 patients lost to follow-up reasons given but don't know from which group. **Baseline differences:** yes, difference in average age. **Selective reporting:** **Study power/sample size:** small, no sample size calculation. **Statistical analysis:** patient demographics compared by Fisher's exact test. Student's t-test used to compare mean changes in dimension, volume, and histopathological data. **Setting:** plastic surgery clinic and inpatient physician referral at Boston Medical Centre, USA. **Treatment period:** 6 weeks **Length of follow-up:**	**Randomised N:** 15 **Completed N:** not sure which group drop-outs were from **Dropouts:** not sure which group drop-outs were from **Age (mean):** 54.4 years **Inclusion criteria:** presence of stage III or IV ulcer for 4 or more weeks; albumin >//=2.0; aged 21-80 years; ulcer volume after debridement = 10-150ml. **Exclusion criteria:** fistulas to organs or body cavities; malignancy in the wound; pregnant or lactating female; hashimoto thyroiditis; graves disease; iodine allergy; systemic sepsis; electrical burn; radiation exposure; chemical exposure; cancer; connective tissue disease; chronic renal or pulmonary disease; uncontrolled diabetes;				treated with VAC and complicated by sepsis, requiring amputation. There were no other treatment complications. Six wounds in the VAC group (30%) and 6 wounds in the HP grup (40%) underwent flap surgery. Three patients with 3 wounds completed 6 weeks of treatment followed by a second 6 weeks with the other treatment. The mean reduction in ulcer volume was 57% with VAC and 25% with HP The mean reductions in length, width and depth were 36.9cm, 40cm

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
3-10 months **Assessment of PUs:** 3-week evaluation included photograph of wound site, a plaster wound impression and measurement of wound dimensions. The 6-week evaluation included a series of post-treatment tests, consisting of a photograph of the wound site, a soft-tissue biopsy, a plaster wound impression and measurement of wound dimensions. If a bone biopsy and MRI were performed as part of pre-treatment testing, then these tests were repeated at 6 weeks.	corticosteroids or immunosuppressive agents; cardiac pacemaker; ferromagnetic clamps; recent placement of orthopaedic hardware.				and 33.6cm in the VAC group compared with 18.7cm, 19cm and 31cm in the HP group, p=0.10, p=0.11 and p=0.90). 3/15 (20%) wounds treated with HP showed improved osteomyelitis (2 by bone biopsy and one by MRI) there was no improvement in osteomyelitis for VAC group (by bone biopsy or MRI).

11. LIGHT THERAPY

11.1. Review protocol

Table 64 – Review protocol

Protocol	Light therapy
Review question	What is the effectiveness of light therapy for the treatment of pressure ulcers?
Population	Individuals of all ages, with at least one pressure ulcer of any category/stage
Intervention	Light therapy (infrared, ultraviolet, laser, monochromatic, polarized light)
Comparison	• No therapy • Comparison between light therapies • Placebo • Sham light therapy • Other type of therapy for pressure ulcer treatment
Outcomes	**Critical outcome for decision-making** • Time to complete healing (time to event data) • Rate of healing (continuous data) • Rate of reduction in size and volume of pressure ulcer (absolute and relative) (continuous data) • Reduction in size and volume of pressure ulcer (absolute and relative) (continuous data) • Proportion of patients completely healed within trial period (dichotomous) **Important outcomes** • Wound related pain • Health-related quality of life o Short-form health survey (SF36) o Manchester Short Assessment of Quality of Life o EQ-5D o WHOQOL-BREF o Cardiff HRQoL tool

	○ HUI ○ Pressure ulcer quality of life (Gorecki) • Acceptability of treatment (e.g. compliance, tolerance) • Time in hospital (continuous data) • Side effects (infection, health skin damage, healthy tissue damage, maceration, treatment related pain, skin irritation, allergic reaction, itching, odour, bleeding, rash, toxicity) • Mortality
Study design	• High quality systematic reviews of RCT's or RCT's only. • Cochrane reviews will be included if they match the inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.
Exclusion	• Studies with another population, intervention, comparison or outcome • Non-English, non-French, non-Dutch language papers
Search strategy	**The electronic databases to be searched are:** • Medline (OVID interface), Cinahl (EBSCO-interface), Embase, Library of the Cochrane Collaboration • All years • Search strategy see Appendix I
Review strategy	**How will individual PICO characteristics be combined across studies)** • Population – any population will be combined except those specified in the strata. Must have active pressure ulcers at time of enrolment. • Intervention – any type of light therapy will be combined for meta-analysis. • Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – same outcomes will be combined for meta-analysis. • Blinding – Blinded and unblinded studies will be meta-analysed together. • Unit of analysis – patients, individual pressure ulcers • Minimum follow up = no minimum. • Minimum total size = no minimum • Use authors data. If there is a 10% differential or higher between the groups or if the missing data is higher than the event rate downgrade on risk of bias. If authors use ACA and ITT, ACA is preferable over ITT.

	• MIDs: 0.75 to 1.25 for dichotomous variables and 0.5 x standard deviation for continuous variables.
Analysis	**The following groups will be considered separately if data are present:** • ICU patients, spinal cord patients, palliative patients, paediatric patients and adults (if not in other subgroup); **Subgroups:** The following groups will be considered separately as subgroups if data are present: • Different categories of pressure ulcers (from category 2 upwards where outcomes are reported separately) • Different locations of pressure ulcers: sacral, heel and others
Other terms	
Notes	

11.2. Search strategy

11.2.1. Search Filters

Table 65 – Search filters Medline (OVID)

Date	03/01/2013	
Database	**Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R)** 1946 to Present	
Search Strategy	41. exp Pressure Ulcer/	9318
	42. decubit*.ti,ab.	4072
	43. (pressure adj (sore* or ulcer* or damage)).ti,ab.	6463
	44. (bedsore* or bed-sore*).ti,ab.	522
	45. ((friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	261
	46. OR/1 – 5	
	47. Exp phototherapy/	13859
	48. Light therap*.tw	25977
	49. Low level light.tw	1075
	50. Low intensity light.tw	67
	51. Phototherapy*.tw	142
	52. Heliotherapy*.tw	4799
	53. infrared.tw	114
	54. ultraviolet.tw	59678

	55. laser.tw	47813
	56. monochromatic.tw	162541
	57. polarized light.tw	3622
	58. light emitting diode.tw	4342
	59. LED.tw	1943
	60. LLLT.tw	271006
	61. UV.tw	573
	62. OR/7 – 21	94339
	63. randomized controlled trial.pt.	623420
	64. controlled clinical trial.pt.	346084
	65. randomi#ed.tw.	86011
	66. placebo.ab.	313368
	67. randomly.tw.	142808
	68. trial.ti	190418
	69. Clinical Trials as topic.sh.	112489
	70. OR/23 – 29	164411
	71. AND/6, 22, 30	847473
	72. Limit language: 'English, Dutch, Flemish, French'	55
		49
Note		

Table 66 – Search filters Embase

Date	03/01/2013	
Database	Embase	
Search Strategy (attention, for PubMed, check « Details »)	1. 'decubitus'/exp	16258
	2. decubit*:ab,ti	5578
	3. (pressure NEAR/1 (sore* OR ulcer* OR damage)):ab,ti	5017
	4. (bed NEAR/2 sore*):ab,ti OR bedsore*:ab,ti	753
	5. ((friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab	316
	6. OR/1 – 5	
	7. 'phototherapy'/exp	17877
	8. (Light near/1 (therap*)):ti,ab	47843
	9. 'Low level light':ti,ab	1477
	10. 'Low intensity light':ti,ab	90
	11. 'phototherap*':ti,ab	135

	12. 'heliotherap*':ti,ab	7250
	13. 'infrared':ti,ab	143
	14. 'ultraviolet':ti,ab	59591
	15. 'laser':ti,ab	50064
	16. 'monochromatic':ti,ab	162856
	17. 'polarized light':ti,ab	3246
	18. 'light emitting diode':ti,ab	3914
	19. 'LED':ti,ab	1765
	20. 'LLLT':ti,ab	326301
	21. 'UV':ti,ab	876
	22. OR/7 – 21	107046
	23. 'clinical trial'/exp	708606
	24. 'clinical trial (as topic)'/exp	1066795
	25. random*':ti,ab	53367
	26. factorial'*:ti,ab	776564
	27. (crossover* or cross over*):ti,ab	20429
	28. ((doubl* or singl*) adj blind*):ti,ab	124331
	29. (assign* or allocat* or volunteer* or placebo*):ti,ab	13
	30. 'crossover procedure'/exp	597594
	31. 'single blind procedure'/exp	36108
	32. 'double blind procedure'/exp	16228
	33. OR/23 – 32	112186
	34. AND/6, 22, 33	1937943
	35. Limit language: 'English, Dutch, French'	101
		93
Note		

Table 67 – Search filters CINAHL (EBSCO-Interface)

Date	03/01/2013	
Database	CINAHL (EBSCO-interface)	
Search Strategy (attention, for PubMed, check « Details »)	109. MH "Pressure Ulcer"	7928
	110. decubit*	498
	111. pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8718
	112. bedsore* OR bed-sore*	
	113. ((friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	160

	114. OR/1 – 5	823
	115. MH “phototherapy+”	
	116. “Light therap*” or “Low level light” or “Low intensity light” or “phototherapy*” or “heliotherapy*” or “infrared” or “ultraviolet” or “laser” or “monochromatic” or “polarized light” or “light emitting diode” or “LED” or “LLLT” or “UV”	9599 1465 33264
	117. OR/7 – 8	
	118. MH "Clinical Trials+"	
	119. “trial*”	
	120. “randomi#ed”	33509
	121. “randomly”	110355
	122. “randomized controlled trial”	141870
	123. PT “randomized controlled trial”	69066
	124. PT “clinical trial”	25948
	125. OR/23 - 29	9465
	126. AND/6, 22, 30	12445
	127. Limit language=’English, Dutch, French’	51940
		173531
		35
		30
Note		

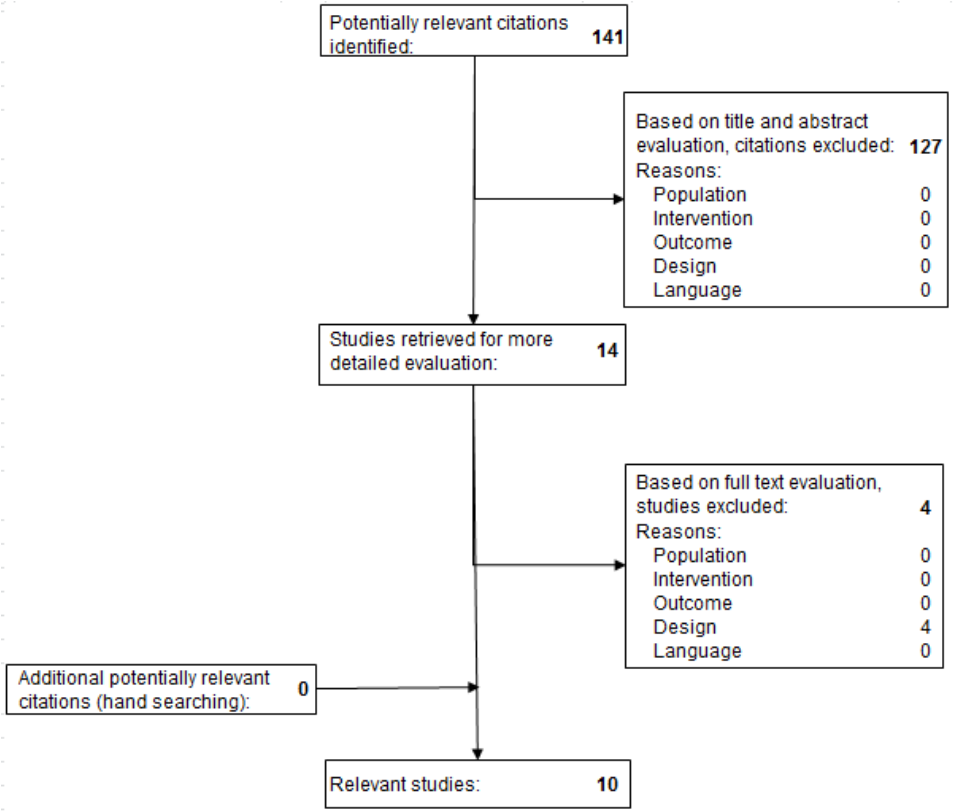
Table 68 – Search filters Cochrane Library

Date	03/01/2013	
Database	The Library of the Cochrane Collaboration	
Search Strategy (attention, for PubMed, check « Details »)):ti,ab,kw,kw	1. “Pressure ulcer”[MeSH]	490
	2. decubit*:ti,ab,kw	357
	3. (pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	879
	4. (bedsore* or bed-sore*):ti,ab,kw	34
	5. ((friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	3
	6. OR/1 – 5	
	7. “phototherapy”[MeSH]	1166
	8. (Light therap*):ti,ab,kw	1882
	9. (Low level light):ti,ab,kw	2185
	10. (Low intensity light):ti,ab,kw	608
	11. (phototherap*):ti,ab,kw	198

	12. (heliotherap*):ti,ab,kw	1181
	13. (infrared):ti,ab,kw	18
	14. (ultraviolet):ti,ab,kw	928
	15. (laser):ti,ab,kw	1687
	16. (monochromatic):ti,ab,kw	7673
	17. (polarized light):ti,ab,kw	87
	18. (light emitting diode):ti,ab,kw	105
	19. (LED):ti,ab,kw	114
	20. (LLLT):ti,ab,kw	25469
	21. (UV):ti,ab,kw	117
	22. OR/7 – 21	895
	23. “Clinical Trial” [publication type]	38253
	24. “Randomized Controlled Trial” [publication type]	16
	25. “clinical trial” as topic	315374
	26. (trial)):ti.	51777
	27. (randomi#ed)):ti,ab,kw	251036
	28. (randomly)):ti,ab,kw	1
	29. OR/27 – 33	86532
	30. AND/10, 26, 34	522435
		65
Note		

11.2.2. Flow chart

Figure 38 – Flow chart search strategy



11.2.3. Excluded Studies

Table 69 – Excluded studies

Reference	Reason of exclusion
Dolan 1989	No RCT
Hawkins 2005	No RCT
Iordonau 2002	No RCT
Karba 1997	No RCT

11.3. Clinical Evidence

Ten randomized controlled trials were included in this review. [19-28]

Various types of light therapy are used to treat pressure ulcers. In this review different types of light therapy were compared to control or each other:

- Laser therapy: any therapy using light delivered by a laser device;
- Monochromatic infrared light: infrared light at one wavelength;
- Polarized light: light can be polarized (vibration of light is going in the same direction) or unpolarized (vibration of light is going in all directions);
- Low level laser therapy: therapy by laser used at a very low energy level per cm^2 or time-unit;
- Multiwave length light: intense pulsed light (broad spectrum lights) with multiple wavelengths;
- Ultraviolet therapy: light therapy using radiation in the ultraviolet range.

11.3.1. Summary table

Table 70 – Summary table

Study	Intervention/comparator	Population	Outcome	Study length
Dehlin 2003[19]	Monochromatic phototherapy Placebo	Geriatric patients with stage II and III PUs (Sterling or Shea classification)	Proportion of ulcers completely healed Time to reduction in ulcer area Reduction in ulcer area Relative reduction in ulcer area Adverse events	11 weeks of treatment and 2 weeks of follow-up
Dehlin 2007[20]	Monochromatic phototherapy Placebo	Geriatric patients with stage II PUs (Sterling or Shea classification)	Proportion of ulcers completely healed Time to complete healing Rate of reduction in ulcer area Normalized percentage reduction in ulcer area Percentage reduction in ulcer area over time Adverse events	11 weeks of treatment and 2 weeks of follow-up
Durovic 2008[21]	Polarized light Standard care	Patients with a PU (Pressure Ulcer Classification System)	Surface area reduction Change of rank of PU Healing (PUSH score)	Four weeks of treatment
Lucas 2000[22]	Low level laser therapy	Nursing home patients with a stage III PU (classification	Median wound area reduction	Until complete healing with a maximum of six weeks

	Standard care	corresponding to EPUAP)	Increase of ulcer area Adverse events	
Lucas 2003[23]	Low level laser therapy Standard care	Nursing home patients with a stage III PU (classification corresponding to EPUAP)	Proportion of patients completely healed Increase of ulcer area Absolute reduction in ulcer area Relative reduction in ulcer area Proportion of patient who developed a stage IV PU Adverse events	Six weeks of treatment
Nussbaum 1994[24]	Laser therapy Ultrasound/ultraviolet-C therapy Standard care	Patients with a spinal cord injury and a PU	Mean weekly healing rate	Until complete closure
Schubert 2001[25]	Pulsed monochromatic light Standard care	Hospitalized patients with a stage II or III PU (Shea classification)	Proportion of patients > 50% healed Time to 90% reduction in ulcer area Constant healing rate Healing rate	Until complete healing with a maximum of ten weeks
Shojaei 2008[26]	Laser therapy Standard care	Veterans with a spinal cord injury and a PU	Proportion of patients with ulcers improved Proportion of patients with ulcers not changed	Three weeks of treatment

			Proportion of patients with ulcers worsened Minimum of 50% reduction in ulcer size	
Taly 2004[27]	Multiwavelength light therapy Sham therapy	Patients with a spinal cord injury and a stage II to IV PU (classification corresponding to EPUAP)	Proportion of ulcers completely healed Proportion of ulcers not improved Proportion of ulcer with a decreased PSST score Time to complete healing Reduction in PU stage Time to reach a PU stage II PSST score at end of study	Until complete healing with a maximum of 14 sessions and a follow-up of two weeks
Wills 1993[28]	Ultraviolet therapy Sham therapy	Patients with a superficial PU (< 5 mm deep)	Time to complete healing	Eight weeks of treatment and two weeks of follow-up

11.3.2. Clinical GRADE evidence tables

Table 71 – Light therapy versus control

Quality assessment							No of patients/ulcers		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Light therapy	Control	Relative (95% CI)	Absolute		
Proportion of patients completely healed – nursing home patients and patients with a spinal cord injury – all stages– NPUAP classification and no system reported[n]												
2 Lucas 2003; Shojaei 2008	randomised trials	very serious[a,b]	no serious inconsistency	no serious indirectness	Serious[c]	none	21/44 (47.7%)	16/51 (31.4%)	RR 1.54 (0.93 to 2.56)	169 more per 1000 (from 22 fewer to 489 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								23.7%		128 more per 1000 (from 17 fewer to 370 more)		
Proportion of patients completely healed - Nursing home patients – stage III – NPUAP classification												
1 Lucas 2003	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	Serious[c]	none	18/36 (50%)	15/43 (34.9%)	RR 1.43 (0.85 to 2.42)	150 more per 1000 (from 52 fewer to 495 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								34.9%		150 more per 1000 (from 52 fewer to 496 more)		
Proportion of patients completely healed - Patients with a spinal cord injury – stage not reported – classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[e]	none	3/8 (37.5%)	1/8 (12.5%)	RR 3 (0.39 to 23.07)	250 more per 1000 (from 76 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								12.5%		250 more per 1000 (from 76 fewer to 1000 more)		

Proportion of patients completely healed – hospitalized patients – stage II – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[g]	none	-	-	P<0.05	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
								0%		not pooled		
Proportion of ulcers completely healed – geriatric patients and patients with a spinal cord injury – stage II to IV – Shea and NPUAP classification[n]												
2 Dehlin 2003; Taly 2004	randomised trials	very serious[a,h]	no serious inconsistency	no serious indirectness	Serious[c]	none	52/113 (46%)	48/115 (41.7%)	RR 1.09 (0.81 to 1.46)	38 more per 1000 (from 79 fewer to 192 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								43.9%		40 more per 1000 (from 83 fewer to 202 more)		
Proportion of ulcers completely healed – geriatric patients – stage II and III – Shea classification												
1 Dehlin 2003	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[c]	none	34/78 (43.6%)	34/86 (39.5%)	RR 1.1 (0.77 to 1.59)	40 more per 1000 (from 91 fewer to 233 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								39.5%		40 more per 1000 (from 91 fewer to 233 more)		
Proportion of ulcers completely healed – patients with a spinal cord injury – stage II to IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	18/35 (51.4%)	14/29 (48.3%)	RR 1.07 (0.65 to 1.75)	34 more per 1000 (from 169 fewer to 362 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								48.3%		34 more per 1000 (from 169 fewer to 362 more)		

Proportion of ulcers healed > 90% – geriatric patients – stage II and III – Shea classification												
1 Dehlin 2003	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[c]	none	44/78 (56.4%)	42/86 (48.8%)	RR 1.16 (0.86 to 1.55)	78 more per 1000 (from 68 fewer to 269 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								48.8%		78 more per 1000 (from 68 fewer to 268 more)		
Proportion of patients > 50% healed after 5 weeks – hospitalized patients – stage II and III – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	Serious[c]	none	26/27 (96.3%)	23/32 (71.9%)	RR 1.34 (1.07 to 1.68)	244 more per 1000 (from 50 more to 489 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								71.9%		244 more per 1000 (from 50 more to 489 more)		
Proportion of patients improved - Patients with a spinal cord injury – stage not reported – classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[e]	none	7/8 (87.5%)	6/8 (75%)	RR 1.17 (0.72 to 1.88)	127 more per 1000 (from 210 fewer to 660 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								75%		127 more per 1000 (from 210 fewer to 660 more)		

Proportion of patients not changed - Patients with a spinal cord injury – stage not reported – classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[e]	none	1/8 (12.5%)	1/8 (12.5%)	RR 1 (0.07 to 13.37)	0 fewer per 1000 (from 116 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								12.5%		0 fewer per 1000 (from 116 fewer to 1000 more)		
Proportion of patients worsened – nursing home patients and patients with a spinal cord injury – stage III PU (stage not reported in Shojaei study) - NPUAP classification and no system reported[n]												
3 Lucas 2000; Lucas 2003; Shojaei 2008	randomised trials	very serious[b,d]	very serious[i]	no serious indirectness	very serious[e]	none	6/52 (11.5%)	5/59 (8.5%)	RR 1.29 (0.47 to 3.59)	25 more per 1000 (from 45 fewer to 219 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								12.5%		36 more per 1000 (from 66 fewer to 324 more)		
Proportion of patients worsened - Nursing home patients – stage III PU - NPUAP classification												
2 Lucas 2000; Lucas 2003	randomised trials	very serious[d]	very serious[i]	no serious indirectness	very serious[e]	none	6/44 (13.6%)	4/51 (7.8%)	RR 1.10 (0.07 to 18.21)	8 more per 1000 (from 73 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								14.8%		15 more per 1000 (from 138 fewer to 1000 more)		
Proportion of patients worsened - Patients with a spinal cord injury – stage not reported – classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[e]	none	0/8 (0%)	1/8 (12.5%)	OR 0.14 (0 to 6.82)	105 fewer per 1000 (from 125 fewer to 368 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								12.5%		105 fewer per 1000 (from 125 fewer to 368 more)		

Proportion of ulcers not changed or worsened – patients with a spinal cord injury – stage II to IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	6/35 (17.1%)	3/29 (10.3%)	RR 1.66 (0.45 to 6.05)	68 more per 1000 (from 57 fewer to 522 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								10.3%		68 more per 1000 (from 57 fewer to 520 more)		
Proportion of patients who developed a stage IV PU - Nursing home patients – stage III PU - NPUAP classification												
1 Lucas 2003	randomised trials	very serious[c]	no serious inconsistency	no serious indirectness	very serious[e]	none	3/37 (8.1%)	5/44 (11.4%)	RR 0.71 (0.18 to 2.79)	33 fewer per 1000 (from 93 fewer to 203 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								11.4%		33 fewer per 1000 (from 93 fewer to 204 more)		
Proportion of patients with an ulcer decreased in stage (stage III to stage II, I or 0) Patients with a spinal cord injury – classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[j]	none	5/8 (62.5%)	?	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
								?		not pooled		
Proportion of patients with an ulcer of unchanged stage - Patients with a spinal cord injury – stage not reported - classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[j]	none	3/8 (37.5%)	?	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
								?		not pooled		
Proportion of ulcers reduced to a stage I after 3 weeks – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	1/4 (25%)	0/5 (0%)	OR 9.49 (0.18 to 489.97)	-	⊕OOO VERY LOW	
								0%		-		

Proportion of ulcers reduced to a stage II after 3 weeks – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	3/4 (75%)	1/5 (20%)	RR 3.75 (0.59 to 23.66)	550 fewer per 1000 (from 82 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								20%		550 fewer per 1000 (from 82 fewer to 1000 more)		
Mean percentage reduction in ulcer area – geriatric patients – stage II – Shea classification												
1 Dehlin 2007	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	no serious imprecision	none	78.5 (SD 41.8)	50.2 (SD (108.2)	-	MD 28.3 higher (3.39 to 53.21 higher)	⊕⊕OO LOW	CRITICAL OUTCOME
Mean percentage reduction in ulcer area – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	very serious[k]	none	28.5 (n=20)	-20 (n=20)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Reduction in ulcer area – geriatric patients – stage II and III – Shea classification												
1 Dehlin 2003	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[l]	none	n=78	n=86	p=0.12	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Median percentage reduction in ulcer area – geriatric patients – stage II – Shea classification												
1 Dehlin 2007	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[k]	none	100 (n=79)	100 (n=84)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Median percentage reduction in ulcer area - Nursing home patients – stage III PU - NPUAP classification												
1 Lucas 2000	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	very serious[l]	none	83 (n=8)	95 (n=8)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME

Mean cm² ulcer area at end of treatment – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	Serious[c]	none	10.8 (SD 19.18)	22.97 (SD15.69)	-	MD 12.17 lower (23.03 to 1.31 lower)	⊕OOO VERY LOW	CRITICAL OUTCOME
Absolute mm² reduction in ulcer area - Nursing home patients – stage III PU - NPUAP classification												
1 Lucas 2003	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	Serious[c]	none	48 (SD 394)	138 (SD 270)	-	MD 90 lower (241.91 lower to 61.91 higher)	⊕OOO VERY LOW	CRITICAL OUTCOME
Relative percentage reduction in ulcer area - Nursing home patients – stage III PU - NPUAP classification												
1 Lucas 2003	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5 (SD 194)	34 (SD 204)	-	MD 29 lower (116.94 lower to 58.94 higher)	⊕⊕OO LOW	CRITICAL OUTCOME
Mean percentage reduction in PUSH score – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	very serious[k]	none	31 (n=20)	-13.4 (n=20)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean PUSH score at end of treatment – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7.35 (SD 3.15)	11.85 (SD 2.35)	-	MD 4.5 lower (6.23 to 2.77 lower)	⊕⊕OO LOW	CRITICAL OUTCOME
Proportion of ulcers with a lower PSST score – patients with a spinal cord injury – stage II to IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	11/35 (31.4%)	12/29 (41.4%)	RR 0.76 (0.4 to 1.46)	99 fewer per 1000 (from 248 fewer to 190 more)	⊕OOO VERY LOW	CRITICAL OUTCOME
								41.4%		99 fewer per 1000 (from 248 fewer to 190 more)		

PSST score at end of study – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	Serious[c]	none	13.3 (SD 2.9)	24.2 (SD 4)	-	MD 5.9 lower (10.41 to 1.39 lower)	⊕⊕OO LOW	CRITICAL OUTCOME
PSST score at end of treatment – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	16.8 (SD 16.5)	22.4 (SD 3.9)	-	MD 5.6 lower (22.13 lower to 10.93 higher)	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean percentage reduction in PSST score at end of treatment – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[k]	none	32.2 (n=4)	12.9 (n=5)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean percentage reduction in PSST score at end of study – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[k]	none	37.8 (n=4)	19.4 (n=5)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean rank of PU at end of treatment – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	no serious imprecision	none	5.95 (SD 2.48)	8.6 (SD 1.05)	-	MD 2.65 lower (3.83 to 1.47 lower)	⊕⊕OO LOW	CRITICAL OUTCOME
Mean percentage reduction in rank of PU – general population – stage not reported – classification system not reported												
1 Durovic 2008	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	very serious[k]	none	19.6 (n=20)	-4.9 (n=20)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean percentage reduction in stage at end of treatment – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[k]	none	17.9 (n=4)	12.5 (n=5)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME

Mean percentage reduction in stage at end of study – patients with a spinal cord injury – stage III and IV –NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[k]	none	35.7 (n=4)	25 (n=5)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (weeks) – geriatric patients – stage II and III – Shea classification												
1 Dehlin 2003	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[l]	none	n=78	n=86	p=0.93	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (days) (stage II) – geriatric patients – stage II – Shea classification												
1 Dehlin 2007	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[l]	None	n=79	n=86	p=0.58	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (weeks) - general population and patients with a spinal cord injury – stage II to IV and superficial Pus - NPUAP classification and no system reported[n]												
2 Wills 1983; Taly 2004	randomised trials	very serious[d,h]	very serious[i]	no serious indirectness	no serious imprecision	none	n=43	n=37	-	MD 0.69 lower (3.43 lower to 2.05 higher)	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (weeks) - General population – superficial Pus – classification system not reported												
1 Wills 1983	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	Serious[c]	none	6.25 (SD 1.56)	8.38 (SD 1.27)	-	MD 2.13 lower (3.52 to 0.74 lower)	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (weeks) (age and initial area as covariates) General population – superficial Pus – classification system not reported												
1 Wills 1983	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	Serious[c]	none	6.26 (SD 1.67)	8.37 (SD 1.41)	-	MD 2.11 lower (3.62 to 0.6 lower)	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to complete healing (weeks) - Patients with a spinal cord injury – stage II to Iv – NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	Serious[c]	none	2.45 (SD 2.06)	1.78 (SD 2.13)	-	MD 0.67 higher (0.36 lower to 1.7 higher)	⊕⊕OO LOW	CRITICAL OUTCOME

Time to 90% reduction in ulcer area (weeks) – hospitalized patients – stage II and III – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[k]	none	5 (n=27)	9 (n=32)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Time of reduction in ulcer area (weeks) – geriatric patients – stage II and III – Shea classification												
1 Dehlin 2003	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[l]	none	n=78	n=86	p<0.0001	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Time to reach stage II (weeks) - Patients with a spinal cord injury – stage III and IV – NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	Serious[c]	none	2.25 (SD 0.5)	4.33 (SD 1.53)	-	MD 2.08 lower (3.51 to 0.65 lower)	⊕⊕OO LOW	CRITICAL OUTCOME
Mean healing rate (%/week) – geriatric patients – stage II – Shea classification												
1 Dehlin 2007	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[k]	none	15.1 (n=79)	10.9 (n=84)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Mean healing rate (%/week) - patients with a spinal cord injury – stage not reported – classification system not reported												
1 Nussbaum 1994	randomised trials	very serious[d]	no serious inconsistency	no serious indirectness	very serious[e]	none	23.7 (SD 17.05)	32.41 (SD 15.65)	-	MD 8.71 lower (27.23 lower to 9.81 higher)	⊕OOO VERY LOW	CRITICAL OUTCOME
Healing rate per week – hospitalized patients – stage II and III – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[k]	none	0.298 (n=27)	0.2 (n=32)	p<0.05	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Healing rate per week – hospitalized patients – stage II – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[m]	none	0.317 (n=?)	0.204 (n=?)	p<0.05	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME

Constant healing rate (exponential fitting) (%/day) – hospitalized patients – stage II and III – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[m]	none	5.3 (n=27)	3.4 (n=32)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Constant healing (exponential fitting) (%/day) (stage II) – hospitalized patients – stage II – Shea classification												
1 Schubert 2001	randomised trials	very serious[f]	no serious inconsistency	no serious indirectness	very serious[m]	none	5.9 (n=?)	3.4 (n=?)	-	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Minimum reduction of 50% in ulcer size - Patients with a spinal cord injury – stage not reported - classification system not reported												
1 Shojaei 2008	randomised trials	very serious[b]	no serious inconsistency	no serious indirectness	very serious[k]	none	n=8	n=8	p=0.007	not pooled	⊕OOO VERY LOW	CRITICAL OUTCOME
Proportion of patients with hypergranulation - Patients with a spinal cord injury – stage II to IV – NPUAP classification												
1 Taly 2004	randomised trials	Serious[h]	no serious inconsistency	no serious indirectness	very serious[e]	none	0/35 (0%)	1/29 (3.4%)	OR 0.11 (0 to 5.64)	31 fewer per 1000 (from 34 fewer to 133 more)	⊕OOO VERY LOW	IMPORTANT OUTCOME
								3.5%		31 fewer per 1000 (from 35 fewer to 135 more)		
Proportion of patients with adverse events – nursing home patients and geriatric patients – stage II and III – NPUAP and Shea classification												
3 Dehlin 2007; Lucas 2000; Lucas 2003	randomised trials	very serious[a,d]	no serious inconsistency	no serious indirectness	very serious[e]	none	9/124 (7.3%)	9/136 (6.6%)	RR 1.06 (0.44 to 2.54)	4 more per 1000 (from 37 fewer to 102 more)	⊕OOO VERY LOW	IMPORTANT OUTCOME
								0%		-		

a Dehlin (2000) and Dehlin (2007): no report on allocation concealment, sequence generation; double blinding, only information on blinding of outcome assessor; no ITT analysis; b Shojaei (2008): no report on allocation concealment and sequence generation; triple blinding, no further information; no ITT analysis; c Confidence interval crossed one MID point
d Durovic (2008), Lucas (2000), Lucas (2003), Nussbaum (1994) and Wills (1983): no report on allocation concealment and sequence generation; single-blinded (outcome assessor or staff members); no ITT analysis; e Confidence interval crossed both MID points; f Schubert (2001): insufficient sequence generation, no report on allocation concealment and blinding; no ITT analysis
g Only a p-value was reported. Unclear how many patients had a stage II PU; h Taly (2004): no report on allocation concealment; unclear if patients were blinded
i Heterogeneity: $p<0.1$ and $I^2 > 50\%$; j Only proportion reported for light therapy group; k No standard deviation or p-value reported; l Only p-value reported; m No standard deviation or p-value; eported. Unclear how many patients had a stage II PU; n Lucas (2000), Lucas (2003) and Taly (2004): NPUAP classification; Shojaei (2008), Wills (1993): no classification system reported; Dehlin (2003): Shea classification

Table 72 – Laser therapy versus ultrasound/ultraviolet-C

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laser therapy	Ultrasound/ ultraviolet-C	Relative (95% CI)	Absolute		
Mean healing rate (week) - patients with a spinal cord injury – stage not reported – classification system not reported												
1 Nussbaum 1994	randomised trials	Very serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	23.7 (SD 17.05)	51.8 (SD 22.91)	-	MD 28.1 lower (50.95 to 5.25 lower)	⊕OOO VERY LOW	CRITICAL OUTCOME

a No report on allocation concealment and sequence generation; single-blinded (outcome assessor); no ITT analysis
b Confidence interval crossed one MID point

Table 73 – Ultrasound/ultraviolet-C versus standard care

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ultrasound/ ultraviolet-C	Standard care	Relative (95% CI)	Absolute		
Mean healing rate (week) - patients with a spinal cord injury – stage not reported – classification system not reported												
1 Nussbaum 1994	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	51.8 (SD 22.91)	32.41 (SD 15.65)	-	MD 19.39 higher (2.81 lower to 41.59 higher)	⊕OOO VERY LOW	CRITICAL OUTCOME

a No report on allocation concealment and sequence generation; single-blinded (outcome assessor); no ITT analysis
b Confidence interval crossed one MID point

11.3.3. Forrest plots

Figure 39 – Light therapy versus control – proportion of patients completely healed

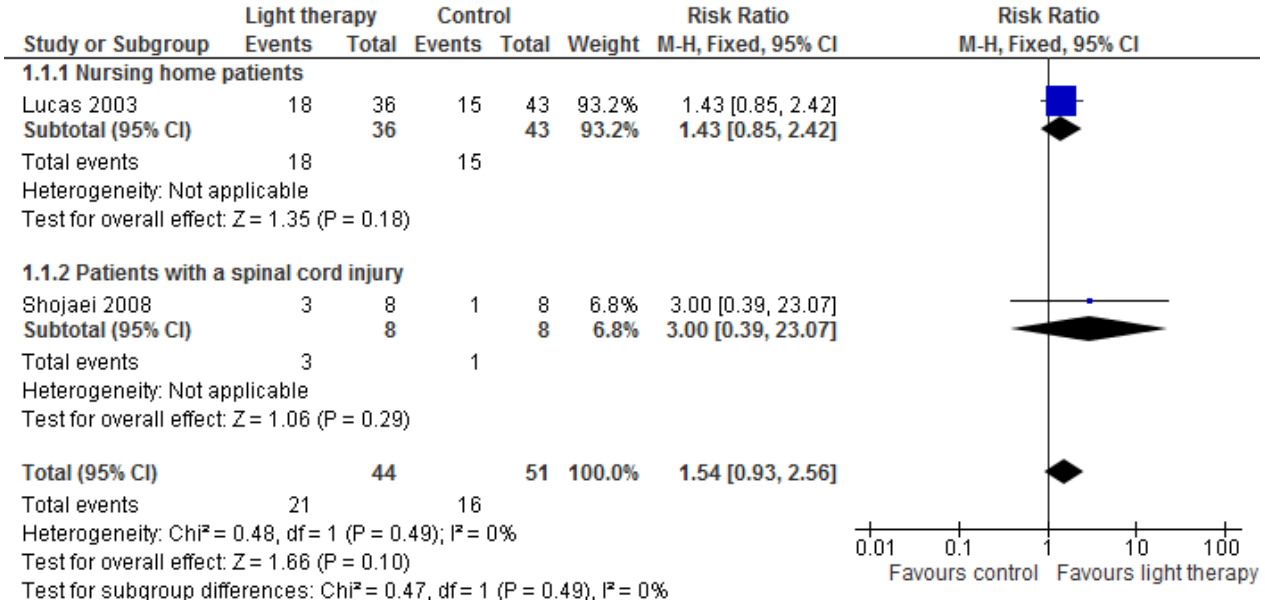


Figure 40 – Light therapy versus control – proportion of ulcers completely healed

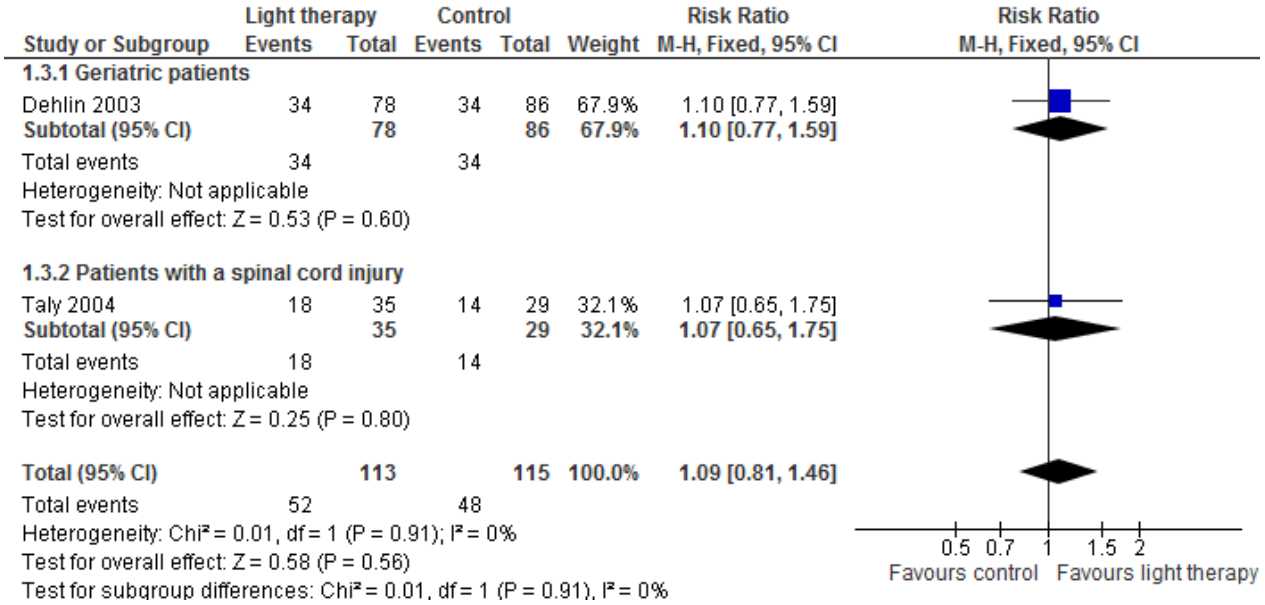


Figure 41 – Light therapy versus control – proportion of ulcers completely healed > 90%

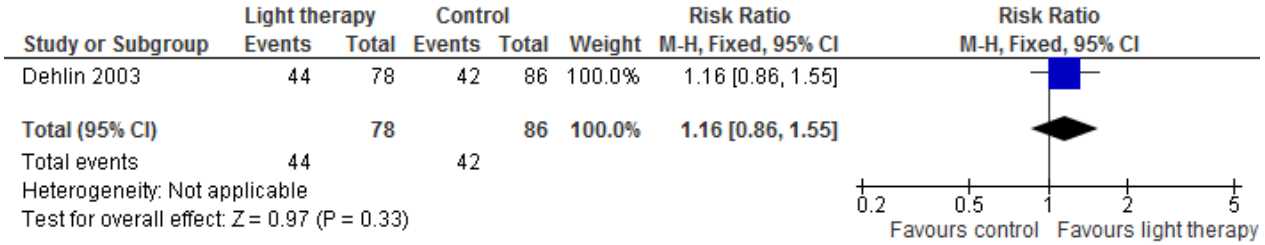


Figure 42 – Light therapy versus control – proportion of patients healed > 50% after 3 weeks

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Schubert 2001	26	27	23	32	100.0%	1.34 [1.07, 1.68]
Total (95% CI)		**27**		**32**	**100.0%**	**1.34 [1.07, 1.68]**
Total events	26		23			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.50 (P = 0.01)

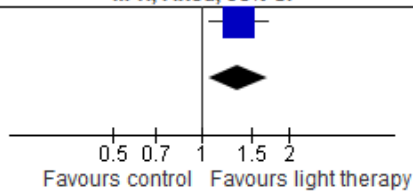


Figure 43 – Light therapy versus control – proportion of patients improved

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Shojaei 2008	7	8	6	8	100.0%	1.17 [0.72, 1.88]
Total (95% CI)		**8**		**8**	**100.0%**	**1.17 [0.72, 1.88]**
Total events	7		6			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.63 (P = 0.53)

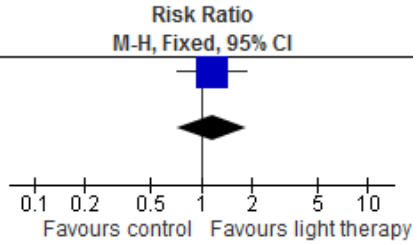


Figure 44 – Light therapy versus control – proportion of patients not changed

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Shojaei 2008	1	8	1	8	100.0%	1.00 [0.07, 13.37]
Total (95% CI)		**8**		**8**	**100.0%**	**1.00 [0.07, 13.37]**
Total events	1		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.00 (P = 1.00)

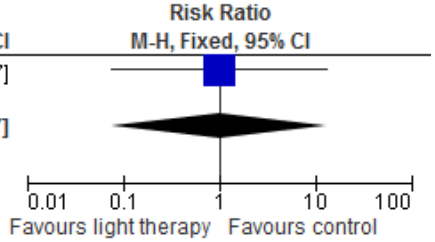


Figure 45 – Light therapy versus control – proportion of patients worsened

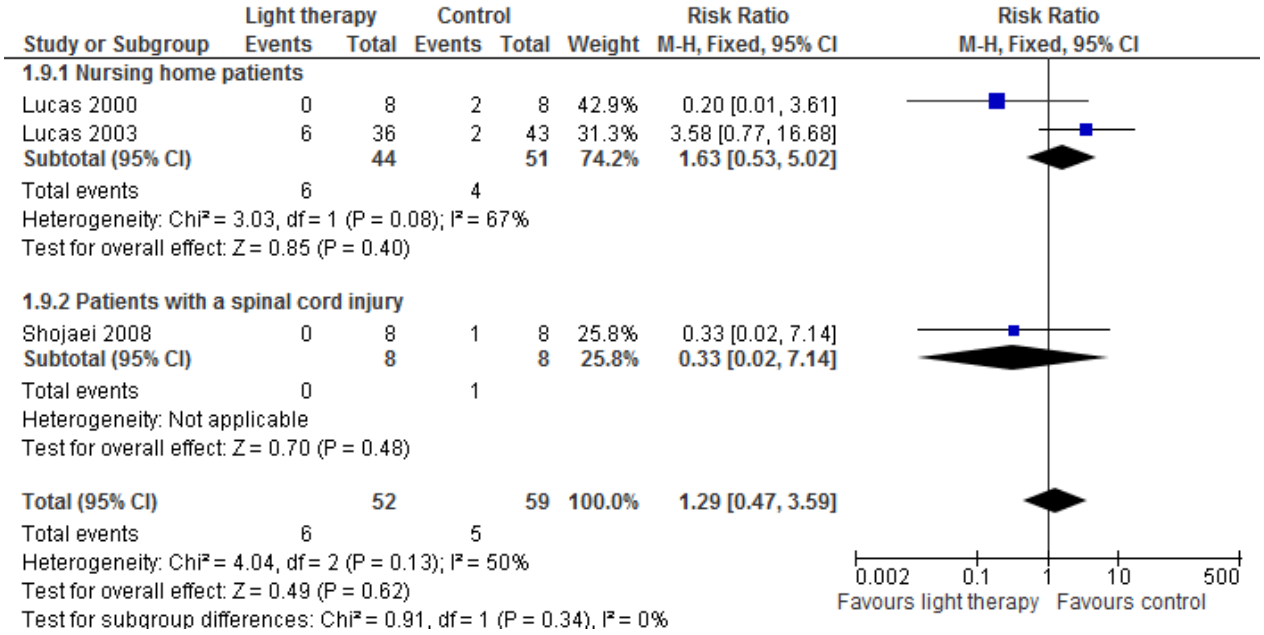


Figure 46 – Light therapy versus control – proportion of patients worsened (Nursing home patients) – stage III PU – NPUAP classification

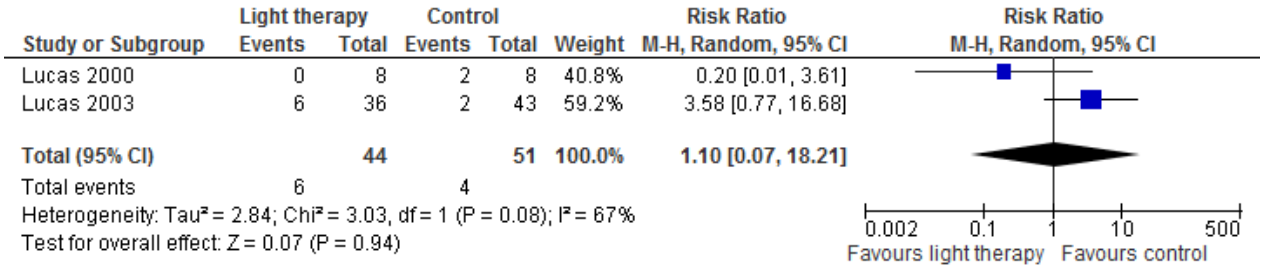


Figure 47 – Light therapy versus control – proportion of patients worsened (spinal cord injury) – stage not reported

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Shojaei 2008	0	8	1	8	100.0%	0.14 [0.00, 6.82]
Total (95% CI)		**8**		**8**	**100.0%**	**0.14 [0.00, 6.82]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.00 (P = 0.32)

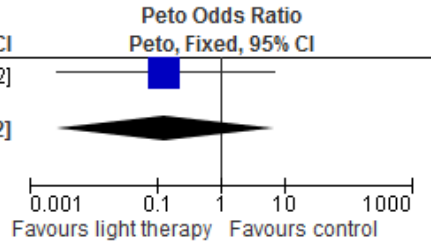


Figure 48 – Light therapy versus control – proportion of ulcers not changed or worsened

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Taly 2004	6	35	3	29	100.0%	1.66 [0.45, 6.05]
Total (95% CI)		**35**		**29**	**100.0%**	**1.66 [0.45, 6.05]**
Total events	6		3			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.76 (P = 0.44)

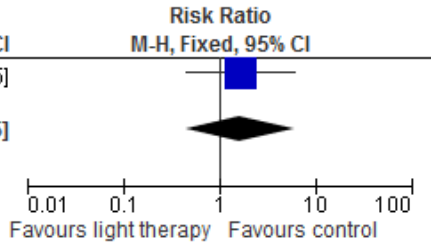


Figure 49 – Light therapy versus control – proportion of patients who developed a stage IV PU

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Lucas 2003	3	37	5	44	100.0%	0.71 [0.18, 2.79]
Total (95% CI)		**37**		**44**	**100.0%**	**0.71 [0.18, 2.79]**
Total events	3		5			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.49 (P = 0.63)

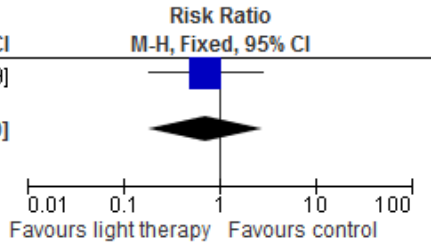


Figure 50 – Light therapy versus control – proportion of stage III and IV ulcers reduced to a stage I

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Taly 2004	1	4	0	5	100.0%	9.49 [0.18, 489.97]
Total (95% CI)		**4**		**5**	**100.0%**	**9.49 [0.18, 489.97]**
Total events	1		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)

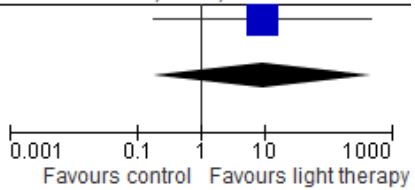


Figure 51 – Light therapy versus control – proportion of stage III and IV ulcers reduced to a stage II after 2 weeks

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Taly 2004	3	4	0	5	100.0%	20.09 [1.45, 278.54]
Total (95% CI)		**4**		**5**	**100.0%**	**20.09 [1.45, 278.54]**
Total events	3		0			

Heterogeneity: Not applicable
Test for overall effect: Z = 2.24 (P = 0.03)

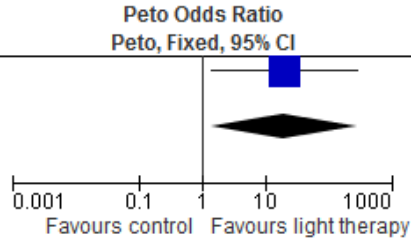


Figure 52 – Light therapy versus control – proportion of stage III and IV ulcers reduced to a stage II after 3 weeks

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Taly 2004	3	4	1	5	100.0%	3.75 [0.59, 23.66]
Total (95% CI)		**4**		**5**	**100.0%**	**3.75 [0.59, 23.66]**
Total events	3		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.41 (P = 0.16)

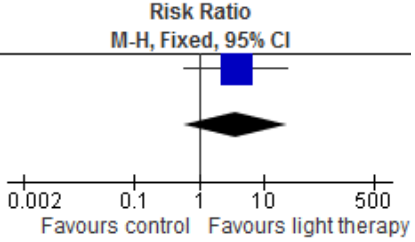


Figure 53 – Light therapy versus control – mean percentage reduction in ulcer area

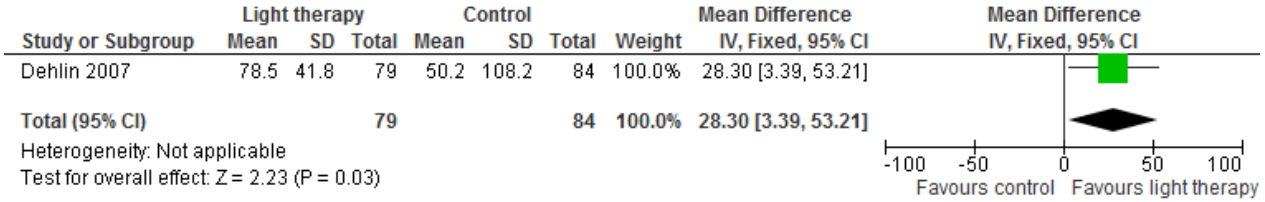


Figure 54 – Light therapy versus control – mean cm² reduction in ulcer area

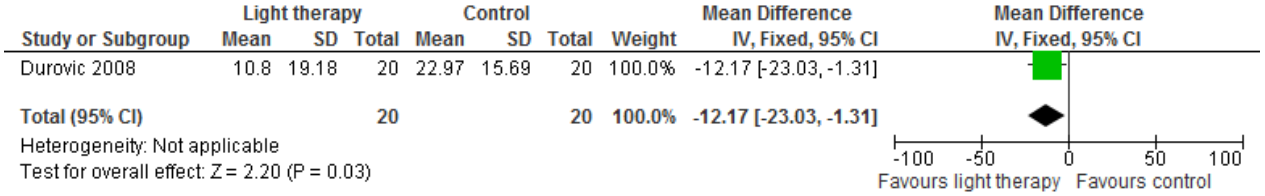


Figure 55 – Light therapy versus control – absolute mm² reduction in ulcer area

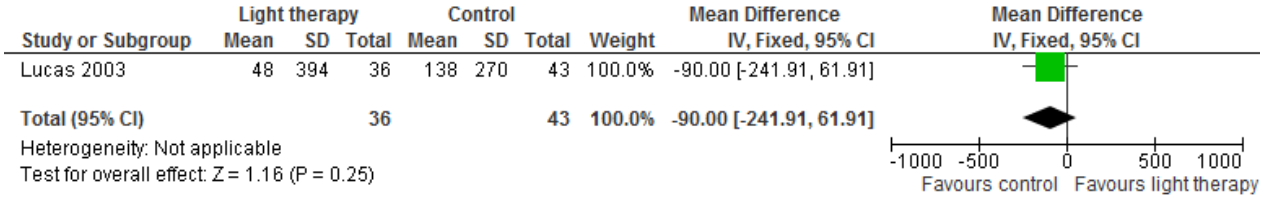


Figure 56 – Light therapy versus control – relative percentage reduction in ulcer area

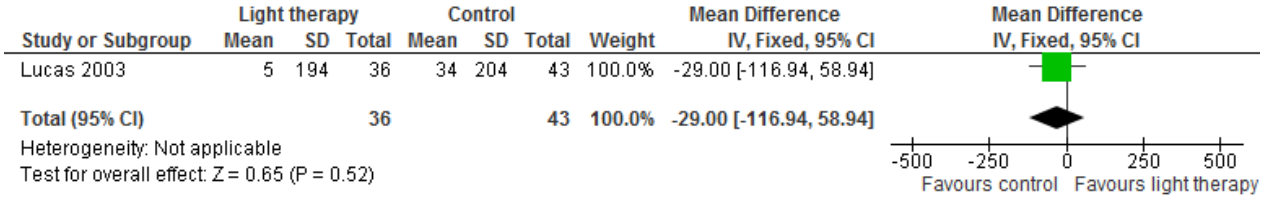


Figure 57 – Light therapy versus control – mean PUSH score at end of treatment

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Durovic 2008	7.35	3.17	20	11.85	2.35	20	100.0%	-4.50 [-6.23, -2.77]
Total (95% CI)			**20**			**20**	**100.0%**	**-4.50 [-6.23, -2.77]**

Heterogeneity: Not applicable
Test for overall effect: Z = 5.10 (P < 0.00001)

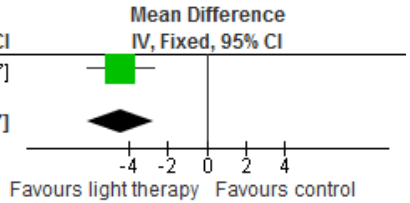


Figure 58 – Light therapy versus control – proportion of ulcers with a lover PSST score

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Taly 2004	11	35	12	29	100.0%	0.76 [0.40, 1.46]
Total (95% CI)		**35**		**29**	**100.0%**	**0.76 [0.40, 1.46]**
Total events	11		12			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.82 (P = 0.41)

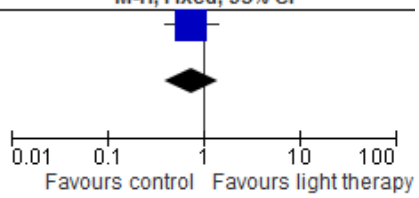


Figure 59 – Light therapy versus control – PSST score at end of study (stage III and IV)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Taly 2004	18.3	2.9	4	24.2	4	5	100.0%	-5.90 [-10.41, -1.39]
Total (95% CI)			**4**			**5**	**100.0%**	**-5.90 [-10.41, -1.39]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.56 (P = 0.01)

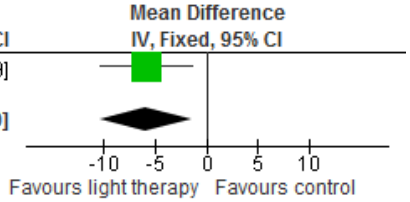


Figure 60 – Light therapy versus control – PSST score at end of treatment (stage III and IV)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Taly 2004	16.8	16.5	4	22.4	3.9	5	100.0%	-5.60 [-22.13, 10.93]
Total (95% CI)			**4**			**5**	**100.0%**	**-5.60 [-22.13, 10.93]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.66 (P = 0.51)

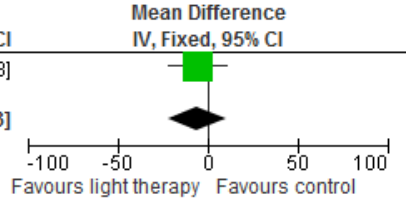


Figure 61 – Light therapy versus control – mean rank of PU at end of treatment

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Durovic 2008	5.95	2.48	20	8.6	1.05	20	100.0%	-2.65 [-3.83, -1.47]
Total (95% CI)			**20**			**20**	**100.0%**	**-2.65 [-3.83, -1.47]**

Heterogeneity: Not applicable
Test for overall effect: Z = 4.40 (P < 0.0001)

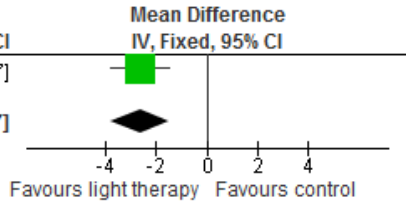


Figure 62 – Light therapy versus control – time to complete healing (weeks)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.39.1 General population								
Wills 1983	6.25	1.56	8	8.38	1.27	8	48.5%	-2.13 [-3.52, -0.74]
Subtotal (95% CI)			**8**			**8**	**48.5%**	**-2.13 [-3.52, -0.74]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.99 (P = 0.003)								
1.39.2 Patients with a spinal cord injury								
Taly 2004	2.45	2.06	35	1.78	2.13	29	51.5%	0.67 [-0.36, 1.70]
Subtotal (95% CI)			**35**			**29**	**51.5%**	**0.67 [-0.36, 1.70]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.27 (P = 0.20)								
Total (95% CI)			**43**			**37**	**100.0%**	**-0.69 [-3.43, 2.05]**

Heterogeneity: Tau² = 3.53; Chi² = 10.01, df = 1 (P = 0.002); I² = 90%
Test for overall effect: Z = 0.49 (P = 0.62)
Test for subgroup differences: Chi² = 10.01, df = 1 (P = 0.002), I² = 90.0%

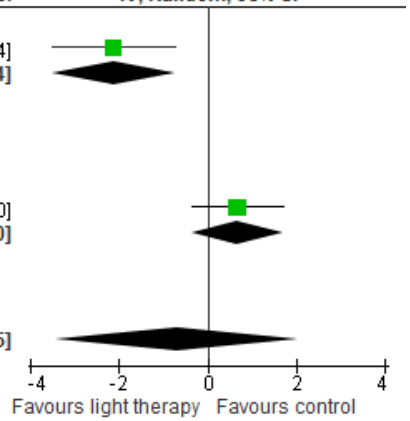


Figure 63 – Light therapy versus control – time to complete healing (weeks) (age and initial area as covariates)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Wills 1983	6.26	1.67	8	8.37	1.41	8	100.0%	-2.11 [-3.62, -0.60]
Total (95% CI)			**8**			**8**	**100.0%**	**-2.11 [-3.62, -0.60]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.73 (P = 0.006)

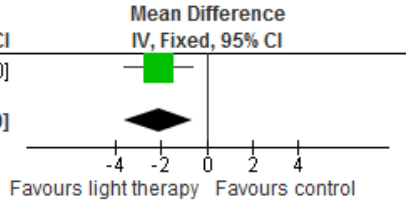


Figure 64 – Light therapy versus control – time to reach stage II (weeks) (stage III and IV)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Taly 2004	2.25	0.5	4	4.33	1.53	5	100.0%	-2.08 [-3.51, -0.65]
Total (95% CI)			**4**			**5**	**100.0%**	**-2.08 [-3.51, -0.65]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.86 (P = 0.004)

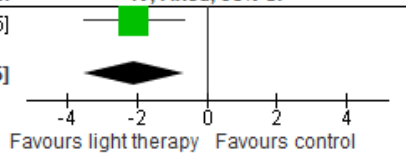


Figure 65 – Light therapy versus control – mean healing rate (%/weeks)

Study or Subgroup	Light therapy Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Nussbaum 1994	23.7	17.05	6	32.41	15.65	6	100.0%	-8.71 [-27.23, 9.81]
Total (95% CI)			**6**			**6**	**100.0%**	**-8.71 [-27.23, 9.81]**

Heterogeneity: Not applicable
Test for overall effect: Z = 0.92 (P = 0.36)

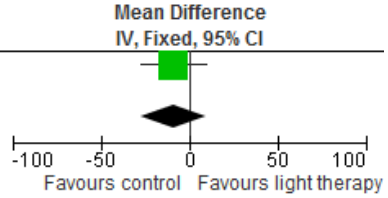


Figure 66 – Light therapy versus control – proportion of patients with hypergranulation

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Peto Odds Ratio Peto, Fixed, 95% CI
Taly 2004	0	35	1	29	100.0%	0.11 [0.00, 5.64]
Total (95% CI)		**35**		**29**	**100.0%**	**0.11 [0.00, 5.64]**
Total events	0		1			

Heterogeneity: Not applicable
Test for overall effect: Z = 1.10 (P = 0.27)

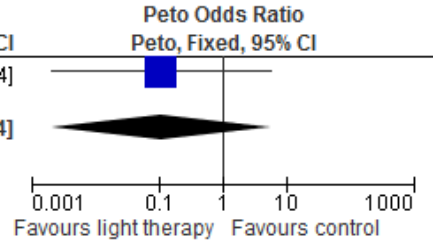


Figure 67 – Light therapy versus control – proportion of patients with adverse events

Study or Subgroup	Light therapy Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Dehlin 2007	9	79	9	84	100.0%	1.06 [0.44, 2.54]
Lucas 2000	0	8	0	8		Not estimable
Lucas 2003	0	37	0	44		Not estimable
Total (95% CI)		**124**		**136**	**100.0%**	**1.06 [0.44, 2.54]**
Total events	9		9			

Heterogeneity: Not applicable
Test for overall effect: Z = 0.14 (P = 0.89)

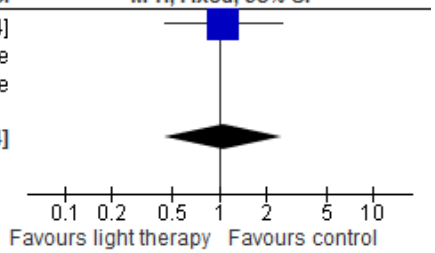


Figure 68 – Laser therapy versus ultrasound/ultraviolet-C – mean healing rate (weeks)

Study or Subgroup	Laser therapy Mean	SD	Total	US/UV-C Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Nussbaum 1994	23.7	17.05	6	51.8	22.91	6	100.0%	-28.10 [-50.95, -5.25]
Total (95% CI)			**6**			**6**	**100.0%**	**-28.10 [-50.95, -5.25]**

Heterogeneity: Not applicable
Test for overall effect: Z = 2.41 (P = 0.02)

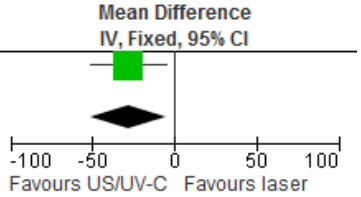
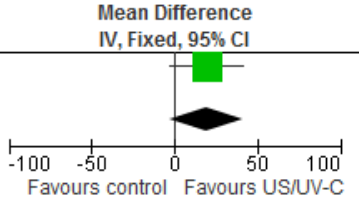


Figure 69 – Ultrasound/ultraviolet-C versus standard care – mean healing rate (weeks)

Study or Subgroup	US/UV-C Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Nussbaum 1994	51.8	22.91	6	32.41	15.65	6	100.0%	19.39 [-2.81, 41.59]
Total (95% CI)			**6**			**6**	**100.0%**	**19.39 [-2.81, 41.59]**

Heterogeneity: Not applicable
Test for overall effect: Z = 1.71 (P = 0.09)



11.3.4. Evidence tables

Table 74 – Dehlin 2003

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Dehlin 2003 **Title:** Monochromatic phototherapy in elderly patients: A new way of treating chronic pressure ulcers? **Journal:** Aging - Clinical and Experimental Research, 15 (3), 259-63 **Study type:** randomized controlled trial **Sequence generation:** not reported **Allocation concealment:** not reported **Blinding:** double blinded, outcome-assessor was blinded, no further information **Addressing incomplete outcome data:** drop-outs were excluded **Statistical analysis:** Time until healing,	**Patient group:** Geriatric in- and out-patients with grade II or III pressure ulcer (according to Sterling or Shea classification) **All patients** **Randomised N:** 198 patients **Completed N:** 164 patients **Drop-outs:** 34 patients (18 in G1 and 22 in G2; protocol violation, wish to withdraw, experience of adverse events; numbers not reported) **Group 1** **Randomised N:** 96 patients **Completed N:** 78 patients **Dropouts:** 18 patients (reason per group not reported) **Baseline characteristics of completed N** **Age (mean years (SD); range):** 83 (6.6); 65-97	**Group 1:** Monochromatic phototherapy: 5 days during week 1; 2 days during weeks 2, 4, 6, 8, and 10; and 3 days during weeks 3, 5, 7, 9, and 11. Treatment duration was 9 min for the first week and 6 min for all remaining weeks. The probe contained 30 diodes emitting infrared light at 965 nm and 80 diodes emitting red light at 637 nm. Infrared light with an irradiance of 55 W/m² was first given, and then red light with an irradiance of 21 W/m². Using a duty cycle of 80% infrared and red light were pulsed at following frequency: infrared light – 287Hz, 31.2Hz, 9900Hz, 8Hz, 15.6Hz ,and 780Hz; red light – 8Hz, 31.2Hz, 9900Hz, 5Hz and 8.6Hz. **Group 2:** placebo with identical appearance and emitting red light. **Both groups:** conventional treatment: protection of ulcer area, a regular turning schedule, emollient or	**Outcome 1:** Proportion of ulcers completely healed at week 12 **Outcome 2:** Proportion of ulcers healed > 90% at week 12 **Outcome 3:** Time to complete healing. **Outcome 4:** Time of reduction in ulcer area (all ulcers) **Outcome 5:** Reduction in ulcer area (all ulcers) at week 12 **Outcome 6:** Relative percentage reduction in ulcer area in grade II ulcers at week 13 **Outcome 7:**	**Group 1:** 34/78 **Group 2:** 34/86 **P value:** 0.93 **Group 1:** 44/78 **Group 2:** 42/86 **P value:** 0.77 **Group 1:** not reported **Group 2:** not reported **P value:** 0.93 **Group 1:** not reported **Group 2:** not reported **P value:** < 0.0001 **Group 1:** not reported **Group 2:** not reported **P value:** 0.18 **Group 1:** 81.2 **Group 2:** 45.6 **P value:** 0.06 141 adverse events were	**Funding:** supported by Biolight International AB **Limitations:** no details on sequence generation and allocation concealment; insufficient information on blinding; no ITT analysis; reporting of results incomplete (time of healing, reduction in size of all ulcers); classification system unclear as both Shea and Sterlin classification are reported; randomization reported as carried out at weekly visit, unclear what is meant by this; no

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
almost complete healing, or partial healing was calculated applying survival analysis. Cumulative survival of pressure ulcers was calculated with the Kaplan-Meier technique. The hypothesis of no difference between groups was tested with the log-rank test. Primary efficacy variables were also tested using a Cox proportional regression model with baseline pressure ulcer size as a covariate. The normalized pressure ulcer area at each visit was analysed with ANOVA for repeated measures. The t-test and Fisher's exact test were also used, and a p-value of less than 0.05 was considered statistically significant. **Baseline differences:** no difference except for systolic blood pressure (p=0.07) **Study power/sample**	**Gender (m/f):** 24/54 **Ulcer age (mean days (SD; range)):** 49 (42; 14-173) **Ulcer location:** foot (n=43); trunk (n=35) **Ulcer grade:** Grade II (n=44); Grade III (n=34) **Group 2** **Randomised N:** 108 patients **Completed N:** 86 patients **Dropouts:** 22 patients (reason per group not reported) **Baseline characteristics of completed N** **Age (mean years (SD); range):** 85 (7.5); 65-105 **Gender (m/f):** 9/53 **Ulcer age (mean days (SD; range)):** 57 (40; 14-171) **Ulcer location:** Foot: n=47 Trunk: n=53 **Ulcer grade:** Grade II: n=43 Grade III: n=43 **Inclusion criteria:** Grade II or III (Shea	moisturizing cream around the ulcer, a pressure reducing mattress, and pressure reducing cushion for wheelchair bounded patients. Hydrocellular/hydrocolloid bandages were applied to clean ulcers. Chemical or enzymatic debridement was not allowed.	Adverse events	reported: tingling in and around the wound during treatment (n=1), pain in wound during treatment (n=2), bleeding in wound (n=1), and redness (n=1). Others were considered not related to treatment.	debridement prior to treatment **Additional outcomes:** Reduction in ulcer size according to BMI (stratified analysis for BMI < 20): Group 1 (n=41): 3.3%; Group 2 (n=42): 1.5%; p<0.01) **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
size: Sample size calculation was based on a variation of the expected ulcer survival time of 0.4 to 0.6, a power of 90% and a p-value < 5%. The estimate sample size was 200 patients. **Setting:** Eight geriatric centres in Sweden and Denmark. Inpatients and outpatients. **Length of study:** 11 weeks of treatment and two weeks of follow up. **Assessment of PUs:** Pressure ulcers were classified according to Sterlin scale or Shea score? The ulcer area was measured twice during week 1 and once weekly for the remaining 11 weeks, or until the ulcer was healed. The ulcer area was measured using a plastic film, marked with a grid with 0.25cm² divisions, placed in the ulcer.	score) pressure ulcer; ulcer location on trunk or foot; ulcer age 2 weeks to 6 months; initial area 1 to 20cm²; age > 65 years. **Exclusion criteria:** unstable diabetes mellitus (HbA1C > 10%); serious or terminal malignancy or terminal illness; treatment with radiotherapy or cytotoxines; suspected or proven osteomyelitis; antibiotic treatment of ulcer within 2 weeks; use of corticosteroids (> 10 mg/day of prednisone); significant abnormal blood test the month before inclusion: pacemaker: photosensitivity or sensitive to electromagnetic radiation: life expectancy < 3 months: participant in any other clinical study during the last month.				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Ulcers were determined by an independent individual using a planimeter. **Multiple ulcers:** not reported					

Table 75 - Dehlin 2007

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Dehlin 2007 **Title:** Monochromatic phototherapy: effective treatment for grade II chronic pressure ulcers in elderly patients . **Journal:** Aging - Clinical and Experimental Research, 19 (6), 478-83 **Study type:** randomized controlled trial **Sequence generation:** a computer generated list was used **Allocation concealment:** patients were randomized in	**Patient group:** Geriatric in- and out-patients with grade II pressure ulcer (according to Shea classification) **All patients** **Randomised N:** 94 patients (in the present study) **Completed N:** 163 patients **Drop-outs:** 18 in the present study (11 died, 2 withdrew consent, 1 developed gangrene, 1 ulcer size to small, 3 unable to perform treatment) **Group 1** **Randomised N:** not reported **Completed N:** 79	**Group 1:** Monochromatic phototherapy: 5 days during week 1; 2 days during weeks 2, 4, 6, 8, and 10; and 3 days during weeks 3, 5, 7, 9, and 11. Treatment duration was 9 min for the first week and 6 min for all remaining weeks. The probe contained 30 diodes emitting infrared light at 965 nm and 80 diodes emitting red light at 637 nm. Infrared light with an irradiance of 55 W/m² was first given, and then red light with an irradiance of 21 W/m². Using a duty cycle of 80% infrared and red light were pulsed at following frequency: infrared light – 287Hz, 31.2Hz, 9900Hz, 8Hz, 15.6Hz ,and 780Hz; red light – 8Hz, 31.2Hz, 9900Hz, 5Hz and 8.6Hz.	**Outcome 1:** Proportion of ulcers completely healed at week 12 **Outcome 2:** Time to complete healing. **Outcome 3:** Rate of reduction in ulcer area **Outcome 4:** Mean (SD) normalized percentage reduction in ulcer area at week 12 **Outcome 5:** Median normalized percentage	**Group 1:** 43/79 **Group 2:** 50/84 **P value:** 0.52 **Group 1:** not reported **Group 2:** not reported **P value:** 0.58 **Group 1:** not reported **Group 2:** not reported **P value:** 0.12 **Group 1:** 78.5 (41.8) **Group 2:** 50.2 (108.2) **P value:** 0.039 **Group 1:** 100 **Group 2:** 100	**Funding:** supported by Biolight International AB **Limitations:** insufficient information on allocation concealment; insufficient information on blinding; no ITT analysis; randomization reported as carried out at weekly visit, unclear what is meant by this; no debridement prior to treatment. **Additional**

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
blocks of appropriate and variables size **Blinding:** double blinded, outcome-assessor was blinded, no further information **Addressing incomplete outcome data:** drop-outs were excluded **Statistical analysis:** The primary efficacy variabke normalized reduction in pressure ulcer size was calculated as the percentage change in ulcer size form baseline to week 12. Analysis of variance was used, which allowed for variations due to treatment and centre and also included the baseline measures. Secondary efficacy variables were percentage of totally healed ulcers, time to totally healed, normalized weekly reduction in pressure ulcer size over time, and the rate of normalized reduction	patients (pooled with earlier study Dehlin 2003) **Dropouts:** not reported **Baseline characteristics of completed and pooled N** **Age (mean years (SD); range):** 84 (7.5); 68-101 **Gender (m/f):** 28/51 **Ulcer age (mean days (SD); range)):** 55 (37); 14-167 **Ulcer location:** Foot: n=32 Trunk: n=47 **Ulcer size (mean (SD); median)):** 4.1 (3.2); 3.0 **Group 2** **Randomised N:** not reported **Completed N:** 84 patients (pooled with earlier study Dehlin 2003) **Dropouts:** not reported **Baseline characteristics of completed and pooled N** **Age (mean years (SD); range):** 84 (7.7); 65-105 **Gender (m/f):** 34/50	**Group 2:** placebo with identical appearance and emitting red light. **Both groups:** conventional treatment: protection of ulcer area, a regular turning schedule, emollient or moisturizing cream around the ulcer, a pressure reducing mattress, and pressure reducing cushion for wheelchair bounded patients. Hydrocellular/hydrocolloid bandages were applied to clean ulcers. Chemical or enzymatic debridement was not allowed.	reduction in ulcer area at week 12 **Outcome 6:** Percentage reduction in ulcer area over time (%/week) **Outcome 7:** Proportion of patient with treatment related adverse events	**Group 1:** 15.1 **Group 2:** 10.9 **Group 1:** 9/79 (tingling in and around ulcer or wound pain) **Group 2:** 9/84 (skin reaction)	**outcomes:** / **Notes:** Data were pooled with results from Dehlin 2003 study (patients with grade II)

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
in pressure ulcer size. These were analysed using the chi-square test and ANOVA and – for survival of ulcers – the Kaplan-Meier technique and the log-rank test. Comparisons between patients' variables were made with the t-test with the Welch correction. All tests were two-sided and a p-value of less than 0.05 was considered as statistically significant. All analyses were performed with SAS version 6.12 for Windows. **Baseline differences:** No significant difference between groups, although there was a tendency toward lower diastolic blood pressure in G1 (p=0.08). **Study power/sample size:** Sample size calculation was based on a variation of the expected ulcer survival	**Ulcer age (mean days (SD); range)):** 59 (41); 15-183 **Ulcer location:** Foot: n=39 Trunk: n=45 **Ulcer size (mean (SD); median)):** 4.7 (4.0); 3.3 **Inclusion criteria:** Grade II (Shea score) pressure ulcer; ulcer location on trunk or foot; ulcer age 2 weeks to 6 months; initial area 1 to 20cm²; age ≥ 65 years. **Exclusion criteria:** unstable diabetes mellitus (HbA1C > 10%); serious or terminal malignancy or terminal illness; treatment with radiotherapy or cytotoxines; suspected or proven osteomyelitis; antibiotic treatment of ulcer within 2 weeks; use of corticosteroids (> 10 mg/day of prednisone); significant abnormal blood test the month before inclusion: pacemaker: photosensitivity or				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
time of 0.4 to 0.6, a power of 90% and a p-value < 5%. The estimate sample size was 160 patients. **Setting:** Eight geriatric centres in Sweden and Denmark. Inpatients and outpatients. **Length of study:** 11 weeks of treatment and two weeks of follow up. **Assessment of PUs:** Pressure ulcers were classified according to Shea classification The ulcer area was measured twice during week 1 and once weekly for the remaining 11 weeks, or until the ulcer was healed. The ulcer area was measured using a plastic film, marked with a grid with 0.25cm² divisions, placed in the ulcer. Ulcers were determined by an independent individual using a planimeter. Photos of each ulcer	sensitive to electromagnetic radiation: life expectancy < 3 months: participant in any other clinical study during the last month.				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
were taken at day 1, week6 and after 12 weeks. **Multiple ulcers:** not reported					

Table 76 – Durovic 2008

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Durovic 2008 **Title:** The effects of polarized light therapy in pressure ulcer healing **Journal:** Vojnosanitetski Pregled, 65 (12), 906-12 **Study type:** randomized controlled trial **Sequence generation:** not reported **Allocation concealment:** not reported **Blinding:** single-blinded (observer) **Addressing incomplete outcome data:** not reported	**Patient group:** patients with a pressure ulcer (according to the Pressure Ulcer Classification System. **All patients** **Randomised N:** 44 patients **Completed N:** 40 patients **Drop-outs:** 4 patients (one deterioration of consciousness after stroke; one because of anticoagulants drug administration; two died) **Group 1** **Randomised N:** 22 patients **Completed N:** 20 patients **Dropouts:** 2 patients (one deterioration of	**Group 1:** Polarized light with following characteristics: wavelength: 400–2000 nm; degree of polarization: > 95%; power density: 40 mW/cm²; light energy: 2,4 J/cm². Polarized light therapy was performed for six min daily, at a distance of 10 cm, five times a week. **Group 2:** Standard wound cleansing and dressing (no additional treatment) **Both groups:** All wounds were cleaned using 2% hydrogen peroxide. The standard dressing implied application of a gauze with normal saline (NaCl), then a dry gauze, next it a cotton wool and adhesive strip	**Outcome 1:** Mean cm² ulcer area at end of treatment **Outcome 2:** Mean percentage reduction in ulcer area **Outcome 3:** Mean rank of PU at end of treatment **Outcome 4:** Mean percentage reduction in rank of PU **Outcome 5:** Mean PUSH score at end of treatment	**Group 1:** 10.80 (19.18) **Group 2:** 22.97 (15.69) **P value:** 0.0005 **Group 1:** 28.5 **Group 2:** -20.0 **Group 1:** 5.95 (2.48) **Group 2:** 8.6 (1.05) **P value:** 0.0005 **Group 1:** 19.6 **Group 2:** -4.9 **Group 1:** 7.35 (3.17) **Group 2:** 11.85 (2.35) **P value:** 0.00003	**Funding:** / **Limitations:** no details on sequence generation and allocation concealment; single-blinded; addressing of incomplete outcomes data not reported; type of classification system unclear; not clear what is meant with rank of PU and how this was measured; no debridement prior to treatment. **Additional outcomes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Statistical analysis: Following tests were used: Kolmogorov-Smirnov test, Shapiro-Wilk test, Mann Whitney Exact test, Exact Wilcoxon signed rank test and Fischers Exact test. Statistical significance was set up $p < 0.05$. **Baseline differences:** Significant difference between Group 1 and Group 2 for age (p=0.06) **Study power/sample size:** No a priori sample size calculation **Setting:** unclear **Length of study:** four weeks of treatment. **Assessment of PUs:** Pressure ulcers were classified according to the Pressure Ulcer Classification System, not specified which one. The Pressure Ulcer Scale for Healing (PUSH) was used. All wounds were described through the	consciousness after stroke; one because of anticoagulants drug administration) **Baseline characteristics of completed N** **Age (mean years (SD)):** 61.85 (16.11) **Gender (m/f):** 11/9 **Ulcer surface (mean cm² (SD)):** 15.10 (17.61) **Rank of PU (mean (SD)):** 7.40 (1.96) **Total PUSH score (mean (SD)):** 10.65 (2.25) **Ulcer location:** Back (n=1), buttocks (n=2), sacral area (n=11), hip (n=3), heel (n=3) **Group 2** **Randomised N:** 22 patients **Completed N:** 20 patients **Dropouts:** 2 patients (two patients died) **Baseline characteristics of completed N** **Age (mean years (SD)):** 68.65 (19.87)		**Outcome 6:** Mean percentage reduction in PUSH score	**Group 1:** 31.0 **Group 2:** -13.4	**Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
surface area measurement, exudates amount and surface appearance. Wound healing process was evaluated in a standard manner (centimeter ruler and some kind of callipers) by two independent blinded observers. **Multiple ulcers:** not reported	**Gender (m/f):** 11/9 **Ulcer surface (mean cm² (SD)):** 19.15 (22.73) **Rank of PU (mean (SD)):** 8.20 (1.51) **Total PUSH score (mean (SD)):** 10.45 (2.74) **Ulcer location:** Back (n=1), buttocks (n=3), sacral area (n=5), spine (n=1), hip (n=4), heel (n=6) **Inclusion criteria:** patients with stage I-III ulcer; absence of relative contraindications for using of polarized light; absence of deterioration of common disease or attack of new disease; informed consent. **Exclusion criteria:** previously in study to treat their current pressure ulcer; skin grafting planned within one week; poor nutrition (albumin level < 3.0g/dL); presence of local or general infection, particularly the				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
	sacral (pylonidal) sinus or the sacral osteomyelitis; intake of drugs that can affect the skin and delay in healing, specially steroids, immunosuppressive agents, antineoplastic drugs and anticoagulants.				

Table 77 – Lucas 2000

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Lucas 2000 **Title:** The Effect of Low Level Laser Therapy (LLLT) on Stage III Decubitus Ulcers (Pressure Sores); a Prospective Randomised Single Blind, Multicentre Pilot Study **Journal:** Lasers in Medical Science, 14, 94-100 **Study type:** randomized controlled trial **Sequence**	**Patient group:** nursing home patients with a stage III pressure ulcer. **All patients** **Randomised N:** 16 patients **Completed N:** 16 patients **Drop-outs:** 0 patients **Group 1** **Randomised N:** 8 patients **Completed N:** 8 patients **Dropouts:** 0 patients **Age (median years (range)):** 87.5 (73-92)	**Group 1:** Low level laser therapy (LLLT) with a microprocessor controlled, multiple monochromatic optical source probe. The handheld probe with 12x70 W monochromatic infrared GaAs-diodes (gallium arsenide) operated at a wavelength of 904 nm in a 830 Hz pulse frequency mode with an average beam power of 8 mW and a radiant exposure of 1 J/cm² covered an area of 30 cm². To obtain an energy density of 1 J/cm2 an exposure time of 2 min and 5 s (125 s) was needed. **Group 2:** Consensus	**Outcome 1:** Median percentage reduction in ulcer area at six weeks **Outcome 2:** Proportion of patients with an increase in ulcer area **Outcome 3:** Adverse events	**Group 1:** 83 **Group 2:** 95 **Group 1:** 0/8 **Group 2:** 2/8 **Group 1:** 0/8 **Group 2:** 0/8	**12. Funding:** granted by Stichting fondsenverwering sacties Volksgezondheid. **Limitations:** no details on sequence generation and allocation concealment; single-blinded; addressing of incomplete outcomes data not reported; no reporting on

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
generation: not reported **Allocation concealment:** not reported **Blinding:** single-blinded (observer) **Addressing incomplete outcome data:** not reported **Statistical analysis:** Baseline characteristics and outcome data were analysed with non-parametric descriptive statistics. Six weeks after intervention the differences in wound sizes between the two treatments were compared, using the Mann Whitney U Test. With respect to differences within both treatment groups we performed the Friedman two-way analysis. We also calculated the wound size reduction in terms of percentage compared to baseline. **Baseline differences:** Group 1 slightly larger	**Gender (m/f):** 2/6 **Ulcer duration (median weeks (range)):** 4 (1-9) **Ulcer location:** gluteal (n=1); sacrum/coccyx (n=2); calcaneus (n=2); lateral malleolus (n=2) **Initial wound size (mm² (range)):** 94 (9-513) **Group 2** **Randomised N:** 8 patients **Completed N:** 8 patients **Dropouts:** 0 patients **Age (median years (range)):** 88 (72-95) **Gender (m/f):** 0/8 **Ulcer duration (median weeks (range)):** 3 (1-10) **Ulcer location:** gluteal (n=3); sacrum/coccyx (n=2); calcaneus (n=2); lateral malleolus (n=1) **Initial wound size (mm² (range)):** 82.5 (30-527) **Inclusion criteria:** Stage III pressure ulcer. **Exclusion criteria:** patients with a wound	decubitus treatment (no additional treatment) **Both groups:** consensus decubitus treatment: information and instruction of the patient, wound cleansing, simple moist dressings, and frequent alteration of the patient's position. Treatments were given over a period of 6 weeks (maximum), five times a week (except for the weekends).			complete healing (one of the primary outcomes); no debridement prior to treatment **Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
initial median wound size and longer decubitus duration. No statistical calculation of difference. **Study power/sample size:** No a priori sample size calculation **Setting:** Four nursing homes. **Length of study:** until complete healing with a maximum of six weeks. **Assessment of PUs:** Decubitus ulcer stage III was defined as a full-thickness skin defect extending into the subcutaneous layers and adipose tissue. Once a week the wound appearance (e.g. colour, presence or absence of necrotic tissue, eschar, and inflammation) was documented. Wound surface area was registered in mm² based on a 1:1 Polaroid Image Exposure® (deviation	surface area > 30cm²; wounds completely occluded by eschar; constant, invariable ulceration for > 1 year; diabetic patients with serious metabolic disorders; terminal patients.				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
≤1%). This instant colour photograph was taken every week to provide a permanent time series record. In addition, an independent and trained evaluator outlined the area of these measurements on a transparent wound diagram consisting of a mm² scaled grid. The perimeter of the vital borderline of the ulceration was transposed to the transparency and the enclosed area (mm²) was determined by an investigator. **Multiple ulcers:** not reported					

Table 78 – Lucas 2003

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Lucas 2003 **Title:** Efficacy of low-level laser therapy in the management of stage III decubitus ulcers: a prospective, observer-blinded multicenter randomised clinical trial **Journal:** Lasers in Medical Science, 18, 72-7 **Study type:** randomized controlled trial **Sequence generation:** Allocation was by means of a central computerized telephone service. A minimization procedure, concentrating on minimizing imbalances in the distribution of treatment numbers within the various values of each individual possible prognostic factor, was performed.	**Patient group:** nursing home patients with a stage III pressure ulcer. **All patients** **Randomised N:** 86 patients **Completed N:** 79 patients **Drop-outs:** 7 patients (four patients died, one was admitted to the hospital, and two developed a stage IV PU after baseline measurement). **Group 1** **Randomised N:** 39 patients **Completed N:** 36 patients **Dropouts:** 3 patients (two patients died, one developed a stage IV PU after baseline measurement) **Age (mean years (SD); median years; range):** 81.3 (9.6); 82; 49-94 **Gender (m/f):** 14/25 **Ulcer duration (mean weeks (SD); median years; range):** 2.9 (4);	**Group 1:** LLLT treatments were administered using a 12 microprocessor-controlled infrared GaAs-diode laser probe (gallium arsenide) at 904 nm, covering an irradiated area of 12 cm² (physical probe dimension 30 cm²). Total peak power was 12x70 W in a 830 Hz pulse frequency mode of 150 ns pulses with an average beam power of 12x8 mW and a radiant exposure of 1 J/cm², which required an exposure time of 125 s. The laser probe was applied to the surrounding normal tissue surface as a so-called contact treatment method. Five times a week for six weeks. **Group 2:** Consensus decubitus treatment (no additional treatment) **Both groups:** consensus decubitus treatment as developed and recommended by the NPUAP: information and instruction of the patient, wound cleansing, simple	**Outcome 1:** Proportion of patients completely healed **Outcome 2:** Proportion of patients worsened **Outcome 3:** Absolute mm² reduction in ulcer area **Outcome 4:** Relative percentage reduction in ulcer area **Outcome 5:** Proportion of patients who development a stage IV PU **Outcome 6:** Adverse events	**Group 1:** 18/36 **Group 2:** 15/43 **Group 1:** 6/36 **Group 2:** 2/43 **Group 1:** 48 (394) **Group 2:** 138 (270) **P value:** 0.23 **Group 1:** 5 (194) **Group 2:** 34 (204) **P value:** 0.42 **Group 1:** 3/37 **Group 2:** 5/44 **P value:** 0.72 **Group 1:** 0/37 **Group 2:** 0/44	**Funding:** / **Limitations:** no details on allocation concealment; single-blinded; analysis reported as intention-to-treat but this is not clear in the result section (report of results of completed patients instead of randomised patients); no debridement prior to treatment. **Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Allocation concealment: not reported **Blinding:** single-blinded (observer) **Addressing incomplete outcome data:** All data was analyzed on an intention-to-treat basis, including all randomized patients with at least one outcome measurement by the last-observation-carried-forward. **Statistical analysis:** Patients' baseline characteristics were summarized with descriptive statistics. Wound size improvement after treatment was expressed in absolute (mm2) and in relative terms (%). The differences between absolute and relative wound size improvements were analysed using the Mann–Whitney U test.	2; 0.5-22; 3 missing **Ulcer location:** gluteal (n=4); sacrum/coccyx (n=14); calcaneus (n=13); lateral malleolus (n=3); medial femoral condyle (n=1); other (n=4) **Wound surface area (mean mm² (SD); median; range):** 317 (396); 155; 8-1821 **Group 2** **Randomised N:** 47 patients **Completed N:** 43 patients **Dropouts:** 4 patients (two patients died, one was admitted to the hospital, and one developed a stage IV PU after baseline measurement). **Age (mean years (SD); median years; range):** 81.5 (8.9); 85; 49-100 **Gender (m/f):** 18/29 **Ulcer duration (mean weeks (SD); median years; range):** 3.3 (5.1); 2; 0.5-30; 3 missing **Ulcer location:** gluteal	moist dressings, and frequent alteration of the patient's position. Treatments were given over a period of 6 weeks (maximum).			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Because the wound sizes were considerably non-normally distributed, we also analysed the primary outcome data after logarithmic transformation of the wound size areas. The difference in mean delta loge scores (= loge baseline scores) loge follow-up scores) between groups was compared using the unpaired t-test. The difference in presence of stage IV decubitus ulcers (secondary outcome) was analyzed using Fisher's exact test. **Baseline differences:** No statistical calculation of difference. **Study power/sample size:** Sample size estimation of 40 patients per group. **Setting:** Four nursing homes in the Netherlands **Length of study:** six weeks of treatment.	(n=8); sacrum/coccyx (n=14); greater trochanter (n=1); calcaneus (n=14); lateral malleolus (n=5); other (n=4) **Wound surface area (mean mm² (SD); median; range):** 350 (378); 232; 40-1750 **Inclusion criteria:** Stage III pressure ulcer; one wound per patient. **Exclusion criteria:** patients with a wound surface area > 30cm²; wounds completely occluded by eschar; constant, invariable ulceration for > 1 year; diabetic patients with serious metabolic disorders; terminal patients.				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Assessment of PUs: Decubitus ulcer stage III was defined as a full-thickness skin defect extending into the subcutaneous layers and adipose tissue. A stage IV decubitus ulcer is defined as a full-thickness skin loss with extensive destruction, tissue necrosis and damage to muscle, bone or supporting structures (tendon, joint capsule etc.). Every 2 weeks the wound surface area was registered in mm2 based on a full scale (1:1) Polaroid Image Exposure (deviation ≤ 1%). An independent and trained evaluator outlined the area of these measurements on a transparent wound diagram consisting of a mm² grid. The perimeter of the vital borderline of the ulceration was					

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
transposed to the transparency and the enclosed area (mm²) was determined by another investigator, blinded to the clinical details. **Multiple ulcers:** not reported					

Table 79 – Nussbaum 1994

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Nussbaum 1994 **Title:** Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury **Journal:** Physical Therapy, 74 (9), 812-23. **Study type:** randomized controlled trial **Sequence generation:** not reported **Allocation concealment:** not reported	**Patient group:** patients with a spinal cord injury and pressure ulcers. **All patients** **Randomised N:** 20 patients and 22 ulcers **Completed N:** 16 patients and 18 ulcers **Drop-outs:** 2 patients (transfer to acute care hospital with medical complications) **Comment:** 1 wound (surgical incision) in G2 was not a pressure ulcer and was therefore removed from the analysis **Group 1**	**Group 1:** Laser treatments were administered using a 800 cluster probe. The unit consists of an 820nm laser diode (beam spot diameter of 4mm, average power of 15mW) and 30 superluminous diodes (10 each at 660, 880 and 950 nm). The unit's power density is 120 mW/cm². Pulse repetition rate was set at 5000 pulses per second (pps) (pulse duration of 160 nanosec.) Energy density was 4J/cm² (treatment time of 35 seconds). The treatment was applied three times weekly. **Group 2:** Ultrasound (US) treatment and ultraviolet-C	**Outcome 1:** Mean weekly healing rate	**Group 1:** 23.70 (17.05) **Group 2:** 51.8 (22.91) **Group 3:** 32.41 (15.65)	**Funding:** funded by the John Labatt Seed Fund Award **Limitations:** no details on sequence generation and allocation concealment; no blinding of patients and health care professionals; no ITT analysis; no a priory sample size calculation; no classification system reported; no debridement

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Blinding: blinding of outcome assessor and statistician. **Addressing incomplete outcome data:** Drop-outs were excluded **Statistical analysis:** Initial ulcer areas were subjected to tests of normality. Because distribution was normal, parametric tests were used for comparisons. Groups were used compared for difference in initial mean ulcer size and mean weekly healing rates using a one-way analysis of variance. A student-Newman-Keuls test was used for comparing differences in healing rates between pairs of groups. The level of significance was set at 0.05 for all statistical tests. **Baseline differences:** No statistical difference between groups in initial mean ulcer size was not	**Randomised N:** 6 patients and 7 ulcers **Completed N:** 5 patients an 6 ulcers **Dropouts:** 1 patients an 1 ulcer (transfer to acute care hospital with medical complications) **Age (mean years; range):** 42; 30-61 **Gender (m/f):** 5/1 **Ulcer duration:** > 6 weeks: n=6 < 1 week: n=0 **Ulcer location:** Ankle: n=1 Trochanter: n=1 Calf: n=1 Chest: n=1 Coccyx: n=1 Thigh: n=1 **Ulcer area (mean cm²; range):** 2.8; 0.9-5.4 **Ulcer depth:** 1-5 mm: n=4 6-10 mm: n=2 **Ulcer aetiology:** Unrelieved pressure: n=4 Cast pressure: n=2 **Group 2** **Randomised N:** 5	(UVC) treatment were alternated daily for 5 days per week. US was applied three times a week, but in case of purulent ulcers, UVC was applied three times weekly. Ultrasound treatment was applied using an Omnisound 3000, which was calibrated by the manufacturer at start of the study. The size of the treatment head was 5cm², and treatment was delivered at a frequency of 3Mhz and at an SATA intensity of 0.2W/cm² (1:4 pulse ratio). US was applied to intact skin surrounding the ulcer using coupling gel for contact for 5 minutes per 5cm² of ulcer area. Ultraviolet-C treatment was applied using a Bitcher cold-quartz lamp (95% emission at 250 nm). A test dose was not performed for each subject. An E1 dose was found to be 15 sec at 2.5cm distance. The dosage was calculated for each session according to the ulcer appearance. **Group 3:** Standard care			prior to treatment **Additional outcomes:** / **Notes:** 1 wound (surgical incision) in G2 was not a pressure ulcer and was therefore removed from the analysis

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
significant. **Study power/sample size:** No a priory sample size calculation. **Setting:** Hospitalized patients at Lyndhurst Spinal Cord Centre **Length of study:** until complete closure. **Assessment of PUs:** Pressure ulcer classification not reported. A baseline tracing of the ulcer perimeter was drawn on a transparency. Maximum depth of the ulcer was recorded by placing a disposable measuring tape directly into the deepest part of the wound. Follow-up measurements were taken on the same day for all subjects and were repeated every 14 days until wound closure. The tracings were analyzed using a digitizer tablet and stylus pen. A computer graphics program was	patients and 6 ulcers **Completed N:** 5 patients an 6 ulcers **Comment:** 1 wound (surgical incision) in G2 was not a pressure ulcer and was therefore removed from the analysis **Dropouts:** 0 **Age (mean years; range):** 42.2; 26-59 **Gender (m/f):** 6/0 **Ulcer duration:** > 6 weeks: n=6 < 1 week: n=0 **Ulcer location:** Heel: n=1 Trochanter: n=1 Ischium: n=1 Coccyx: n=2 Chest: n=1 (removed from analysis; surgical incision) **Ulcer area (mean cm²; range):** 1.9; 0.9-3.1 **Ulcer depth:** 1-5 mm: n=6 6-10 mm: n=0 **Ulcer aetiology:** Unrelieved pressure: n=5 Surgical incision: n=1	**All groups:** Subjects without a pressure ulcer on or around the buttocks were allowed to sit and participate in their regular rehabilitation program. Subjects with a pressure ulcer that would be subjected to pressure in sitting were restricted to prone lying on a wheeled cart, and they participated in a rehabilitation program designed to accommodate their 'grounded' status.			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
used to calculate the area of each ulcer. **Multiple ulcers:** Two subjects had each 2 ulcers. 16 patients and 18 ulcers were analysed.	**Group 3** **Randomised N:** 7 patients and 7 ulcers **Completed N:** 6 patients an 6 ulcers **Dropouts:** 1 patients an 1 ulcer (transfer to acute care hospital with medical complications) **Age (mean years; range):** 36; 15-46 **Gender (m/f):** 5/1 **Ulcer duration:** > 6 weeks: n=4 < 1 week: n=2 **Ulcer location:** Ankle: n=3 Trochanter: n=1 Coccyx: n=2 **Ulcer area (mean cm²; range):** 2.1; 0.7-3.3 **Ulcer depth:** 1-5 mm: n=6 6-10 mm: n=0 **Ulcer aetiology:** Unrelieved pressure: n=4 Friction: n=2 **Inclusion criteria:** Patients with a spinal cord injury and a PU. **Exclusion criteria:** /				

Table 80 – Schubert 2001

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Schubert 2001 **Title:** Effects of phototherapy on pressure ulcer healing in elderly patients after a falling trauma. A prospective, randomized, controlled study **Journal:** Photodermatology Photoimmunology & Photomedicine, 17, 32-8 **Study type:** randomized controlled trial, permuted blocks of six patients **Sequence generation:** not reported **Allocation concealment:** not reported **Blinding:** not reported **Addressing incomplete outcome data:** not reported **Statistical analysis:** For ulcer area, group means and standard error of the mean (SE)	**Patient group:** hospitalized patients with a stage II or III pressure ulcer (according to Shea classification). **All patients** **Randomised N:** 72 patients with 116 ulcers **Completed N:** 59 patients **Drop-outs:** 13 patients (one need to be operated, nine patients died, and two were not accessible for measurement after 2 weeks, one interrupted the study after 5 weeks) **Group 1** **Randomised N:** 35 patients with 55 ulcers **Completed N:** 27 patients **Dropouts:** 8 patients (one need to be operated, six patients died, and one was not accessible for measurement after 2 weeks) **Age (mean years**	**Group 1:** Pulsed monochromatic light (PML). A probe contained both 30 diodes, which could emit infrared light at 956 nm, and 80 diodes, which could emit red light at 637 nm. Infrared and red PML were used in sequence. First, infrared light with an irradiance of 55 W/m2 was used. Then red light with an irradiance of 21 W/m2 was used. Using a duty cycle of 80%, both the infrared light and the red light were pulsed with the following pulse frequencies: during the first five treatments: 78 Hz, 702 Hz, 8.58 kHz; during the following treatments: 15.6 Hz, 287 Hz, 31.2 Hz. Treatments were given for 9 min each time by two trained nurses. The number of treatments given per week was as follows: week 1: 5 times; week 2: 4 times; week 3: twice; week 4 and beyond: once a week. **Group 2:** Standard treatment (no additional treatment)	**Outcome 1:** Time (weeks) to 90% reduction in ulcer area **Outcome 2:** Constant healing rate all ulcers (exponential fitting) (%/day) **Outcome 3:** Constant healing rate ulcers stage II (n=62) (exponential fitting) (%/day) **Outcome 4:** Healing rate per week (healed proportion of the baseline ulcer area) (patients who completed the study; n=59) **Outcome 5:** Healing rate per week of stage II PU (healed proportion of the baseline ulcer area) (patients	**Group 1:** 5 **Group 2:** 9 **Group 1:** 5.3 **Group 2:** 3.4 **Group 1:** 5.9 **Group 2:** 3.4 **P value:** / **Group 1:** 0.298 **Group 2:** 0.200 **P value:** < 0.05 **Group 1:** 0.317 **Group 2:** 0.204 **P value:** < 0.05	**Funding:** / **Limitations:** no details on sequence generation and allocation concealment; no blinding; addressing of incomplete outcomes data not reported; unclear if analysis was performed based on patients or ulcers. **Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
were computed weekly. Demographic data were evaluated as group means and SE. Normality tests were performed. For normally distributed data, Student's *t*-test was used. When data deviated from normal distributions, the Mann–Whitney U-test was used to compare the group distributions. The healing process was described in three different ways: rate constant, healing rate and ulcer healing level. The latter was calculated using the Kaplan-Meier method. **Baseline differences:** No significant difference between the two groups. **Study power/sample size:** no a priory sample size calculation. **Setting:** Huddinge University Hospital in Sweden. **Length of study:** until healed with a	**(SD)):** 85 (0.9) **Gender (m/f):** 14/21 **Ulcer location on trunk (%):** 83 **Ulcer stage:** Stage II (n=47); Stage II (n=8) **Group 2** **Randomised N:** 37 patients with 61 ulcers **Completed N:** 32 patients **Dropouts:** 5 patients (three patients died, one was not accessible for measurement after 2 weeks, and one interrupted the study after 5 weeks). **Age (mean years (SD)):** 85 (0.8) **Gender (m/f):** 12/25 **Ulcer location on trunk (%):** 68 **Ulcer stage:** Stage II (n=52); Stage II (n=9) **Inclusion criteria:** Elderly patient with a stage II or III PU. **Exclusion criteria:** /	**Both groups:** Patients were informed not to lie on the pressure ulcer, but instead to lie in 30¾ side position. Patients used foam mattresses of good quality (14–18 cm thick). Wheel-chair bound patients were given cushions (Roho or foam) when sitting. Except in particular situations (infection or necrosis) ulcers were cleansed gently from topical substance with physiological saline moistened gauze and dried. Ulcers that demonstrated a local infection were also treated with an absorbent gel containing cadexomer iodine. Necroses were mostly removed by sharp debridement with a pair of scissors, or a scalpel, or otherwise by hydrogel treatment. A topical anaesthetic such as EMLA cream (lidocaine–prilocaine) was applied on the ulcer for at least 30 min before debridement. These treatments were mostly used during the first 2 weeks to get the ulcer surface clean as soon as possible. The	who completed the study; n=53) **Outcome 6**: Proportion of patients > 50% healed after 2 weeks **Outcome 7**: Proportion of patients > 50% healed after 5 weeks **Outcome 8**: Proportion of patients with stage II Pus healed after 5 weeks	**Group 1:** 18/27 **Group 2:** 16/32 **P value:** Ulcer healed to 50%: p<0.01 Ulcer healed to 90%: p=0.01 Ulcer completely healed: p<0.05 **Group 1:** 26/27 **Group 2:** 23/32 **P value:** Ulcer healed to 50%: p<0.01 Ulcer healed to 90%: p=0.01 Ulcer completely healed: p<0.05 **P value:** Ulcer healed to 50%: p<0.01 Ulcer healed to 90%: p=0.01 Ulcer completely healed: p<0.05	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
maximum of 10 weeks. **Assessment of PUs:** Pressure ulcers were classified according to the Shea classification. An adhesive transparent plastic film was placed tightly over the ulcer and attached to the surrounding skin. This film consists of two sheets, one on top of the other. The boundary of the pressure ulcer was outlined with a fine-tipped indelible marker pen on the top sheet. The sheet was then removed, but was retained for evaluation of the ulcer area. The sheet was placed on a flat horizontal board and the outlined ulcer boundary was traced with the tip of a digital planimeter. A numeric display on the planimeter gave a direct read-out of the plane area enclosed by the ulcer tracing. The planimeter had an		cleaned ulcer surface was kept moistened with a semipermeable hydrocolloid treatment. Careful inspection of the ulcer edges was done to avoid maceration.			

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
accuracy of ±0.2% and a resolution of 0.1 cm². **Multiple ulcers:** a total of 116 ulcers in 72 patients were included in the study. Range: 1-6 ulcers per patient.					

Table 81 – Shojaei - 2008

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Shojaei 2008 **Title:** Low Level Laser Therapy in the Treatment of Pressure Ulcers in Spinal Cord Handicapped Veterans Living in Tehran **Journal:** Iran Journal of Medical Science, 33 (1), 44-8 **Study type:** randomized controlled trial **Sequence generation:** not reported **Allocation concealment:** not reported **Blinding:** triple	**Patient group:** veterans with a spinal cord injury and afflicted with a pressure ulcer. **All patients** **Randomised N:** 16 patients **Completed N:** 16 patients **Drop-outs:** 16 patients **Group 1** **Randomised N:** 8 patients **Completed N:** 8 patients **Dropouts:** 0 patients **Age (mean years (SD)):** 38.2 (5) **Injury duration (mean years (SD)):** 18 (2.7)	**Group 1:** Laser therapy: infrared: 980 nm, 200mw continuous (Gallium-Aluminium-Arsenide), and red: 650 nm, 30mw continuous (Gallium-Aluminium-Indium-Phosphate) with an at every other day dose of 4-6 J/cm² for 3 weeks **Group 2:** Conventional treatment (no additional treatment) **Both groups:** conventional treatment, not further specified.	**Outcome 1:** Proportion of patients completely healed **Outcome 2:** Proportion of patients improved **Outcome 3:** Proportion of patients not changed **Outcome 4:** Proportion of patients worsened **Outcome 5:** Proportion of patients with an ulcer decreased	**Group 1:** 3/8 **Group 2:** 1/8 **Group 1:** 7/8 **Group 2:** 6/8 **Group 1:** 1/8 **Group 2:** 1/8 **Group 1:** 0/8 **Group 2:** 1/8 **Group 1:** 5/8 **Group 2:** ?	**Funding:** / **Limitations:** very little description of methodology: no details on sequence generation and allocation concealment. Classification of PU unspecified. Assessment of ulcers and outcomes not reported. Not all outcomes are reported in the result section; no debridement prior to treatment.

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
blinded **Addressing incomplete outcome data:** not reported **Statistical analysis:** Data regarding the size and stage of ulcer in spinal cord veterans before and after treatment was evaluated by paired *t* test while the size and stage of ulcers in both case and control groups were compared using the Mann Whitney test. Considering the small sample size, a non-parametrical statistical test such as Wilcoxon was used. **Baseline differences:** No statistical calculation of difference. **Study power/sample size:** A priory sample size estimation of 15 patients. **Setting:** Veteran's hospitals and spinal cord Veterans care homes in Tehran.	**Ulcer duration (mean months (SD)):** 36.8 (3.9) **Ulcer stage:** Stage I (n=3); Stage II (n=3); Stage III (n=2) **Ulcer location:** ischial (n=6), sacral (n=2) **Group 2** **Randomised N:** 8 patients **Completed N:** 8 patients **Dropouts:** 0 patients **Age (mean years (SD)):** 41.1 (9.4) **Injury duration (mean years (SD)):** 19.3 (3.8) **Ulcer duration (mean months (SD)):** 36.4 (7.2) **Ulcer stage:** Stage I (n=6); Stage II (n=1); Stage III (n=1) **Ulcer location:** ischial (n=4), sacral (n=2), ankle (n=2) **Inclusion criteria:** Spinal cord injured veterans with stage I, II, and III pressure ulcer in sites such as		in stage **Outcome 6:** Proportion of patients with an ulcer of unchanged stage **Outcome 7**: Minimum reduction of 50% in ulcer size	**Group 1:** 3/8 **Group 2:** ? **Group 1:** / **Group 2:** / **P value:** 0.007	**Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Length of study: three weeks of treatment **Assessment of PUs:** Pressure ulcers classification not specified. Assessment not reported. **Multiple ulcers:** not reported.	knee, ankle, occiput, and around pelvis, which confirmed by primary clinical examination; Lack of any history or signs for diabetes mellitus, vascular disorder, vasculitis, and chronic renal failure according the clinical examination and previous medical records; Lack of indicative signs of ulcer infection (malodorous, yellow secretion, fever); Negative history for consuming any immunity compromising drugs; Lack of any laser treatment contraindications such as seizure, cancer, and hypersensitivity to light. **Exclusion criteria:** /				

Table 82 – Taly 2004

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Taly 2004 **Title:** Efficacy of Multiwavelength Light Therapy in the Treatment of Pressure Ulcers in Subjects With Disorders of the Spinal Cord: A Randomized Double-Blind Controlled Trial **Journal:** Archives of Physical Medicine and Rehabilitation, 85, 1657-61 **Study type:** randomized controlled trial **Sequence generation:** ulcers received an unique identification number and were randomized by using a random number table. **Allocation concealment:** not reported **Blinding:** double blinded, nurses (dressings) and investigator (measurements) were blinded. Unclear if	**Patient group:** Spinal cord patients with a pressure ulcer stage II, III or IV. **All patients** **Randomised N:** 35 patients with 64 ulcers **Completed N:** 30 patients with 54 ulcers **Drop-outs:** 5 patients with 10 ulcers (two patients (seven ulcers) died; one opted out of the study; and two developed an ulcer infection) **Age (mean years (SD); range)):** 31.71 (1.23); 8-65 **Ulcer location:** scrum (n=21), trochanter (n=18), gluteal region (n=9), lateral malleolus (n=2), elbow (n=2), ischial tuberosity (n=1), heel (n=1), and other (n=10) **Group 1** **Randomised N:** 35 ulcers, number of patients not reported **Completed N:** 27 ulcers, number of	**Group 1:** Multiwavelength light therapy. During every session, each 10cm² square was exposed for 60 seconds. The 46 probes had wavelengths of 660 – 820 nm; power of 15 mW or 25 mW; a frequency of 20 Hz. multiwavelength light therapy source are given in table 1. Energy applied to the ulcer was 4.5J/cm2. **Group 2:** Mutiwavelength light therapy were the beam was switched off. **Both groups:** Patients received daily dressing with sterile gauze soaked in normal saline and pressure relief with either a water mattress or a split mattress. Ulcers were debrided if thought necessary. Eschars, if any, were removed. Education regarding care of the ulcer was given to all patients.	**Outcome 1:** Proportion of ulcers completely healed **Outcome 2:** Proportion of ulcers which did not improved **Outcome 3:** Proportion of ulcers with a lower PSST score (better status) **Outcome 4:** Time (weeks) to complete healing **Outcome 5:** Reduction of stage III or IV PU to a stage II after 2 weeks **Outcome 6**: Reduction of stage III or IV PU to a stage II after 3 weeks **Outcome 7**: Reduction of stage III or IV PU	**Group 1:** 18/35 **Group 2:** 14/29 **P value:** 0.802 **Group 1:** 6/35 **Group 2:** 3/29 **Group 1:** 11/35 **Group 2:** 12/29 **Group 1:** 2.45 (2.06) **Group 2:** 1.78 (2.13) **P value:** 0.330 **Group 1:** 3/4 **Group 2:** 0/5 **Group 1:** 3/4 **Group 2:** 1/5 **Group 1:** 1/4 **Group 2:** 0/5 **P value:** /	**Funding:** Supported by National Institute of Mental Health and Neurosciences. **Limitations:** no details on allocation concealment; not clear if patients were blinded; stage at start of treatment different from stage at randomization. **Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
patients were blinded. **Addressing incomplete outcome data:** Intention-to-treat analysis was used, and in patients who did not complete the study after entry, the last available observations or measurements were considered for analysis. **Statistical analysis:** Ulcers were unit of analysis. The number of ulcers that healed in each group was compared by using the chi-square test. When the cell size was less than 5, the Fisher exact coefficient was used. The significance level was set at *P* less than .05. Time taken by the ulcers to heal was compared using an independent sample *t* test, with the significance level set at *P* less than .05. The PSST score and the pressure ulcer stage are ordinal scales. Hence, the differences in the PSST scores	patients not reported **Dropouts:** 8 ulcers **PSST score (mean (SD); median; range):** 21.9 (5); 22; 14-32 **Ulcer duration (mean days (SD)):** 34.2 (45.5) **Ulcer stage:** Stage II (n=31); Stage III (n=3); Stage IV (n=1) **Group 2** **Randomised N:** 29 ulcers, number of patients not reported **Completed N:** 27 ulcers, number of patients not reported **Dropouts:** 2 ulcers **PSST score (mean (SD); median; range):** 22.7 (4.4); 23; 14-31 **Ulcer duration (mean days (SD)):** 57.1 (43.5) **Ulcer stage:** Stage II (n=24); Stage III (n=4); Stage IV (n=1) **Inclusion criteria:** Patients with a spinal cord disorder and a pressure ulcer stage II, III, or IV. **Exclusion criteria:** Subjects with		to a stage I after 3 weeks **Outcome 8**: Time (weeks) to reach stage II **Outcome 9**: PSST score of ulcers not healed at end of treatment **Outcome 10**: PSST score of ulcers not healed at end of study **Outcome 11**: Mean percentage reduction in PSST score of ulcers not healed at end of treatment **Outcome 12**: Mean percentage reduction in PSST score of ulcers not healed at end of study **Outcome 13**: Mean percentage reduction in stage of ulcers not	**Group 1:** 2.25 (0.5) **Group 2:** 4.33 (1.53) **P value:** 0.047 **Group 1:** 21.1 (4.6) **Group 2:** 20.7 (4.6) **P-value:** 0.955 **Group 1:** 19.9 (6.4) **Group 2:** 19.0 (4.9) **P value:** 0.806 **Group 1:** 12.8 **Group 2:** 15.5 **Group 1:** 17.8 **Group 2:** 22.4 **Group 1:** 9.1 **Group 2:** 4.3	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
and the pressure ulcer stage between the 2 groups were analyzed with the Mann-Whitney *U* test, with the significance level at *P* less than .05. **Baseline differences:** No statistical difference between both groups. **Study power/sample size:** No a priory sample size calculation. **Setting:** Neurologic rehabilitation ward in Bangalore, India. **Length of study:** until complete healing with a maximum of fourteen sessions (three sessions per week) and follow-up two weeks after treatment **Assessment of PUs:** Pressure ulcers were divided into the conventional 4 stages: stage 1, nonblanching erythema of intact skin; stage 2, partial thickness skin loss; stage 3, full-thickness skin loss; and stage 4, extension into muscle	photosensitivity, ulcers from other causes, necrotic tissue in ulcers that would interfere with the application of laser, flask-shaped ulcers that cannot be adequately exposed to laser, pressure ulcers with underlying osteomyelitis, or pressure ulcers requiring surgical intervention.		healed at end of treatment **Outcome 14**: Mean percentage reduction in stage of ulcers not healed at end of study **Outcome 15**: PSST score at end of treatment in stage III or IV ulcers **Outcome 16**: PSST score at end of study in stage III or IV ulcers **Outcome 17**: Mean percentage reduction in PSST score of stage III or IV ulcers at end of treatment **Outcome 12**: Mean percentage reduction in PSST score of stage III or IV ulcers at end of study	 **Group 1:** 9.1 **Group 2:** 8.7 **Group 1:** 18.3 (2.9) **Group 2:** 24.2 (4.0) **P value:** 0.047 **Group 1:** 16.8 (16.5) **Group 2:** 22.4 (3.9) **P value:** 0.049 **Group 1:** 32.2 **Group 2:** 12.9 **Group 1:** 37.8 **Group 2:** 19.4	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
and bone The wound was assessed by using the Pressure Sore Status Tool9 (PSST), which scores pressure ulcers from 0 to 60; lower scores indicate a better status. This tool includes the following parameters: size, depth, edges, undermining, necrotic tissue type, necrotic tissue amount, exudate type, exudate amount, skin color surrounding wound, peripheral tissue edema, peripheral tissue indurations, granulation tissue, and epithelialization. Photographs of all ulcers were taken at the beginning of treatment, end of treatment, and 14 days after last treatment session. **Multiple ulcers:** 64 ulcers in 35 patients.			**Outcome 13**: Mean percentage reduction in stage of stage III or IV ulcers at end of treatment **Outcome 14**: Mean percentage reduction in stage of stage III or IV ulcers at end of study	**Group 1:** 17.9 **Group 2:** 12.5 **Group 1:** 35.7 **Group 2:** 25.0	

Table 83 – Wills 1983

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Wills 1983 **Title:** A Randomized Placebo-controlled Trial of Ultraviolet Light in the Treatment of Superficial Pressure Sores. **Journal:** Journal of American geriatrics Society, 31 (3), 131-3 **Study type:** randomized controlled trial **Sequence generation:** not reported **Allocation concealment:** not reported **Blinding:** single-blind, staff members were unaware of group to which each patient belonged **Addressing incomplete outcome data:** not reported **Statistical analysis:** Not reported. **Baseline differences:** No statistical calculation of difference. Initial area	**Patient group:** patients with a superficial pressure sore (< 5mm deep). **All patients** **Randomised N:** 18 patients **Completed N:** 16 patients **Drop-outs:** 2 patients (two patients (one died; one was transferred to an acute-care hospital) **Group 1** **Randomised N:** not reported **Completed N:** 8 patients **Dropouts:** not reported **Age (mean; range):** 87.1; 63-103 **Gender (m/f):** 4/4 **Initial ulcer area (mean (SEM)):** 144.5 (36.3) **Ulcer location:** sacrum or ischium (n=7); other (n=1) **Group 2** **Randomised N:** not reported **Completed N:** 8 patients	**Group 1:** Ultraviolet therapy. The UV emission extends between 200 nm and 400 nm. Skin testing of each patient was determined. The treatment comprised twice weekly doses of 2.5 MED (second degree erythema). Each dose of UV was increased by 50% over the previous dose. **Group 2:** Similar treatment but the UV light was obstructed by a mica cap left in place over the quartz window. **Both groups:** daily nursing care: continual relief of pressure form the sore; cleaning and dressing of sore twice daily and sterile water was used as daily cleansing agent.	**Outcome 1:** Time (weeks (SEM)) to complete healing **Outcome 2:** Time (weeks (SEM)) to complete healing (analysis with age and initial area as covariate)	**Group 1:** 6.25 (0.55) **Group 2:** 8.38 (0.45) **P value:** <0.02 **Group 1:** 6.26 (0.59) **Group 2:** 8.37 (0.50) **P value:** <0.02	**Funding:** Supported by grant from the Canadian Geriatrics Research Society **Limitations:** very little description of methodology: no details on sequence generation and allocation concealment; single-blinded; statistical analysis not reported; no a priory sample size calculation; few results; no debridement prior to treatment. **Additional outcomes:** / **Notes:** /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
of sores tended to be higher in placebo group. **Study power/sample size:** No a priory sample size calculation. **Setting:** Extend Care Unit of the Health Sciences Centre Hospital, University of British Columbia. **Length of study:** eight weeks of treatment and two weeks of follow-up **Assessment of PUs:** Superficial pressure sores were defined as being less than 5 mm deep. Sores were measured before treatment and at weekly intervals. Measurements were made by tracing the outline of the sore onto sterile cellophane and transferring this tracing to 1mm squared graph paper. **Multiple ulcers:** not reported	**Dropouts:** not reported **Age (mean; range):** 80.6; 62-91 **Gender (m/f):** 2/6 **Initial ulcer area (mean (SEM)):** 196.8 (31.2) **Ulcer location:** sacrum or ischium (n=6); other (n=2) **Inclusion criteria:** Patients with a superficial pressure sores. **Exclusion criteria:** /				

12. HEEL ULCER PREVENTION

12.1. Review protocol

Table 84 – Review protocol

Protocol	Heel ulcer prevention
Review question	What is the most clinically effective method for management of pressure ulcers of the heel?
Population	Individuals of all ages, with at least one pressure ulcer of any category/stage
Intervention	Interventions for management of heel ulcers: • Pressure-redistributing devices • Repositioning • Nutrition and hydration • Electrotherapy • NPWT • HBOT • Debridement • Antimicrobials • Antibiotics • Dressings • Skin massage/rubbing
Comparison	• Each other • No intervention
Outcomes	**Critical outcome for decision-making** • Time to complete healing (time to event data) • Rate of healing (continuous data) • Rate of reduction in size and volume of pressure ulcer (absolute and relative) (continuous data) • Reduction in size and volume of pressure ulcer (absolute and relative) (continuous data)

	• Proportion of patients completely healed within trial period (dichotomous) **Important outcomes** • Wound related pain • Health-related quality of life o Short-form health survey (SF36) o Manchester Short Assessment of Quality of Life o EQ-5D o WHOQOL-BREF o Cardiff HRQoL tool o HUI o Pressure ulcer quality of life (Gorecki) • Acceptability of treatment (e.g. compliance, tolerance) • Time in hospital (continuous data) • Side effects (infection, health skin damage, healthy tissue damage, maceration, treatment related pain, skin irritation, allergic reaction, itching, odour, bleeding, rash, toxicity) • Mortality
Study design	• High quality systematic reviews of RCT's or RCT's only. • Cochrane reviews will be included if they match the inclusion criteria and have appropriate assumptions for missing data such as available case analysis or ITT (with the appropriate assumptions) • Cohort studies will be considered if no RCTs are available.
Exclusion	• Studies with another population, intervention, comparison or outcome • Non-English, non-French, non-Dutch language papers
Search strategy	**The electronic databases to be searched are:** • Medline (OVID interface), Cinahl (EBSCO-interface), Embase, Library of the Cochrane Collaboration • All years
Review strategy	**How will individual PICO characteristics be combined across studies)** • Population – any population will be combined except those specified in the strata. Must have active pressure ulcers at time of enrolment. • Intervention – any type of light therapy will be combined for meta-analysis.

	• Comparison – any comparison which fits the inclusion criteria will be meta-analysed • Outcomes – same outcomes will be combined for meta-analysis. • Blinding – Blinded and unblinded studies will be meta-analysed together. • Unit of analysis – patients, individual pressure ulcers • Minimum follow up = no minimum. • Minimum total size = no minimum • Use authors data. If there is a 10% differential or higher between the groups or if the missing data is higher than the event rate downgrade on risk of bias. If authors use ACA and ITT, ACA is preferable over ITT. • MIDs: 0.75 to 1.25 for dichotomous variables and 0.5 x standard deviation for continuous variables.
Analysis	**The following groups will be considered separately if data are present:** • ICU patients, spinal cord patients, palliative patients, paediatric patients and adults (if not in other subgroup); **Subgroups:** The following groups will be considered separately as subgroups if data are present: • Different categories of pressure ulcers (from category 2 upwards where outcomes are reported separately) • Different locations of pressure ulcers: sacral, heel and others
Other terms	
Notes	

12.2. Search strategy

12.2.1. Search Filters

Table 85 – Search filters in OVID Medline

Search strategy	Heel ulcers		Results
Date	April 2013		
Database	Medline-Ovid		
Search strategy	1	letter/	778041
	2	editorial/	318116
	3	news/	154433
	4	exp historical article/	310106
	5	Anecdotes as Topic/	4410
	6	comment/	518833
	7	case report/	1596123
	8	(letter or comment*).ti.	86220
	9	or/1-8	3125048
	10	randomized controlled trial/ or random*.ti,ab.	710524
	11	9 not 10	3109418
	12	animals/ not humans/	3693714
	13	exp Animals, Laboratory/	690006
	14	exp Animal Experimentation/	5594
	15	exp Models, Animal/	384076
	16	exp Rodentia/	2547958
	17	(rat or rats or mouse or mice).ti.	1060980

Search strategy	Heel ulcers		Results
	18	or/11-17	7356197
	19	pressure ulcer/	9153
	20	decubit*.ti,ab.	3964
	21	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6308
	22	(bedsore* or bed-sore*).ti,ab.	506
	23	(incontinen* adj2 dermatitis).ti,ab.	59
	24	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	658
	25	or/19-24	13940
	26	limit 25 to english language	11177
	27	(seat* or chair* or wheelchair* or pillow*).ti,ab.	38008
	28	wheelchairs/	3369
	29	(bed or beds).ti,ab.	72259
	30	(cutfoam or padding or sheepskin* or sheep-skin* or gels).ti,ab.	36682
	31	(alternat* adj2 pressure).ti,ab.	283
	32	shoes/	4464
	33	exp orthotic devices/	8883
	34	(orthotic adj2 (device* or therap* or treat*)).ti,ab.	528
	35	(shoe* or boot* or footwear or foot-wear).ti,ab.	15693
	36	(orthos* or insole).ti,ab.	13804
	37	((contact or walk*) adj2 cast*).ti,ab.	350
	38	(aircast* or scotchcast*).ti,ab.	105
	39	((foot or feet or heel*) adj2 (pressure or protect* or device*)).ti,ab.	1064
	40	((foot or feet or heel* or leg*) adj2 trough*).ti,ab.	5

Search strategy	Heel ulcers		Results
	41	(heel* adj2 (lift* or splint* or float* or glove* or suspen* or elevat*)).ti,ab.	168
	42	or/27-41	183438
	43	26 and 42	1634
	44	43 not 18	1453
	45	randomized controlled trial.pt.	337759
	46	controlled clinical trial.pt.	85231
	47	randomi#ed.ab.	303090
	48	placebo.ab.	139805
	49	drug therapy.fs.	1570595
	50	randomly.ab.	185146
	51	trial.ab.	262281
	52	groups.ab.	1202801
	53	or/45-52	3026183
	54	Clinical Trials as topic.sh.	162630
	55	trial.ti.	108851
	56	or/45-48,50,54-55	827236
	57	Meta-Analysis/	36479
	58	Meta-Analysis as Topic/	12450
	59	(meta analy* or metanaly* or metaanaly*).ti,ab.	47365
	60	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.	56098
	61	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	21617
	62	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	23254
	63	(search* adj4 literature).ab.	21585

Search strategy	Heel ulcers		Results
	64	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	69072
	65	cochrane.jw.	9100
	66	or/57-65	159531
	67	56 or 66	941051
	68	44 and 67	213
	69	(shaped adj3 (pad* or dressing*)).ti,ab.	56
	70	(heel* adj3 (pad* or cushion*)).ti,ab.	301
	71	heel/	2307
	72	heel*.ti,ab.	8187
	73	prevent*.ti,ab.	852809
	74	71 or 72	8981
	75	73 and 74	650
	76	69 or 70 or 75	983
	77	26 and 76	127
	78	77 not 18	115
	79	67 and 78	27
	80	68 or 79	215
	1	pressure ulcer/	9185
	2	decubit*.ti,ab.	4000
	3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	6387
	4	(bedsore* or bed-sore*).ti,ab.	509
	5	(incontinen* adj2 dermatitis).ti,ab.	62

Search strategy	Heel ulcers		Results
	6	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	665
	7	or/1-6	14064
	8	limit 7 to english language	11277
	9	heel*.ti,ab.	8239
	10	heel/	2309
	11	or/9-10	9027
	12	8 and 11	295
	13	letter/	777117
	14	editorial/	319425
	15	news/	149964
	16	exp historical article/	309193
	17	Anecdotes as Topic/	4402
	18	comment/	519725
	19	case report/	1600014
	20	(letter or comment*).ti.	87288
	21	or/13-20	3125471
	22	randomized controlled trial/ or random*.ti,ab.	716973
	23	21 not 22	3109678
	24	animals/ not humans/	3661514
	25	exp Animals, Laboratory/	680311
	26	exp Animal Experimentation/	5635
	27	exp Models, Animal/	379882
	28	exp Rodentia/	2509509

Search strategy	Heel ulcers		Results
	29	(rat or rats or mouse or mice).ti.	1052606
	30	or/23-29	7311672
	31	12 not 30	244
	32	from 31 keep 1-244	244

Table 86 – Search filters in Embase

Search strategy	Heel ulcers		Results
Date	April 2013		
Database	Embase-OVID		
Search strategy	1	decubitus/	12961
	2	decubit*.ti,ab.	4912
	3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	7353
	4	(bedsore* or bed-sore*).ti,ab.	675
	5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	797
	6	(incontinen* adj2 dermatitis).ti,ab.	65
	7	or/1-6	17570
	8	limit 7 to english language	13657
	9	(seat* or chair* or wheelchair* or pillow*).ti,ab.	42492
	10	exp wheelchair/	5376
	11	(bed or beds).ti,ab.	92526
	12	(cutfoam or padding or sheepskin* or sheep-skin* or gels).ti,ab.	36575

Search strategy	Heel ulcers		Results
	13	(alternat* adj2 pressure).ti,ab.	307
	14	orthopedic shoe/	221
	15	shoe/	5954
	16	orthotics/	3070
	17	(orthotic adj2 (device* or therap* or treat*)).ti,ab.	637
	18	(shoe* or boot* or footwear or foot-wear).ti,ab.	19021
	19	(orthos* or insole).ti,ab.	16742
	20	((contact or walk*) adj2 cast*).ti,ab.	404
	21	(aircast* or scotchcast*).ti,ab.	130
	22	((foot or feet or heel*) adj2 (pressure or protect* or device*)).ti,ab.	1282
	23	((foot or feet or heel* or leg*) adj2 trough*).ti,ab.	5
	24	(heel* adj2 (lift* or splint* or float* or glove* or suspen* or elevat*)).ti,ab.	188
	25	or/9-24	210737
	26	8 and 25	1795
	27	random*.ti,ab.	754182
	28	factorial*.ti,ab.	19468
	29	(crossover* or cross over*).ti,ab.	62717
	30	((doubl$ or singl$) adj blind$).ti,ab.	141908
	31	(assign* or allocat* or volunteer* or placebo*).ti,ab.	576484
	32	crossover procedure/	35085
	33	double blind procedure/	110991
	34	single blind procedure/	16412
	35	randomized controlled trial/	329510

Search strategy	Heel ulcers			Results
		36	or/27-35	1238630
		37	letter.pt. or letter/	795546
		38	note.pt.	531057
		39	editorial.pt.	412693
		40	case report/ or case study/	1866558
		41	(letter or comment*).ti.	139266
		42	or/37-41	3469718
		43	randomized controlled trial/ or random*.ti,ab.	839007
		44	42 not 43	3442785
		45	animal/ not human/	1341058
		46	nonhuman/	3916857
		47	exp Animal Experiment/	1537681
		48	exp experimental animal/	427225
		49	animal model/	656256
		50	exp Rodent/	2601891
		51	(rat or rats or mouse or mice).ti.	1132895
		52	or/44-51	9101147
		53	systematic review/	53173
		54	meta-analysis/	65909
		55	(meta analy* or metanaly* or metaanaly*).ti,ab.	60872
		56	((systematic or evidence) adj2 (review* or overview*)).ti,ab.	64712
		57	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.	25777
		58	(search strategy or search criteria or systematic search or study selection or data extraction).ab.	27383

Search strategy	Heel ulcers		Results
	59	(search* adj4 literature).ab.	26367
	60	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.	82031
	61	((pool* or combined) adj2 (data or trials or studies or results)).ab.	33209
	62	cochrane.jw.	11437
	63	or/53-62	238591
	64	36 or 63	1406727
	65	26 and 64	315
	66	65 not 52	305
	67	(shaped adj3 (pad* or dressing*)).ti,ab.	55
	68	(heel* adj3 (pad* or cushion*)).ti,ab.	313
	69	heel/	3638
	70	heel*.ti,ab.	9834
	71	prevent*.ti,ab.	1016005
	72	69 or 70	10671
	73	71 and 72	835
	74	67 or 68 or 73	1173
	75	8 and 74	144
	76	75 not 52	126
	77	64 and 76	29
	78	66 or 77	309
	1	decubitus/	13299
	2	decubit*.ti,ab.	5021

Search strategy	Heel ulcers		Results
	3	(pressure adj (sore* or ulcer* or damage)).ti,ab.	7546
	4	(bedsore* or bed-sore*).ti,ab.	686
	5	((moist* or friction or shear) adj2 (sore* or ulcer* or damage or wound* or injur* or lesion*)).ti,ab.	819
	6	(incontinen* adj2 dermatitis).ti,ab.	68
	7	or/1-6	17994
	8	limit 7 to english language	14056
	9	heel*.ti,ab.	10078
	10	heel/	3769
	11	or/9-10	10932
	12	8 and 11	326
	13	letter.pt. or letter/	806895
	14	note.pt.	543764
	15	editorial.pt.	420357
	16	case report/ or case study/	1891928
	17	(letter or comment*).ti.	141589
	18	or/13-17	3523253
	19	randomized controlled trial/ or random*.ti,ab.	865786
	20	18 not 19	3495777
	21	animal/ not human/	1351212
	22	nonhuman/	3986236
	23	exp Animal Experiment/	1561870
	24	exp experimental animal/	435748
	25	animal model/	674807

Search strategy	Heel ulcers		Results
	26	exp Rodent/	2643124
	27	(rat or rats or mouse or mice).ti.	1147609
	28	or/20-27	9243723
	29	12 not 28	261

Table 87 – Search filters in CINAHL

Search strategy	Heel ulcers		Results
Date	April 2013		
Database	CINAHL		
Search strategy	S30	S29 Limiters - English Language; Exclude MEDLINE records	79
	S29	S7 and S28	238
	S28	S25 or S26 or S27	600
	S27	heel* AND prevent*	533
	S26	heel* N3 pad* OR heel* N3 cushion*	74
	S25	shaped N3 pad* OR shaped N3 dressing*	10
	S24	S22 NOT S23	1502
	S23	PT anecdote or PT audiovisual or PT bibliography or PT biography or PT book or PT book review or PT brief item or PT cartoon or PT commentary or PT computer program or PT editorial or PT games or PT glossary or PT historical material or PT interview or PT letter or PT listservs or PT masters thesis or PT obituary or PT pamphlet or PT pamphlet chapter or PT pictorial or PT poetry or PT proceedings or PT "questions and answers" or PT response or PT software or PT teaching materials or PT website	1E+06
	S22	S7 and S21	2517
	S21	S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20	43464
	S20	heel* AND (lift* OR splint* OR float* OR glove* OR suspen* OR elevat*)	187
	S19	(foot or feet or heel* or leg*) and trough*	22
	S18	(foot OR feet OR heel*) AND (pressure OR protect* OR device*)	3585
	S17	contact N2 cast* OR walk* N2 cast*	157
	S16	orthotic N2 treat* OR orthotic N2 therap* OR orthotic N2 device*	242
	S15	alternat* N2 pressure	134

	S14	bed or beds or cutfoam or padding or sheepskin* or sheep-skin* or gels or shoe* or boot* or footwear or foot-wear or orthos* or insole or aircast* or scotchcast*	26881
	S13	(MH "Orthopedic Footwear")	96
	S12	(MH "Seating")	651
	S11	(MH "Orthoses+")	6013
	S10	(MH "Shoes+")	2401
	S9	seat* or chair* or wheelchair* or pillow*	13407
	S8	(MH "Wheelchairs+")	3071
	S7	S1 or S2 or S3 or S4 or S5 or S6	9952
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1430
	S5	incontinen* n2 dermatitis	80
	S4	bedsore* OR bed-sore*	157
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8568
	S2	decubit*	488
	S1	(MH "Pressure Ulcer")	7783
	S10	s9 Limiters - English Language; Exclude MEDLINE records	112
	S9	S7 AND S8	340
	S8	heel*	2.444
	S7	S1 or S2 or S3 or S4 or S5 or S6	10147
	S6	((moist* or friction or shear) and (sore* or ulcer* or damage or wound* or injur* or lesion*))	1.450
	S5	incontinen* n2 dermatitis	83
	S4	bedsore* OR bed-sore*	159
	S3	pressure n1 sore* OR pressure n1 ulcer* OR pressure n1 damage*	8732
	S2	decubit*	499
	S1	(MH "Pressure Ulcer")	7944

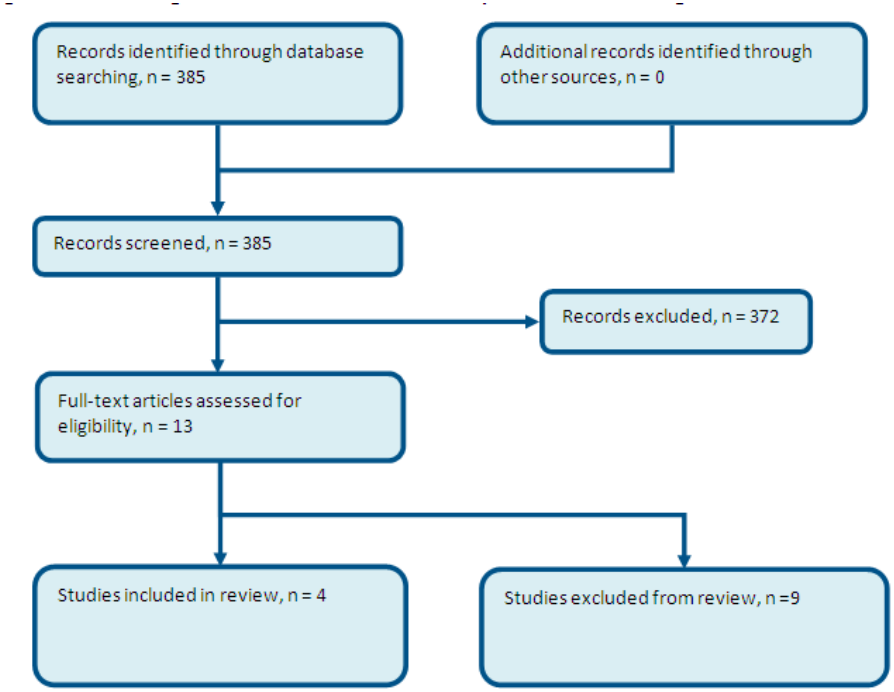
Table 88 – Search filters in Cochrane

Search strategy	Heel ulcers		Results
Date	April 2013		
Database	Cochrane (- CDSR [3/2012]; DARE; Central [3/2012]; NHS EED; HTA)		
Search strategy	#1	MeSH descriptor: [Pressure Ulcer] explode all trees	489
	#2	decubit*:ti,ab,kw	353
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	867
	#4	(bedsore* or bed-sore*):ti,ab,kw	34
	#5	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	64
	#6	#1 or #2 or #3 or #4 or #5	1204
	#7	(seat* or chair* or wheelchair* or pillow*):ti,ab,kw	2696
	#8	MeSH descriptor: [Wheelchairs] explode all trees	128
	#9	MeSH descriptor: [Shoes] explode all trees	237
	#10	MeSH descriptor: [Orthotic Devices] explode all trees	719
	#11	(bed or beds or cutfoam or padding or sheepskin* or sheep-skin* or gels or shoe* or boot* or footwear or foot-wear or orthos* or insole or aircast* or scotchcast*):ti,ab,kw	12844
	#12	(alternat* near/2 pressure):ti,ab,kw	45
	#13	(orthotic near/2 (device* or therap* or treat*)):ti,ab,kw	454
	#14	((contact or walk*) near/2 cast*):ti,ab,kw	55
	#15	((foot or feet or heel*) near/2 (pressure or protect* or device*)):ti,ab,kw	151
	#16	((foot or feet or heel* or leg*) near/2 trough*):ti,ab,kw	1
	#17	(heel* near/2 (lift* or splint* or float* or glove* or suspen* or elevat*)):ti,ab,kw	26
	#18	#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17	15831
	#19	#6 and #18	300
	#20	(shaped near/3 (pad* or dressing*)):ti,ab	8
	#21	(heel* near/3 (pad* or cushion*)):ti,ab	19
	#22	(heel* and prevent*):ti,ab,kw	73
	#23	#20 or #21 or #22	95
	#24	#6 and #23	29
	#25	#19 or #24	302
	#1	MeSH descriptor: [Pressure Ulcer] explode all trees	490
	#2	decubit*:ti,ab,kw	357
	#3	(pressure near/2 (sore* or ulcer* or damage)):ti,ab,kw	879

Search strategy	Heel ulcers		Results
	#4	(bedsore* or bed-sore*):ti,ab,kw	34
	#5	(incontinen* near/2 dermatitis):ti,ab,kw	10
	#6	((moist* or friction or shear) near/2 (sore* or ulcer* or damage or wound* or injur* or lesion*)):ti,ab,kw	66
	#7	#1 or #2 or #3 or #4 or #5 or #6	1230
	#8	heel*:ti,ab,kw	648
	#9	#7 and #8	55

12.2.2. Flow chart

Figure 70 – Flow chart



12.2.3. Excluded Studies

Table 89 – excluded studies

Reference	Reason for exclusion
Taylor 1979	Intervention does not match protocol – cleansing sponge
Houwing 2008	Prevention not management of heel ulcers
Cheneworth 1994	Not an RCT
Collier 2000	Review
Dekeyser 1994	Outcomes do not match protocol
Frain 2008	Not an RCT
Hampton 2010	Not an RCT
Zernike 1997	Outcomes do not match protocol

12.3. Clinical Evidence

A Cochrane Review (McGinnis 2011)[29] was found for pressure-relieving devices for treating heel pressure ulcers, plus one study (Russell 2000)[30] which looked at two different types of mattress. One study looked at topical agents – nerve growth factors compared to placebo (Landi 2003)[31], this is reported in the topical agents review and reported feet and heel ulcers. As this present review focuses on heel ulcers, only one outcome was extricable from the study (reduction in ulcer area) as all other outcomes related to foot and heel ulcers. One study (Muller 2001) [32] looked at collagenase-containing ointment compared to hydrocolloid dressing to treat pressure ulcers. Meaume (2009)[33] looked at ornithine alpha-ketoglutarate, an amino acid salt, compared to placebo as a supplement to treat heel pressure ulcers.

No randomized controlled trials were identified regarding repositioning, electrotherapy, NPWT, HBOT, debridement, antimicrobials, antibiotics, skin massage/rubbing.

12.3.1. Summary table

Table 90 – Summary of studies included in the review

Study	Intervention/comparator	Population	Outcome	Study length
Landi 2003[31]	Nerve growth factor Placebo	Nursing home patients with a stage II to V foot PU (Yarkony classification)	Reduction in ulcer area	Six weeks of treatment or until complete healing
Meaume 2009[33]	10g sachet of ornithine alpha-ketoglutarate versus one sachet of placebo	Elderly patients (geriatrics, internal medicine, physical medicine and rehabilitation, trauma, plastic surgery, cardiology, neurology and dermatology settings) who had pressure ulcers of the heel of stage II or II (NPUAP classification)	% reduction in pressure ulcer surface area; >90% reduction by week 6; rate of complete healing (cm^2/day); all cause mortality	6 weeks
Muller 2001[32]	Hydrocolloid dressing Collagen dressing	Female inpatients with a grade IV heel PU	Proportion of patients completely healed Time to healing	Maximum 16 weeks
Russell 2000[30]	2 types of alternating cell mattress systems with pressure-relieving cushions: Huntleigh Nimbus 3 with Aura cushion and 4-hourly turning vs Pegasus Cairwave Therapy System with Proactive 2 seating cushion and 8-hourly turning.	Patients from care of the elderly units with pressure ulcer of ≥grade 2 (Torrance classification system). Average age 83.9 and 84.6 years in the 2 groups.	Ulcer healing at 12 and 18 months	18-month follow-up

12.3.2. Clinical GRADE evidence tables

Table 91 – Clinical evidence profile: Nimbus system vs Cairwave system for Management of heel ulcers

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nimbus system	Cairwave system	Relative (95% CI)	Absolute		
Proportion of patients completely healed												
1 Russell 2000	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	24/55 (43.6%)	17/58 (29.3%)	RR 1.49 (0.9 to 2.45)	144 more per 1000 (from 29 fewer to 425 more)	⊕⊕OO LOW	Critical outcome
								29.3%		144 more per 1000 (from 29 fewer to 425 more)		

(a) No details of randomisation method; unclear allocation concealment.
(b) Confidence interval crossed one MID point.

Table 92 – Clinical evidence profile: nerve growth factor versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nerve growth factor	Placebo	Relative (95% CI)	Absolute		
Reduction in ulcer area (mm^2) (Better indicated by higher values)												
1 Landi 2003	randomised trials	Serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	623 (SD 451) N=18	485 (SD 384) N=18	-	MD 138 higher (135.64 lower to 411.64 higher)	⊕⊕OO LOW	Critical outcome

(a) Allocation according to age, group, sex and ulcer area and blinding of nurses and outcome assessor, but no blinding of patient.
(b) Confidence interval crosses one MID point.

Table 93 – Clinical evidence profile: Hydrocolloid dressing versus collagen dressing

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydrocolloid dressing	Collagen dressing	Relative (95% CI)	Absolute	Quality	Importance
Proportion of patients completely healed (heel ulcers) – general population – stage IV – classification system not reported												
Müller 2001	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	Serious[b]	none	7/11 (63.6%)	11/12 (91.7%)	RR 0.69 (0.43 to 1.12)	284 fewer per 1000 (from 522 fewer to 110 more)	⊕OOO VERY LOW	Critical outcome
								91.7%		284 fewer per 1000 (from 523 fewer to 110 more)		
Mean time to healing (weeks) (heel ulcers) – general population – stage IV – classification system not reported												
Müller 2001	randomised trials	very serious[a]	no serious inconsistency	no serious indirectness	very serious[c]	none	14 (SD 4.6)	10 (SD 4.6)	-	MD 4 higher (0.24 to 7.76 higher)	⊕OOO VERY LOW	Critical outcome
								2.8%		not pooled		

(a) Müller (2001): no report on sequence generation, allocation concealment and blinding.
(b) Confidence interval crossed one MID point
(c) Confidence interval crossed both MID points

Table 94 – Clinical evidence profile: ornithine alpha-ketoglutarate versus placebo

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	10g Ornithine alpha-ketoglutarate	Placebo	Relative (95% CI)	Absolute	Quality	Importance
Rate of complete healing (cm2/day) – elderly patients who had pressure ulcers of the heel of stage II or IIIg (unclear if nutritionally deficient)												
1 Meaume (2009)	randomised trials	very serious [a]	no serious inconsistency	no serious indirectness	serious[b]	none	0.07 (s.d 0.11) N= 85	0.04 (s.d 0.08) N= 75	MD 0.03 higher (0 to 0.06 higher)	-	⊕OOO VERY LOW	Critical
Mean % reduction in ulcer size – elderly patients who had pressure ulcers of the heel of stage II or IIIg (unclear if nutritionally deficient)												
1 Meaume (2009)	randomised trials	very serious [a]	no serious inconsistency	no serious indirectness	no serious	None[f]	59.5 (s.d 71.4) N= 85	54 (s.d 69) N= 75	MD 5.5 higher (16.28 lower to 27.28 higher)	-	⊕OOO VERY LOW	Critical
Mean surface area reduction (cm2) – elderly patients who had pressure ulcers of the heel of stage II or IIIg (unclear if nutritionally deficient)												
1 Meaume (2009)	randomised trials	very serious [a]	no serious inconsistency	no serious indirectness	no serious	None[f]	2.3 (s.d 4.2) N= 85	1.7 (s.d 1.7) N= 75	MD 0.6 higher (0.37 lower to 1.57 higher)	-	⊕OOO VERY LOW	Critical
90% reduction by week 6– elderly patients who had pressure ulcers of the heel of stage II or IIIg (unclear if nutritionally deficient)												
1 Meaume (2009)	randomised trials	very serious [a]	no serious inconsistency	no serious indirectness	Serious[b]	none	23.4% N=85	13% N=75	OR 0.49 (CI 0.16 to 14.6)[e]	-	⊕OOO VERY LOW	Critical

(a) Very high drop-out in both arms. Due to problems in recruitment the study was opened up to other centres so some centres had 2 patients and randomisation balanced by blocks of four. Baseline differences. Missing data higher than event rate.
(b) Confidence interval crossed one MID point.
(c) Confidence interval crossed both MID points.
(d) value reported by study
(e) Odds ratio reported by study.
(f) ANCOVA used. Non-parametric tests detected between-group differences (p=0.044) which were confirmed by parametric tests after log-transformation to normalise distribution (p=0.027 for group comparisons).
NPUAP classification of pressure ulcers.

12.3.3. Forrest plots

12.3.3.1. Interventions for management of heel ulcers

Figure 71 – Nerve growth factor versus placebo – reduction in ulcer area (mm^2)

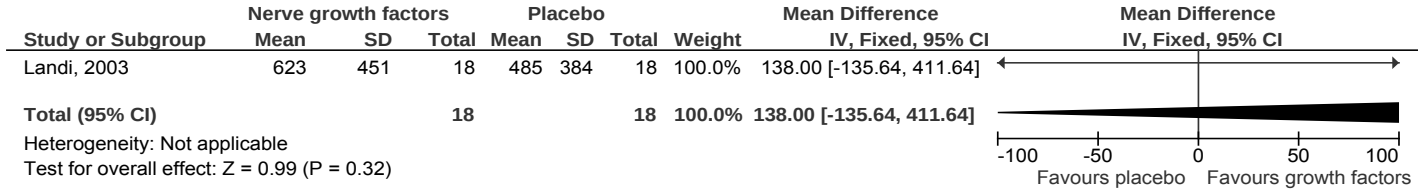


Figure 72 – Nimbus system versus Carewave system – proportion of patients completely healed

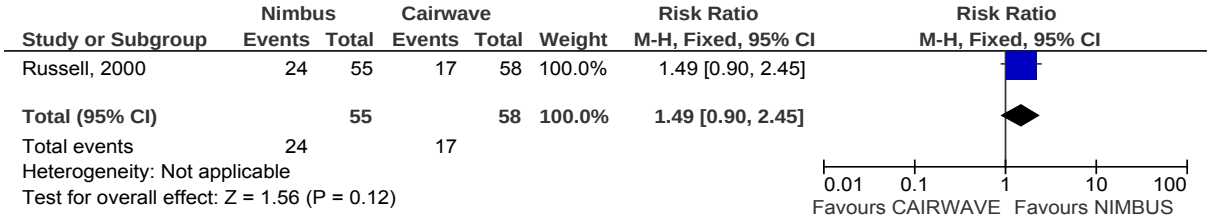


Figure 73 – Hydrocolloid dressing versus collagen – proportion of patients completely healed

Study or Subgroup	Hydrocolloid Events	Hydrocolloid Total	Collagen Events	Collagen Total	Weight	Risk Ratio M-H, Fixed, 95% CI
4.1.4 Heel ulcers						
Müller 2001	7	11	11	12	100.0%	0.69 [0.43, 1.12]
Subtotal (95% CI)		**11**		**12**	**100.0%**	**0.69 [0.43, 1.12]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.50 (P = 0.13)						
Total (95% CI)		**11**		**12**	**100.0%**	**0.69 [0.43, 1.12]**
Total events	7		11			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.50 (P = 0.13)						
Test for subgroup differences: Not applicable						

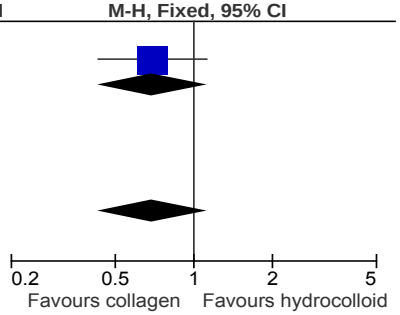


Figure 74 – Hydrocolloid dressing versus collagen - mean time to healing (weeks)

Study or Subgroup	Hydrocolloid Mean	Hydrocolloid SD	Hydrocolloid Total	Collagen Mean	Collagen SD	Collagen Total	Weight	Mean Difference IV, Fixed, 95% CI
4.6.2 Heel ulcer								
Müller 2001	14	4.6	11	10	4.6	12	100.0%	4.00 [0.24, 7.76]
Subtotal (95% CI)			**11**			**12**	**100.0%**	**4.00 [0.24, 7.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.08 (P = 0.04)								
Total (95% CI)			**11**			**12**	**100.0%**	**4.00 [0.24, 7.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.08 (P = 0.04)								
Test for subgroup differences: Not applicable								

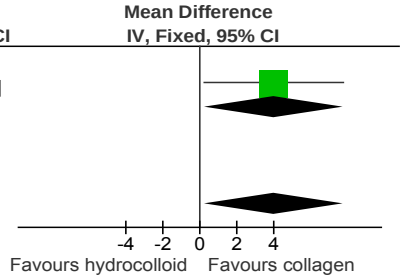


Figure 75 – Ornithine alpha-ketoglutarate versus placebo – rate of complete healing at week 6 (cm^2/day)

Study or Subgroup	Ornithine alpha Mean	Ornithine alpha SD	Ornithine alpha Total	Placebo Mean	Placebo SD	Placebo Total	Weight	Mean Difference IV, Fixed, 95% CI
Meaume, 2009	0.07	0.11	85	0.04	0.08	75	100.0%	0.03 [0.00, 0.06]
Total (95% CI)			**85**			**75**	**100.0%**	**0.03 [0.00, 0.06]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.99 (P = 0.05)								

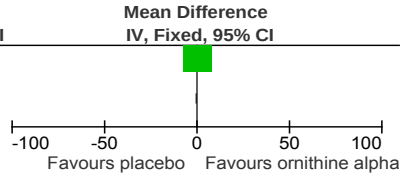


Figure 76 – Ornithine alpha-ketoglutarate versus placebo – mean % reduction in ulcer size

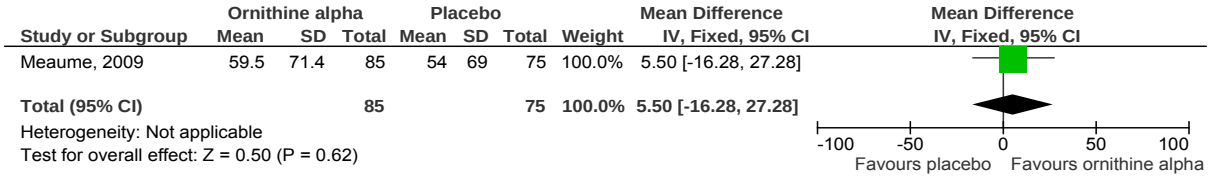
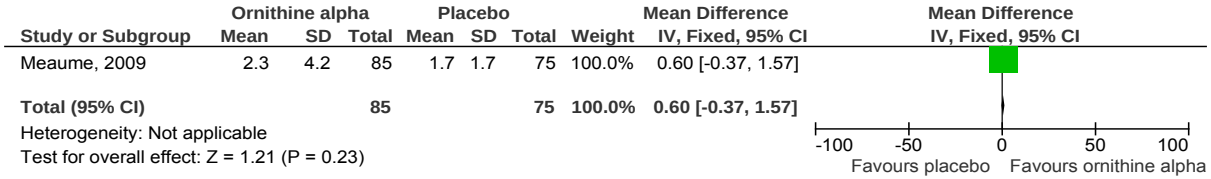


Figure 77 – Ornithine alpha-ketoglutarate versus placebo – mean surface area reduction (cm2)



12.3.4. Evidence tables

Table 95 – LANDI 2003

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Landi (2003) Title: Topical Treatment of Pressure Ulcers with Nerve Growth Factor: A Randomized Clinical Trial. Journal: Annals of Internal Medicine, 139 (8); 635-642. Study type: randomized controlled trial	Patient group: Nursing home patients a stage II or V PU to the foot (according to the Yarkony-Kirk classification). All patients Randomised N: 38 Completed N: 36 Drop-outs: 2 (1 died, and 1 lost to follow up) Group 1	Group 1: topical nerve growth factor (2.5 S murine nerve growth factor). One mg of nerve growth factor was dissolved in 20 ml of balanced salt solution, with a final concentration of 50 μg/ml. The nerve growth factor solution was dropped daily on the lesion and allowed to dry for 2 to 3 minutes. Group 2: Balanced salt solution. The solution was	Outcome 1: Reduction in ulcer area (mm²)	Group 1: 623 (SD 451) Group 2: 485 (SD 384)	Funding: Grant from the Progetto Finalizzato Invecchiamento of the Italian National Research Council. Support was also provided by interRAI, an international group of clinicians and researchers who collaborate to promote

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Sequence generation: a computer-generated list was used. Allocation concealment: randomly stratified according to age group, sex, and ulcer surface area Blinding: double blind, nurses and outcome assessor Addressing incomplete outcome data: unclear Statistical analysis: Quantitative variables are presented as mean values (±SD). Differences in baseline characteristics between patients in the control and treatment groups were analysed in several ways. Quantitative outcomes were tested by using the Student t-test after a pretest for homogeneity of variance. The Mann–Whitney test was used for cases in which the normality assumption	Randomised N: 19 Completed N: 18 Dropouts: 1 (died) Age (mean years (SD); range): 80.2 (3.0); 75-85 Gender (m/f): 5/13 BMI (mean kg/m²): 24.0 (1.4) Duration of PU (mean days (SD)): 13 (4) Ulcer stage: Stage II: n=3 Stage III: n=9 Stage IV: n=5 Stage V: n=1 Ulcer location: Heel: n=14 Lateral malleolus: n=4 Surface area (mean mm² (SD)): 1012 (633) Group 2 Randomised N: 19 Completed N: 18 Dropouts: 1 (lost to follow-up) Age (mean years (SD); range): 80.2 (4.7); 73-93 Gender (m/f): 5/13	dropped daily on the lesion and allowed to dry for 2 to 3 minutes. Both groups: All ulcers received daily local care: irrigation with normal saline, use of debriding enzymes, and application of opaque hydrocolloid occlusive barriers. Al patient received the same preventive skin regimen (turning, repositioning and use of pressure relieving mattress)			research on resident assessment instruments and quality outcomes for elderly persons. Dr. Aloe (co-author) was supported by a grant from the Italian National Institute of Health (ICG 120/4RA00-90) and by a grant from the Italian National Research Council, FISR/ Neurobiotechnology (192/03). Limitations:; inadequate allocation concealment; no patient blinding; no a priory sample size calculation; no ITT. Additional outcomes: /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
was not reasonable. Categorical variables were analysed by using the Fisher exact test. Analysis of covariance was used to compare reduction in pressure ulcer area from baseline to 6-week follow-up after adjustment for baseline ulcer area, location, and duration. Because the distribution of reduction in pressure ulcer area was not normal, this analysis was performed after natural log transformation of this variable. Statistical analyses were performed by using SPSS, version 10.0 (SPSS Inc., Chicago, Illinois). Baseline differences: No statistical differences between group according to a p <0.2. Study power/sample	BMI (mean kg/m²): 23.8 (1.4) Duration of PU (mean days (SD)): 12 (5) Ulcer stage: Stage II: n=3 Stage III: n=13 Stage IV: n=1 Stage V: n=1 Ulcer location: Heel: n=15 Lateral malleolus: n=3 Surface area (mean mm² (SD)): 1012 (655) Inclusion criteria: PU of the foot that ranged from 1 cm2 to 30 cm2 in total area Exclusion criteria: developed the lesion more than 1 month before admission; terminal illnesses; diabetes; peripheral vascular diseases				Notes: /

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
size: No a priory sample size calculation. Setting: teaching nursing home of Catholic University of the Sacred Heart, Fontecchio, Italy. Length of study: 6 weeks of treatment or until completely healed Assessment of PUs: PU were classified according to the Yarkony-Kirk classification (1990). The ulcer perimeter was traced onto sterile, transparent block paper and the blocks were counted. Digital photographs were taken at baseline and every week during the follow-up period. Multiple ulcers: indirect: one ulcer per patient					

Table 96 – MEAUME2009

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Meaume 2009[3] Title: Efficacy and safety of ornithine alpha-ketoglutarate in heel pressure ulcers in elderly patients: results of a randomised controlled trial Study type: multi-centre double-blinded RCT Sequence generation: randomised in blocks of four, randomisation codes generated by using computer. A randomisation no. attributed to chronological order of entry of patients into the double-blind period within each investigational site. Allocation concealment: adequate Blinding: placebo had similar aspect and taste. Investigators and assessors were	Patient group: hospitalised or outpatient elderly patients All patients Randomised N=165 ITT N: 160 Drop-outs: 72 Group 1 Randomised N: 89 ITT N:85 (see analysis details) Completed N: 45 Dropouts:44 Age (mean):80.8+/-8.8 years (ITT) Sex (m/f): 34.1/65.9 BMI: 27.1+6.5 Ulcer area (cm2): mean 8.7+/-6.7 Median: 6.6 Min-Max: 0.71-39.05 Log-transformed ulcer area: 0.816+/-0.349 >8 area </=12cm2: 18.8% Group 2	Group 1: one 10g sachet of ornithine alpha-ketoglutarate Group 2: one sachet of placebo Both sachets given during or after lunch, preferably in 200ml of water or mixed with food. Other ulcer management included mechanical debridement, cleaning, heel elevation, dressings, heel offloading with a suspension boot, management of pain with analgesics and topical corticosteroids and topical antibacterials for excessive granulation tissue. Compliance tested with by collecting treatment kits.	Outcome 1: wound area changes at week 6	Group 1: -2.3+/-4.2cm2 Group 2: -1.7+/-1.cm2 p=0.006	Funding: grant from CHIESI France and Italy. Limitations: well-reported trial with clear details of methodology. Study powered for 70 in each arm which was met for studies randomised but there was a very high drop-out rate in both arms. Due to difficulties in patient recruitment the study was opened to many more centres than initially planned and 2 or 3 of the centres recruited no more than 2 patients while randomisation was balanced by blocks of four. Randomisation did not balance
			Outcome 2:% regression in wound area	Group 1:-59.5+/-71.4% Group 2:-54.0+/-69% Relative risk: p=0.477	
			Outcome 3: >90% regression by week 6	Group 1:23.4% Group 2:13.0% OR: 0.49 95% CI: 0.16/1.46	
			Outcome 4: adverse events in patients	Group 1: 13/85 Group 2: 7/75	
			Outcome 5: severe adverse events in patients (all were considered unrelated to study treatment by investigators)	Group 1: 13/85 Group 2: 15/75	
			Outcome 6: Mortality (unrelated to drug):	Group 1: 5/89 (5.6%) Group 2: 3/76 (3.9%) Relative risk: 1.42 95% CI: 0.35 to 5.76	
			Outcome 7: Rate of complete healing at week 6	Group 1: -0.07 +/- 0.11cm2/day Group 2: - 0.04 +/- 0.08	

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
blinded. Addressing incomplete outcome data: adequate Type of analysis: ITT on efficacy analyses – who take at least one dose of study medication and who had at least one post-treatment evaluation. LOCF applied to deal with missing efficacy time-points. Statistical analysis: ANCOVA (age, history of lesion and patients weight as covariates). Baseline differences: more males in OKG than placebo group; significant difference in ulcer area. Study power/sample size: power calculations 70 patients per group based on previous studies of OKG in pressure ulcer treatment. Setting: 67 investigational centres in six European	Randomised N: 76 ITT N:70 (see analysis details) Completed N:43 Dropouts:33 Age (mean):80.5+/-9.6 Sex (m/f): 52.6/47.4, p=0.017 BMI: 26.7+5.9 Ulcer area (cm2): mean 8.2+/-8.9 Median: 3.9, p=0.044 Min-Max: 0.23-48.14 Log-transformed ulcer area: p=0.027 >8 area </=12cm2, p=0.001 Inclusion criteria: males or females over age of 60 years; heel pressure ulcer (NPUAP stage II or III) occurring after accidental immobilisation; ulcer in process of recovery with early signs of granulation tissue (at least 10% of red tissue on colour scale). Exclusion criteria:		(cm2/day)	cm2/day P=0.007	baseline pressure ulcer characteristics and ulcer area distribution deviated from normal distribution as healing is strongly related to baseline ulcer are the abnormal distribution was a major bias so was subgrouped. Additional outcomes: particular adverse events.

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
countries. Study length: 6 weeks Categorisation of PUs: NPUAP Assessment of PUs: assessed once a week for 6 weeks.	patients confined to bed 24 hours a day before the episode triggering development of the pressure ulcer; pressure ulcer entirely covered by necrosis or fibrin, infected ulcer; poorly controlled type I or II diabetes, dialysed patient, active neoplastic disease; parenteral nutrition; serum albumin <22g/l; advanced peripheral arterial occlusive disease [[ABPI (ankle brachial pressure index)ranging between 0.80 and 1.3 with presence of distal pulses]				

Table 97 – RUSSELL2000

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
Author and year: Russell 2000 Title: Randomised controlled trial of two pressure-relieving systems. Journal: Journal of Wound Care 2000; 9(2):52-5. Type of study: RCT Sequence generation: "on admission to the study, subjects were randomly allocated to trial equipment". Method of randomisation not described (unclear risk) Allocation concealment: unclear (unclear risk) Blinding: "images [of the pressure ulcers] were stored on compact discs, using codes that ensured image analysis could be carried out 'blind' to treatment group" Addressing incomplete outcome data: no	Patient group: patients from elderly units with pressure ulcer of grade 2 or above All patients Randomised N: 141 Completed N: 112 Drop-outs: 29 Age: average 83.9 and 84.6 years Group 1 Randomised N: 70 Completed N: 57 Dropouts: 13 Age (mean): 83.9 years Group 2 Randomised N: 71 Completed N: 55 Dropouts: 16 Age (mean): 84.6 years Inclusion criteria: patients from care of the elderly units; pressure ulcer of > grade 2; Exclusion criteria: patients excluded if	2 types of alternating cell mattress systems with pressure-relieving cushions: Group 1: Huntleigh Numbus 3 with Aura cushion and 4-hourly turning Group 2: Pegasus Cairwave Therapy System with Proactive 2 seating cushion and 8-hourly turning.	Outcome 1: proportion of patients completely healed	Group 1: 24/55 (43.6%) Group 2: 17/58 (29.3%)	Funding: not reported Limitations: no details of randomisation method; unclear allocation concealment. Additional outcomes: Ulcer healing: all types, and divided into heel and sacral ulcers at 12 and 18 months

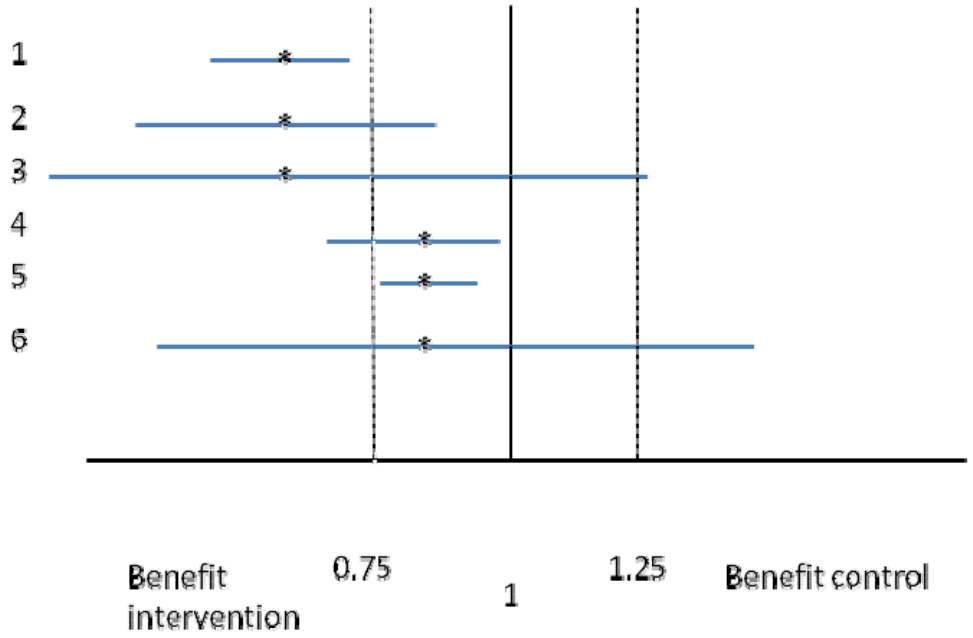
Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
missing outcome data Selective reporting: all of the study's pre-specified outcomes were reported. Analysis: not specified in study report (high risk) Statistical analysis: Wilcoxon-Mann-Whitney rank sum test Baseline differences: baseline comparability for initial area of ulcer also reported (low risk) Study power/sample size: a priori sample size calculation of 80% power was 100 patients per group, the study was underpowered. Setting: care of elderly unit, hospital Length of study: Length of intervention period unclear. 18 month follow-up Assessment of PUs: insufficient information on outcome measurements. Ulcer healing was recorded by weekly camera and	randomised equipment unavailable (not stated how often this occurred)				

Reference	Patient Characteristics	Intervention Comparison	Outcome measures	Effect sizes	Comments
nurse gradings – called 'improvement factor'. Classification of Pus: Torrance classification system Multiple ulcers: if patient had two ulcers areas this counted as two separate ulcers. Timing of outcome assessment similarity: ulcers photographed weekly and patients surveyed at 7 days after trial entry. Not stated when comfort was assessed (low risk)					

13. EVIDENCE STATEMENTS

Figure 78 illustrates how the clinical importance of effect estimates and imprecision were considered in the evidence statements throughout this guideline.

Figure 78 – Six examples of point estimates and confidence intervals for relative risks



The evidence statements are linked with the GRADE-tables and Forest plots included in the evidence plots. The **Point estimates** are used to determine if a result is clinical important. In figure 1 we show 6 examples (more scenario's are possible) of relative risks. The dotted line indicates from which moment a result can be considered as 'clinical important' (i.e. a relative risk <0.75 or a relative risk >1.25). In the figure below this is the case in examples 1,2 and 3. This is of course only a 'rule of thumb' that was discussed with the clinical experts of the GDG and the external expert panel on a case-by-case basis.

The '**Confidence Intervals'** are used to specify the level of **precision or imprecision** of the point estimates. When point estimates are based on small studies, for instance, confidence intervals are wide, indicating a high level of imprecision.

In case of a **high level of precision** the evidence statements are formulated as follows: 'x studies showed intervention is more clinical effective than control' (**situation 1**) or 'x studies showed there is **no** clinical difference in effect between intervention and control" (**situation 5**)

In case of '**serious imprecision**, 'potentially' is used as terminology: X studies showed intervention **is potentially** more clinically effective at preventing pressure ulcers compared to control (**situation 2**); X studies showed there is **potentially no** clinical difference in effect between intervention and control (**situation 4**)

In case of '**very serious imprecision**' the wording '**May be'** is used (**situations 3 and 6**)

The above examples are not set in stone. The formulation of evidence statements could be altered after discussions within the GDG or with the external experts.

Evidence statements will be used as input together with other considerations (e.g. costs; user-friendliness of an intervention,…) to formulate recommendations.

14. ASSESSMENT OF EXISTING GUIDELINES

A scoping review was carried out to prepare the development of the guidelines for the prevention and treatment of pressure ulcers. A three step search strategy was performed to identify clinical practice guidelines on the prevention and/or treatment of pressure ulcers. The first step involved a search of electronic databases were search using index-terms and free-text words. Following databases were included for this search: Medline (OVID), CINAHL (EBSCO-interface), Embase, and the Library of the Cochrane Collaboration. Secondly, websites of guideline developers and wound care organisations were searched using free-text words: American Medical Directors Association (AMDA), Australian Wound Management Association, Canadian Medical Association (CMA), Deutsches Netzwerk für Qualitätsentwicklung in der Pflege (DNQP), European Wound Management Association, Guidelines International Network (GIN), Haute Autorité de Santé (HAS), Institute for Clinical Systems Improvement (ICSI), Joanna Briggs Institute (JBI), Kwaliteitsinstituut voor de Gezondheidszorg (CBO), Landelijke Eerstelijns Samenwerkings Afspraken (LEVA'S), National Institute of Health and Clinical Excellence (NICE), National Pressure Ulcer Advisory Panel and European Pressure Ulcer Advisory Panel (NPUAP and EPUAP), Registered Nurses' Association of Ontario (RNAO), Scottish Intercollegiate Guidelines Network (SIGN), US National Guideline Clearinghouse, Verpleegkundigen & Verzorgenden Nederland, Wound, Ostomy, and Continence Nurses Society (WOCNS), Wounds international, Wounds UK, and 1ste lijn Amsterdam. Thirdly, the reference lists of all retrieved guidelines were searched to identify additional guidelines.

Eighteen clinical practice guidelines[34-50] were identified trough the search of electronic databases and websites of guidelines developers and national/international wound care organizations.

The retrieved guidelines were evaluated by three independent reviewers using the Appraisal of Guidelines Research & Evaluation II (AGREE II). The AGREE II scores, particularly the scores of the domain 'Rigour of development', was used to guide the research team in the decision-making process whether to (1) include, (2) exclude or (3) adapt a guideline. None of the retrieved guidelines were considered to be suitable to be used in an ADAPTE-process. The most common reason for exclusion was the absence of a systematic search for evidence and a lack of quality appraisal of included studies.

It was decided to develop the guidelines de novo. However, the guidelines of NPUAP/EPUAP[39] and NICE[43] were considered as useful to support the formulation of best-practices for our purposes as they both made use of a systematic and extensive consultation process to gather expert opinion.

15. RECOMMENDATIONS: COMMENTS EXPERT PANEL

Item	Recommendations prior to meeting	Comments experts prior to meeting	Min	Max	Mean	Median	% 4 or 5	To be discussed	Decision Taken on Expert meeting
	Treatment Pressure Ulcers								
Tailoring pressure ulcer treatment for each individual - Best practices general	**Pressure ulcer treatment should be a combined approach, tailored to individual needs and situations and should be based on the principles of shared decision making:** **• Treatment should take into account several factors such as the individual's medical condition, the overall plan of care and the individual's preferences. The needs of the individual and the context should be re-assessed regularly;** **• An individual plan of care should be adopted based on assessment data, identified risk factors for delayed healing and individual goals and preferences. The plan is developed in interaction with the individual, informal caregivers and the healthcare professionals. The planned and agreed/refused actions are documented in the individual record and communicated to all relevant caregivers (also in case transition between care settings takes place).**	R3: What is meant with the principles of shared decision making? Interaction with the individual, informal careegivers and healthcare professionals?	4	5	5	5	100%		Pressure ulcer treatment should be a combined approach, tailored to individual needs and situations and should be based on the principles of shared decision making: • Treatment should take into account several factors such as the individual's medical condition, the overall plan of care and the individual's preferences. The needs of the individual and the context should be re-assessed regularly; • An individual plan of care should be adopted based on assessment data, identified risk factors for delayed healing and individual goals and preferences. The plan is developed in interaction with the individual, informal caregivers and the healthcare professionals. The planned and agreed/refused actions are documented in the individual record and communicated to all relevant caregivers (also in case transition between care settings takes place).
Holistic assessment and individual plan of care for patients with pressure ulcers - Best practices general	**Patients with pressure ulcers should receive an initial and ongoing holistic assessment.** **• This assessment should entail the individual's medical condition, the individual's preferences, risk factors for development and deterioration of pressure ulcers (see prevention guideline), the overall plan of care and a focused physical examination including** **o Factors that may affect healing (e.g., impaired perfusion, impaired sensation, systemic infection…….);** **o Vascular assessment in the case of extremity ulcers (e.g., physical examination, history of claudication, and ankle-brachial index or toe pressure);** **o Pain assessment (see below);** **o Ulcer assessment (see below).** **• Reassess on regular basis (at least weekly) and document the findings**	R1: het deel van de titel ("and individual plan of care) past eerder bij 1e best practice // "entail"?// kan the overall plan of care bij de assesment horen (eerder als gevolg van de assessment?)// impaired perfusion wordt meer in detail uitgewerkt in vascular assesslment// is mobility niet even belangrijk? (mis ik trouwens ook elders in de tekst)// het kan toch niet de bedoeling zijn om alles wekelijks te reëvalueren: akkoord voor wond assessment, niet voor vascular assessment R2: Digestive derivation R3: As below is mentionned that nutritional assessment is part of the general assessment, I would add 'nutritional assessmen' here. What is toe pressure? Is it realistic to reasses all the items at least weekly?	3	5	4	4,5	88%	x	Patients with pressure ulcers should receive an initial and ongoing holistic assessment including: - the individual's medical condition, - the individual's preferences, - risk factors for development and deterioration of pressure ulcers (see prevention guideline), - a focused physical examination that includes: o Factors that may affect healing (e.g., impaired perfusion, impaired sensation, systemic infection…….); o Vascular assessment in the case of extremity ulcers (e.g., physical examination, history of claudication, and ankle-brachial index or toe pressure measurement); o Pain assessment (see below); 0 Nutritional assessment (see below); o Ulcer assessment (see below). • Reassess on regular basis and document the findings

	Patients with pressure ulcers should receive an initial and ongoing ulcer assessment. The aim of ulcer assessment is to establish the severity of the ulcer, to develop a treatment plan, to evaluate treatment interventions, to assess for complications and to communicate information about the pressure ulcer to the relevant members of the multidisciplinary team. **• The ulcer assessment should include:** **o Cause of ulcer;** **o Site/location;** **o Stage or category;** **o Dimensions of ulcer and type of tissue;** **o Exudate amount and type;** **o Local signs of infection;** **o Pain;** **o Wound appearance (e.g. wound edges, undermining/tracking (sinus or fistula), necrotic tissue, presence/absence of granulation tissue, and epithelialisation).** **o Surrounding skin;** **o Odour;** **o Dressing appearance (exsudate, color, adhesion, …).** **• A structured approach for ulcer assessment and monitoring should be used. This structured approach could include:** **o The consistent use of uniform measurement methods of the dimensions of the pressure ulcer (i.e. wound length and width, depth, tunneling, and undermining) to facilitate meaningful comparisons of wound measurements across time. The deepest part of the wound should be measured using a sterile probe and care should be taken to avoid causing injury;** **o The use of clinical judgment to assess signs of healing such as decreasing amount of exudate, decreasing wound size, and improvement in wound bed tissue;** **o The use of photographs to monitor pressure ulcer healing over time;** **o The initial assessment of the pressure ulcer category based on a standardized classification system (e.g. NPUAP/EPUAP Classification System).** **o The regular assessment (e.g. PUSH-tool)**	R1: ik mis duration of the ulcer (kan belangrijk zijn naar prognose)// wat wordt bedoeld met cause? (cfr. zal hier druk zijn), eerder vraag naar uitlokkende factor? // bij dressing appearance: eerder absorption of exsudate// care should be taken to avoid injury R2: precedent surgeries, scars R3: Initial assessment of PU should be at the beginning. Why is the PUSH tool mentionned? R5: Advice of matras, semi - fowler, education to the patiënt. R6: Initial assessment to complete with date of appearance of ulcer?	4	5	4	4	100%		Patients with pressure ulcers should receive an initial and ongoing ulcer assessment. The aim of ulcer assessment is to establish the severity of the ulcer, to develop a treatment plan, to evaluate treatment interventions, to assess for complications and to communicate information about the pressure ulcer to the relevant members of the multidisciplinary team. • The ulcer assessment should include: o Cause of the ulcer (e.g. pressure ulcer due to nasogastric tube, oxygen mask; pressure on bony prominences); o Site/location; o Time since pressure ulcer occurence; o Stage or category; o Dimensions of ulcer and type of tissue; o Exudate amount and type; o Local signs of infection; o Pain; o Wound appearance (e.g. wound edges, undermining/tracking (sinus or fistula), necrotic tissue, presence/absence of granulation tissue, and epithelialisation). o Surrounding skin; o Odour; o Dressing appearance (exsudate saturation, color, adhesion, …). • A structured approach for ulcer assessment and monitoring should be used. This structured approach could include: o The consistent use of uniform measurement methods of the dimensions of the pressure ulcer (i.e. wound length and width, depth, tunneling, and undermining) to facilitate meaningful comparisons of wound measurements across time. The deepest part of the wound should be measured using a sterile probe and care should be taken to avoid causing injury; o The use of clinical judgment to assess signs of healing such as decreasing amount of exudate, decreasing wound size, and improvement in wound bed tissue; o The use of photographs to monitor pressure ulcer healing over time; o The initial assessment of the pressure ulcer category based on a standardized classification system (e.g. NPUAP/EPUAP Classification System). o The regular assessment and monitoring (e.g. PUSH-tool; PSST; Sessing scale) with

	with the frequency depending on the condition of the wound and the result of the holistic assessment of the patient. With each dressing change, observe the pressure ulcer for developments that may indicate the need for a change in treatment (e.g., wound improvement, wound deterioration, more or less exudate, signs of infection, or other complications).								the frequency depending on the condition of the wound and the result of the holistic assessment of the patient. With each dressing change, observe the pressure ulcer for developments that may indicate the need for a change in treatment (e.g., wound improvement, wound deterioration, more or less exudate, signs of infection, or other complications). 0 All assessments and actions should be documented and time stamped.

	Any changes in the wound characteristics should be documented, made accessible and communicated to the members of the multidisciplinary team.	R1: any relevant changes (best te specifiëren, anders onwerkbaar om telkens elke verandering door te geven)	4	5	5	4,5	100%		Any relevant changes in the wound characteristics should be documented, made accessible and communicated to the members of the multidisciplinary team.
Primary and secondary prevention of pressure ulcers - Best practices general	**Patients with a pressure ulcer should be considered being at risk to develop additional pressure ulcers. Therefore the general principles of pressure ulcer prevention (see prevention guideline: risk and skin assessment; repositioning) should be applied to: • Prevent the development of new pressure ulcers; • Prevent the pressure ulcers to get worse; • Support the healing process. For nutrition and re-distributing devices specific recommendations for the treatment of pressure ulcers are formulated (see below)**		4	5	5	5	100%		
Pain assessment and management - Best practices general	**Pain assessment and management is part of the general plan of care. The evidence about treatment of pain related to pressure ulcers is not studied as part of this guideline. Therefore we refer to general pain assessment and treatment procedures that are used in the healthcare providers' organisation.**	R1: misschien toch explicieter stellen dat pain assessment en management essentieel is. Kunnen we ervan uitgaan dat er overal procedures zijn inzake pijnmeting en pijn aanpak? Ook nood aan regelmatig herzien van de pijn aanpak (reëvaluatie) R3: Mention pain in the guideline? R5: Must be seen as an important item in woundcare	3	5	4	4	57%	X	Pain assessment and management are of utmost importance and have to be integrated in the general plan of care. The evidence about treatment of pain related to pressure ulcers is not studied as part of this guideline. Therefore we refer to general pain assessment and treatment procedures that are used in the healthcare providers' organisation.
Educating and training of professional care-givers in pressure ulcer treatment - Best practices general	**Training and education should be tailored both to the needs of individual caregivers and to the responsibilities of the group of professionals. At least following components should be considered as part of each educational/training programme: • Holistic assessment and individual patient planning; • Ulcer assessment; • Normal healing process; • Pain assessment; • Recognising inflammation and infection signs; • Exudates management; • Local treatment options, methods for debridement and/or protection of tissue; • Skin protection; • proprerties and effectiveness of different types of dressing; • Positioning, proprieties and effectiveness of different types of support**	R1: moeten alle opgesomde elementen in elke opleiding aan bod komen (zo staat het nu geformuleerd)// knowledge of the normal healing process, assessment of inflammation and signs of infection // wat wordt bedoeld met protection of tissue (wondbodem?)// properties ipv proprieties// wat wordt bedoeld met positioning of support surfaces (is dit de onderlinge vergelijking)// door elkaar gebruik van support surfaces and redistribution device R3: Positioning and repositioning? R6: add: use of devices preventing shear: ex. gliding sheet	4	5	5	5	100%	x	Training and education should be tailored both to the needs of individual caregivers and to the responsibilities of the group of professionals. Consider following components as part of educational/training programmes: • Holistic assessment and individual patient planning; • Ulcer assessment; • Normal healing process; • Pain assessment; • Nutrition • Recognising inflammation and infection signs; • Exudates management; • Local treatment options, methods for debridement and/or protection of tissue; • Skin protection; • Properties and effectiveness of different types of dressing; • Positioning/repositioning, ,• Properties and effectiveness of different

	surfaces.								types of support surfaces (e.g. mattresses; devices for heel elevation; seat cushions).
Nutrition - Recommendation	**A care professional with specific competencies in nutritional care can recommend nutritional supplements for patients with pressure ulcers. As clinical studies did not demonstrate the superiority of one nutritional intervention such as oral nutritional supplements and/or tube feeding over another, we do not recommend a specific complementary diet (type and quantity) with nutritional supplements to contribute to the healing process of pressure ulcers.**	R1: stelling is niet zo duidelijk: 1e zin: advies kan gegeven worden inzake supplementen, verder in zelfde tekst: we do not recommend…	3	5	4	4	83%	x	A care professional with specific competencies in nutritional care may recommend nutritional interventions (e.g. nutritional supplements) for patients with pressure ulcers. As clinical studies did not demonstrate the superiority of one nutritional intervention such as oral nutritional supplements and/or tube feeding over another, we cannot recommend a specific complementary diet (type and quantity) with nutritional supplements to contribute to the healing process of pressure ulcers.
Nutrition - Best practice	**Best practice includes monitoring the nutritional status of individuals with pressure ulcers as part of a general assessment procedure and as an ongoing process throughout an individual's episode of care. Initially, this assessment should include documentation and monitoring of the following factors:• current weight and height;• recent weight loss;• usual eating habits;• recent changes in eating habits and intake;• the adequacy of total nutrient intake (food, fluid, oral supplements, enteral/parenteral feedings).**	R1: wat is "adequacy of total nutrient intake" (slaat dit op het feit of dit al dan niet aan de behoeften voldoet? R(: Controle of the refrigerator shows interesting lacks of not eating healthy (cfr control diabetic patients in homecare)	4	5	4	4	100%		Best practice includes monitoring the nutritional status of individuals with pressure ulcers as part of a general assessment procedure and as an ongoing process throughout an individual's episode of care. Initially, this assessment should include documentation and monitoring of the following factors:• current weight and height;• recent weight loss;• usual eating habits;• (recent changes in) eating habits and intake;• the adequacy of total nutrient intake (food, fluid, oral supplements, enteral/parenteral feedings).

	The nutritional support for the treatment of patients with pressure ulcers should be based on: **• a formal nutritional assessment;** **• general medical condition;** **• patient preferences;** **• an intervention of a care professional with specific competencies in nutritional care to adjust the diet according to the needs of the patients with pressure ulcers, in order to provide sufficient calories, protein, fluid, micronutrients, particularly when dietary intake is poor or deficiencies are confirmed or suspected.**	R1: is dit niet in tegenstelling met de stelling 2 hoger, waar men stelt dat het niet aangeraden wordt. // persoonlijk zou ik ook eerder opteren om geen dieet of supplementen aan te raden, tenzij er manifeste tekorten zijn, welke liefst in het bloed geconfirmeerd zijn R3: what is meant with a formal nutritional assessment? Using a specific form (as MNA). Should this be mentioned in the best practice above? R5: nurses should be able to look at the nutrition (but mostly have no time)	3	5	4	4,5	67%	X	The nutritional support for the treatment of patients with pressure ulcers should be based on: • a formal nutritional assessment, (e.g. Mini-Nutritional Assessment); • general medical condition; • patient preferences; • an intervention of a care professional with specific competencies in nutritional care to adjust the diet according to the needs of the patients with pressure ulcers, in order to provide sufficient calories, protein, fluid, micronutrients, particularly when dietary intake is poor or deficiencies are confirmed or suspected.
Redistributing devices - recommendation	**• The use of pressure redistributing devices (low-tech constant low pressure surfaces or high-tech support surfaces) is recommended for individuals who have a pressure ulcer. Redistributing devices should be used in combination with regular repositioning.**	R1: support surface vs. redistributing devices. R5: semi-fowler. And if one is paralised, you know he must buy a hight tech support in case of first buying a low tech matras	2	5	4	4,5	88%		• The use of pressure redistributing devices (low-tech constant low pressure surfaces or high-tech support surfaces) is recommended for individuals who have a pressure ulcer. Redistributing devices should be used in combination with regular repositioning.
	• As clinical studies did not demonstrate the superiority of one pressure redistributing device over another (e.g. air-fluidised therapy, alternating-pressure mattress), decisions about which pressure redistributing device to use should be based on an overall assessment of the individual, including wound evolution and off loading possibilities, level of risk, comfort and general health state. Appropriateness of each device in different care settings, and other considerations (e.g. cleaning, type of mattress cover, cardiopulmonary resuscitation-function, disinfection and cost) can contribute to guide the choice.	R1: laatste zinsnede: should be taken into account R3: Can there be a different level of risk in patients with a PU? The very strict criteria for the evidence result in no difference in the different suport surfaces.	3	5	4	4	86%		• As clinical studies did not demonstrate the superiority of one pressure redistributing device over another (e.g. air-fluidised therapy, alternating-pressure mattress), decisions about which pressure redistributing device to use should be based on an overall assessment of the individual, including wound evolution and off loading possibilities, level of risk, comfort and general health state. Appropriateness of each device in different care settings, and other considerations (e.g. cleaning, type of mattress cover, cardiopulmonary resuscitation-function, disinfection and cost) can contribute to guide the choice.
Redistributing devices - best practice	**When pressure ulcers deteriorate or fail to heal, or when there is an increase in risk status:** **• the professional caregiver should consider replacing the existing support surface with one that will reduce time of applied pressure and/or improve pressure redistribution, reduce shearing forces, and control microclimate (heat and moisture control) for the individual.** **• Preventive interventions and local wound care should also be intensified.** **• Before replacing the existing mattress:** **o Evaluate the effectiveness of previous**	R1: change ipv replace// wat wordt bedoeld met microclimate? Wat wordt bedoeld met intensifiëring van wondzorg? R3: I think it is difficult for the professional caregivers to consider the support surfaces as scientific literature gives no result as clinical studies did not demonstrate the superiority of one pressure redistributing device over another. Is microclimate important in healing PU? I cannot find the rationale in the scientific document. Should	3	5	4	4	86%		When pressure ulcers deteriorate or fail to heal, or when there is an increase in risk status: • the professional caregiver should consider changing the existing redistributing device with one that will reduce time of applied pressure and/or improve pressure redistribution and reduces shearing forces for the individual. • Preventive interventions and local wound care should also be intensified. • Before replacing the existing mattress: o Evaluate the effectiveness of previous and current prevention and treatment plans.

	and current prevention and treatment plans.	repositioning frequence not be mentioned? R6: crtl good functioning of (high-tech) device before replacing							
Debridement - best practice	**• Debride devitalized tissue within the wound bed or edge of pressure ulcers when appropriate to the individual's condition and consistent with overall goals of care.**	R1: when the individual's condition allows it	4	5	5	5	100%		• Debride devitalized tissue within the wound bed or edge of pressure ulcers when appropriate to the individual's condition and consistent with overall goals of care.
	• If clinicians consider to debride pressure ulcers, the choice of the debridement method(s), chemical, bioactive, surgical , autolytic, enzymatic, mechanical debridement) will be based on: the individual's condition; goals of care; ulcer/peri- ulcer status; type, quantity, and location of necrotic tissue; care setting; availability of products for debridement and professional accessibility/capability.	R1: komma te veel na debridement/// know-how ipv capability	4	5	5	4,5	100%		• If clinicians consider to debride pressure ulcers, the choice of the debridement method(s), chemical, bioactive, surgical , autolytic, enzymatic, mechanical debridement) will be based on: the individual's condition; goals of care; ulcer/peri- ulcer status; type, quantity, and location of necrotic tissue; care setting; availability of products for debridement and professional accessibility/capability.
Dressing & topical agents - recommendation	**We suggest to offer an optimal wound healing environment by using hydroactive dressings/topical agents in preference to basic non hydroactive dressing types . • As clinical studies did not demonstrate the superiority of one type of hydroactive dressing/topical agent over another, decisions about which type of dressing/topical agents to use should be based on: o ulcer assessment (condition of wound: issue, exudate, depth, degree of infection, odor, pain, wound edges and wound environment,); o general skin assessment; o treatment objective; o dressing characteristics; o previous positive effect of particular dressing/topical agent; o manufacturer's indications for use and contraindications; o risk of adverse events; o and patient preference (lifestyle, abilities and comfort).**	R1: We suggest? Eerder met passieve zin // wat is hydro-active dressing (wordt active bedoeld? Eerder The use of active wounddressings enhances wound healing and is preferred in comparison to basis, passive dressings. // wat zijn topical agents (cfr. onduidelijk gedefinieerd in PDF tekst)// cave manufacturer's indication for use and contraindications (is dit de meest betrouwbare bron?); hoe kan je risk of adverse events hier interpreteren? is het het risico van het verband om een adverse event te veroorzaken?// wordt comfort niet steeds nagestreefd? R3: Previous positive effect of particular dressing/topical agent: experience based? Not completely clear how to select a dressing/topical agent based on the different items. Are financial considerations relevant?	3	5	4	4	71%	X	We suggest to offer an optimal wound healing environment by using modern dressings and topical agents (e.g. hydrocolloids, hydrogels, hydrofibres, foams, alginates, silver dressings) in preference to basic dressing types – (e.g. gauze, paraffin gauze and simple dressing pads) . • As clinical studies did not demonstrate the superiority of one type of modern dressing and topical agent over another, decisions about which type of modern dressing/topical agent to use should be based on: o ulcer assessment (condition of wound: issue, exudate, depth, degree of infection, odor, pain, wound edges and wound environment,); o general skin assessment; o treatment objective; o dressing characteristics; o previous positive effect of particular dressing/topical agent; o manufacturer's indications for use and contraindications; o risk of adverse events;

									o and patient preference (lifestyle, abilities and comfort).
Indications for surgery to close pressure ulcer - best practices	**Referral for surgical interventions for patients with pressure ulcers should be based on:** **• ulcer assessment;** **• level of risk (anaesthetic and surgical intervention);** **• general medical condition;** **• competing care needs;** **• failure of previous conservative management interventions.**	R1: geldt dit ook voor debridement? Wat wordt bedoeld met competing care needs? R2: previous evaluation of risks of relapse (irreversible cause of pressure ulcers or reversible (sub)acute state, efficiency and compliance with the preventive mesures) R3: level of which risk? Level of risk of the anaesthetic and surgical intervention?	4	5	4	4	100%		Referral for the surgical treatment of pressure ulcers should be based on: • level of risk (anaesthetic and surgical intervention; recurrence) • patient preference (lifestyle, abilities and comfort) • ulcer assessment (e.g. anatomical site, staging) • general skin assessment • general health status • competing care needs • assessment of psychosocial factors for the risk of recurrence • previous positive effect of surgical techniques, and • failure of previous conservative management interventions.
Systemic agents-best practices	**In the presence of systemic and/or local clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy will be considered at the discretion of the treating physician.**	R1: is er niets steeds nood aan systemische antibiotica als er echt infectie is? bloedonderzoek en beeldvorming kan hier nuttig zijn.	3	5	4	4	88%		In the presence of systemic and/or local clinical signs of infection in the patient with a pressure ulcer, systemic anti-microbial therapy will be considered at the discretion of the treating physician.

Adjuvant-recommendation	**As clinical studies failed to demonstrate the clinical effectiveness of negative pressure wound therapy, electrotherapy, light therapy, hyperbaric oxygen therapy, we cannot recommend any of these technologies as routine treatments for pressure ulcers.**	R4: Réserve sur la formulation de "non" recommandations et risque que la liste ne soit pas exhaustive… R5: NPTW is ideal to prepare a chirurgical closure or to loose devitalised tissue. Scientific proove is needed. R7: pas en routine pour la plupart des adjuvants mais la pratique de la pression négative utilisée par des experts pouvant poser les indications adéquates , des objectifs précis et un suivi performant s'avère efficace	2	5	4	3	38%	X	As clinical studies failed to demonstrate the clinical effectiveness of negative pressure wound therapy, electrotherapy, light therapy, hyperbaric oxygen therapy, we cannot recommend any of these technologies as routine treatments for pressure ulcers.

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