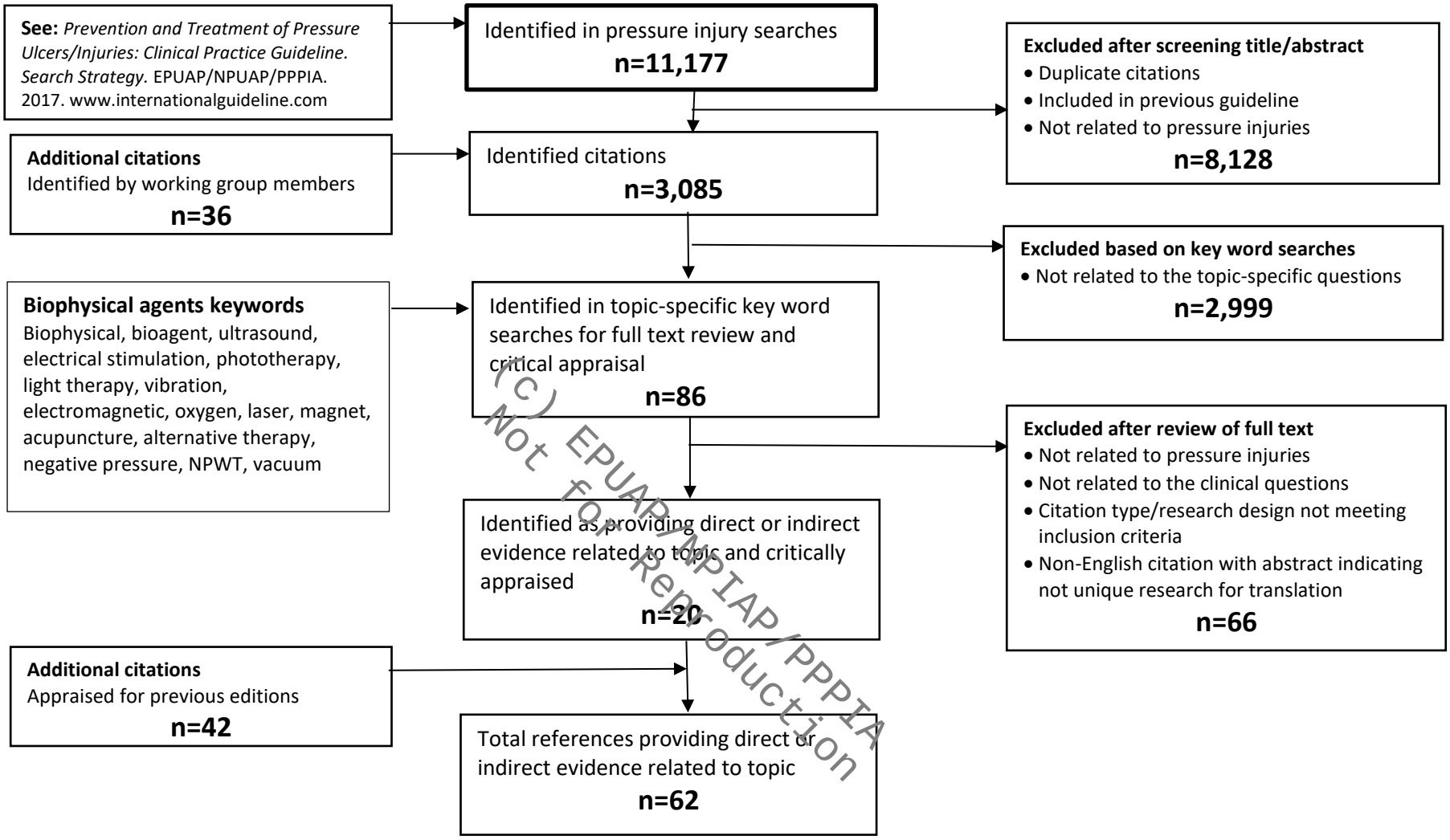
Search results for 2019 International Pressure Injury Guideline: Biophysical agents



European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline. The International Guideline. Emily Haesler (Ed.). EPUAP/NPIAP/PPPIA; 2019

Articles Reviewed for International Pressure Injury Guideline

The research has been reviewed across three editions of the guideline. The terms pressure ulcer and pressure injury are used interchangeably in this document and abbreviated to PU/PI. Tables have not been professionally edited. Tables include papers with relevant direct and indirect evidence that were considered for inclusion in the guideline. The tables are provided as a background resources and are not for reproduction.

European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline. The International Guideline. Emily Haesler (Ed.). EPUAP/NPIAP/PPPIA; 2019

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
Clinical Question 1: Electrical Stimulation							
(Polak et al., 2017)	RCT to determine if electro-stimulation (ES) by high voltage monophasic pulsed current (HVMPC) differs in pressure injury healing outcomes if delivered through the cathode (CG) only compared to a combination of cathode and anode (CAG) current delivery	Participants were recruited in three nursing homes (n=63) Inclusion criteria: • Age >60 years • High risk score for pressure injuries • Category/Stage II or III pressure injury of up to 50cm² present • Duration of pressure injury 1 to 12 months • Located in the pelvic girdle Exclusion criteria: • Could not receive ES • Conditions impeding wound healing • Critical wound infection Participant characteristics: No statistical differences between the two groups	Participants were randomized to one of three groups: • Electrostimulation (twin-peak monophasic pulse, 154 µs, 100pps, 0.25 A 50mins/day. 5days/week) delivered through the cathode as mode of delivery attended 5 times/week in 50 minute sessions (n=23) • Electrostimulation with a combination of cathode and anode mode of delivery – regimen as for cathode only group except the cathode intervention was delivered for 1 week, followed by anode delivery for 5 weeks (n=20) • Control group receiving placebo electrostimulation with no current delivered (n=20)	• 7 measurements done before trial started • Wounds measured once a week in the duration of the trial • Outcome was healing achieved over total time and time until 50% healing was achieved • Follow up period of 6 weeks	**Percent area reduction at six weeks** Cumulative wound surface area reduction was 82.34% (95% CI 70.06 to 94.63) in cathode-only group compared with 70.77% (95% CI 53.51 to 88.04) in cathode-anode group. These reductions were significantly greater than in the placebo ES group (40.53%; 95% CI 23.60 to 57.46); p=0.0006 and p =0.0124 respectively. The cathode-only group and the cathode-anode group were not statistically significantly different regarding treatment results (p=0.9932). **Time to 50% approximation** Cathode only group had fastest time to 50% healing (1.92 weeks, 95% CI 1.62-2.23) compared to cathode-anode group (2.60 weeks, 95% CI 2.08-3.13) and placebo group (10.60 weeks, 95% CI 7.25-13.95). The differences were statistically significant between the cathode ES group and the placebo ES group (p <0.05) and between the cathode+anode ES group and the placebo ES group (p <0.05). But they	• Triple blinded trial • Outcome measure of 50% closure is not a strong indicator of effectiveness • Short observation time of 6 weeks failed to elucidate ideal regimen • Approx 9.3% dropped out of the treatment groups (not different from placebo group)	**Level of Evidence: 1** **Quality: High**

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					were not statistically significant between the two groups in which ES was applied (p>0.05). **Complete wound closure** Highest ratio of final wound closure was achieved by cathode group and lowest in the placebo group, but there was no significant difference between the two treatment groups **Author conclusions: HVMPC 5 times a week with the cathode as mode of delivery or the cathode & anode combination, are both effective in treatment of Category/Stage II or III pressure injuries.**		
(Polak, Kloth, et al., 2016)	RCT To determine if electro-stimulation (ES) by high voltage monophasic pulsed current (HVMPC) delivered through the cathode (CG) improves pressure injury healing times	• Participants were recruited in two nursing homes (n=49) Inclusion criteria: • Age >60 years • High risk score for pressure injury development • Category/Stage II or III pressure injury of up to 50cm^2 present • Duration of pressure injury 1 to 12 months • Located in the pelvic girdle Exclusion criteria: • Could not receive ES • Conditions impeding wound healing • Critical wound infection	Participants were randomized to receive either: • HVMPC electrostimulation delivered through the cathode as mode of delivery (ES group, n=35) or • placebo electrostimulation with no current delivered(n=24)	• 7 measurements done before trial started • Wounds measured once a week in the duration of the trial • Outcome was healing achieved over total time and time until 50% healing was achieved • Follow up period of 6 weeks	**Percent reduction in wound size** After 1 week the pressure injury area reduction in the ES group was 35% compared to 17.07% in the control group (p<0.032). **Decreases in wound surface area** Largest decrease of wound surface area at weeks 1, 2 and 3 with 35%, 32.78% and 45% achieved respectively in the ES group when compared to the control group where wound surface area reduction was 17.07%, 12.78% and 20.32% on weeks 1, 2 & 3. (p<0.032) **Author conclusions: HVMPC delivered five times per week with the cathode proves effective in treatment of Category/Stage II and III pressure injuries**	• Outcome measure of 50% closure is not a strong indicator of effectiveness • Short observation time of 6 weeks failed to elucidate ideal regimen • 16.7% drop out from treatment group (similar to placebo group)	**Level of Evidence: 1** **Quality: High**

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		Participant characteristics: • No statistical differences between the two groups					
(Karsli, Gurcay, Karaahmet, & Cakci, 2017)	RCT comparing high voltage ES to low frequency ultrasound for healing pressure injuries	Participants were recruited in a medical clinic Turkey (n=35, 8 excluded due to concurrent medical diagnoses) • Inclusion criteria: • Hospitalized for neurologic rehabilitation. • Category/Stage II to IV pressure injury Exclusion criteria: • Cardiac dysrhythmia or pacemaker, epilepsy, osteomyelitis, pregnancy, malignancy, and/or uncontrolled autonomic dysreflexia. Participant characteristics: • Majority had SCI, (TBI, CVA, myelitis and combination of SCI/TBI) • Duration of neurologic disease, Smoking, voiding status, ambulation level not statistically significant different between groups • Baseline severity of pressure injuries were significantly different, with the HVES group having significantly worse profile in terms of classification	Participants were assigned to either: • HVES applied using twin peaked monophasic pulsed current with 100PPS 10-50-100 us pulse width and 2 second ramp up time in continuous mode. Intensity between 50 and 150 V. 60 minute duration 3x per week x 4-12 weeks (n=25), or • Ultrasound at 3 MHz 20% duty cycle and 0.3 W/cm^2 frequency 1 MHz in continuous mode in the wound bed for 1-2 mins. 1-1.5 W/cm^2 dose for 2-3 mins around the wound (n=22)	• Did not specify who was assessing wounds if consistent. • Did utilize wound evaluation scales to calculate dimensions • NPUAP Staging system • Follow up 4 to 12 weeks.	**Wound surface area change** • 43% decrease in wound surface area in HVES group versus 63% WSA decrease in US group • Analysis based on Category/Stage and intervention group showed significant improvements in Category/Stage II, III and IV pressure injuries in both treatment groups (baseline compared to follow-up) • Wound surface area showed significant decrease in HVES group over time (p<0.001) and in US group over time (p<0.001) **Regression analysis on factors that impact wound healing** Level of ambulation (r=4.365 P<.001), pretreatment Category/Stage (r=3.335 P=.002) and smoking (95% CI 0.535 to 2.046; P = 0.001) all impacted healing outcomes **Conclusions: Both groups demonstrated statistically significant improvement in wound surface area with difference in groups likely due to more advanced stage/increased initial surface area in the HVES group.**	• No control group • All pressure injuries were Category/Stage IV were in the HVES group which may alter realistic findings	**Level of Evidence: 1** **Quality: Low**

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		(p=0.018) and wound surface area (p=0.036)					
(Lawson & Petrofsky, 2013)	Comparative study to compare a biphasic and monophasic wave form electrical stimulation for promoting blood flow and healing rates of chronic stage III and IV pressure injuries over 4 weeks of treatment	Participants were recruited at an outpatient wound center in US (n=40 participants, n=20 had pressure injuries) Inclusion criteria: • English speaking adult • non-smoking, • only one wound • > 40 years • no diabetes plus a Category/stage III or IV pressure injury Exclusion criteria: • Pacemaker • peripheral vascular disease • long term radiation therapy, steroid therapy, or chemotherapy • Pregnancy • poor nutritional status • prior wound treatment beyond traditional interventions	• All groups received sharp debridement, hydrogel to wound bed, wet-to-dry sterile gauze, 3 times per week. • All groups received electrical stimulation via Challenge 8000 device for 30 minutes in a 32°C room. The waveform was generated by a Biopac MP 100 (Biopac Systems, Goleta, CA) data analysis system delivering pulse width of 200µs, frequency 30Hz and current up to 20mA. • Participants received either: ○ biphasic waveform ○ or monophasic waveform	• wound healing over 4 weeks using unreported methods • Blood flow using Laser Doppler flow meter at 5 and 10 mins pre-stimulation and at 5, 10, 15, 20, 25 and 30 minutes during stimulation and at 10 minutes post stimulation, at initial treatment, 2 weeks and 4 weeks. • Follow up for 4 weeks	**Percent wound healing over 4 weeks** No significant difference between monophasic and biphasic groups for percent wound healing **Blood flow** Pressure injuries demonstrated significantly greater blood flow with biphasic current than monophasic at initial test ($p<0.001$) and week 2 ($p<0.001$) **Author conclusions: Biphasic current electrical stimulation was significantly more effective in healing neuropathic wounds vs pressure ulcers. Healing rate not significant when comparing the two currents for pressure ulcers.**	• Study also included 20 participants with neuropathic ulcers, results not reported here but neuropathic group had significantly better healing with biphasic ES • No blinding • Methods of outcome assessment not reported	**Level of Evidence: 2** **Quality: Moderate**
{Jercinovic, 1994 #17864}	RCT	Participants were people with SCI and PU (n=73 people, n=109 ulcers) Characteristics: mean 36 years, SD 15 years Control group had larger ulcers at baseline but ES	• Individuals were randomized to received either: ○ Low frequency, biphasic, asymmetric, charge-balanced pulsed current electrical stimulation(2 hours/day, 5 times/week) plus standard wound care. Delivered by two	• Trial duration 4 weeks • wound area values evaluated using exponential and linear fitting • Weekly wound area • changes in wound depth and tissue appearance	**mean healing rate** • The electrical stimulation group had mean healing rate of 2.2% (SD 2.1) per day using linear fitting method or 5.7% (SD 7.1) per day using exponential fitting method • The control group had mean healing rate of 1.5% (SD 1.7) per	• Unclear how many completed study • No information on randomization and allocation concealment • No double blinding	**Level of evidence: 1** **Quality: low**

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		group had ulcers with more complex tissue characteristics	electrodes placed on healthy skin approx 3cm from ulcer edge. Frequency 40pps, pulse duration 205us, amplitude individualized (up to 35mA) to achieve minimal muscle contraction, or ○ Standard wound care • For all patients, initial debridement, application of standard dressing two or more times per day and antibiotic as required		day (linear) or 2.7% (3.6) per day (exponential)	• No statistical comparisons of results • Severity of pressure injuries is not reported	
{Franek, 2012 #461}	RCT	n=57 (7 did not complete treatment and not considered in analysis) Inclusion: •Physician's discretion •Non healing Category/Stage II or III pressure injuries Exclusion: •Diabetes mellitus •ABPI < 0.9 •cancer Characteristics: • All PUs on lower extremities • Mean age 56 to 59 yrs • Primarily stage II PU • Mean PU area 3.97 to 4.54cm^2 • Mean PU duration 2 to 3 months	All participants received standard care: Range of wound dressings (e.g. non-adhesive, hydrogels, moist gauze), topical treatments, pressure relieving surface if required. Participants received either: • Only standard care (n=24) • High-Voltage Electrical Stimulation (HVES) at 100V;100 µs; 100 Hz for 50 minutes once daily, five times a week (n=26)	• Wounds photographed on weekly basis and digital planimetry to determine wound area • Wound area measured using callipers at deepest point • Patient were followed until healing for a maximum of 6 weeks	• Mean PU areas decreased significantly in both groups • Mean PU area was statistically significantly different from week 3 (p=0.008) • Average granulation area increase was statistically significantly superior in treatment group only in week 5 (p=0.02) • Week 6 surface area change was 88.9% (SD=14) the treatment group and 44.4% (SD= 63.1) in the control group (p=0.00003) • Correlation coefficients between changes in wound surface area, longest length and longest width were R=0.96 and R=0.98 in the treatment and R=0.94 and R=0.89 in the control	• Study length of 4 years • No blinding • Lower extremity PU only • Variety of other treatments may not have been consistent between groups	**Level of evidence: 1** **Quality: moderate**
{Franek, 2011 #462}	RCT	n = 58 participants	All patients received standard care: local bath of potassium	• Per cent change in wound surface area	• Both groups had statistically significant reduction in (p≤0.0001)	• Non-blinded study	**Level of evidence: 1**

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		Inclusion: •Stage I, II or III PU Exclusion: •SCI or paralysis •ABPI <0.9 •Diabetes mellitus •Arrhythmias •Post-steroid therapy Characteristics: • Mean age 59 to 60 yrs • Primarily leg PU • Mean PU duration 2 to 3 mths • Mean PU area 4.5 to 5cm^2 • Mean PU volume 0.04cm^3 • About 50% participants were smokers	permanganate, compresses of fibrolan, colistin, iruxol, and wet dressings containing 10% sodium chloride Participants received either: • Standard care only (n=29) • Monophasic pulsed current generator high voltage monophasic stimulation (HVMS) at 100 µs, 100 Hz, 100 V once daily, five times a week for 6 weeks (n=29)	• Per cent change in wound depth • Per cent change in wound volume • Per cent change in wound length	wound surface area, wound volume, wound depth, wound length and pus covered area • In HVMS group 8/29 PUs healed versus 4/29 PUs in control group • Relative changes : ○ total surface area: 85.38% in HVMS group versus 40.08% in control group) ○ Length: 71.22% in HVMS group versus 30.38% in control group ○ Width: 76.09% in HVMS group versus 32.48% in control group ○ volume 20.69% in HVMS group versus 9.39% in control group • The Gilman Index (0.64 cm in HVMS group versus 0.28 cm in control group) indicated a difference in favor of group A (p≤0.001) • More efficient decrease of pus and greater granulation growth were observed in group A but difference was not statistically significant (p=0.07) • In HVMS group the correlation between change of total area and length of ulcers was 0.85 (p=0.002), total area and width was 0.84 (p=0.002), and total area and volume was 0.66 (p=0.01). • In control group the correlation between change of total area and length of ulcers was 0.55 (p=0.02), total area and width was 0.54 (p=0.02), total area and volume was 0.49 (p=0.04).	• Wide variety in participants and PU characteristics • Authors unable to confirm the mechanism by which HVMS influences healing	**Quality: moderate**
{Houghton, 2010 #466}	Single-blind RCT	Participants (n=67 screened, n=34 included) with SCI living in the community	Patients were stratified based upon wound severity and	Percentage decrease in wound surface area over	• Percentage decrease in wound surface area over 3 months significantly greater in EST group	• Small single-blinded study sample size	**Level of evidence: 1**

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		Inclusion: • Stage II to IV PU between 1 and 20cm^2 of at least 3 month duration Exclusion: • Serious comorbidity • Contraindications to electrical stimulation therapy (e.g. pacemaker) • Deep tunneling PU • Three or more abnormal blood values Characteristics: • Mean age 50 years • primarily stage IV PUs • mean wound duration 1.2 to 3 years	duration to four groups prior to randomisation. All participants received standard wound care of nutritional assessment and program, activity program, blood analysis, customised wound care, seating cushion. Participants received either: • Standard wound care (SWC) • Electrical stimulation therapy (EST): - Silver dressing regimen to facilitate therapy - 2 to 30 30 minute education sessions - Individualised electrical stimulation (generally single electrode placed directly over wound with larger dispersive electrode placed 20cm away from wound), twin-peak monophasic pulsed current with 50µs pulse duration at 50 to 150V intensity. 40 minutes therapy followed by 20 minutes with no therapy for an 8 hour cycle daily.	3 months assessed by digital planimetry Proportion of wounds achieving at least 50% reduction in wound surface area Wound appearance assessed using a photographic wound assessment tool Assessed monthly over 3 months then followed for 4 months to assess recurrence.	(70% ± 25% versus 36% ± 61%, p=0.048) • All stage II PUs healed in both groups • Proportion of wounds achieving at least 50% reduction in wound surface area significantly greater in EST group (80% versus 36%, p=0.02) • photographic wound assessment tool score was improved in more PUs in the EST group (75% versus 44%, p=0.07) • Adverse reactions included red itchy skin beneath dispersive electrode (resolved within 24 hours)., one patient acquired a burn. • Mean treatment time was 3.0±1.5 hrs per day (lower than recommended time) • 8 subjects in each treatment group had recurrent or new PUs develop within 4 months of closure	• EST treatments were applied in combination with silver dressings • High PU recurrence rate	**Quality: moderate**
{Gentzkow, 1993 #189}	Baseline-controlled study exploring pulsed electrical stimulation for healing Category/Stage III and IV pressure injuries	Participants were recruited at a spinal cord injury center, a long term care facility and a specialist pressure injury center, all in US (n=61) Inclusion criteria: • All participants had a lead in period of 4 weeks with baseline treatment only.	• In lead in phase, pressure injuries received moist saline gauze only. Whirlpool or hyperbaric oxygen (this is the comparator group) • For pressure injuries not progressing, treatment with pulsed electrical stimulation using Dermapulse® for two 30-minute sessions per day,	Improvement in pressure injury stage or wound character at 2 weeks Follow-up of 4 weeks	60.7% improved after 2 weeks of electrical stimulation (p<0.000001) 80.4% improved after 4 weeks of treatment Complete healing achieved in 23% of pressure injuries No safety issues occurred	• Unit of measurement was the pressure ulcer, not the individual (some participants had 2 pressure injuries) • Used reverse staging as a	**Level of evidence: 3** **Quality: low**

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		Only pressure injuries without improvement in this phase received electrical stimulation. • Eschar, necrotic or exudative wounds were selected Exclusion criteria: • Pace maker • Active phlebitis • Osteomyelitis, thrombosis, malignancy, epilepsy • Long-term steroids, chemotherapy, radiation • Pregnancy Participant characteristics: • Age range 25-100 (mean 62-63) • 37.7% of pressure injuries were less than 2 months in duration,, 26.2% unknown duration, 18% >6 months duration • 62.3% were Category/Stage IV pressure injuries and remainder were Category/Stage III pressure injuries	monophasic, square wave current in pulse duration of 140 µsec, 128 pulses per second at 35 milliamps (n=21) • Treatment continued for at least 2 weeks but up to 4 weeks			measure of healing • Comparison was baseline treatment	
{Kloth, 1988 #257}	RCT exploring pulsed electrical stimulation for healing Category/Stage IV pressure injuries	Participants were recruited (n=16) Participant characteristics: • Age range 20-89 years (mean 66-77) • Ulcers had previously been unresponsive to treatments	All wounds debrided enzymatically or manually Participants were randomized to receive either • pulsed electrical stimulation high voltage, monophasic at 105Hz with intraphase duration of 50µsec and voltage just	Methods of wound measurement not reported	**Percent healing per week** • Electrical stimulation had greater healing per week than control group (44.80% versus –11.59%) **Complete healing** • All wounds in treatment grouped achieved 100% healing after mean 7.3 weeks of treatment	• Methods of randomization not valid • No allocation concealment • Inclusion/exclusion criteria not reported	**Level of evidence: 1** **Quality: low**

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			sufficient for visible muscle contraction (n=9) or • sham treatment for 4,5 or 16 weeks (n=7) • Treatment for 45 minutes daily, five days/week		• No pressure injuries in control group completely healed	• Very small sample, likely not sufficient to measure significant effect •	
{Wood, 1993 #450}	RCT exploring pulsed electrical stimulation for healing Category/Stage II and III pressure injuries	Participants were recruited in four centers (n=74) Inclusion criteria: Chronic pressure injury with no sign of improvement for preceding 5 weeks Participant characteristics: • Mean age 74-75 years • Pressure injury duration average 4.9 months in control group and 5.5 in treatment group	Participants were randomized to receive either • pulsed low intensity direct current electrical stimulation at 300-600µA (n=43) or • sham treatment (n=31)	Surface area calculated from cross-section diameters and from wound tracings transferred to a grid Response was considered as a decrease in surface area of at least 80% after 8 weeks Followup of 8 weeks	**Percent healing per week** Electrical stimulation had greater healing per week than control group (11.04% versus 4.10%, p<0.0001) **Complete healing** 58% in treatment group healed by 8 weeks compared with 3% in control group (p<0.001)	• Double blinded study • Method of randomization and allocation concealment not reported • Inclusion/exclusion criteria not clear	**Level of evidence: 1** **Quality: moderate**
{Griffin, 1991 #202}	RCT exploring pulsed electrical stimulation for healing pressure injuries	Participants with SCI were recruited in a SCI center in US (n=20 randomized, n=17 completed and analyzed) Inclusion criteria: • SCI • Pelvic pressure injury of Category/Stage II to IV Exclusion criteria: • Pacemaker • Cardiac diseases Participant characteristics: All males Mean age 26-32 years	Participants stratified based on Category/Stage of pressure injury then were randomized to receive either • High voltage pulsed electrical stimulation delivered for 1 hour/day for 20 consecutive days with frequency at 100pps, intensity at 200V (n=8) or • sham treatment (n=9)	Measurements of wound at baseline and days 5,10,15 and 20 Wound tracings projected to grid to calculate surface area	**Healing outcomes** • Treatment group showed significantly better change in wound surface area at day 5 (p=0.03), day 15 (p=0.05) and day 20 (p=0.05) compared with sham treatment group • 100% of Category/Stage II pressure injuries in treatment group healed completely • After 20 days, median change was –80% in treatment group versus –52% in control group	• Sample size calculation indicated a need for 10 per group • 2 patients withdrew due to medical complications and 1 withdrew to have surgical repair) • Methods of randomization and allocation concealment not reported	**Level of evidence: 1** **Quality: low**

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		Individuals in treatment group had SCI duration significantly longer (P<0.05)					
{Stefanovska, 1993 #401}	Experimental study reporting outcomes when using electrical stimulation to promote healing	Participants were people with SCI received electrical stimulation for pressure injuries in Slovenia (n=170 treated, n=150 with complete data for analysis but data only presented for n=88)	• Participants received either: ○ ES with direct currents with amplitude 600µA for two hours daily plus standard wound care ○ ES with AC low frequency pulsed currents, biphasic with pulse duration 0.25ms and repetition rate of 40Hz, plus standard wound care ○ Control group receiving standard wound care only • For delivering ES in both groups the electrodes were placed on healthy skin on either side of the wound	• Wound area and wound depth • Methods of measurement not reported	• AC electrical stimulation group showed significantly greater rate of healing compared to control group (p=0.003) • DC group was not significantly different to control group for rate of healing • AC electrical stimulation was less effective for wounds with initial greater surface area • DC electrical stimulation was less effective for wound with initial greater depth **Author conclusions: AC electrical current has a stronger influence on healing than other wound healing parameters, although results are not consistent across participants**	• Unclear how individuals were assigned to groups • Does not stay how wounds were measured • Contains detailed discussion on how to measure wound healing rate • Blinding not discussed • Unclear exactly how many participants, DC group appears to have much less	**Level of evidence: 2** **Quality: low**
{Baker, 1996 #57}	RCT comparing different types of electrical stimulation	Participants were inpatients and outpatients with SCI (n=80 participants with n=192 pressure injuries) Inclusion criteria: • pressure injury • Spinal Cord Injury Participant characteristics: Age range 17-76 years Did not differ significantly on duration of SCI disease or biochemical results	• Participants were randomized to receive: ○ Asymmetric biphasic electrical stimulation, phase duration 100µsec, 50 pulses/second (n=20 with n=67 wounds) ○ Symmetric biphasic electrical stimulation, phase duration 300µsec, 50 pulses/second (n=21 with n=58 wounds) ○ Microcurrent, 4mA amplitude, 10µsec, 1 pulse/second (n=20 with n=42 wounds)	Pressure injury healing Acetate wound tracings and wound volume performed weekly for inpatients and 2-4 weekly for outpatients	• The Asymmetric electrical stimulation was associated with significantly more individuals achieving a good response (61%) compared with good responders for Microcurrent group (56%) (p<0.02) • Asymmetrical (61%) and Symmetrical (70%) had similar amount of good responders but the percent healing per week was higher in the asymmetric group (63.7%±7.2 versus 50.6%±5.6, p=not reported)	• Blinded study • Does not report methods of randomization or allocation concealment • Treatment as inpatients vs outpatients may have led to other variations in care • Level of analysis was the wound, not the patient	**Level of evidence: 1** **Quality: low**

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			○ Control group receiving sham treatment (n=19 with n=25 wounds) • All groups had three treatment sessions of 30 minutes each		**Author conclusions: Asymmetric electrical stimulation is most effective for promoting healing**	• Approx 25% of participants withdrew • Does not report pressure injury severity • Statistical analysis limited to participants described as "good responders"	
Clinical question 2: Pulsed electromagnetic therapy							
{Gupta, 2009 #464}	Double-blind RCT	Participants with neurological disorders who were hospitalized(n=12) Inclusion: • Category/Stage III or IV pressure injuries Excluded: • Osteomyelitis • Non-ischaemic pressure injuries Characteristics: • Mean age 27 to 28 years • Mean duration of PU 103.75±113.70 days • A total of 24 PUs were included (13 Category/Stage IV and 11 Category/Stage III)	• All pressure injuries were debrided and treated with antibiotics as required prior to study. • Both groups were given standard wound care including daily dressing changes. • Participants randomised either: ○ PEMT (n=6, 13 pressure injuries) administered in 'Pulsatron' delivering low frequency PEMF therapy (1Hz frequency sine waves with 30 miliampere current intensity). ○ Sham therapy (n=6, 11 pressure injuries) in 'Pulsatron' without machine switched on • Therapy was administered for 30 sessions, 5 days a week for 6 weeks, for 45 minutes/session.	Wound healing assessed based on Bates-Jensen wound assessment (BJWAT) tool score Staging assessed on NPUAP criteria	• Significant improvement in BJWAT scores in both PEMT group (p=0.001) and sham group (p=0.003) but no significant difference between the two groups (p=0.361) • Both groups achieved significant healing of pressure injuries assessed on NPUAP staging criteria (PEMF group p=0.008 and sham group p=0.014) but no significant difference between the two groups (p=0.649)	• Small sample size • Non-standard assessment of healing outcomes	**Level of evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
{Comorosan, 1993 #121}	RCT exploring electromagnetic field therapy	Participants were recruited in a social care unit in Romania (n=30) Inclusion criteria: Pressure injury of long duration Participant characteristics: • Primarily in palliative end-of-life care • Age range 60-84 years • Category/Stage II and III pressure injuries • Co morbidities included SCI, CVA, dementia and atherosclerosis	• Participants were randomly assigned to receive: ○ Diapulse® sessions 1 to 2 times daily in 30 minute sessions applied through dressings at 600pps with peak power of 6, plus conventional treatment (n=20) ○ Conventional treatment only (hydrogen peroxide cleansing, application of talcum powder, methylene blu, tetracycline (n=5) ○ Sham Diapulse plus conventional therapy (n=5) ○ Treatment for 1-4 weeks	Wounds photographed on a weekly basis Wounds were assessed on the following scale: excellent (healed), very good (75-95% healed, good 50-75% healed, fair 25-50% healed, poor <25% healed, no improvement unhealed.	• 85% of pressure injuries in treatment group were ranked as excellent and 15% ranked as very good • 80% sham treatment group rated as no improvement and 20% ranked as poor improvement • Control group 60% no improvement and 40% poor improvement	• Methods of randomization and allocation concealment not reported • Double blinded study • The standard word care regimen is not used in contemporary wound care and may have impeded healing • Subjective evaluation of healing	**Level of evidence: 1** **Quality: low**
{Salzberg, 1995 #377}	RCT exploring PEF energy for healing Category/Stage II and III pressure injuries	Participants were recruited in a veteran hospital in USA (n=30) Inclusion criteria: • Category/Stage II or III pressure injury • SCI Exclusion criteria: • More than one pressure injury • Pacemaker • Cellulitis, sepsis, terminal illness, total joint replacement or other metal implant • Category/Stage I or Stage IV pressure injury Participant characteristics: All male	• After stratification based on pressure injury category/stage, participants received either: • Non thermal, pulsed high frequency, peak power electromagnetic energy on frequency 27.12MHz with pulse repetitions rates of 80 to 600 pulses/second and pulse width of 65micoseconds and pulse power peak at 293-975 peak watts delivered through wound dressing (n=10) • Sham therapy • Treatment for up to 12 weeks • All participants received saline gauze dressings	Pressure inures measured as width x length by a single observer All pressure injuries photographed weekly	**Healing for Category/Stage II pressure injuries** • At 1 weeks, active therapy group had 84% of pressure injuries healed compared with 40% of sham group (p=0.01) • At one week, mean wound size was significantly smaller in active therapy group 16.5 cm^2 versus 2.7cm^2, p=0.015 **Time to healing for Category/Stage II pressure injuries** Active group had significantly faster healing with mean 31.5 days to complete healing versus 13 days (p<0.001) **Healing for Category/Stage III pressure injuries** • Active therapy group had 60% of pressure injuries healed	• Double blind study • Does not report methods of randomization or allocation concealment	**Level of evidence: 1** **Quality: moderate**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		No difference in wound size or condition at baseline between groups			compared with 0% of sham group (p=not reported) • 70.6% of active therapy pressure injuries decreased in size versus 20.7% of the sham therapy group (p=not reported) No adverse events occurred		
{Seaborne, 1996 #386}	RCT to explore the best regimen for PEMF therapy	Participants were recruited in a non-ambulatory hospital for men (n=20) Inclusion criteria: • Aged 60 to 101 years • Trochanter or sacral pressure injuries Exclusion criteria: Pacemaker Participant characteristics: • Mean duration of pressure injury 13.5 weeks • Pressure injury descriptions indicate Category/Stage II to IV pressure injuries were involved • Negative swab cultures	• Participants were randomized to receive high frequency PEMF energy at 27.12MHz with pulse power 1000watts ○ Regimen 1: magnetic field, 20 pps, 700W peak power, power density 0.036 W/cm^2 (n=5) ○ Regimen 2: electric field, 20 pps, 700W peak power, power density 0.042 W/cm^2 (n=5) ○ Regimen 3: magnetic field, 110 pps, 700W peak power, power density 0.199 W/cm^2 (n=5) ○ Regimen 4: electric field, 110 pps, 700W peak power, power density 0.230 W/cm^2 (n=5) • All patients had 20 minute regimens daily for 5 days/week for two weeks • Study design was ABAB repeated measures (baseline, treatment, no treatment, treatment)	Wound surface area measured with wound tracings transferred to graph paper Wound measurement on a weekly basis for 5 weeks	**Mean wound surface area** • Differences in mean wound surface area was significant at 4th and 5th weeks compared to baseline (p<0.001) • No significant differences between regimens	• One person administered all treatment • Blinded outcome measurement • Small sample, with four groups there may be insufficient participants to truly measure effect	**Level of evidence: 1** **Quality: moderate**
Clinical question 3: Pulsed radio frequency energy							

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
{Frykberg, 2011 #463}	Retrospective case series	Database review of records of patients treated with PRFE (n=413, 28 patients had 34 pressure injuries) from 100 facilities in USA. Inclusion: •Wound duration ≥ 4 weeks •PREF treatment for ≥ 4 weeks •Mean age 71±14 yrs, 91% male •PU duration 9±10 mths •PU size 15±24.4 cm^2 (range 0.4 to 115.2) •Chronic PUs non-responsive to debridement, NPWT, moist wound healing, offloading, growth factors, bioengineered skin equivalents.	• Pulsed radio frequency energy administered 30 mins, x2 daily • By placing applicator adjacent to wound dressing • Administered by patients (community-based) or staff (facility-based) • Frequency not reported.	• Per cent reduction in wound area at 4 weeks • Wound healing trajectory at 4 weeks ([initial wound area-final wound area]/number days treatment) • Proportion of wounds achieving ≥ 50% reduction in size at 4 weeks	• Mean per reduction cent wound surface area for pressure injuries at 4 weeks 49% ± 6% (range 100% to –386%, p<0.0001) • 59% PUs achieved ≥ 50% reduction in size at 4 weeks • Wound healing trajectory at 4 weeks: 0.34 ±0.60 cm^2 per day	• Selection bias favoured severe wounds • Assumed reliable database entries • Compliance with therapy regimen is known as self-administered for patients in the community • Took data from a registry maintained by the product manufacturer	**Level of Evidence: 4** **Quality: low**
{Conner-Kerr, 2012 #458}	Retrospective record case series analysis	Data was taken from a device manufacturer's registry consisting of cases from 99 different facilities in USA. (n=89 participants, 110 pressure injuries) Inclusion: • PU of at least 1 month duration • At least 4 wks of outcome data Characteristics: • Treated with PRFE due to failure of other treatments and primarily following surgical intervention.	Wound and additional PU care was as per individual institution standards PRFE performed by carer or participant All facilities had been instructed to use Provant Therapy System by placing applicator over wound dressings for 30 minutes twice daily	• Median wound surface area reduction at 4 weeks • Per cent of wound achieving 50% reduction or greater in wound surface area • Rate of healing • Method of assessing the outcome measures is not reported	• Median wound surface area was 9.8cm^2 at baseline and 4.5cm^2 at 4 weeks • Median wound surface area reduction at 4 weeks was 44%±54%, mean 51%, range 100% to –386% (i.e. increased) • 51% of wound achieving 50% reduction or greater in wound surface area at 4 weeks • Wound healing trajectory at 4 weeks was 0.36±0.63cm^2/day (mean 0.13, range 3.06 to –1.29) • Greatest reduction in wound size was seen in Stage II PUs (median wound surface area reduction of 82%)	• No control group • Database records • Excluded all cases without 4 weeks of outcome data, thereby favouring treatment • Adherence to instructions for administration is not checked • Method of assessing the outcome measures is not reported and	**Level of Evidence: 4** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Median age 69 yrs (range 28 to 75) • 82% participants had only one PU • 89% treated in inpatient facilities • PUs ranged from 1 to 82 mths duration (median 6 mths) • 43% stage IV, 20% stage III, 19% stage II, 18% unstaged.				may differ between facilities	
Clinical question 4: Phototherapy							
(Taradaj et al., 2013)	RCT to assess the efficacy of phototherapy (laser therapy) at different wavelengths (940, 808 and 658nm on Category/Stage II and III pressure injury healing.	• Participants were recruited from medical setting in Poland (n=72) Inclusion criteria: • Lower extremity pressure injury Exclusion criteria: • Infection, • Medication that interfere with wound healing • use of special dressings or any type of non-routine therapeutic procedure • nonattendance to program • pregnancy • ABPI <0.8 • diabetes mellitus • systemic sclerosis, cancer, paralysis • pressure injury requiring surgical intervention	• All received standard wound care (daily simple dressings with sterile gauze and 1% hydrophilic silver sulfadiazine cream) • Participants were randomized to receive either: ○ Placebo laser, or ○ One of three different laser treatments, all provided by a physiotherapist using gallium-aluminium-arsenide diode laser, 50mW, spot size 0.1cm^2, average dose 4J/cm^2 wavelengths in one of three doses: ○ Group 1: 940nm ○ Group 2: 808nm ○ Group 3: 658nm Therapy for a duration based on wound size, once daily, five	• Infrared camera measurement, data collection by a nurse • Statistical analysis by a technician • Complete wound healing by a nurse and physiotherapist. • Staging system used :EPUAP • Follow up period: 3 months after end of study	**Percentage reduction of ulcer surface area** Group 1: 940nm laser- 33.23% Group 2: 808nm laser- 71.09% Group 3: 658nm laser- 33.23% Placebo- 28.34% **Percentage of completely healed wounds at 1 month** Group 1: 940nm laser- 11.11% Group 2: 808nm laser- 11.11% Group 3: 658nm laser- 47.05% Placebo- 11.11% P<0.001 **Ulcer healing rate at 3 months after end of study** Group 1: 940nm laser- 16.66% Group 2: 808nm laser- 16.66% Group 3: 658nm laser- 58.82% Placebo- 16.66% P<0.001 **Author conclusions: Wavelength of laser beam is extremely important in wound healing process. No**	• No power calculation • No conflict of interest declared. • No commercial association with the manufactures of the equipment	**Level of Evidence: 1** **Quality: High**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Participant characteristics • Age range 24 – 88, • Category/Stage range IIA to III pressure injuries • Baseline differences not statistically significant	times per week for one month		**justification to use wavelength 808nm or 940nm. Use of 658nm gave promising clinical results.**		
{Lucas, 2003 #17866}	RCT comparing phototherapy (low level laser therapy) for healing Category/Stage III pressure injuries with standard wound healing	Participants were recruited in three nursing homes in the Netherlands (n=86) Inclusion criteria: Category/Stage III pressure injuries	Participants were randomized to receive either: • Low level laser therapy (LLLT) using an irradiated area of 12cm2 with total peak power at 904nm 830Hz pulse frequency mode of 150ns pulses. Laser was applied to normal peri-wound tissue with applicator held just off contact with wound surface. (n=39) • Control group: standard wound therapy (n=47)	• Absolute and relative pressure injury reduction at 6 weeks compared to baseline • Number of individuals developing a Category/Stage IV pressure injury	**Rate of healing** • There was no difference in rate of change in absolute improvement in wound surface area between the two groups (p=0.23) • There was no difference in rate of change in relative improvement in wound surface area between the two groups (p=0.42) **Adverse events** • 8% of laser group and 11% in control group experience an adverse event, one of which was a Category/Stage IV pressure injury (treatment group) (p=0.72 between groups)	• 7% withdrawal with no reasons given, but used ITT analysis • Methods of randomization not reported • No information about potential blinding of participants • Outcome assessors were blinded • No ITT analysis	**Level of Evidence: 1** **Quality: low**
{Wills, 1983 #444}	RCT comparing phototherapy (UV light) to conventional therapy for healing pressure injuries	Participants were recruited in an aged care facility in British Columbia (n=18 randomized, n=16 analyzed) Inclusion criteria: • Superficial pressure injuries recently occurring and <5mm Participant characteristics> • 81% of pressure injuries were on sacrum or ischium • Age range 62 to 103 years	Participants were randomized to receive: • Conventional treatment plus phototherapy with UV light twice daily at dose of 2.5 minimal erythema dosage, delivered twice weekly for 10 weeks for total exposure of 7.5 minutes (n=8) • Conventional treatment (twice daily sterile water wound dressings) plus sham light (n=8)	• Time to complete healing • Adverse events	**Time to complete healing** Phototherapy group had a shorter time to complete healing (mean 6.26±1.6688 weeks versus 8.37±1.4142 (p<0.02) (mean difference -2.11, 95% CI -3.63 to -0.59)	• Randomization and allocation concealment methods not reported • Category/Stage of pressure injury was unclear • Blinding was attempted but may not have been sufficient • No ITT analysis • Small sample size	**Level of Evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
{Schubert, 2001 #381}	RCT comparing phototherapy (infrared light) for healing Category/Stage II or III pressure injuries	Participants were recruited at a hospital in Sweden (n=72) Inclusion criteria: Aged over 65 years Category/Stage II or III pressure injuries Orthopedic or geriatric ward inpatient Participant characteristics: 82% had a fracture Mean age 85 years	• Participants were randomized to receive: ○ Pulsed monochromatic infrared light at 956nm with red light at 637nm. Treatments for 9 minutes with pulse repetition frequency of 15.6Hz to 8.58kHz (n=37 randomized) or, ○ Control group (n=37 randomized, n=35 analyzed) • All pressure injuries had necrosis removed with sharp debridement and moist wound healing (e.g. hydrocolloids were used. Treatment for 10 weeks of until complete healing	• Pressure injury surface area • Wound tracings on a weekly basis with planimetry used to determine surface area	**Healing rate** • Mean wound surface area decreased by 10% by 5 weeks, compared to 9 weeks for control group • Healing rate in phototherapy group was 0.298 per week versus 0.200 in control group (i.e. Rate of healing was 49% greater in the phototherapy group compared to the control group.)	• Allocation concealment methods not reported • No blinding of participants or outcome assessors • 18% withdrawal rate (death and transfers, malnutrition and ulcer revisions), no ITT analysis	**Level of Evidence: 1** **Quality: moderate**
{Shojaei, 2008; #1473}	RCT comparing phototherapy (laser)	Participants were recruited from a veteran's center in Iran (n=16) Inclusion criteria: • SCI • Category/Stage I to III pressure injuries Participant characteristics: • More than half the participants (9/16) had • Category/Stage I pressure injuries (more in the phototherapy group (75% vs 37.5%)	Participants were recruited to either: • Phototherapy with a gallium-aluminium-arsenide laser plus gallium-aluminium-indium-phosphate diode laser with continuous emission (IR 980 nm, 200 m continuous at dose 4-6J/cm² applied alternate days for three weeks (n=8), or • Standard treatment group (n=8)	• Reducing the size of pressure injuries • Pressure injury stage before and after treatment • Pressure injury size before and after treatment • Difference in cure rate	**Proportion of healed pressure injuries** Healing rate was significant in favour of the intervention group (p=0.001) **Rate of healing** There was no significant difference between groups (p=0.236)	• Randomization and allocation concealment methods not reported • No blinding of participants • There were no withdrawals in this study • Non-equivalent samples with respect to Category/Stage • Small sample size	**Level of Evidence: 1** **Quality: low**
{Dehlin, 2003 #1472}	RCT comparing phototherapy (monochromatic	Participants were recruited in eight aged care centers in	• Participants were randomized to receive either:	• Shea score to classify pressure injuries	**Proportion of healed pressure injuries at 12 weeks**	• Randomization and allocation concealment	**Level of Evidence: 1**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	light therapy) to placebo for healing pressure injuries	Sweden and Denmark (n=164) Inclusion criteria: Category/Stage II or III pressure injuries	○ Phototherapy with pulsed monochromatic light (infrared at 956 nm and red light at 637nm pulsed) (n=78) ○ Placebo therapy group: white light diode painted red (n=86) • For both group therapy was 5 days per week in first week, then alternating between 2 or 3 days per week until week 12. With sessions being between 6 and 9 minutes duration. • All participants received same conventional local wound treatment including hydrocellular or hydrocolloid dressings. • No debridement was performed.	• Proportion of healed pressure injuries at 12 weeks • Rate of healing • Time to complete healing	• Healing rate was higher in the phototherapy group compared to placebo (43.6% versus 39.5%) **Rate of healing** There was no difference in rate of change in wound surface area between the two groups (p=0.18) **Adverse events** • Adverse events were higher in the phototherapy group (78 individuals with 141 events) compared with the placebo group (86 individuals with 174 events) although most were unrelated to the phototherapy treatment • Five cases were potentially related and included tingling, pain, bleeding and redness.	methods not reported • No blinding of participants but outcome assessors were blinded • 17% withdrawal due to protocol violations or due to adverse events	**Quality: low**
{Nussbaum, 1994 #334}	RCT exploring phototherapy (ultrasound combined with ultraviolet C (UVC) light therapy) for healing pressure injuries	Participants recruited from a SCI center in Canada (n=20 participants with n=22 pressure injuries) Inclusion/exclusion criteria: No reported Participant characteristics: • Age range 15 to 61 years • Primarily males • Approx 25% had malnourishment	Participants were randomized to one of three groups: • Ultrasound/UVC: pulsed ultrasound at 3 MHz frequency, average intensity 0.2Wcm2 for 5 minutes per 5cm2 wound area plus UVC dose calculated based on wound appearance. US and UVS was alternated daily for 5 days/week (n=5) • Laser therapy: three times weekly administration of laser using 820nm diode and 30 superluminous diodes at energy density of 4 J/cm2 (n=6)	• Time to complete healing • Mean percent change in ulcer size	**Mean weekly healing rate** • Overall in the study 36.54% **Mean percent change in wound size** Mean change was significantly greater I the US/UVC group (53.5%) compared with laser group (23.7%) and control group (32.4%, p=0.032). • • No adverse events were reported	• Category/Stage of pressure injury was not reported • Randomization and allocation concealment methods not reported • Appears to have no blinding • 20% withdrew from study and were not analyzed	**Level of Evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
			• Control group: standard wound care (twice daily cleansing, paraffin gauze dressing (n=9)				
{Nussbaum, 2013 #469}	Double-blind RCT investigating phototherapy (ultraviolet C light therapy) for healing Category/Stage II to IV pressure injuries	Participants recruited from two inpatient facilities, and an outpatient wound center in Canada (n=43 participants with n=58 pressure injuries) Inclusion: • Adults over 18 years • SCI at C2 to L2 • Category/Stage II to IV pressure injuries Exclusion: • NPWT • Surgical repair in previous 3 months • Neoplasm Participant characteristics: • Primarily buttock and lower extremity PUs • Mean age 54 to 55yrs • Mean PU size stage 2 PUs 2.44 to 4.22cm2 • PU duration primarily 1-8 wks in both groups, UVC group had more PUs of 9-52 wks than placebo group and placebo group had more PUs >52 wks than UVC group.	• All participants received standard pressure relieving measures. Wound care regimen not reported. • Participants were stratified by pressure injury location and randomized to either: ○ Placebo UVC attained using regular light bulb and regimen as per treatment group (n=28) ○ Ultraviolet C light therapy (UVC) applied x3 weekly (wound edges and peri-wound irradiated for 15 seconds at 15mW/cm^2 then PU irradiated on a regimen based on PU severity (n=30) • Therapy until 100% PU closure or discharge from facility	• Weekly wound area as per cent of baseline • Mean per cent wound area change between consecutive weeks • Weeks to wound closure Assessed weekly by wound photography and imaging software to calculate area Subgroup analysis for stage 2 and stage 3-4 PUs	• 13 PUs(43.3%) in UVC group and 12 (42.8%) in placebo group closed during treatment time (p=ns overall or by subgroup) • At any weekly time point, number of PUs closed was similar between groups (p=ns) • 5 PUs reopened within 1 month (p=ns between groups) • 15 PUs were unhealed after 12 months (p=ns between groups) • Stage 2 PUs showed significant healing at some weekly time points (weeks 3, 5 and 7) with respect to per cent of baseline size for UVC group versus placebo group (p<0.03 to 0.05).	• Homogeneity between PU location and severity was considered responsible for lack of significant results. • Large drop out not included in analysis • Unit of analysis is the pressure injury, not the patient	**Level of Evidence: 1** **Quality: high**
{Durovic, 2008 #460}	Prospective randomized single-blind study investigating phototherapy	Participants (n=40) Inclusion: • Category/Stage I to III pressure injuries	All participants received standard wound cleaning and dressings. Participants randomised to receive either:	• Surface of PU measured using callipers	There were significant differences between the groups at the end of the treatment regarding: • The surface of PU (experimental group 10.80 ±19.18 versus control	• Non-blinded and poorly described randomisation and inclusion criteria.	**Level of Evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	(polarised light therapy) for healing Category/Stage I to III pressure injuries	• no contraindications for polarised light • no deterioration of a common disease or development of a new disease Exclusion: • Intended skin graft within 7 days • Previous PU study participation • Albumin levels < 3.0g/dL • Local or general infection including pilonidal sinus or osteomyelitis • Steroids, immunosuppressants, antineoplastics or anticoagulants. Characteristics: • Mean age 61.86 to 68.65 yrs • Mean PU surface area 15.10 to 19.15 • More PUs in experimental group had light (50%) or moderate (25%) exudate and more in control group had no exudate (65%) p=0.04 • More PUs in control group were "closed" or epithelialized at baseline (75% versus 65%, p=0.01)	• Polarized light therapy with wavelength: 400–2000 nm; degree of polarization: > 95%; power density: 40 mW/cm2; light energy: 2,4 J/cm2. Therapy performed for 6 minutes daily at 10cm distance for 5 days/week for 4 weeks. (experimental group, n=20) • No additional therapy (control group, n=20)	• Rank of PU (this outcome is not described) • PUSH score	group 22.97±15.69, p=0.00005); however, 50% of the PUs in control group were described as "closed" at baseline • Rank of PU (experimental group 5.95±2.48 versus control group 8.6±1.05, p =0.0005) • Total PUSH score (experimental group 7.35±3.17 versus control group 11.85±2.35, p=0.00003)	• Outcome measure of "rank of PU) not described • Did not address if an individual assessor was involved in assessing the results • Did not use gold standard for PU assessment (wound tracings and/or digital planimetry) • Control PUs were less severe at baseline therefore less opportunity for improvements	
{Onigbinde, 2010 #467}	Non-randomised controlled study with participants serving as own	Participants were bed ridden patients at a teaching hospital in Nigeria (n=10)	All PUs were dressed with Ringer's solution dressings. • Left limbs were radiated with ultraviolet radiation type B	• Mean surface area using wound tracings	• 78.9% decrease in the mean surface area of the experimental group limb (initial = 76.5 cm^2; final 16.6 cm^2) compared with 37.4%	• Experimental pressure injuries had much larger baseline size	**Level of Evidence: 2** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	controls comparing phototherapy (ultraviolet B) for healing pressure injuries	Inclusion: • Bilateral pressure injuries on lower limbs • Stable medication regimen including ciproflaxin • Aged 35 to 55 years Exclusion: • Diabetes • Malnutrition • Dermatitis • Metallic implants Characteristics: • Mean age 45.3±18.3 yrs • Mean PU surface area 76.5±63.7cm^2 for experimental PUs and 43.8±32cm^2 for control PUs • Mean PU volume at baseline was 34.9±34.2ml for experimental PUs and 26.1±25.5ml in control PUs	(UVR – B) every, 3 days for 6 weeks with gradual increase in session duration for ¾ to 5 minutes • The right limbs only received the normal wound dressing for 6 weeks	• Mean wound volume measured by lining the wound with foil • Bacterial growth assessed by Likert score (0 being no growth and 5 being very heavy growth)	decrease in the control group (initial = 43.8 cm^2; final 27.4 cm^2, p=not reported) • 74.7% decrease in the mean volume of the experimental group (initial = 34.9 ml; final 8.2 ml) versus 46.3% decrease in the control group (initial = 26.1 ml; final 14.0 ml, p=not reported) • Significant decrease in the growth of bacteria (X^2 = 37.01, p<0.00)	therefore had greater opportunity for improvement • Participants received oral ciprofloxacin that confounded results • Volumetric measurements for depth lined the wound with "foil" – not the usual gold standard • Assessed bacteria growth by Likert scoring • Category/Stage of pressure injuries not reported	
Clinical question 5: Ultrasound therapy							
Non-contact low frequency ultrasound							
(Wagner-Cox, Duhame, Jamison, Jackson, & Fehr, 2017)	Retrospective observational **study to evaluate efficacy of non-contact low frequency ultrasound (NCLFUS) for treating SDTIs**	Retrospective chart review over 1 year in a single hospital (n=44 records, n=22 hospital acquired, n=22 present on admission) Inclusion criteria: • Received NCLFUS for a DTI Exclusion criteria: • Multiple DTIs • Incomplete medical record	Protocol in place for managing DTIs included: • Mandatory staff education • Skin assessment every shift by an RN • WOC nurse review all patients with DTI • NCLFUS administered as per manufacturer protocol – daily for 5 days over total surface area then 3 times weekly until resolved	• It was unclear who performed the evaluation of DTI, or how often this was performed	**Outcomes from NCLFUS therapy** • 23% of DTI resolved • Significant decrease in size of injury from commencement to completion of therapy (24.6 cm^2 vs 14.4 cm^2, p=0.02) • Number of NCLFUS treatments was not correlated with resolution or otherwise of the DTI (p=0.40) • Change in DTI size was not correlated with age (p=0.79), BMI (p=0.30), baseline glucose	• No control group – DTIs may have resolved naturally, particularly as there was no correlation between status and number of treatments • Small sample size • Unclear outcome measurement –	**Level of evidence: 4** **Quality: Low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		Participant characteristics: • Mean age 71.3±16.3 years • 48% females • Approx 71% Caucasian • Mean BMI 25.5±14.1 • 27% diabetes • Mean Braden scale score 12.1±2.1 • 93% urine incontinence, 96% fecal incontinence • Median length of stay 12.5 days (range 5 to 27) with significantly longer LOS in cohort with hospital acquired DTI, p<0.001			(p=0.76), baseline albumin (p=0.97) • For cohort with heel DTI (n=8) there was a significant reduction in size from baseline to cessation of NCLFUS treatment (15.9cm^2 vs 13.4cm^2, p=0.045) • No heel DTIs fully resolved **Comparison between HADTI and DTI present on admission** • HADTI had significantly more treatments (6.8 vs 4.6, p=0.03) • Delay in receiving treatment was shorter for HADTI than present on admission (p=0.001)	who performed it and when was it performed	
(Honaker et al., 2016)	Case-control study **investigating efficacy of non-contact low frequency ultrasound for deep tissue injury**	Treatment group identified prospectively over 3 years (n=30) Control group were identified via a retrospective chart review of patients with DTPI in 2008 (n=30) Inclusion criteria: • Treatment group: ○ diagnosis of DTPI documented ○ hemodynamically stable ○ ability to tolerate lateral laying position • Control group: ○ diagnosis of DTPI documented by WOC nurse at two time points at least 10 days apart (if the DTI was ascribed to a PU at the second time	Control group care: (n=30) • standard PU repositioning, assistive turning device and application of trypsin-balsam of peru ointment twice daily • silicon border foam dressing • low air loss bed, or static overlay if ICU • dietitian consultation Treatment group: (n=30) • Noncontact low frequency ultrasound (NLFU) daily for 5 days until healed or discharged • MIST therapy at 0.2-0.6W/cm at 40kHz ultrasound frequency for 3 mins (area <10cm^2) or 4 mins (10-120cm^2) • mean NLFU number of treatments was 7.55 (CI 95% 6.5–8.6), with a mean dose of	Assessed using Honaker Suspected Deep Tissue Injury Severity Scale (HSDTISS) score that measures wound surface area (range 1–8), skin integrity (range 1-3), and wound/color tissue assessment (range 1–7)	**Implementation of treatment** • There was no significant difference between control group (mean 0.96 days, range <1 to 5 days) and treatment group (mean 0.93 days, range <1 to 4 days) for timeframe between identification of DTPI to implementation of treatment **Efficacy of treatment** • The treatment group had significantly greater change in total surface area compared with control group (mean decrease 8.8cm^2 versus 0.3cm^2, p=0.014, r^2=0.10) • The treatment group had significantly greater change in mean HSDTISS (mean decrease 2.2 versus mean increase 1.6, p=0.001, r^2=0.39) • Final category of injury was most commonly unstageable (57%) for	• Assumed that the PI scaling is progressive • Psychometric testing of HSDTISS is reported previously • Non-randomized • Relied on database entries • Non-blinded HSDTISS scoring	**Level of evidence: 3** **Quality: High**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		point it met inclusion criteria) Exclusion criteria: Treatment group: • Actively dying • Scheduled for discharge within 7 days of DTI identification • DTI over an electronic implant • malignancy • pregnancy Participant characteristics: Mean age approx. 66 years Mean length stay approx. 18 days Approx 40% smokers Approx 50% diabetes Approx 90% anemia Predominantly Caucasian DTPI predominantly located at coccyx, sacrum or buttocks	5.32 minutes (95% CI 4.83 to 5.83) Long wave-length of kHz has been hypothesized to be more effective for DTPI due to increased deep tissue penetrance in comparison to the mHz waveform		the control group and Stage 2 in treatment group (50%) • Time before participant was discharged or a pressure injury stage could be ascribed to the evolving DTPI was longer in control group (average 12.6 days, 95% CI 9.9–15.33) compared with treatment group (average 11.1 days, 95% CI 8.9–13.3 days, p=not reported) **Factors identified as predictors of HSDTISS** • Length of stay (p=0.017, r^2=0.10) • Treatment/control group (p=0.0001, r^2=0.40) **Factors identified as predictors of DTPI total surface area** • Hypertension (p=0.02, r^2=0.06) • Anemia (p=0.04, r^2=0.60) • Treatment/control group (p=0.014, r^2=0.10)		
{Honaker, 2013 #896}	Retrospective cohort study comparing NCLFUS for STDIs with standard care	Retrospective record review (n = 43 cases of SDTI treated with NCLFUS and n=42 control STDIs) Characteristics: • Control group had larger wound surface area at baseline but significance was not reported • Cases had NCLFUS if the STDI was presumed to be <5 days old • No difference in severity score at baseline (p<0.913)	• Records were reviewed as either cases or controls • All participants received standard pressure ulcer prevention • Cases received the same treatment as controls plus NCLFUS delivered with MIST™ Therapy System (Celleration) daily for 5 days then every second day (mean number of treatments = 10) • Controls received trypsin-balsam-of-Peru ointment	• Development of a new assessment tool to assess SDTI, validity and reliability not reported • Tool used three scales on which total surface area, skin integrity and wound color were assessed from photos in patient records • Severity score was assigned based on three scales (score 3-	• NC-LFUS group achieved significant reduction in severity score at follow up compared to the control group (t = 5.67, p < 0.000) • 18% of SDTI in NC-LFUS resolved spontaneously versus 2% in control group	• Assessment of wound color using digital photography requires a validated photographic strategy – unclear if this was used. • Non blinded • Relies on documentation • Underpowered study	**Level of Evidence: 3** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
			twice daily or soft-silicone bordered foam dressing.	18 with higher score = greater severity)			
{Serena, 2009 #895}	Case series exploring NCFLU for Category/Stage III pressure injuries to decrease bioburden and facilitate healing	Participants were recruited from 3 centers (n = 18, n = 11 eligible based on requirement for bioburden) Inclusion: • Aged > 18 years • Category/Stage III pressure injury with volume <160cm^3 • No clinical signs of infection • Had not taken antibiotics in preceding 24 hours • Quantitative tissue biopsy indicating >10^5 CF/.g Exclusion: • Head or neck wounds • Malignancy • Electronic prothesis Participant characteristics: • Primarily dark skinned • Mean wound duration 27 days • Primarily ischial pressure injuries	• All wounds received debridement at baseline • Noncontact low frequency ultrasound (NC-LFUS) applied for duration based on wound size for three times per week for two weeks (3 minutes for wounds <10cm^2 and 20 minutes for wounds >170cm^2) • Treatment administered was a mean of 6 administrations for mean duration of 4 minutes/session	• Per-protocol analysis • Wound biopsy at baseline and 2 weeks for wound culture	• Mean reduction in bacterial bioburden from 4 x 10^7 to 2 x 10^7, p not reported • 26% reduction in mean wound area from 13.8cm^2 to 10.8cm^2 (p not reported) • 20% mean wound volume (p not reported)	• No analysis by center • No control • No blinding • Small sample size • Unclear how wound size was assessed • No statistical analysis	**Level of Evidence: 4** **Quality: low**
High frequency ultrasound							
(Polak, Taradaj, et al., 2016)	RCT exploring high voltage pulsed current (ES) plus high frequency ultrasound to	Participants were recruited in residential care and temporary care facilities in Poland (n=90 randomized, n=77 completed and analyzed)	• All received standard wound care, and pressure injury prevention • Participants were randomized to receive either:	• Average change in wound area relative to baseline • Percent reduction in wound area • Complete healing at 6 weeks	**Mean wound surface area** • At 6 weeks, all groups achieved significant reduction in wound surface area versus baseline: • US group g from 10.86±11.59 cm^2 at baseline to 3.69±6.23 cm^2,p<0.0001	• 14.4% dropout • Pressure injury rather than individual was the unit of analysis	**Level of Evidence: 1** **Quality: High**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	heal pressure injuries	Inclusion criteria: • >60 years of age • Category/Stage II to IV pressure injuries of 1-50 cm^2 and 1-12 months duration • Exclusion criteria: • Cancer • electronic implants • necrotic or tunneling pressure injuries • Osteomyelitis • Requiring surgical intervention Participant characteristics: The majority of participants were aged over 80 years 50% of ES group and about 30% of the other two group had diabetes Primarily Category II pressure injuries	○ Standard wound care plus electrical stimulation (HVMPC, 154 µs, 100 pps, 100 V, 250 µC/sec, 50 minutes/day) (n=30 randomized, n=25 completed) or ○ standard wound care plus high frequency ultrasound (1MHz; 0.5 W/cm2; 20%; 1–3 minutes/cm2) (n=30 randomized, n=24 completed) ○ standard wound care (n=31 randomized, n=28 completed) • Treatments were administered once a day, 5 days a week for 6 weeks	• Wound measurements at baseline, week 4 and week 6 •	• ES group from 7.48±6.20 cm^2 to 2.65±4.33 cm^2, p<0.0001 • control group from 9.31±7.27cm^2 to 5.33±46.41 cm^2 , p<0.0001 • Percent area reduction at 6 weeks was 77.48±11.59% in US group, 76.19±32.83% in ES group and 48.87±53.42% in standard wound care. (p=0.014 between all three, US and ES were not significantly different to each other p=0.99, US was significantly better than control (p=0.024) and ES was significantly better than control p=0.03 **Complete healing** • Not significantly different between all three groups US 46.4%, ES 51.7% and standard wound care 22.6% (p=0.79) US was not significantly better than control (p=0.097) and ES was significantly better than control p=0.031)	• No patient blinding,	
(Karsli, Gurcay, Karaahmet, & Cakci, 2017)	RCT comparing high voltage ES to high frequency ultrasound for healing pressure injuries	Participants were recruited in a medical clinic Turkey (n=35, 8 excluded due to concurrent medical diagnoses) • Inclusion criteria: • Hospitalized for neurologic rehabilitation. • Category/Stage II to IV pressure injury Exclusion criteria: • Cardiac dysrhythmia or pacemaker, epilepsy,	Participants were assigned to either: • HVES applied using twin peaked monophasic pulsed current with 100PPS 10-50-100 us pulse width and 2 second ramp up time in continuous mode. Intensity between 50 and 150 V. 60 minute duration 3x per week x 4-12 weeks (n=25), or • High frequency ultrasound at 3 MHz 20% duty cycle and 0.3 W/cm^2 frequency 1 MHz	• Did not specify who was assessing wounds if consistent. • Did utilize wound evaluation scales to calculate dimensions • NPUAP Staging system • Follow up 4 to 12 weeks.	**Wound surface area change** • 43% decrease in wound surface area in HVES group versus 63% WSA decrease in US group • Analysis based on Category/Stage and intervention group showed significant improvements in Category/Stage II, III and IV pressure injuries in both treatment groups (baseline compared to follow-up) • Wound surface area showed significant decrease in HVES group	• No control group • All pressure injuries were Category/Stage IV were in the HVES group which may alter realistic findings	**Level of Evidence: 1** **Quality: Low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		osteomyelitis, pregnancy, malignancy, and/or uncontrolled autonomic dysreflexia. Participant characteristics: • Majority had SCI, (TBI, CVA, myelitis and combination of SCI/TBI) • Duration of neurologic disease, Smoking, voiding status, ambulation level not statistically significant different between groups • Baseline severity of pressure injuries were significantly different, with the HVES group having significantly worse profile in terms of classification (p=0.018) and wound surface area (p=0.036)	in continuous mode in the wound bed for 1-2 mins. 1-1.5 W/Cm^2 dose for 2-3 mins around the wound (n=22)		over time (p<0.001) and in US group over time (p<0.001) **Regression analysis on factors that impact wound healing** Level of ambulation (r=4.365 P<.001), pretreatment Category/Stage (r=3.335 P=.002) and smoking (95% CI 0.535 to 2.046; P = 0.001) all impacted healing outcomes **Conclusions: Both groups demonstrated statistically significant improvement in wound surface area with difference in groups likely due to more advanced stage/increased initial surface area in the HVES group.**		
(Polak et al., 2014)	RCT exploring the use of the use of high-frequency ultrasound (HFUS) as part of a interdisciplinary wound care program in a geriatric population at high risk of pressure injuries	Participants were recruited in four nursing/ and care centers in Poland (n=42) Inclusion criteria: • >70 years old • Category/Stage II or III pressure injury • Wound size >1cm^2 • Wound on trunk or buttocks • Wound persisting >4 weeks Exclusion criteria: • >2 pressure injuries	• All received standard wound care, debridement, nutritional intervention, continence management and two hourly repositioning if immobile. • Participants were randomized to receive either: ○ high-frequency ultrasound (HFUS) 5 x weekly for 1-3 minutes/cm^2: 1 MHz, 0.5 W/cm^2/SATP, Duty cycle 20% for 6 weeks or until healed, (n=20 with n=21 pressure injuries) or	• Change in wound surface area after treatment • % decrease in wound surface area at 6 weeks • Wound healing rate • Average weekly change in wound surface area • % of wounds where wound surface area has reduced by ≥50% at 6 weeks • Wound size measured by a clinician by	**Change in wound surface area after treatment (cm^2)** Intervention group had significantly greater change in surface area compared with control group (68.8 ± 37.23 vs 37.24 ± 57.04, p = 0.047) **Decrease wound surface area at 6 weeks (cm^2)** • Intervention group showed a significant improvement in wound surface area from baseline to week 6 (15.38 ± 12.92 cm^2 versus 6.16 ± 8.26 ^{cm2,} p = 0.000069) • Control group showed non-significant reduction in wound surface area at 6 weeks (11.08 ±	• Small sample size of Category/Stage III pressure injuries • Non-blinding of patients • Includes data on mechanisms of ultrasound • No sham control • Care between participants may have varied	**Level of Evidence: 1** **Quality: High**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Pressure injury needs surgical intervention • Neoplasm, lymphatic, systemic disease, CNS demyelinating disease or cirrhosis Participant characteristics: • 17 females • age range 71 – 95 • no significant difference in population characteristics between groups	○ no additional treatment (n=22 with n=23 pressure injuries)	copying the wound contour onto a transparent sheet and measured using a planimeter, before treatment and at week 6 • EPUAP Staging system	7.52cm^2 at baseline versus 8.28 ± 8.79 at 6 weeks, p= 0.0062) **Wound healing rate %** No significant difference between intervention group (38.1%) and control group (11.04 %, p = 0.083) **Average weekly change in wound surface area (cm^2)** No significant difference between intervention group (2.63 ± 2.49cm^2) versus control group (1.52 ± 2.02cm^2, p=0.07) **% of wounds where wound surface area has reduced by ≥50% at 6 weeks** No significant difference between intervention group (66.67%) and control group (43.48%, p=0.14) **Author conclusions: High-frequency ultrasound (HFUS) 5 x weekly for 6 weeks reduces surface area more effectively than standard care alone**		
(Shanmuga, Suryanarayana Reddy, Venkat, Sachin, & Bhagya, 2017)	RCT to evaluate the effect of continuous ultrasound therapy in healing of Category/Stage II and III pressure injuries	Participants were recruited in India (n=30) Inclusion criteria: • Age 22-66 years • One or more pressure injuries Exclusion criteria: • Postoperative infected pressure injuries • Diabetic ulcers • Carcinoma	• Participants were randomized to receive either: ○ Continuous ultrasound (US) therapy (3 MHz; 0.8W/cm^2 for10 min) applied at surrounding wound surface area (n=15), or ○ Control group: no additional treatment, received saline (0.9%) and sterile gauze dressing	Wound assessment using PUSH tool Digital photographs taken at initial of treatment, end of treatment and 20 days after last treatment session The initial ulcer area was carried out using graph papers to detect the injuries perpendicular linear dimensions	**Wound surface area** Intervention group had significantly smaller wound surface area following treatment compared to control group (0.124±0.26cm^2 vs 6.27±5.12cm^2, p=0.0003) **Absolute improvement in wound surface area** Intervention group had significantly better absolute improvement in wound surface area following treatment compared to control	• Does not report methods of randomization, allocation concealment • No blinding • Small sample size • Authors measured linear dimensions but reported area	**Level of Evidence: 1** **Quality: Low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Mental health problems • Metal implants Participant characteristics: • Mean age 40-45 years (range 22-66 years) • Primarily male • Mean duration of pressure injury 4 months • Mean size approx. 10cm^2 • No differences between groups	changed 6 times per week (n=15)		group (9.97±5.34cm^2 vs 4.05±5.12cm^2, p=0.0072)		
{McDiarmid, 1985 #302}	RCT comparing high frequency ultrasound to sham therapy for healing Category/Stage I and II pressure injuries	Participants were recruited in three hospitals in UK (n=40) Inclusion criteria: Category/Stage I or II pressure injuries Aged > 18 years Able to relieve pressure Exclusion criteria: Malignancy Radiotherapy in preceding 6 months Deep vein thrombosis Participant characteristics: Mean age 80 years	Participants were randomly assigned to received either: • Ultrasound at 3 MHz, 0.8Wcm^2 peak intensity, pulse duration of 2ms, for five minutes (pressure injuries <3cm^2) with one addition minute for each 0.5cm^2 over 3cm^2., three times per week. (n=21) • Sham ultrasound (n=19)	• Transparent film tracing • Maximum length x maximum width for wound surface area • No bacteriological investigations • Pressure injury survival time • Pressure injuries classified as 'clean' or 'infected', but the method of classification is not reported and no interrater reliability	**Complete healing** • No significant difference between ultrasound group (48%) and sham therapy group (42%, p>0.05) • Median healing time was 32 days in ultrasound group vs 36 days in sham therapy group (p=0.80)	• Less than 50% (n=18) followed to complete healing, n=22 censored due to death, discharge or failure to completely heal • Double-blinded • Did not report randomization or allocation concealment methods	**Level of Evidence: 1** **Quality: moderate**
{Nussbaum, 1994 #334}	RCT exploring phototherapy (ultrasound combined with ultraviolet C (UVC) light therapy) for healing pressure injuries	Participants recruited from a SCI center in Canada (n=20 participants with n=22 pressure injuries) Inclusion/exclusion criteria: No reported Participant characteristics: • Age range 15 to 61 years • Primarily males	Participants were randomized to one of three groups: • High frequency ultrasound/UVC: pulsed ultrasound at 3 MHz frequency, average intensity 0.2Wcm2 for 5 minutes per 5cm2 wound area plus UVC dose calculated based on wound appearance. US and	• Time to complete healing • Mean percent change in ulcer size	**Mean weekly healing rate** • Overall in the study 36.54% **Mean percent change in wound size** Mean change was significantly greater I the US/UVC group (53.5%) compared with laser group (23.7%) and control group (32.4%, p=0.032). • • No adverse events were reported	• Category/Stage of pressure injury was not reported • Randomization and allocation concealment methods not reported • Appears to have no blinding	**Level of Evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Approx 25% had malnourishment	UVS was alternated daily for 5 days/week (n=5) • Laser therapy: three times weekly administration of laser using 820nm diode and 30 superluminous diodes at energy density of 4 J/cm2 (n=6) • Control group: standard wound care (twice daily cleansing, paraffin gauze dressing (n=9)			• 20% withdrew from study and were not analyzed	
{ter Riet, 1996 #413}	RCT investigating high frequency ultrasound for healing pressure injuries	Participants were recruited in 11 nursing homes and a hospital in Netherlands (n=88) Inclusion criteria: • Category/Stage II to IV pressure injuries • Category II pressure injuries were required to have no epithelialization for 7 days Exclusion criteria: • Osteomyelitis • Pregnancy • Radiotherapy • Requiring surgical	Participants were randomly assigned to received either: • Ultrasound at 3.28 MHz, 0.1Wcm^2 peak intensity, pulse duration of 2ms, pulse repetition frequency 100Hz, for five times per week for 12 weeks. (n=45) • Sham ultrasound (n=43) • Equipment delivered by a physical therapist	• Wound photography on week 1,2,4,6,8,10 and 12 • Wound surface reduction in cm2 at 12 weeks •	**Complete healing** 18/45 (40%) of pressure injuries healed in the ultrasound group compared with 19/43 (44%) in the sham group (p=0.61) **Surface area reduction** There was no significant difference in mean reduction in wound surface area between ultrasound group and sham group (22.91% vs 13.82%, p=0.10, adjusted difference 8.27%, 95% CI -2.31% to18.85%) Healing rate There was no significant difference in mean healing rate between ultrasound group and sham group (0.18cm vs 0.13cm, p=0.18, adjusted difference 0.05cm, 95% CI -0.04 to 0.13)	• ITT analysis • Blinded outcome assessment • The study also investigated effect of vitamin C • ITT analysis reported here, Per protocol analysis was also not significant	**Level of Evidence: 1** **Quality: high**
Clinical question 6: Negative pressure wound therapy (NPWT)							
(Srivastava et al., 2014)	Controlled trial to compare pressure injury healing with	Participants were recruited in a trauma center in India (n=48) Inclusion criteria:	• All pressure injuries cleaned and packed with saline gauze, with dressings twice daily	• Wound surface area, depth and tissue type (slough to red granulation tissue)	**Change wound condition at week 3** In intervention group, wound bed slough converted to granulation tissue in 33.3% pressure injuries	• Unclear who performed wound assessment	**Level of Evidence: 2** **Quality: high**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	conventional dressing and with negative pressure	• Traumatic paraplegia • Age 16-60 years • Category/Stages 3-4 pressure injury (according to • NPUAP scale) Exclusion criteria: • wounds with necrotic tissue • unlikely to tolerate debridement • chronic • osteomyelitis not treatable by antibiotics • diabetes mellitus • rheumatoid disease • vasculitis • neuropathy, chemotherapy, or radiation therapy • poor nutritional status (in Braden scale 1-2) • serum albumin < 2.5 g/l • haemoglobin < 9.0 g/l Participant characteristics: • mean age 53 -54 years • active infection in majority of pressure injurie sin both groups • Upper respiratory tract infection or urinary tract infection in majority of participants in both groups	• Participants in intervention group received NPWT for 9 weeks (mean pressure -80 mmHg (range -60 to -120 mmHg)	• Evaluated weeks 0, 3, 6 and 9 • Pathologic organisms evaluated at week 0 and week 9 • Greatest length and width measured and surface area estimated • Ulcer depth measured with cotton-tipped applicator • Exudate – subjective evaluation • Necrotic tissue, slough and granulation tissue were assessed by visual inspection at dressing changes.	(p=0.0001) compared with no change in the control group. **Change wound condition at week 6** In intervention group, wound bed slough converted to granulation tissue in 73.8% pressure injuries (p=0.0001), and in 37.5% pressure injuries in the control group (p=0.0001). **Change wound condition at week 9** In the intervention group, slough converted to granulation tissue in 100% pressure injuries, while it was still present in 41.7% control group **Infection status** In week 0, 100% of pressure injuries in both groups had positive cultures for pathogenic organisms In week 9, 100% of the intervention group had no pathogenic organisms (p=0.0001) but 41.6% (p>0.05) had positive cultures in control group **Ulcer size and depth** Ulcer size and depth decreased significantly (p=0.0001) from week 0 to weeks 3, 6, and 9 in intervention group but there were no statistically significant differences for surface area or depth in the control group (p>0.05) **Cost** The total cost of a 9-week treatment of one PU was approximately 46% less than the costs of conventionally treated comparable ulcer.	• Subjective evaluations used without reporting interrater reliability • This procedure was ineffective in low sacral ulcers in which the ulcer involves the area close to the natal cleft because the adhesive dressing could not be properly applied to obtain an airtight seal. • Sterile foam used in the negative pressure apparatus has a tendency to disintegrate and make the secretion viscous	

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
(Fulco, Erba, Valeri, Vournakis, & Schaefer, 2015)	Pilot RCT **exploring the use of poly-N-acetyl glucosamine nanofibers (sNAG) as a hemostatic agent used in conjunction with NPWT** The treatment was designed to test as management for active wound bleeding that interferes with NPWT, which can be an issue in patients on antiplatelet therapy following debridement. sNAG is expected to decrease risk of bleeding without ceasing antiplatelets.	Participants were undergoing ischial or sacral PU repair flap surgery at a center in Switzerland (n=26) Inclusion criteria: • Consenting Exclusion criteria: • Immunosuppression, hemodialysis, steroids, pregnancy, connective tissue disorder, sepsis Participant characteristics: • Mean age 58 years (range 28 to 85) • Primarily ischial PU, three participants had sacral PU and they were all in the control group • No significant difference in wound base area at baseline • No significant differences between three groups on serum albumin, zinc, lymphocyte count, BMI, diabetes or CV disease	All participants had surgical wound debridement (until wound bed bleeding), NPWT for 2 weeks then flap repair. Bleeding was controlled with light compression and bipolar coagulation. NPWT applied on day 2 with participants (who were not treated with antiplatelet therapy) were randomized to either: NPWT alone (n=10) NPWT with sNAG (n=10) A control group continued antiplatelet therapy with sNAG with NPWT (n=6)	• Wound base area and wound surface area measured using digital planimetry • Mean wound epithelization assessed by digital planimetry • Granulation tissue measurements performed on histological wound cross sections • Bleeding assessed by % of dressing covered in blood at day one	**Mean wound area** superior reduction in sNAG-NPWT group versus NPWT group (second group tended to have increase in wound area), p<0.05 **Mean wound epithelization** 462mm in sNAG-NPWT group versus 361mm in NPWT group, p=non-significant **Granulation tissue** 2.9±0.7mm thick in sNAG-NPWT group versus 3.3±0.8mm in NPWT alone group, p=ns **Adverse reactions** No adverse reactions were experienced in the study **Bleeding** patients in the control group receiving anti-platelets had the highest level of bleeding (36%) compared with NPWT alone (22%) and NPWT with sNAG (23%) **Study conclusions: sNAG increases the effectiveness of NPWT in promoting wound contracture**	• Small sample size, uncertain if this study is adequately powered • Patient inclusion criteria is not defined	**Level of Evidence: 1** **Quality: Moderate**
(Dwivedi et al., 2017; Dwivedi et al., 2016)	RCT exploring the **effectiveness of negative pressure devices compared to standard wound dressings for promoting PU closure in**	Participants were recruited in SCI unit in a hospital in India (n=65 screened, n=60 randomized, n=16 withdrew, n=44 analyzed) Inclusion criteria: • Traumatic paraplegia • Aged 16 to 60 years • Stage III or IV PU	Pressure ulcers were debrided prior to randomization. Participants were randomized to receive either: Standard care consisting of normal saline and sterile gauze packing changed 1-2 times daily (n=30 allocated, n=23 analyzed) or	• Measurement using ruler at greatest length and width and cotton tip measurement of depth; PUSH tool; clinical photography • Assessment conducted weekly • Patients followed until on closure of wound or	**Pressure ulcer length** • No significant difference week 2-6 • NPWT group had significantly shorter length in week 7 (p=0.04), week 8 (p=0.005) and week 9 (p=0.001) **Pressure ulcer width** • No significant difference week 1-5	• Power calculation conducted but required population not explicitly stated • Appears to be non-blinded • Withdrawals were not	**Level of Evidence: 1** **Quality: Low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	individuals with paraplegia.	Exclusion criteria: • Necrotic tissue incompatible with debridement • Chronic osteomyelitis • Exposed blood vessels or nerves • Diabetes mellitus, rheumatoid disease, vasculitis, neuropathy, chemo or radiation therapy • Braden scale assessment indicating poor nutrition • Serum albumin <2.5g/L or hemoglobin <9.0g/L Participant characteristics: • Mean age 32.52 to 38.30 (standard care group significantly younger, p<0.05) • >80% male • Standard care group had significantly more stage III PU (56.5% versus 19.0%) and significantly less stage IV PU (53.5% vs 81%), p<0.01	NPWT: using a sterile foam and transparent film dressing changed weekly (n=30 allocated, n=21 analyzed)	until trial completion 9 weeks • Cost effectiveness (consumables) calculated on a daily basis based on two representative PUs from each group and multiplied for number of days to achieve granulation	• NPWT group had significantly shorter length in week 6 (p=0.01), week 8 (p=0.02) and week 9 (p=0.006) **Pressure ulcer depth** • Standard care group significant improvement compared to NPWT group in week 1 (p=0.001), week 2 (p=0.003) and week 3 (p=0.02) • NPWT significantly better than standard care group at week 9 (p=0.01) **Other characteristics** • NPWT group had significant better exudate scores using PUSH for weeks 3-9 (p=0.001 for all) • NPWT group had significantly less discharge (mls) for weeks 2-6 (p=0.001 for all) and no discharge in weeks 7-9 • NPWT group had significant better tissue type scores using PUSH for weeks 4-9 (p=0.001 for all) **MMP-8 levels** By week 3, levels were significantly lower in the NPWT group (p =0.46 at week 3, p=0.006 at week 6 and p<0.001 at week 9) **Wound dimensions** • By week 6, the difference between groups in length was significant (p=0.04) favoring NPWT, which continued at week 9 (p=0.001) • By week 9, NPWT group had 79.7% reduction vs dressing group 54.7% reduction)	included in analysis • Groups were not similar with respect to PU stage at baseline but there was no significant difference in length, width or depth at baseline • No reason given for withdrawals • Cost only included dressing materials • Note: Both trials report the same study (same results week 0 and 8, same ethics number) but the participants in groups are slightly different • Methods of randomization and allocation concealment not reported • Approx 30% of participants were withdrawn for various reasons including deteriorating wound, no ITT analysis	

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
					• Width became significant favoring NPWT group by week 9 (81.7% reduction vs 59.5% reduction, p=0.006 for cm reduction) • Depth became significant favoring NPWT group by week 9 (89.4% reduction vs 78.1% reduction, p=0.01 for cm reduction) **Wound condition** • Conversion of slough into red granulation was significantly higher in NPWT after week 6. • Exudate was significantly lower in NPWT group after week 3. **Cost** • 9 week treatment cost was US$105 for NPWT and US$200 for standard care group **Author conclusions: NPWT is a reasonable treatment for promoting closure of stage IV PU and is cost effective in low resource setting. The treatment was not effective in low sacral ulcers due to inability to apply dressing to create an airtight seal. Sterile foam can block the drain.**	• 10 participants withdrawn from NPWT group due to deterioration of wound/ Infection, or inability to maintain seal • Randomization, allocation concealment and blinding not reported	
{Wild, 2008 #472}	RCT	Recruited from nursing home, n=10 Inclusion: • PU stage III or IV Exclusion: • Palliative care Mean age 78 to 83 years	NPWT with either: • V.A.C.® system (n=5) with dressings changed x3 weekly • Redon surgical drain bottles (n=5) delivering pressure between –900mmHg and 0mmHg, but pressure level is uncontrolled. Dressings changed as required. All wounds surgically debrided and all patients received appropriate nutritional support.	• Absolute and relative proportion of wound area consisting of granulation tissue, fibrin and necrosis assessed by an independent observer using Wound Healing Analysing Tool (WHAT) • Frequency of dressing change	**Dressing changes:** • Significantly more frequently for Redon group (3 times daily versus 0.5 times daily, p<0.05) **Healing:** • Mean change in granulation tissue favoured V.A.C.® system (54% versus –7.1%, p=0.01) • Mean change in fibrin favoured V.A.C.® system (–27% versus 21.8%, p=0.035)	• Unable to recruit sufficient participants to meet a priori power calculation • Study ceased early • Ethics not obtained (states not required in country research performed)	**Level of evidence: 1** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
				Mean follow-up of 8.5 days	• Mean change in necrotic tissue favoured V.A.C.® system but there was no statistically significant differences (p=0.598) Redon system: • Seal checked two hourly • Bottles reapplied when vacuum insufficient • Bottles changed up to 10 times daily • Leakage and suction of stool • Complaints of pain from participants		
{de Laat, 2011 #459}	Prospective RCT (Nb: the RCT included two study arms – PUs and surgical wounds. Only data from PUs included in evidence table)	n= 12 patients with 16 PUs Inclusion: Spinal cord injury patient with PU grade IV Mean age approx. 48 years, mean BMI approximately 23.9kg/m^2	All wounds debrided, all SCI patients managed in hospital. Random assignment to either: • Patients were assigned to either treatment with NPWT using VAC® system (n=6 patients with 9 PUs) : foam dressing changed x3 weekly • sodium hypochlorite wound dressings (n=6 patients with 7 PUs): wet to moist dressings changed x3 daily	• Time to reach 50% reduction in wound volume • Maximum follow-up was 6 weeks	Only 14 PUs reached 50% healing within 6 weeks. Median treatment time to 50% reduction of would volume: • NPWT group 2.0 weeks (interquartile range [IQR]=1 to 2) versus sodium hypochlorite group 3.0 weeks (IQR = 3 to 4, p=0.001 • Unadjusted hazard rate ratio (HRR) 0.188 (p=0.014) and HRR adjusted for baseline wound volume and smoking status was 0.833 (p=0.021) Complications associated with NPWT included clinical infection (2 wound) and 1 patient had an arterial bleed requiring surgical repair.	• Used wound as a point of analysis rather than patient • Used non-conventional comparative treatment that may favour NPWT • Excluded patients who did not reach 50% healing within 6 weeks from analysis	**Level of evidence: 1** **Quality: moderate**
{Wallin, 2011 #468}	Retrospective record analysis (Nb: Included patients with wounds of other aetiology. Only	Consecutive selection of patients treated with NPWT in one general hospital between 2005 to 2007. n=14 patients with PUs	NPWT using VAC® device with continuous sub atmospheric pressure of 125 mm Hg. Dressings changed x2 to 3 weekly or more frequently depending on exudate	Patient demographic Comorbidities Clinical infection Wound complications Treatment outcome: • successful: wound much improved and/or	• 86% wounds treated with NPWT had positive wound swab, primarily *E.Coli, Pseudomonas, Streptococci, Enterococci* and *Bacteroides* • 50% (n=7) cases classified as successful	• Retrospective chart review • No controls • Small number of patients	**Level of evidence: 3** **Quality: moderate**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	data from PUs included in evidence table)			left to heal by secondary granulation; wound healed; wound bed improved and skin graft performed, • unsuccessful: wound not improved, wound bed larger or worse, treatment discontinued due to complications. Follow up ranged from 24 to 48 months.	• Median treatment time was not significantly different (p=0.48) between cases that were successful (median 28 days ± 71 days, range 8 to 210) and those that were unsuccessful (median 23 days ± 23 days, range 4 to 75 • Patients with infectious, postoperative, and traumatic wounds had greater treatment success than those with PU (p=0.001). • In the full sample (n=87) there were complications in 10 patients including infection (n=5), breakdown of surrounding skin (n=3) and hemotoma (n=2).		
{Ho, 2010 #465}	Observational study	Participants (n=86) with SCI recruited from 10 Veterans Affairs medical centres Inclusion: • stage III or IV PU in the pelvic region (sacral, coccygeal, ischial, buttock • age ≥ 18 years age Exclusion: • reconstructive flap surgery • unresolved osteomyelitis • palliative care • coronary artery disease, vascular disease, congestive heart failure • malignant disease Characteristics: • Mean age 55 years	All patients received low air loss mattress, regular turning, wound debridement, hydrotherapy, routine wound cleansing and dressing changes. At discretion of physician patients received either: • NPWT (n=33) • standard wound care alone (n=53)	Change in wound surface area Digital planimetry on day 1, during weeks 2 and 3 and on day 28 Laboratory data (serum albumin) was collected on day 1 and 28 (± 2 days) PUs were classified as healing (wound surface area decreasing) or non-healing (wound surface area increasing	• No significant difference in number of patients classified as healing between NPWT group (70%) versus standard care group (67%, p=ns) • In patients who were classified as healing, there was no significant difference in size of wound surface area decreased amount between the NPWT group (–43% ± 22%) versus standard care group (–50% ± 26%, p=ns) • In the NPWT group there was a significant difference in serum albumin levels between patients classified as healing versus non-healing (2.9 ± 0.4 vs. 3.3 ± 0.5 mg/dL, p<0.05) • Standard care group had no significant difference in serum albumin levels between patients classified as healing versus non-	• Wound depth, which is a consideration in selection of NPWT, was not measured • Prealbumin, which is a better indicator of nutritional status, was not measured	**Level of evidence: 4** **Quality: low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Primarily male patients (96 to 100%)			healing (3.2 ± 0.3 vs. 3.2 ± 0.3 mg/dL)		
{Joseph, 2000 #247}	RCT comparing NPWT with standard therapy for chronic non-healing wounds	Participants were recruited in a medical center in USA (n=24 participants with n=36 pressure injuries) Inclusion criteria: • Open wound that had failed to heal for four weeks or longer Exclusion criteria: • Infection of any sort • Low albumin • Chronic renal disease, thyroid disease, unstable diabetes, taking anticoagulants, pregnancy or breast feeding • Osteomyelitis • Malignant wounds • Fistulas Participant characteristics: 79% of wounds were pressure injuries Wound volumes ranged from 3cc to 150cc	• Sharp debridement of necrotic tissue before application of treatment • Participants were randomized to receive either: ○ NPWT with open cell foam dressing and controlled atmospheric pressure, with dressing changed every two days (n=) or, ○ Standard wound care (saline gauze dressings changed three times daily	• Wound photography • Alginate impression molds to measure wound volume • Six week follow-up	**Wound dimensions** • NPWT was associated with greater reduction in wound depth (68% versus 20%, p=0.00001) • NPWT was associated with greater reduction in wound width (62% versus 35%, p=0.02) • NPWT was associated with greater reduction in wound volume (48% versus 39%, p=0.038) • No significant between group differences in wound length (NPWT 46% reduction, standard care 38% reduction, p=0.38) **Adverse events** • Osteomyelitis occurred in one case • Calcaneal fractures occurred in two cases when patients ambulated against advice • Standard wound management was related to 2 fistulas, 6 wound infections and 2 cases of osteomyelitis • Rate adverse events was 44% in standard care vs 17% in NPWT)	• Unit of analysis was pressure injury, not participant • Reported methods of randomization and allocation concealment • Blinded outcome assessment	**Level of evidence: 1** **Quality: High**
{Isago, 2003 #237}	Cohort study evaluating response to NPWT	Participants were bedridden medical patients recruited in Japan (n=10) Inclusion criteria: Category/Stage IV pressure injuries	Participants received treatment with a V.A.C.™ system using polyurethane foam Wounds debrided prior to treatment Pressure at 125mmHg, continuous for 48 hours then intermittent Second daily dressings	Wound length x width and depth Weekly wound assessment Surface area of wound calculation Bloods – white blood cells, CRP, Sodium, potassium and calcium	• Wound dimensions • NPWT was associated with greater reduction in wound surface area over time after one week of treatment (mean reduction 55.1% by seven weeks p<0.05) • NPWT was associated with greater reduction in wound depth after two weeks of	• Does not report recruitment strategy • Minimal information on participant characteristics • Unclear wound severity • No comparator	**Level of evidence: 3** **Quality: Low**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
					treatment (mean reduction 61.2% by seven weeks p<0.05) • No changes in blood values		
{Deva, 2000 #148}	Case series exploring NPWT for Category/Stage III and greater pressure injuries	Participants were recruited in a plastics unit (n=30) Inclusion criteria: Category/Stage III and greater pressure injuries Participant characteristics: Mean age 50.7 years 50% had SCI and the rest were immobilized from other causes Mean duration of pressure injuries was 418 days (range 8 to 1650)	Some pressure injuries surgically debrided Participants received NPWT using V.A.C. device with suction at 75-125mmHg continuous for first 48 hours and thereafter intermittent	Complete wound healing Reduction in wound cavity Closure by skin graft or suture Wound photography Wound volume estimated based on volume of foam dressing Follow up for 3 months	• NPWT was successful for 87% of pressure injuries • Mean time to healing was 35 days (range 8 to 124)	• Unclear how representative these cases are • Minimal data on wound size and how success was evaluated	**Level of evidence: 4** **Quality: Low**
{Wanner, 2003 #915}	Quasi experiment comparing NPWT to wet-to-dry/wet-to-wet dressings	People with SCI (n=22) with Category/Stage II or deeper pressure injuries Mean size larger in NPWT at baseline	Surgical debridement Participants received treatment with either: V.A.C.™ system with a foam dressing at –125 mmHg with dressings change every 2-7 days (n=11) wet-to-dry or wet-to-wet dressings with Ringer's solution (n=11)	Endpoint was 50% reduction in size in preparation for flap surgery	• Time to reach 50% reduction in size was not significantly different (27 days VAC vs 28 days control)	• Reducing frequency of dressings decreases pain	**Level of evidence: 2** **Quality: Low**
Clinical question 7 kinetic energy							
Pulsatile lavage							
{Ho, 2012 #488}	Double blind prospective RCT	Participants recruited from an inpatient facility (n=28) Inclusion: • aged > 18 yrs with SCI • stage III and IV pelvic PUs, presenting as clean with no	All participants received standard care according to clinical guidelines. Participants were randomised to receive either: • Daily low-pulsatile lavage treatment with 1 litre of normal saline at 11 psi	• Length, width and depth of PU obtained weekly for 3 weeks • PU depth using saline injection method	• Random-coefficient models for analysis of linear and volume measurements revealed improvements over time for both groups	• Small number of participants and underpowered • Strict exclusion criteria excluded 221 participants	**Level of Evidence: 1** **Quality: moderate**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		odor, necrosis, minimal exudate, no tunnelling or fistula, no cellulitis, no erythema of surrounding tissue • PU maximum diameter of 3 to 15cm at baseline • No antibiotics within preceding 7 days • no malignancy or vascular disease associated with PU • no diabetes, heart disease or renal failure Characteristics: • Primarily ischial PUs • No significant demographic differences • Mean age 55 to 57 years	applied over 10 to 20 mins using a device designed for the procedure (n=14) or • Sham treatment in which no lavage was administered directly to the PU but participants were given the impression it had been (n=14) Dressings were removed before the commencement of treatment and replaced at the completion of treatment	• PU healing rate over the 3-week study period	• Time trend analysis revealed greater measurement decreases for the treatment groups • Differences in rates of change over time (95% CI) for treatment and control groups respectively (p<0.001): ○ Depth: –0.24 (0.09 to –0.58) cm/wk ○ Width: –0.16 (0.06 to –0.39) cm/wk ○ Length: –0.47 (0.18 to –1.12) cm/wk ○ Volume: –0.33 (0.13 to –0.80) cm^3/wk All 95% CIs span the null value, decreasing confidence in the significance of the results.	• All 95% CIs span the null value, decreasing confidence in the significance of the results.	
Whirlpool							
{Burke, 1998 #106}	RCT comparing whirlpool to standard wound care for healing Category/Stage III to IV pressure injuries	Participants were recruited in a veteran's hospital in USA (n=18 participants with n=42 pressure injuries) Inclusion criteria: Category/Stage III to IV pressure injuries Exclusion criteria: Wound not followed for at least 2 weeks Coexisting medical conditions precluding whirlpool Clinical infection of the wound	• Whirlpool at 96 to 98°F with no jet stream directly position to a pressure injury for 20 minutes daily plus dressings as per the control group (n=24), or • Control group: Irrigation with saline, wet-to-wet saline dressings changed twice daily (n=18)	• Follow-up for two weeks • Ulcer dimensions over time	**Wound healing rates** • Whirlpool was associated with superior healing based cm/week (p=0.0435) No adverse effects were reported	• No blinding, or allocation concealment • Randomization method not reported • Analysis at the level of pressure injury rather than the individual	**Level of Evidence: 1** **Quality: low**
Vibration therapy							

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
{Arashi, 2010 #456}	Non-randomised blinded trial investigating vibration for accelerating PU healing	Participants recruited from a hospital facility. (n=31 participants with 41 PUs) Inclusion: • Aged > 65 years • Stage I PU defined as moderate to severe skin discoloration with non-blanching. Exclusion: • Considered unsuitable by medical practitioner • Marker contractures • PU located above shoulders Characteristics: • Mean age 80 years • Primarily bedridden • Mean BMI 15 to 16 kg/m^2 • Primarily cared for on an alternating air mattress • Mean Braden score 10.6 to 12.7 • Primarily sacral PU	All participants received standard care according to the PU care guidelines. • Experimental group (n=16 participants, n=20 PUs) received vibration therapy in which a vibrator (RelaWave) was used to apply vibration (frequency: 47 Hz; time 10 seconds; amplitude modulation cycle: 15 seconds) for 15 minutes 3 times a day for up to 7 days • Control group (n=15 participants, n=21 PUs) received only standard care	Primary outcomes: • Healing Rate • Healing Period Secondary Outcomes: • Ulcer areas • Intensity of redness	• More PUs in experimental group healed compared to control group (40% versus 9.5%, p=0.033) • Mean relative change per day of wound area was superior in the experimental group (20.4±27.2% versus 6.4±6.9%, p=0.007) • The healing rate during the study was significantly higher in the experimental group than in the control group (P = .018, log rank test) • The hazard ratio adjusted for baseline risk factors was 0.031 (95% CI 0.002 to 0.594, p=0.021) • No participants experienced physical discomfort from vibration	• Non blinded, non randomised study • Groups followed at different time periods and authors suggest seasonal conditions may have influenced microclimate • Interrater reliability for evaluating healing was not assessed • Difficult to measure real intensity of vibration level reaching/impacting on the skin was hard to assess – used a method of– main method of checking was placing hand under patient to feel the vibration	**Level of Evidence: 2** **Quality: moderate**
Clinical question 8: Atmospheric							
Topical oxygen therapy							
(Azimian, Nayeri, Pourkhalegh i, & Ansari, 2015)	Single blinded RCT **investigating effectiveness of TWOT on healing PUs.**	Convenience sample of participants recruited from two intensive care units in Iran (n=100) Inclusion criteria: • Aged ≥18 years	• All participants received routine care at the study site (not described). • Participants were randomized to receive: ○ only routine care (n=50)	Wound status assessed using Pressure Ulcer Scale for Healing (PUSH) assessed at baseline and then every second day for ten days by two different assessors.	**Complete healing (complete epithelialization)** • Greater for TWOT compared with control (16 wounds versus 1 wound, p<0.01) **Wound area**	• Routine care was not reported but may have consisted of gauze dressings. • Assessors not blinded, but	**Level of Evidence: 1** **Quality: Moderate**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• Category/stage II to IV PU Sacral or ischial PU Exclusion criteria: • Peripheral vascular disease, diabetes Participant characteristics: • Mean age 69 to 70 years • Mean wound area 28 to 32 cm^2 • Approx. half of PUs were Category II and the rest category III or IV • No significant differences between groups on age, gender, previous cerebrovascular disease, level of consciousness, mobility, baseline wound state or wound size.	○ direct application via a disposable of humidified high pressure oxygen (10L/min) to the wound site for 20 minutes, three times a day for 12 days. Oxygen was delivered using a disposable catheter. ○ Saline soaked gauze dressings changed every shift. (n=50)		• Experimental group had greater healing evident at every observation time point compared with control but the difference was only significant from day 6. • Experimental group showed significant reduction (p=0.001) in wound area from baseline to day 12. • Control group had no significant change in wound area from baseline to day 12 (p=0.16)	there was high interrater correlation between the two assessors • 3 participants dropped out but reason not stated (included in analysis)	
Hyperbaric oxygen							
{Rosenthal, 1971 #367}	Comparative study exploring hyperbaric oxygen therapy for pressure injuries	Participants were recruited in unknown facility (n=21 participants) Inclusion criteria: Not stated Participant characteristics: Age range 15 to 67 years Primarily had SCI	• Hyperbaric oxygen therapy (at 3 atmospheres of pressurized air), 2 hours per day, 5 days per week plus standard wound care (n=18, n=38 pressure injuries) • Standard wound care only (cleansing, frequent dressing changes and mechanical debridement) (n=3, n=6 pressure injuries) • Average 37 treatments	Wound diameter and width	**Complete healing** 58% of pressure injuries completely healed **Reduction in wound surface area** • 13% of pressure injuries had a 50% or greater reduction in size • Control group did not have reduction in wound size	• No randomization and unclear method of group assignment • Poor comparative analysis • Unclear severity of pressure injuries • Limited information about participants	**Level of Evidence: 3** **Quality: Low**
Atmospheric plasma							
(Chuangsuwanich,	RCT exploring low –temperature	Participants recruited in plastic surgery nit in Thailand	Regimen for intervention group:	• Wound exudate and size by wound	**Wound size reduction** Intervention 88.5% vs control 52.2%	• "LTAPP has several active	**Level of Evidence: 1**

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
Assadamongkol, & Boonyawan, 2016)	atmospheric-pressure plasma	(n=50 RANDOMIZED, N=42 COMPLETED) Inclusion criteria: • Pressure injury Category/Stage III or IV • Not heal within 3 weeks Exclusion criteria: • Cancers, wounds from radiation, • clinical sepsis • unavailable for at least twice monthly follow up Participant characteristics: • Primarily female • Mean age 70 to 74 years • Initial PUSH score mean 14-15 • Demographics and wound characteristics statistically similar at P>0.05	Standard wound care (debridement, proper wound dressing) plus unipolar low – temperature atmospheric-pressure plasma delivered using one using argon as the gas medium with direct noncontact short distance plasma, 2- to 3-mm micro beam to wound surface. Therapy administered weekly after wound dressing (N=23) Regimen for control/comparison group: Standard wound care (debridement, proper wound dressing) (N=19)	specialist nurse, weekly • Bacterial load by tissue culture weekly • Wound healing score PUSH Tool 3.0 • VISITRAK device for wound size • NPUAP staging guidelines, 2007 • Follow up period 8 weeks	P < 0.001 **Exudate reduction** Intervention 80.8% vs control 30.4% P < 0.001 **Number of wounds with less bacterial load (%) week 8** Intervention 88.5% Control 82.7% P=0.002 **PUSH score improvement week 8** Intervention 96.2% VERSUS Control 52.2% P<.001 No side effects were reported **Author conclusions: LTAPP group had significantly better wound healing than the control group**	components, including charged particles, metastable-state molecules or atoms, ultraviolet ray, and reactive species, which are free radicals and some ground state molecules of oxygen such as ozone and peroxides." • Assessing nurse blinded to treatment arm. • LTAPP is dose dependent and may vary depending on manufacturer.	**Quality: High**

Full references in direct and indirect evidence tables

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