NKR - 02 for Udredning og behandling af diabetiske fodsår

Review information

Authors

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Citation example: S. NKR - 02 for Udredning og behandling af diabetiske fodsår. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Characteristics of studies

Characteristics of included studies

Akbari 2007

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1: vacuum compression therapy VCT ● *Age, mean (SD)*: 58.2 ± 8.07 ● *Female, N (%)*: 7 (78%) ● *BMI, mean (SD)*: 23.44 ± 3.7 ● *Current smoker, N (%)*: 0% ● *Wound area (cm2), mean (SD)*: 46.88 ±9.28 mm2 Kontrol 1: conventional therapy ● *Age, mean (SD)*: 57.6 ± 8.02 ● *Female, N (%)*: 8 (89%) ● *BMI, mean (SD)*: 23.44 ± 37 ● *Current smoker, N (%)*: 0% ● *Wound area (cm2), mean (SD)*: 46.62 ± 10.03 mm2 **Included criteria:** a diabetic foot ulcer corresponding to grade 2 of the University of Texas Diabetic Foot Wound Classification System (wound penetrat-ing to tendon or capsule, not involving bone or joint) [9–10], no history of deep venous thrombosis, and no hemor-rhage in ulcer. **Excluded criteria:** Subjects were excluded if they had signifi-cant loss of protective sensation, hemorrhage, or vertigo or had not completed their treatment
Interventions	**Intervention Characteristics** Intervention 1: vacuum compression therapy VCT ● *Description*: In addition to the conventional therapy to be described later, the experimental group received vacuum compression therapy VCT 1 hour a day,4 times a week, for 10 sessions (a total of 12 sessions dur-ing 3 weeks; the first and last sessions were considered forevaluation only). The VCT was produced with theVasotrain-447, which can produce both positive and nega-tive pressure. ● *Duration*: 3 weeks ● *Dose*: 12 sessions, 1 hour pr day 4 times per week Kontrol 1: conventional therapy ● *Description*: he control group received only the conventional therapy, which included debride-ment, blood glucose control agents, systemic antibiotics,wound cleaning with normal saline, offloading (pressurerelief), and daily wound dressings. All patients were instructed to use an ankle-foot cast splint for pressure redistribution at all times during ambulation. ● *Duration*: 3 weeks ● *Dose*: daily wound dressings
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: Adverse Event ● **Reporting**: Not reported *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Not reported *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Not reported *Sårareal, efter endt behandling* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint, 3 weeks *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Not reported *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: Adverse Event ● **Reporting**: Not reportedr *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Not reported *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: Dichotomous Outcome

	● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: Continuous Outcome ● **Reporting**: Not reported *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint (3 weeks)
Identification	**Sponsorship source:** This work was unfunded at the time of manuscript preparation. **Country:** iran **Setting:** A single-blind, single center randomized controlled trial, n 18 **Authors name:** Asghar Akbari **Institution:** Department of Physiotherapy, Razmejo-Moghadam Labo-ratory, **Email:** akbari_as@yahoo.com **Address:** yatollah Kafami St, 98136-64855, Zahedan, Iran
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were ran- domly assigned through a computerized randomization schedule to either an experimental or a control group. Patients were randomized and assigned to their groups after the initial screening."
Allocation concealment (selection bias)	High risk	Quote: "Neither participants nor research staff administrating the interventions or assess- ing the outcomes were blinded to group assignment."
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: pt and personnel were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Quote: "However, to avoid bias, a technician blinded to the group allocation performed all tracings and area determinations in both pretreatment and posttreatment stages."
Incomplete outcome data (attrition bias)	Low risk	Quote: "total of 20 patients met the inclusion/exclusion cri- teria, but only 18 were actually enrolled in the study. Nine patients (nonsmokers, seven females and two males) received VCT in addition to conventional therapy and nine patients (nonsmokers, eight females and one male) received conventional treatment. Two patients (one in each group) did not complete their treatment sessions." Judgement Comment: Per protocol analysis.
Selective reporting (reporting bias)	Low risk	Quote: "ClinicalTrials.gov, NCT00477022," Judgement Comment: No deviations from protocol.
Other bias	Low risk	Judgement Comment: No reasons to suspect other sources of bias.

Armstrong 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 57.2 (13.4) ● *Female, N (%)*: 11 (14%) ● *BMI, mean (SD)*: 30.8 (7.8) ● *Type 2 diabetes, N (%)*: 69 ● *HBA1C, mean (SD)*: 8.2% (1.9) ● *Current smoker, N (%)*: 15 ● *Distal blood pressure (mmHg), mean (SD)*: 1.1 (0.22) ● *Wound area (cm2), mean (SD)*: 22.3 (23.4) ● *Peripheral neuropathy, N (%)*: 74 (96%) Kontrol 1 ● *Age, mean (SD)*: 60.1 (12.2) ● *Female, N (%)*: 19 (22%) ● *BMI, mean (SD)*: 31.4 (9.4) ● *Type 2 diabetes, N (%)*: 79 ● *HBA1C, mean (SD)*: 8.2% (1.9) ● *Current smoker, N (%)*: 4 ● *Distal blood pressure (mmHg), mean (SD)*: 1·1 (0.19) ● *Wound area (cm2), mean (SD)*: 22.3 (23.4) ● *Peripheral neuropathy, N (%)*: 76 (89%) Overall ● *Age, mean (SD)*: 59 (12.8) ● *Female, N (%)*: 30 (19%) ● *BMI, mean (SD)*: 31.1 (8.6) ● *Type 2 diabetes, N (%)*: 146 ● *HBA1C, mean (SD)*: 8.2% (1.8)

	● *Current smoker, N (%)*: 11 ● *Distal blood pressure (mmHg), mean (SD)*: 1·1 (0.20) ● *Wound area (cm2), mean (SD)*: 20.7 (20.6) ● *Peripheral neuropathy, N (%)*: 149 (92%) **Included criteria:** people aged18 years or older, presence of a wound from a diabetic foot amputation to the transmetatarsal level of the foot,and evidence of adequate perfusion (defined as either transcutaneous oxygen measurements on the dorsum ofthe foot 30 mm Hg or ankle brachial indices 0·7 and1·2, and toe pressure at 30 mm Hg). All wounds corresponded to University of Texas grade 2 or 3 in depth. **Excluded criteria:** patients presenting with active Charcot arthropathy of the foot, wounds resulting from burns, venous insufficiency, untreated cellulitis orosteomyelitis (after amputation), collagen vascular disease, malignant disease in the wound, or uncon-trolled hyperglycaemia (glycosylated haemoglobin[HbA1c]12%). Patients were also excluded if they were being treated with corticosteroids, immunosuppressive drugs, or chemotherapy. Finally, previous VAC therapyin the past 30 days, present or previous treatment withgrowth factors, normothermic therapy, hyperbaricmedicine, or bioengineered tissue products in the past30 days were also regarded as exclusion criteria.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: Patients randomly assigned to NPWT receivedtreatment delivered through the VAC system, withdressing changes every 48 h according to standardisedtreatment guidelines. Wounds were treated with NPWTuntil the wound was closed or until completion of the112-day assessment. All patients received off-loading therapy, preventativelyand therapeutically, as indicated. A pressure-reliefwalker or sandal (Active Offloading Walker, RoyceMedical, Camarillo, CA, USA) was provided for allpatients. ● *Duration*: 112 days ● *Dose*: evry 48 hour Kontrol 1 ● *Description*: Patients randomly assigned tostandard care were treated with moist wound therapywith alginates, hydrocolloids, foams, or hydrogels,adhering to standardised guidelines at the discretion ofthe attending clinician.26Dressing changes in the controlgroup occurred every day unless otherwise recommendedby the treating clinician.All patients received off-loading therapy, preventativelyand therapeutically, as indicated. A pressure-reliefwalker or sandal (Active Offloading Walker, RoyceMedical, Camarillo, CA, USA) was provided for allpatients. ● *Duration*: 112 days ● *Dose*: dressing changed every day
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: 16 weeks *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint 16 weeks *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint (3 weeks) *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint (3 weeks) *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline

	Tid til heling, efter endt behandling ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint (3 weeks) *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint (3 weeks)
Identification	**Sponsorship source:** funded by KCI USA, the manufacturer of the VAC Therapy Systems. **Country:** USA **Setting:** 162 patients into a 16-week, 18-centre, randomised clinical trial in the USA **Authors name:** David G Armstrong **Institution:** Scholl's Center for LowerExtremity AmbulatoryResearch (CLEAR), RosalindFranklin University of Medicineand Science, Chicago, IL 60064,USA **Email:** Armstrong@usa.net **Address:** Rosalind Franklin University of Medicine and Science, Chicago, IL 60064,USA
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The study sponsor prepared the randomisation scheme" Quote: "162 patients were recruited and randomly allocated a treatment at a 1:1 ratio of study patients to controls" Judgement Comment: Likely random sequence generation however, not specified in detail. Likely no baseline imbalances (not statistically tested).
Allocation concealment (selection bias)	Low risk	Quote: "The study sponsor prepared the randomisation scheme and sites were distributed in sealed envelopes containing the treatment assignment, to be opened sequentially as patients were enrolled."
Blinding of participants and personnel (performance bias)	High risk	Quote: "Neither patients nor investigators were masked to the randomised treatment assignment."
Blinding of outcome assessment (detection bias)	Low risk	Quote: "The masking component of the study dealt specifically with the planimetry measurements from digital photographs taken during every study visit. Given the effect of NWPT on the wound bed, an experienced observer would recognise an NPWT-treated wound; therefore observer masking was not regarded as viable. A standard protocol for the photography of the wound, including all photographic equipment, was supplied by a third-party vendor (Canfield Scientific, Fairfield, NJ, USA). The concordance between the investigator and the digital planimetry provided independent confirmation of the primary efficacy endpoint of complete wound closure." Quote: "Assessments were based on data from wound investigations and photographs done by the treating clinician."
Incomplete outcome data (attrition bias)	Unclear risk	Quote: "Analysis was by intention to treat." Quote: "The 3·4% difference in the proportion of patients who withdrew between treatment groups was not significant (two-tailed Fisher's exact test p=0·753)." Judgement Comment: Substantial attrition rate (19 withdrew from both groups. 22% / 25%)
Selective reporting (reporting bias)	High risk	Quote: "with a logistic regression model. This study has been registered with ClinicalTrials.gov, number NCT00224796. Role of the funding source" Judgement Comment: Protocol stated secondary outcome: To determine the effect of V.A.C. ® Therapy on the quality of life. However Quality of life not reported.
Other bias	High risk	Quote: "most challenging group of patients. Contributors Both D G Armstrong and L A Lavery participated in the design, enrolment, and analysis of the study. Conflict of interest statement D G Armstrong and L A Lavery received research funding and are members of the speakers' bureau for KCI USA, manufacturer of the NPWT therapy system used in this study. Acknowledgments We thank the members" Quote: "This study was funded by KCI USA, the manufacturer of the VAC Therapy Systems. KCI USA organised and implemented the study design by engaging a committee of wound healing experts; employed a staff of study monitors to ensure compliance with source documen- tation at all sites throughout the study; was not involved in the analysis or write-up of the manuscript, but did review the work before it was released;" Judgement Comment: Study funded by manufacturer of the VAC therapy system and are the two authors..

Blume 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 58 (12) ● *Female, N (%)*: 28 (17) ● *BMI, mean (SD)*: 32.4 ● *Type 2 diabetes, N (%)*: 154 (91.1) ● *HBA1C, mean (SD)*: 8.3 (2) ● *Current smoker, N (%)*: 34 (21.1) ● *Distal blood pressure (mmHg), mean (SD)*: 1 (0.2) ● *Wound area (cm2), mean (SD)*: 13.5 (18.2) ● *Peripheral neuropathy, N (%)*: 150 (90.4) Kontrol 1 ● *Age, mean (SD)*: 59 (12) ● *Female, N (%)*: 44 (27) ● *BMI, mean (SD)*: 30.6 ● *Type 2 diabetes, N (%)*: 152 (91.6) ● *HBA1C, mean (SD)*: 8.1 (1.9) ● *Current smoker, N (%)*: 32 (19.4) ● *Distal blood pressure (mmHg), mean (SD)*: 1 (0.2) ● *Wound area (cm2), mean (SD)*: 11 (12.7) ● *Peripheral neuropathy, N (%)*: 143 (88.8) **Included criteria:** "The patient population consisted of diabetic adults >18 years with a stage 2 or 3 (as defined by Wagner'sscale) calcaneal, dorsal, or plantar foot ulcer >2cm 2 in area after debridement. Adequate blood circulation (perfu-sion) was assessed by a dorsum transcu-taneous oxygen test >30 mmHg, ankle-brachial index values >0.7 and <1.2 with toe pressure >30 mmHg, or Doppler arterial waveforms that were triphasicor biphasic at the ankle of the affected leg." **Excluded criteria:** "Patients with recognized active Charcotdisease or ulcers resulting from electrical,chemical, or radiation burns and thosewith collagen vascular disease, ulcer ma-lignancy, untreated osteomyelitis, or cel-lulitis were excluded from the study. Patients with uncontrolled hyperglyce-mia (A1C >12%) or inadequate lower ex-tremity perfusion were not enrolled. Exclusion criteria also included ulcertreatment with normothermic or hyper-baric oxygen therapy; concomitant medications such as corticosteroids, im-munosuppressive medications, or chemotherapy; recombinant or autologousgrowth factor products; skin and dermal substitutes within 30 days of study start;or use of any enzymatic debridementtreatments. Pregnant or nursing motherswere excluded from study participation." **Pretreatment:** "The data suggest that no statistically significant demographic differences ex-isted between treatment arms (Table 1)" Note: Weight 99.2 vs 93.8kg, female 17 vs 27%.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: The NPWT system used in this studywas vacuum-assisted closure therapy.The system consists of three components:a negative pressure generating unit with adisposable canister, a pad with evacuationtube, and a reticulated, open cell sterilepolyurethane or a dense open-pore poly-vinyl alcohol foam dressing cut to fit thewound. The system unit is programmedto deliver controlled negative pressureranging from 50 to 200 mmHg. NPWTwas applied to the ulcer as specified bymanufacturer's guidelines (14), and treat-ment was continued until ulcer closure,sufficient granulation tissue formation forhealing by primary or secondary inten-tion, by day 112. ● *Duration*: 112 days or ulcer closure by any means. Kontrol 1 ● *Description*: AMWT dressings were used accord-ing to Wound, Ostomy and ContinenceNurses Society guidelines (6) and institu-tional treatment protocols, consistentwith standards of care for treating DFUs.Skin substitutes, cytokines, recombinanthuman platelet-derived growth factors, orsimilar therapies as outlined in the exclu-sion criteria were not used in either groupduring the active treatment phase (ATP). ● *Duration*: 112 days or ulcer closure by any means. **Comment:** Treated for ulcer infection prior to randomization NPWT: 50 (29.6%), 45 (27.1%)
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Number of Amputations ● **Direction**: Lower is better ● **Data value**: Endpoint *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome

	● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** KCI USA Incorporated (San Antonio, TX) supported this study. **Country:** USA **Setting:** This study was a prospective RCT initiated at 37 diabetic foot and wound clinics and hospitals. **Authors name:** PETER A. BLUME **Institution:** North American Center for Limb Preservation, New Haven, Connecticut **Email:** peter.b@snet.net
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The data suggest that no statistically significant demographic differences ex- isted between treatment arms" Quote: "Randomization was accomplished by generating blocks of numbers through http://www.randomizer.org."
Allocation concealment (selection bias)	Low risk	Quote: "Numbers were assigned to a treatment group and sealed in opaque envelopes containing black paper labeled with treatment and patient ID. Envelopes were sequentially numbered before clinical trial site distri- bution. At patient randomization, treat- ment was assigned on the basis of the next sequentially labeled envelope."
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: NI about personnel, likely unblinded participants
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: NI likely unblinded assessors
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: missing data was balanced across intervention groups n=54 (32%) and n=43 (26%) in NPWT and AMWT respectively discontinued treatment with reasons. ITT analysis however, moderate-large attrition in both groups
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No protocol available however, expected outcomes thoroughly reported.
Other bias	Low risk	Judgement Comment: No reasons to suspect other sources of bias.

Chiang 2017

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 61.0 (12.9) ● *Female, N (%)*: 4 ● *BMI, mean (SD)*: 27.4 (6.8 ● *Current smoker, N (%)*: 2 ● *Distal blood pressure (mmHg), mean (SD)*: 1.18 (0.41) ● *Wound area (cm2), mean (SD)*: 38.8 (16.6)

	Kontrol 1 ● *Age, mean (SD)*: 62.0 (13.9) ● *Female, N (%)*: 4 ● *BMI, mean (SD)*: 27.1 (6.8) ● *Current smoker, N (%)*: 4 ● *Distal blood pressure (mmHg), mean (SD)*: 1.21 (0.70) ● *Wound area (cm2), mean (SD)*: 32.9 (16.2) **Included criteria:** The inclusion criterion was an acutewound after surgical débridement or minor amputationthat had an adequate blood supply without requiringfurther revascularization procedures and was deemed suit-able for TNP therapy. This included patients who hadundergone recent revascularization to assist wound healing **Excluded criteria:** Previous treatment with corticosteroids, immuno-suppressive drugs, chemotherapy, VAC therapy,hyperbaric oxygen therapy, growth factors, or otherbioengineered tissue products in the previous30 days.dAn acute wound with signs of infection or osteomy-elitis or necrotic tissue that would not be suitablefor TNP therapy.dKnown ankle pressure<50 mm Hg or toepressure<30 mm Hg.dWounds from chronic venous insufficiency.dBeing unsuitable for the trial in the opinion of theoperating surgeon, based on clinical equipoisewhich, for example, excluded patients with a woundsize too small for a TNP dressing and wounds withinadequate perfusion or active infection
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: In the treatment group, TNP was applied by wardnurses with the settings on continuous suctionat125 mm Hg for thefirst 24 hours and intermittentthereafter. Dressings were changed every48 hours in each group unless advised by the surgeonor the wound care nurse specialists. ● *Duration*: 2 w Kontrol 1 ● *Description*: In the control group, modern traditionaldressings, typically topical hydrofiber or hydrogel dress-ings, were applied. Dressings were changed every48 hours in each group unless advised by the surgeonor the wound care nurse specialists. ● *Duration*: 2w
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Number of Amputations ● **Direction**: Lower is better ● **Data value**: Endpoint *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported

	● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** All patients received off-loading therapy, preventativelyand therapeutically, as indicated. A pressure-reliefwalker or sandal (Active Offloading Walker, RoyceMedical, Camarillo, CA, USA) was provided for allpatients. **Country:** new zealand **Setting:** 22 patients who completedthe study were randomly allocated to a treatment group receiving TNP or to a control group receiving regular topicaldressings. **Authors name:** Nathaniel Chiang, **Institution:** Department of Vascular Surgery, Waikato Hospital, Hamilton **Email:** odette.rodda@svha.org.au **Address:** Department of Vascular Surgery,St. Vincent's Hospital, 41 Victoria Parade, Fitzroy VIC 3065, Australia
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization codes were formulated by SPSS software (IBM Corp, Armonk, NY) on a 1:1 basis. Neither the investigators nor the patients were blinded; however, the outcomes were objectively measured." Quote: "There were no differences between the two groups, including for wound location, history of major and minor amputations, and ABI."
Allocation concealment (selection bias)	High risk	Judgement Comment: allocation codes by spss software which investigators or participants could break Likely no adequate allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Quote: "Neither the investigators nor the patients were blinded;"
Blinding of outcome assessment (detection bias)	Low risk	Quote: "the condition of the wound. Randomization codes were formulated by SPSS software (IBM Corp, Armonk, NY) on a 1:1 basis. Neither the investigators nor the patients were blinded; however, the outcomes were objectively measured. On day 0, relevant demographic information was collected,"
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: Substantial attrition rate 44% vs 33% (per protocol analysis)
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: no available protocol.
Other bias	Unclear risk	Quote: "This work was supported by the Waikato Medical Research Foundation, Fac- ulty Research Development Fund, Braemar Charitable Trust Research Grant, Bayers Health Care Fund, Department Grant-in-aid, Performance- Based Research Fund Allocation, Postgraduate Student Fund, and the PReSS Fund. There were no significant relationships with HyperMed Inc (developer of OxyVu), Intermed (manufacturer of VAC), and ARANZ (manufacturer of the FastScan and Silhouette Mobile). The devices were bought and leased using independent research funds. There were no con- flicts of interest that were directly relevant to the content of this manuscript."

James 2019

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 55.85 (35-95) ● *Female, N (%)*: 11 (40.74) ● *BMI, mean (SD)*: 22.99 ● *HBA1C, mean (SD)*: 8.7 ● *Wound area (cm2), mean (SD)*: 70.9 Kontrol 1 ● *Age, mean (SD)*: 52.89 (28-70) ● *Female, N (%)*: 12 (44.44) ● *BMI, mean (SD)*: 23.26 ● *HBA1C, mean (SD)*: 8.54 ● *Wound area (cm2), mean (SD)*: 80.44 **Included criteria:** The study included all diabetic patients >18 years of age admitted with a DFU **Excluded criteria:** The study excluded patients with coagulopathy, venous disease, ulcer with the underlying osteomyelitis, Charcot's joint, and peripheral vascular disease. The study also excluded patients with ulcer with Wagner Grades III and IV and involving both feet. **Pretreatment:** The number of patients with Wagner Grade 1 and 2 was unequally distributed in the two groups (p=0.036)
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: In the study group, the wound bed was filled with a saline-soaked gauze piece after it was thoroughly cleaned. VAC was applied by placing sterile pads in two layers with a 16Fr Ryle's tube placed between the two layers and then the wound was sealed by a sterile transparent polyurethane sheet. The tube was connected to a wall-mounted suction device and the pressure was set at −125 mmHg [Figure 1]. Mode of NPWT was continuous. This dressing was changed every 48 h. At any point of time during the study, if the treating surgeon noticed any adverse wound parameter, VAC therapy was immediately discontinued.

	● *Dose*: Changing every 2. day ● *Duration*: 34 days, until wound healing Kontrol 1 ● *Description*: In the control group, conventional dressing was given. This consisted of placing a saline-soaked gauze piece over the wound bed after cleaning the wound. Two layers of sterile gauze piece were placed on the dressing and secured with roller bandages. The dressing was changed daily, and assessment of the wound was done every 48 h by the treating surgeon for improvement or any adverse wound parameters. ● *Dose*: changed every day ● *Duration*: 34 days, until wound healing
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Scale**: Adverse events ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Higher is better ● **Data value**: Endpoint *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Partially reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint, median time (for wounds >10cm) *Frafald, alle årsager, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** financially supported by the department of surgery, india **Country:** India **Setting:** RCT study, n: 60, carried out at a surgical department in india comparing VAC and conventional theapy in terms of wound healing **Authors name:** Sangma M. D. James **Institution:** Department of surgery, Jawaharial instute of postgraduate mediacal education and research, Puducherry 605 006 india **Email:** drsureshkumar08@gmail.com **Address:** Department of surgery, Jawaharial instute of postgraduate mediacal education and research, Puducherry 605 006 india
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	COMMENTS: Stratified block randomization using a computer program with randomly selected block sizes of four and six.
Allocation concealment (selection bias)	Low risk	COMMENTS: allocation concealement was ensured using serially numbered opaque sealed envelope technique

Blinding of participants and personnel (performance bias)	Unclear risk	COMMENTS: No information about blinding.
Blinding of outcome assessment (detection bias)	High risk	COMMENTS: No information about blinding. Likely unblinded.
Incomplete outcome data (attrition bias)	Unclear risk	COMMENTS: 3 vs 3 patients excluded. 1 adverse event in NPWT group (MCI). Per protocol analysis.
Selective reporting (reporting bias)	Unclear risk	COMMENTS: No protocol, thorough reporting of expected outcomes.
Other bias	Low risk	COMMENTS: no other risk of bias, funded by the surgical department, however that shouldn't be a risk(vac treatment)

Nain 2011

Methods	**Study design:** **Study grouping:**
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 61.33 ± 7.63 ● *Female, N (%)*: 20% Kontrol 1 ● *Age, mean (SD)*: 55.40 ± 11.54 ● *Female, N (%)*: 13.33% **Included criteria:** Age group 20-75 years.-Ulcer area ranging between 50cm2 and 200cm2.-Diagnosis of diabetes mellitus made by American Diabetes Association Criteria **Excluded criteria:** Age <20 years or > 75 years.-An obvious septicemia.-Osteomyelitis. -Wounds resulting from venous insufficiency. -Malignant disease in a wound.-Patients being treated with corticosteroids, immunosuppressive drugs or chemotherapy.-Any other serious pre-existing cardiovascular, pulmonary and immunological disease
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: After the debridement, foam-based dressing was done over the wounds of the study group under all aseptic conditions. The dressing was covered with an adhesive drape to create an airtight seal. An evacuation tube embedded in the foam was connected to a fluid collection canister contained within a portable vacuum/suction machine [Figures 1 and 2]. Subatmospheric (negative) pressure was applied within a range of −50 mmHg to −125 mmHg intermittently three times a day. NPWT dressings were changed as and when required ● *Duration*: 8w ● *Dose*: change when required Kontrol 1 ● *Description*: the control group received twice daily saline-moistened gauze dressings. Weekly cultures were taken from the floor of the ulcers to assess for the bacterial flora. Standard antibiotic regimes were administered to all the patients which consisted broad spectrum antibiotics initially and later according to the culture sensitivity report. ● *Duration*: 8w ● *Dose*: twice daily
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Not reported *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported

	● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** no funding **Country:** india **Setting:** 30 patients were divided into two groups. One group received negative pressure dressing while other group received conventional saline moistened gauze dressing. Results were compared for rate of wound healing **Authors name:** Prabhdeep Singh Nain **Institution:** Departments of General Surgery, 1Plastic Surgery, Dayanand Medical College and Hospital, **Email:** drramneeshgarg@rediffmail.com **Address:** Department of Plastic Surgery, Dayanand Medical College and Hospital, Ludhiana−141001, Punjab, India.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "They were then randomized to either of the groups." Judgement Comment: Unclear method of sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: No information about blinding.
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: No information about blinding.
Incomplete outcome data (attrition bias)	Unclear risk	Quote: "The patients who underwent below knee amputation were excluded from this analysis." Judgement Comment: Likely no attrition (no information). No information about n patients were excluded due to amputations.
Selective reporting (reporting bias)	High risk	Judgement Comment: No potocol nor reporting of n of amputations (critical outcome)
Other bias	Unclear risk	Judgement Comment: No conflicts of interest statements nor information about funding.

Ravari 2013

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Female, N (%)*: 3 ● *Type 2 diabetes, N (%)*: 9 ● *Wound area (cm2), mean (SD)*: 39.5 Kontrol 1 ● *Female, N (%)*: 5 ● *Type 2 diabetes, N (%)*: 13 ● *Wound area (cm2), mean (SD)*: 36.5 **Included criteria:** patients with DFU's **Excluded criteria:** pt with renal failure, dialysis, history of poor compliance with medical treatments, radiation therapy or chemotherapy, ischemic ulcer with need of open or endovascular revascularisation.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: NPWT system as VAC therapy, negative pressure up to 125mmHg ● *Duration*: 2w ● *Dose*: change every 3. day Kontrol 1 ● *Description*: moist dressings ● *Duration*: 2w

	● *Dose*: change every day
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Number of Amputations ● **Direction**: Lower is better ● **Data value**: Endpoint *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Scale:** Patient satisfaction (yes/no). ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** no funding **Country:** iran **Setting:** 13 pt with DFU's enrolled in the moist dressing group and 10 pt in the VAC at a hospital in iran. **Comments:** obs, baseline imbalance, history of ulcer treatment. **Authors name:** Hassan ravari **Institution:** Trauma research center, department of general surgery, shirez university of mediacal sciences shiraz, iran **Email:** ghoddusih@yahoo.com **Address:** department of general surgery, shiraz university of medical sciences, P.O Box 71345-1876, iran
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Judgement Comment: Randomly assigned by simple randomisation method according to the date of admission.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information
Blinding of participants and personnel (performance bias)	Unclear risk	Judgement Comment: No information about blinding.
Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: No information about blinding of participants (reporting satisfaction) nor personnel (reporting ulcer size, ulzer closure nor amputations)
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Likely no attrition (no information)
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No protocol available.
Other bias	Unclear risk	Judgement Comment: No reasons to suspect other sources of bias.

Sajid 2015

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 56.83 (11.3) ● *Female, N (%)*: 32 ● *Type 2 diabetes, N (%)*: 137(98.6) ● *Wound area (cm2), mean (SD)*: 15.09 (2.81) ● *Peripheral neuropathy, N (%)*: 61 (43.9) Kontrol 1 ● *Age, mean (SD)*: 55.88 (10.97) ● *Female, N (%)*: 25 ● *Type 2 diabetes, N (%)*: 137(98.6) ● *Wound area (cm2), mean (SD)*: 15.07 (2.92) ● *Peripheral neuropathy, N (%)*: 69 (49.6) **Included criteria:** Inclusion criteria were diabetic adults of bothgenders aged >18 years with calcaneal, dorsal oraged >18 years with calcaneal, dorsal orplantar foot ulcer. **Excluded criteria:** Patients with recognized activecharcot disease, collagen vascular disease, malignancy,untreated osteomyelitis, HbA1c > 12% and usingconcomitant medications such as corticosteroids,immunosuppressive medications or chemotherapy wereexcluded from the study.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: whileNPWT changes were performed every 48 - 72 ho ● *Duration*: 2w Kontrol 1 ● *Description*: Moist dressings werechanged on daily basis using surgical gauze ● *Duration*: 2w
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Not reported *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported

	● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** no sponsors **Country:** Rawalpindi (india?) **Setting:** Methodology:The study consisted of 278 patients, with 139 patients each in Group 'A' and 'B', who were subjected toAMWT and NPWT, respectively. Wound was assessed digitally every week for 2 weeks. **Authors name:** Muhammad Tanveer Sajid **Institution:** Department of general surgery, military hospital, Rawalpindi **Email:** doc_tanveersajid@hotmail.com **Address:** Ezzy traders, Hakeem jee building, jinnah road, abbottabad
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were divided into two groups by random allocation based on computer generated table of random numbers."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information about concealment.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information about blinding. Likely no blinding.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "or trained dedicated nursing staff. The wounds were assessed weekly for 2 weeks. The wounds were photographed digitally following initial debridement, if required, and at weekly interval with reference marker including patient ID, date and scale in three dimensions. Moreover, wound dimensions and surface areas were determined in a blind fashion using UTHCSA image tool version 3.0 (Figure 1a,b). All the data collected through the proforma was entered into"
Incomplete outcome data (attrition bias)	Unclear risk	Judgement Comment: no obvious missing data, but a large pt group with no defined dropouts og predefined per protocol analysis or ITT
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No protocol available.
Other bias	Low risk	Judgement Comment: No reason to suspect other sources of bias.

Seidel 2020

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 67.6 (12.3) ● *Female, N (%)*: 38 of 171 (22.2%) ● *HBA1C, mean (SD)*: 16.8 (16.7) ● *Wound area (cm2), mean (SD)*: 1060mm2 (1536) ● *Peripheral neuropathy, N (%)*: 125 of 166 (73.1%) Kontrol 1 ● *Age, mean (SD)*: 68.1 (11.5) ● *Female, N (%)*: 40 of 174 (23.0%) ● ● *HBA1C, mean (SD)*: 14.7 (19.6) ● *Wound area (cm2), mean (SD)*: 1141mm2 (3247) ● *Peripheral neuropathy, N (%)*: 125 of 168 (71.8%

	Included criteria: Adult patients (age >18 years) with at least 4-week-old chronic DFUs corresponding to Wagner 2–4 were screened for study participation by the local investigators. Before inclusion, the study protocol required either a debridement or, if necessary, an amputation of foot parts, or a thorough wound cleansing, depending on the indi-vidual needs of the patients. Thus, chronic diabetic foot wounds after adequate wound pretreatment as well as postsurgical amputation wounds below the upper ankle joint were eligible for inclusion. The initially planned minimum ulcer age of 6 weeks was reduced to 4 weeks 3Seidel D, et al. BMJ Open 2020;10:e026345. doi:10.1136/bmjopen-2018-026345Open accessduring the course of the study. As in clinical practice, the assessment of patients' suitability for a specific wound therapy with the aim of complete wound closure and (due to randomisation) for both study treatment arms (NPWT and SMWC) was at the discretion of the treating physicians (clinical investigators of the study). Particular attention was to be paid to the diagnosis and therapy of concomitant diseases. **Excluded criteria:** inclusion and exclusion criteria were selected based on manufacturers' contraindications and US Food and Drug Administration (FDA) warnings, the necessity to exclude patients in need of protection and who are unable to give their consent, and the intention to avoid general study-related and treatment specific influences on the results.Patients estimated to be at risk of non-compliance with study requirements, with wounds with necrotic tissue present that could not be removed by debridement or amputation, with exposed blood vessels within or directly surrounding the wound not possible to be suffi-ciently covered or with an increased risk of bleeding with haemodynamic consequences (mainly relevant for poste-rior tibial artery dorsalis pedis artery), and outpatients receiving anticoagulation therapy or suffering from a high-grade impaired clotting function with a heightened risk of bleeding with haemodynamic consequences were excluded from the DiaFu study. The use of NPWT devices on the study wound within 6 weeks prior to study start represented an exclusion criterion in order to demon-strate a clear therapeutic effect of each treatment arm
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: In the intervention arm commercially available CE-marked NPWT devices of the manufacturers Kinetic Concepts Incorporated (KCI) and Smith & Nephew (S&N) were used in the discretion of the clinical inves-tigator according to clinical routine and manufacturers' instructions.23 Intermittent and continuous NPWT was allowed to be used with the negative pressure to be adapted as recommended for the dressing applied (V.A.C.-Granufoam Black or Silver; V.A.C.-White Foam; Renassys−F/P; Renassys−G) and adapted to the wound needs. Recommendations for use are available on the manufacturers' websites. As part of the European tender for the overall project, the German statutory health insur-ance funds awarded lots for the provision of the medical 4Seidel D, et al. BMJ Open 2020;10:e026345. doi:10.1136/bmjopen-2018-026345Open accessproducts by the respective manufacturers. Germany was divided into four supply areas. During the award proce-dure, S&N received one lot and KCI three lots. Thus, devices and consumables of S&N were used for the north and northern east region of Germany, and for the rest of Germany, the therapy systems of KCI were used. Within the study, NPWT was required to be used for wound bed preparation in order to achieve at least 95% gran-ulation of the wound area. After optimal preparation of the wound, complete closure could be achieved either by secondary intention with dressings or by surgical closure with subsequent removal of the suture. ● *Duration*: 16w Kontrol 1 ● *Description*: Control therapy was defined as any SMWC according to local clinical standards and guidelines.25 26 Healthcare providers were obligated to provide patients with best practice. In the control arm, it was permitted to apply any local wound treatment standard used in the respec-tive study site that did not have an experimental status or was NPWT. To ensure the best quality of local wound treatment, the study sites were trained for both the inter-vention arm by the manufacturers and the control arm by the German Society for Wound Healing and Wound Treatment, which provided parts of its curriculum and experienced instructors.The maximum study treatment time was 16 weeks after randomisation. Study visits needed to be performed at week 1, 3, 5, 12 and 16, and in the event of end of treat-ment, hospital discharge, wound closure and for wound closure confirmation after a minimum of 14 days. Study participants were followed up until 6 months after randomisation. ● *Duration*: 16w
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Number of Amputations ● **Direction**: Lower is better ● **Data value**: Endpoint *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling, mean (SD)* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint

	Recidiv af sår, længste follow-up (op til 1 år) ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** The study was initiated by a consortium of 19 statutory German health insurance funds, which provided integrated care contracts for all study partic-ipants and for up to 7000 patients with acute and chronic wounds in Germany, defined basic rules for study design based on the requirements of the German authorities; and provided a critical review of the study protocol and the final report. The study was funded by the manufacturers KCI (Acelity) and S&N. Both companies provided the NPWT devices and associated consumable supplies in the assigned regions of Germany as well as all necessary support and information about the used material. **Country:** Germany **Setting:** This German national study was conducted in 40 surgical and internal medicine inpatient and outpatient facilities specialised in diabetes foot care **Authors name:** Dörthe Seidel **Institution:** Institut für Forschung in der Operativen Medizin (IFOM), Universität Witten/Herdecke, Köln, Germany **Email:** Doerthe.Seidel@uni-wh.de **Address:** Institut für Forschung in der Operativen Medizin (IFOM), Universität Witten/Herdecke, Köln, Germany
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Patients were randomly allocated to the treatment arms in a 1:1 ratio using a computer- generated list located on a centralised web- based tool. The randomisation list consisted of permuted blocks of variable length which were randomly arranged. Patients were stratified by study site and by Wagner- Armstrong stage within each site (<Wagner- Armstrong stage 2C and ≥Wagner- Armstrong stage 2C). The randomisation lists were generated with the help of a self- created Java program and integrated into the study database."
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Each registered investigator received individual access to the randomisation tool via the study website but without knowledge of future treat- ment assignment, which provided adequate allocation concealment."
Blinding of participants and personnel (performance bias)	High risk	SUPPORTING ANNOTATIONS: "The investigators were responsible for adequately implementing the assigned therapy. Due to the physical differences between the treatment regimens, it was not possible to blind either participant or physician to the treatment assignment."
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "Verification of complete wound closure was performed by independent, blinded assessment of wound photographs. Determination of wound size and percentage wound tissue quality was also performed by central, blinded outcome assessors based on the wound photographs using the Wound Healing Analyzing Tool (W.H.A.T.)."
Incomplete outcome data (attrition bias)	High risk	COMMENTS: "Substantial attrition. ITT and PP analysis showing bias due to missing data (the ITT-analysis underestimating the effect of NPWT). Large imbalanced attrition"
Selective reporting (reporting bias)	Low risk	SUPPORTING ANNOTATIONS: "More detailed information on the study design can be found in the study protocol publication that is available open access. COMMENTSpreregistered trial, primary and secondary outcomes predefined"
Other bias	Low risk	SUPPORTING ANNOTATIONS: "The study was funded by the manufacturers KCI (Acelity) and S&N. Both companies provided the NPWT devices and associated consumable supplies in the assigned regions of Germany as well as all necessary support and information about the used material. The manufacturers had no role in study design, data collection, data analysis, data interpretation or writing of the report. All authors had full access to all of the data (including statistical reports and tables) in the study and take full responsibility for the accu- racy of the data analysis." COMMENTS: Despite the involvement of the manufactures of the NPWT devices no reason to suspect other sources of bias.

Sepulveda 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention 1 ● *Age, mean (SD)*: 61.5 (10) ● *Female, N (%)*: 2 (16.7) ● *BMI, mean (SD)*: 28.1 (4) ● *Type 2 diabetes, N (%)*: 12 ● *HBA1C, mean (SD)*: 9.5 (2) ● *Current smoker, N (%)*: 2 (16.7) ● *Distal blood pressure (mmHg), mean (SD)*: 1.05 (0.5) Kontrol 1 ● *Age, mean (SD)*: 62.1 (8) ● *Female, N (%)*: 3 (25.0) ● *BMI, mean (SD)*: 26.6 (4) ● *Type 2 diabetes, N (%)*: 12 ● *HBA1C, mean (SD)*: 9.7 (2) ● *Current smoker, N (%)*: 3 (25.0) ● *Distal blood pressure (mmHg), mean (SD)*: 1.16 (0.6) **Included criteria:** Subjects older than 18 years old, type II diabetics, with a transmetatarsal amputation wound of 2 or more contiguous toes or the first toe (Figure 1a) from resolved infectious or vascular causes, with adequate perfusion of the affected member and that would accept to participate in the study. **Excluded criteria:** Subjects with active Charcot feet were excluded from the study as well as those with uncontrolled hyperglucaemia (glycated haemoglobin [HbA1C] greater than 12%), being treated with steroids, immunosuppressive drugs or chemotherapy, with severe malnutrition (albumin lower than 2.1 mg/dL).7,35-38and being treated with growth factors or with hyperbaric oxygen in the last 30 days **Comment:** Population is post-operation.
Interventions	**Intervention Characteristics** Intervention 1 ● *Description*: The patients assigned to group A received a treatment that consisted of covering the wound with a polyurethane ester sponge with large pores (400-600 µm) and a fenestrated drainage tube (Nelaton No. 16), inserted between the sponge and a transparent impermeable adhesive bandage placed as a seal over the entire system (Figure 1b). The system was connected to a central suction system and it was kept at a continuous sub-atmospheric pressure of 100 mmHg until the next treatment ● *Duration*: until 90 % of granulation. ca 54 days ● *Dose*: The wound was treated every 48 to 72 hours Kontrol 1 ● *Description*: The patients of group B received treatment according to the saturation of the secondary bandage. If the bandage presented a rate of saturation lower than 50%, the wound was covered with a gel hydrocolloid, tulle (woven gauze impregnated with a petrolatum emulsion), and a bandage. If on the contrary it presented saturation greater than 50%, the wound was covered with alginate and a bandage. The patients of both groups received treatment before being assigned,. according to the clinical guides of the Chilean Health Ministry (shower-therapy, saline solution, and debridement) ● *Duration*: until 90 % of granulation. ca 54 days ● *Dose*: The wound was treated every 48 to 72 hours
Outcomes	*Underekstremitets amputationer, længste follow-up (op til 1 år)* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Unit of measure**: Number of reamputations ● **Direction**: Lower is better ● **Data value**: Endpoint (timepoint not reported) *Sårheling (total sårlukning (ja/nej)), efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Proportion with ulcer healing ● **Direction**: Higher is better ● **Data value**: Endpoint *Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Not reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Endpoint *Sårareal, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Surface area (cm2) ● **Direction**: Lower is better ● **Data value**: Endpoint *Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Infections ● **Direction**: Lower is better ● **Data value**: Endpoint *Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported

	● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Recidiv af sår, længste follow-up (op til 1 år)* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Events ● **Direction**: Lower is better ● **Data value**: Endpoint *Behandlings adherence/kompliance, i interventionsperioden* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Higher is better ● **Data value**: Change from baseline *Tid til heling, efter endt behandling* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: Days ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Unit of measure**: n/N ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** no funding or sponsorship **Country:** Chile **Setting:** 22 Diabetic patients with a foot amputation wound were assigned to treatment with NPWT or standard wound dressing **Authors name:** Gustavo Sepúlveda **Institution:** Servicio de Cirugía Vascular, Hospital Dipreca, Santiago de Chile **Email:** dr.gsepulveda@gmail.com **Address:** Servicio de Cirugía Vascular, Hospital Dipreca, Santiago de Chile, Chile
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "The random sequence was elaborated using a computer programme."
Allocation concealment (selection bias)	Low risk	SUPPORTING ANNOTATIONS: "Closed envelopes were created with an arbitrary identification number and inside the previously determined treatment assignment was found, which was hidden until the end of the study."
Blinding of participants and personnel (performance bias)	High risk	SUPPORTING ANNOTATION: "Send of the study. A nurse that was trained and had experience in each type of treatment carried out the treatments. Given the physical differences between the treatments, it was impossible to hide the random assignment from the patient or the treatment team. The patients assigned to group"
Blinding of outcome assessment (detection bias)	Low risk	SUPPORTING ANNOTATIONS: "saline solution, and debridement). 40 The wound was treated every 48 to 72 hours and evaluated weekly with digital photography. The photography was crosshatched and analyzed square by square to determine the fraction of granulated tissue in each square. The total percentage of granulation of the wound came from the average of all of the fractions of all of the squares of the image. An independent group of the research team masked from the assigned treatment, conducted the evaluation of the percentage of granulation."
Incomplete outcome data (attrition bias)	Low risk	SUPPORTING ANNOTATIONS: "The statistical analysis was performed with the intention to treat and mask the assigned treatment." COMMENTSLikely no attrition
Selective reporting (reporting bias)	Unclear risk	COMMENTS: No protocol available. Thorough reporting of expected outcomes
Other bias	Low risk	COMMENTS: No reasons to suspect other sources of bias.

Footnotes

Characteristics of excluded studies

Borys 2018

Reason for exclusion	Wrong study design

DallaPaola 2010

Reason for exclusion	Wrong patient population

Eginton 2003

Reason for exclusion	Wrong intervention

Frykberg 2007

Reason for exclusion	Wrong study design

Hu 2018

Reason for exclusion	Wrong intervention

Kirsner 2019

Reason for exclusion	Wrong comparator

Lone 2014

Reason for exclusion	Wrong study design

McCallon 2000

Reason for exclusion	Wrong comparator

Nather 2010

Reason for exclusion	Wrong study design

Peinemann 2008

Reason for exclusion	Wrong study design

Saraiya 2013

Reason for exclusion	Wrong study design

Stansby 2010

Reason for exclusion	Wrong study design

Vassallo 2015

Reason for exclusion	Wrong intervention

Footnotes

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Data and analyses

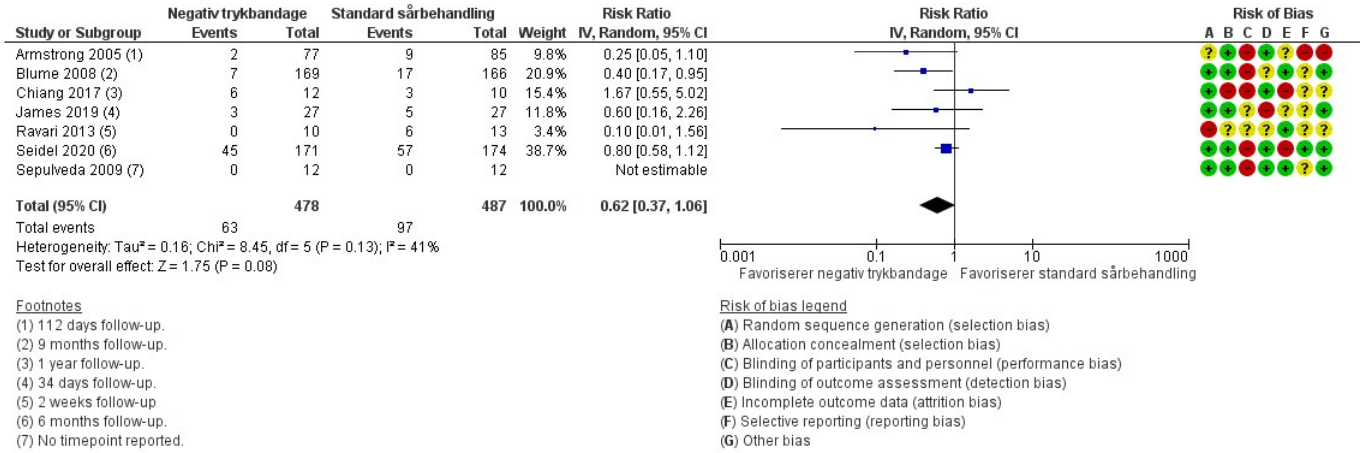
1 Negativ trykbandage vs standard sårbehandling

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Underekstremitets amputationer, længste follow-up (op til 1 år)	7	965	Risk Ratio (IV, Random, 95% CI)	0.62 [0.37, 1.06]
1.2 Sårheling (total sårlukning (ja/nej)), efter endt behandling	7	941	Risk Ratio (IV, Random, 95% CI)	1.33 [1.10, 1.59]
1.3 Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden	4	575	Risk Ratio (IV, Random, 95% CI)	2.00 [0.99, 4.04]
1.4 Recidiv af sår, længste follow-up (op til 1 år)	1	46	Risk Ratio (IV, Fixed, 95% CI)	2.54 [0.11, 59.23]
1.5 Behandlings adherence/kompliance, i interventionsperioden	5	920	Risk Ratio (IV, Random, 95% CI)	1.00 [0.98, 1.01]

1.6 Frafald, alle årsager	7	980	Risk Ratio (IV, Random, 95% CI)	1.31 [0.91, 1.89]
1.7 Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden	5	832	Risk Ratio (IV, Random, 95% CI)	1.10 [0.67, 1.81]
1.8 Sårareal, efter endt behandling, std. mean difference	6	425	Std. Mean Difference (IV, Random, 95% CI)	-0.83 [-1.18, -0.47]
1.9 Sårareal, efter endt behandling, mean difference	6	425	Mean Difference (IV, Random, 95% CI)	-8.80 [-14.79, -2.80]
1.10 Tid til heling, efter endt behandling, std. mean difference	5	758	Std. Mean Difference (IV, Random, 95% CI)	-0.42 [-0.57, -0.28]
1.11 Tid til heling, efter endt behandling, mean difference	5	758	Mean Difference (IV, Random, 95% CI)	-14.82 [-19.50, -10.14]
1.12 Patientrapporteret helbredsrelateret livskvalitet målt med standardiseret spørgeskema, efter endt behandling	0	0	Risk Ratio (IV, Fixed, 95% CI)	Not estimable

Figures

Figure 1 (Analysis 1.1)

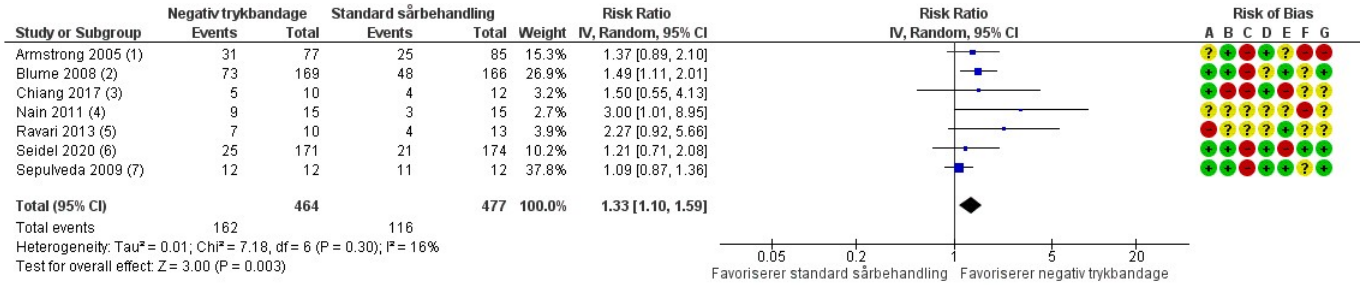


Footnotes
(1) 112 days follow-up.
(2) 9 months follow-up.
(3) 1 year follow-up.
(4) 34 days follow-up.
(5) 2 weeks follow-up
(6) 6 months follow-up.
(7) No timepoint reported.

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.1 Underekstremitets amputationer, længste follow-up (op til 1 år).

Figure 2 (Analysis 1.2)



Footnotes
(1) 16 ugers intervention. Complete closure.
(2) Intervention 4-16 uger (until closure)
(3) 2 ugers intervention. Complete closure.
(4) 8 ugers intervention. Complete closure.
(5) 2 ugers intervention. Complete closure.
(6) 16 ugers intervention. Complete closure (withour surgical interventions).
(7) Ikke rapporteret interventionslængde (Until 90% granulation)

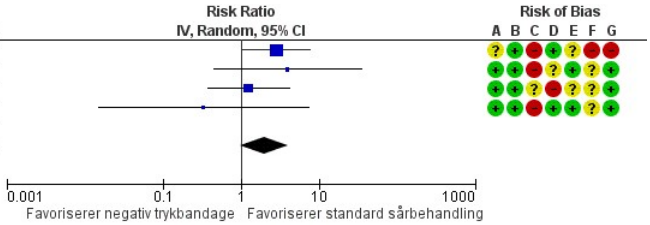
Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.2 Sårheling (total sårlukning (ja/nej)), efter endt behandling.

Figure 3 (Analysis 1.3)

Study or Subgroup	Negativ trykbandage Events	Total	Standard sårbehandling Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Armstrong 2005 (1)	13	77	5	85	50.6%	2.87 [1.07, 7.68]
Blume 2008 (2)	4	169	1	166	10.3%	3.93 [0.44, 34.79]
James 2019 (3)	5	27	4	27	34.0%	1.25 [0.38, 4.16]
Sepulveda 2009 (4)	0	12	1	12	5.1%	0.33 [0.01, 7.45]
Total (95% CI)		**285**		**290**	**100.0%**	**2.00 [0.99, 4.04]**
Total events	22		11			

Heterogeneity: Tau² = 0.00; Chi² = 2.75, df = 3 (P = 0.43); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)



Footnotes
(1) Population is post-operation. Patients with infection pretreatment likely included in study.
(2) Patients treated for infection pretreatment included in study (29.6 vs 27.1%).
(3) Patients with infection (CONS (coagulase negative stafylokokker) pretreatment likely included in study.
(4) Population is post-operation. Patients with infection pretreatment likely included in study.

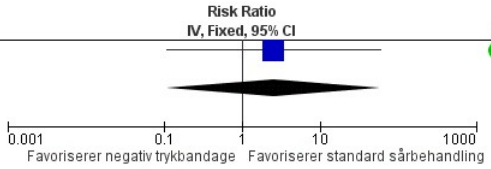
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.3 Infektion (positiv dyrkning, eller klinisk (rødme, pus, lugt, hævelse, smerte)), i interventionsperioden.

Figure 4 (Analysis 1.4)

Study or Subgroup	Negativ trykbandage Events	Total	Standard sårbehandling Events	Total	Weight	Risk Ratio IV, Fixed, 95% CI
Seidel 2020 (1)	1	25	0	21	100.0%	2.54 [0.11, 59.23]
Total (95% CI)		**25**		**21**	**100.0%**	**2.54 [0.11, 59.23]**
Total events	1		0			

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



Footnotes
(1) Recurrent ulcer after epithelisation

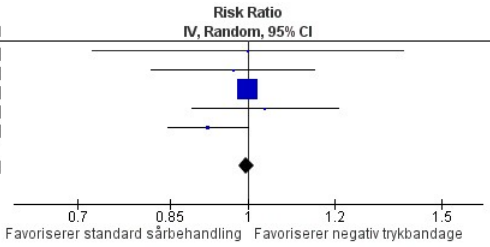
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

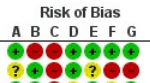
Forest plot of comparison: 1 NPWT vs standard wound care, outcome: 1.7 Recidiv af sår, længste follow-up (op til 1 år).

Figure 5 (Analysis 1.5)

Study or Subgroup	Standard sårbehandling Events	Total	Negativ trykbandage Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Akbari 2007	8	9	8	9	0.3%	1.00 [0.72, 1.39]
Armstrong 2005	58	77	66	85	0.9%	0.97 [0.82, 1.15]
Blume 2008	169	169	166	166	93.9%	1.00 [0.99, 1.01]
James 2019	28	30	27	30	1.1%	1.04 [0.89, 1.21]
Seidel 2020	142	171	157	174	3.8%	0.92 [0.85, 1.00]
Total (95% CI)		**456**		**464**	**100.0%**	**1.00 [0.98, 1.01]**
Total events	405		424			

Heterogeneity: Tau² = 0.00; Chi² = 4.07, df = 4 (P = 0.40); I² = 2%
Test for overall effect: Z = 0.36 (P = 0.72)





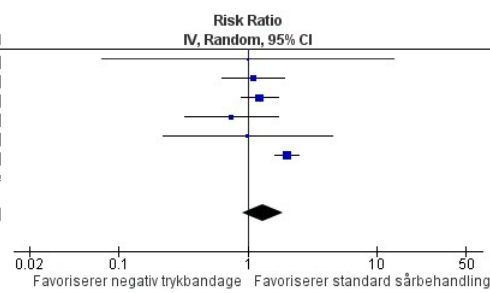
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.5 Behandlings adherence/kompliance, i interventionsperioden.

Figure 6 (Analysis 1.6)

Study or Subgroup	Negativ trykbandage Events	Total	Standard sårbehandling Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Akbari 2007	1	9	1	9	1.8%	1.00 [0.07, 13.64]
Armstrong 2005	19	77	19	85	19.8%	1.10 [0.63, 1.93]
Blume 2008	54	169	43	166	28.0%	1.23 [0.88, 1.73]
Chiang 2017	6	18	8	18	12.6%	0.75 [0.33, 1.72]
James 2019	3	30	3	30	5.0%	1.00 [0.22, 4.56]
Seidel 2020	127	171	64	174	32.8%	2.02 [1.63, 2.50]
Sepulveda 2009	0	12	0	12		Not estimable
Total (95% CI)		**486**		**494**	**100.0%**	**1.31 [0.91, 1.89]**
Total events	210		138			

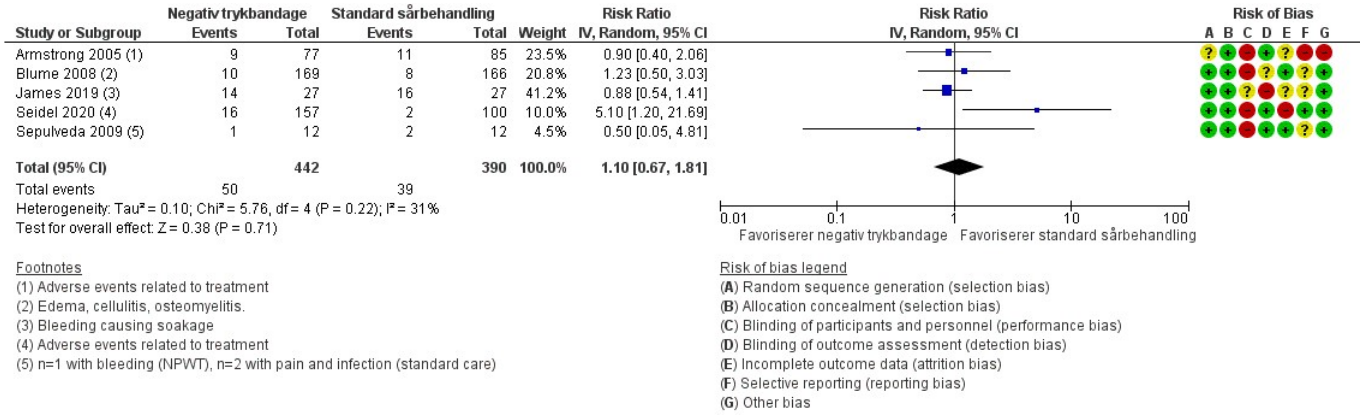
Heterogeneity: Tau² = 0.09; Chi² = 12.19, df = 5 (P = 0.03); I² = 59%
Test for overall effect: Z = 1.47 (P = 0.14)



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 NPWT vs standard wound care, outcome: 1.9 Frafald, alle årsager.

Figure 7 (Analysis 1.7)

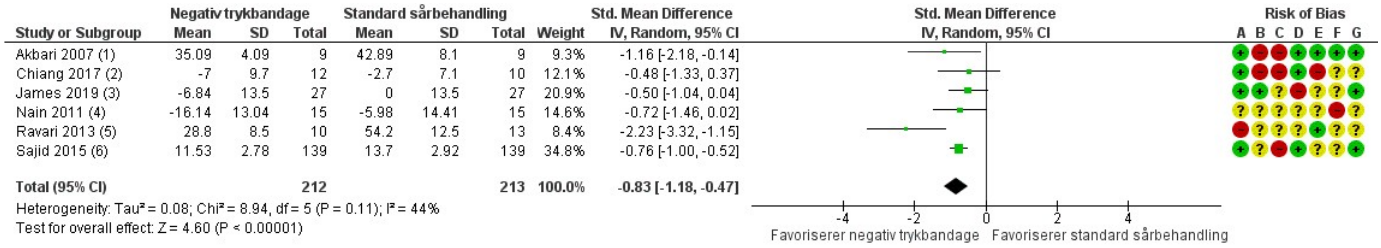


Footnotes
(1) Adverse events related to treatment
(2) Edema, cellulitis, osteomyelitis.
(3) Bleeding causing soakage
(4) Adverse events related to treatment
(5) n=1 with bleeding (NPWT), n=2 with pain and infection (standard care)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.7 Bivirkninger (f.eks. trykskader og påvirkning af hudomgivelser (rødme, vabler, eksem)), i interventionsperioden.

Figure 8 (Analysis 1.8)

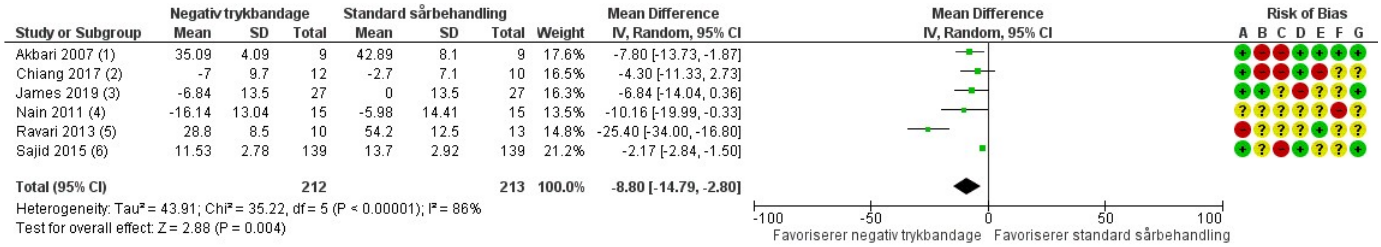


Footnotes
(1) Endpoint wound size (mm2) 3 weeks.
(2) Change in wound size (cm2) 2 weeks.
(3) Calculated between group difference in 34-days end point wound size (cm2) from median change and p-value
(4) Change in wound size (cm2) 8 weeks.
(5) 2 weeks endpoint wound size (cm2).
(6) 2 weeks endpoint wound size (cm2)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 NPWT vs standard wound care, outcome: 1.1 Sårareal, efter endt behandling.

Figure 9 (Analysis 1.9)

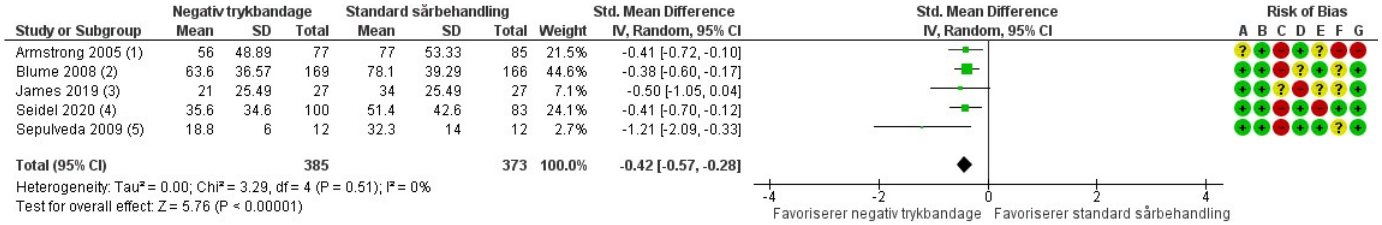


Footnotes
(1) Endpoint wound size (mm2) 3 weeks.
(2) Change in wound size (cm2) 2 weeks.
(3) Calculated between group difference in 34-days end point wound size (cm2) from median change and p-value
(4) Change in wound size (cm2) 8 weeks.
(5) 2 weeks endpoint wound size (cm2).
(6) 2 weeks endpoint wound size (cm2)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.9 Sårareal, efter endt behandling, mean difference.

Figure 10 (Analysis 1.10)

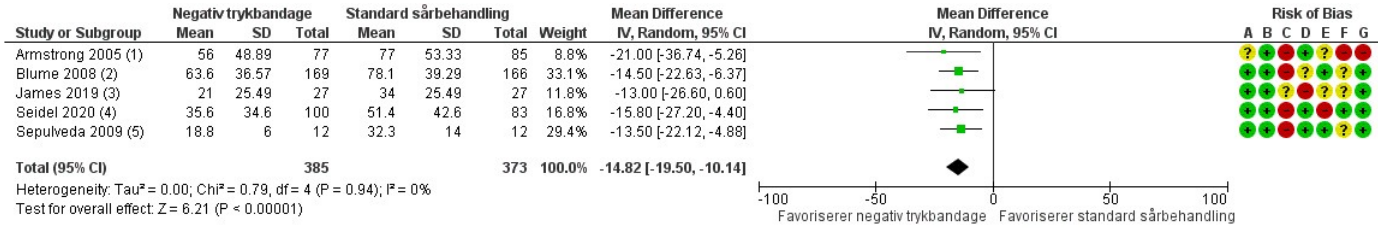


Footnotes
(1) Days. 16 weeks intervention. Mean imputed from median and SD from IQR.
(2) Days. Intervention 4-16 weeks (until closure)
(3) Days. 34 days intervention. Mean imputed from median time to heal and p-value from between group...
(4) Days. Intervention 16 weeks
(5) Days. Intervention until 90% granulation.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 NPWT vs standard wound care, outcome: 1.2 Tid til heling, efter endt behandling.

Figure 11 (Analysis 1.11)

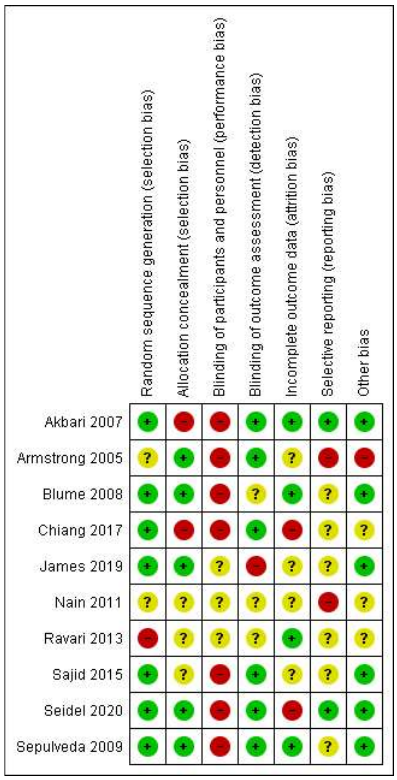


Footnotes
(1) Days. 16 weeks intervention. Mean imputed from median and SD from IQR.
(2) Days. Intervention 4-16 weeks (until closure)
(3) Days. 34 days intervention. Mean imputed from median time to heal and p-value from between group...
(4) Days. Intervention 16 weeks
(5) Days. Intervention until 90% granulation.

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

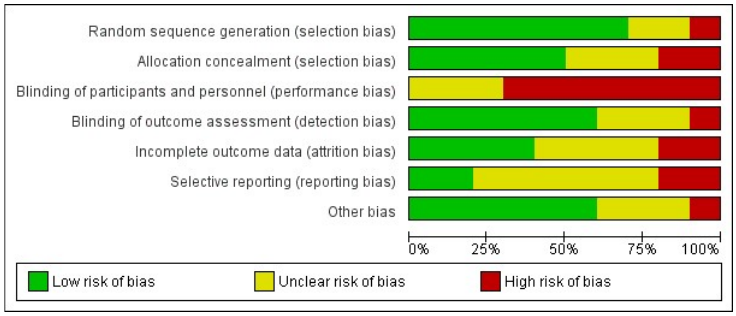
Forest plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.11 Tid til heling, efter endt behandling, mean difference.

Figure 12



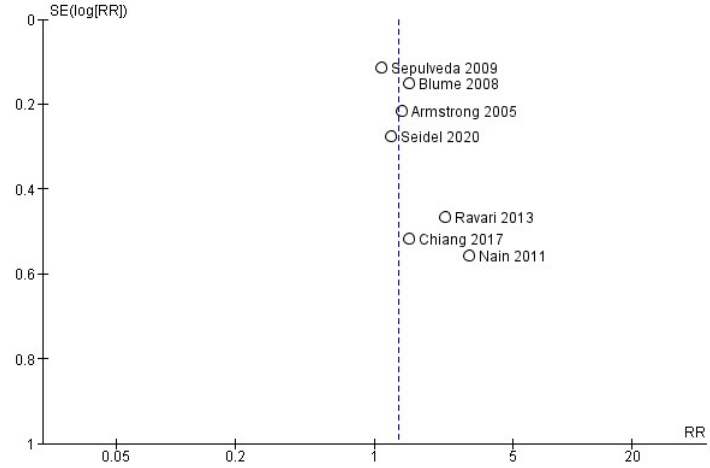
Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 13



Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Figure 14 (Analysis 1.2)



Funnel plot of comparison: 1 Negativ trykbandage vs standard sårbehandling, outcome: 1.2 Sårheling (total sårlukning (ja/nej)), efter endt behandling.