Appendix 1 Supplementary Tables

Supplementary Table 1. Methods of Debridement

Debridement Methods	Explanation	Advantages	Disadvantages	Indications	Contraindications
Non-Mechanical		Selective & Specific for non-viable tissue Convenient application None to minimal discomfort Less cost	Slower (days to weeks)	1. Removal of potential infection source, i.e. non-viable tissue. 2. Removes critically colonized tissue, reduced bacterial burden, reduced resistance related to antibiotic treatment. 3. Facilitates cultures taken to evaluate requirements for antibiotic treatment 4. Stimulates wound bed support in healing and for procedures not limited to grafting, flaps, skin substitutes.	1.Contraindications pertain to specific method of debridement used. 2. Avoid debridement of dry intact eschars without clinical evidence of underlying infection as this can serve as a biological dressing.
Autolytic	Dressing-type specific, sustains moist wound healing environment facilitating autolysis of devitalized tissue.	Selective in non-viable tissue. No or little discomfort. Convenient Less cost	Slow (days to weeks) May result in periwound maceration with very exudative wounds. Can be colonized and infected. Less ideal in the infected wound. Less cost	Similar to above	If active infection and extensive amounts of devitalized tissue needing removal including gangrenous tissue, a different method of debridement should be considered.
Enzymatic	Uses an enzyme applied to the wound	More rapid effect than autolytic debrideme	Slow (days to weeks) Could be	Similar to above	1. Relative contraindication are significantly

	(collagenase) that lyses non-viable tissue.	nt Selective & specific to non-viable tissue. None or little discomfort. Convenient	associated with periwound maceration in heavily exudative wounds. Less ideal in infected wounds. Can be deactivated by other treatments in wound care. Expensive		infected wounds. 2. Collagenase to avoided with silver-containing products or Dakin solution.
Mechanical		Relatively faster method than non-mechanical debridement	May be selective or non-selective depending on specific method used. Less convenient. Associated with more pain. Expensive	1. Removal of source of infection, primarily non-viable tissue. 2. Removes critically colonized tissue, decreases bacterial burden, reduces the resistance from antibiotic treatment, and permits obtaining accurate cultures. 3. Facilitates deeper cultures immediately post-debridement. 4. Stimulates wound bed to support healing and facilitates procedures including grafts, flaps, skin substitutes. 5. Could require local or general anesthesia which has inherent risk.	1. Depends on the method of mechanical debridement used. 2. Avoid is granulation tissue covers the wound bed and no devitalized tissue is present. 3. Insufficient pain control. 4. Inadequate tissue perfusion and/or hypoxia involving the anatomic area. 5. Eschar without clinical evidence infection and serving as a biological dressing.
Sharp/Surgical	Uses a sharp instrument	Quick	Relatively more post-	Similar to above	1. Operative debridement

	including a scalpel or scissor to remove non-viable tissue in outpatient or operating room setting.	Specific Painful Expensive	procedure pain. Expensive i.e may require operating room setting.		requires surgical risk assessment. 2. Avoid in eschar without clinical evidence of infection where eshcar may serve as biological dressing.
Wet to Dry	Uses saline moistened gauze that is allowed to dry and is removed when adherent to tissues causing non-selective mechanical removal of non-viable tissue.	Quick Nonspecific Painful More cost	Nonspecific & nonselective, potential removal of granulating tissue. Relatively more pain or discomfort.	Similar to above	Similar.
Aqueous High-Pressure Lavage Irrigation, or Whirlpool	Uses high pressure irrigation done manually with a 20 ml syringe and an 18-gauge angiocatheter, delivers 12 psi; alternatively high-pressure jet aqueous stream from a whirlpool or alternate mechanical irrigation device.	Quick Preferable for large wounds.	Nonspecific & Nonselective Less specific, Cross-contamination of other wounds and infection. Relatively more pain or discomfort. Immersion of patient may be required. Expensive	Similar to above	Similar to mechanical debridement. Risks cross-contamination if multiple wounds present
Ultrasound debridement	Uses a cavitation	Quick	Relatively more post-	Similar to above	Contraindications: Similar to that

	method to generate sound energy by a handheld instrument mechanicall y dislodging removing nonviable tissue.	Specific	procedure pain or discomfort. Risk of exposure to aerosolized infectious organisms and debris to healthcare provider from the patients wound. Expensive		discussed in mechanical debridement.
Biosurgery **Maggot Debridement Therapy**	Uses maggots applied in larva stage consuming non-viable tissue selectively and removed usually around day 3.	Relatively quick Specific	Possibly minor pain or discomfort. Patient aversion, psychological factors.	Similar to above	1. Abdominal wounds contiguous with the intraperitoneal cavity. 2. Pyoderma gangrenosum with immunosuppressio n therapy. 3. Wounds in areas close to those afflicted by septic arthritis.

Supplementary Table 2: ***A table displaying the inclusion and exclusion criteria for included studies.***

Trial Author	Inclusion Criteria	Exclusion Criteria
1) Ali 2013[1]	1) Texas 2nd grade diabetic foot ulcer	Not reported.
2) Amini 2013[2]	1) Diabetes (type 1 and type 2) 2) Diabetic foot ulcer 3) Wagner Grade 3 chronic (>1 month)	1) 0.6 </= ABI* </= 1.2 (*Ankle Brachial Index)
3) Apelqvist 1990[3]	1) Previous diabetes mellitus	1) Patch test positive individuals.

	2) Superficial skin ulcer below the ankle 3) Systolic toe pressure > 45 mmHg or an absence of cutaneous erythema. 4) Ulcers between 1 - 25 cm^2 and > 50% covered by dry or wet necrotic tissue. 5) Only one ulcer the largest was chosen for study in each patient.	2) Clinical signs of cellulitis. 3) Ulcers where application of intervention dressings would be inappropriate.
4) Baker 1993[4]	1) Patients with neuropathic foot ulcer in a diabetic foot center Type of DM unspecified	Not reported
5) Belcaro 2010[5]	1) Patients who had ulcers resulting from chronic venous insufficiency or diabetes	Not reported.
6) Blackman 1994[6]	1) Diabetes Type 1 or Type 2 2) Partial or full thickness open wound or foot ulcer free; free of hard eschar	1) Ulcers with Wagner stage 3 or higher 2) Ulcers progressing to Wagner stage 3 or higher 3) Subjects needing vascular surgery 4) Ulcers from Charcot joints 5) Ulcers of non-diabetic origin
7) Bowling 2011[7]	1) Type 1 or Type 2 DM 2) Foot ulcer, full thickness, distal to malleoli 2) Chronic > 4 weeks 3) Non-clinically infected foot ulcers 4) Necrotic tissue present and mechanical debridement indicated. 5) One ulcer per patient included	1) Ulcers larger than 25 cm^2 2) Texas Classification grade 3 3) Osteomyelitis 4) Peripheral arterial disease (ABI < 0.8/absent pulses. 5) Prescription use of anticoagulants, immunosuppressive drug treatment 6) Allergies to chlorine 7) Clinically infected wounds excluded on grounds of antibiotic use.
8) Clever 1995[8]	1) Age 18 - 80 years 2) Pure neuropathic superficial ulcer 1-5 cm in diameter	Diabetics with an ankle-brachial pressure index < 0.8 (measured using Doppler ultrasound) Clinical or radiological signs of osteomyelitis or tendon involvement. Large vessel disease Ulcers requiring additional topical treatment

		Known allergies to any product used
9) D'Hemecourt[9] (1998): written consent needed	1) 19 years or older 2) Type 1 or type 2 diabetes 3) At least 1 full thickness ulcer (stage 3 or 4) chronic diabetic foot ulcer present for at least 8 weeks. 4) Target area (Length x Width) 1cm^2-10cm^2 post debridement 5) Transcutaneous oximetry in the affected limb (TcpO2) >/= 30 mmHg	1) Osteomyelitis affecting area of ulcer 2) Target area < 1cm^2 OR > 10 cm^2 post-debridement 3) More than 3 ulcers present at baseline 4) A cause of ulcer other than diabetes e.g. electrical, chemical or radiation 5) Patients with cancer at time of enrollment 6) Concomitant medication known to affect wound healing e.g. corticosteroids, chemotherapy, immunosuppressant's 7) Pregnant, nursing or of child bearing potential not using acceptable contraception.
10) Donaghue 1998[10]	1) At least 21 years of age 2) Adequate nutritional intake (albumin > 2.5 gms/dl) 3) Adequate blood flow to lower extremity (palpable pulses, normal noninvasive tests) 4) Foot ulceration at least 1 cm^2 post-debridement.	1) Severe renal impairment (creatinine >) 2) Severe liver impairment (liver function tests >/= 2 times normal levels. 3) Serious medical disorder that can interfere with wound healing. 4) Osteomyelitis (deep ulcer probing to bone, or radiographic evidence) 5) Clinical signs of infection 6) History of alcohol or drug abuse.
11) EhsanUrRehman 2013[11]	1) Diabetic patients of either gender 2) All age groups 3) Diabetic foot ulcers Wagner grade I & II	1) Nonconsenting patients 2) Systemic infection and other comorbidities
12) Foster 1994[12]	1) At least 18 years' old 2) A clean diabetic foot ulcer 3) Willing and able to comply with study protocol	1) Slough, necrotic, or infected ulcer
13) Goretti (2008)[13]	1) Infected foot lesions post-surgical debridement 2) surgical outcomes > 5 cm^2	Not reported

	3) ankle-brachial index > 0.9, 4) presence of at least two arteries in the ankle documented by palpable pulses or Doppler CW	
14) Hammouri 2004[14]	1) Diabetic foot ulcers	Not reported
15) Jeffcoate 2009[15]	1) Type 1 and type 2 Diabetes 2) Age > 18 yrs. 3) Chronic (>/= 6 weeks) full thickness foot ulcer on or below malleoli 4) Cross sectional area 25 mm^2 - 2500 mm^2 5) Able and willing to give informed consent 6) Reasonably accessible by car to the hospital	1) Known allergy to treatment preparations 2) Ulcer extending to tendon, periosteum, or bone 3) Osteomyelitis 4) Soft tissue infection requiring systemic antibiotics 5) Ulcer on a limb being considered for revascularization 6) Management with a non-removable cast without a dressing window. 7) Gangrene on affected foot 8) Eschar not removable by clinical debridement 9) Sinus or deep track 10) Hallux amputation preventing toe pressure measurement 11) ABI < 0.7 or toe systolic pressure < 30 mmHg 12) Ulceration by disease other than diabetes 13) Any other serious disease likely to compromise outcome 14) Cr > 300 µMol/L 15) Immunosuppressant's, systemic steroids other than inhalation, or any other preparation that could interfere with healing. 16) Living > 10 miles from clinic 17) Those withholding consent
16) Jensen (1997)[16]: written consent needed	1) Diabetic foot ulcer of at least 1cm diameter 2) No evidence of infection in ulcer or peri-wound tissue	No exclusion criteria specified

	3) Wagner grade 2 ulcer, full thickness into subcutaneous tissue, not involving tendon, joint capsule, or bone 4) Documented blood supply consistent with the ability to heal (palpable pulses, non-invasive vascular study) 5) Willingness to comply with protocol.	
17) Lalau 2002[17]	1) Age < 75 yrs. 2) Diabetes either Type 1 or Type 2 3) Foot lesion in the phase of cleansing (granulation tissue < 50% for wound area) 4) Surface area between 1 - 50 cm^2. Acute (< 2 months) and Chronic lesions 2) Surface area of 1 - 50 cm^2	1) Hgba1c > 10% 2) Presence of clinical infection (redness, swelling, warmth, periwound erythema) 3) Osteomyelitis (on plain radiography, or probing of bone) 4) Tunneled wound 5) Severe hypo-vascularization ($TcPO_2$ < 30mmHg)
18) Markevich (2000)[18]	Diabetic Neuropathic Foot wounds	No exclusion criteria specified
19) Mazzone 1993[19]	1) Diabetic subjects with chronic foot ulcers Type of DM unspecified. No other inclusion criteria pre-specified.	No exclusion criteria specified.
20) Munter 2006[20]	1) 18 years or older 2) Not pregnant or lactating 3) Chronic wounds 4) Mixed etiology wounds including burns, donor sites, post-operative wounds, but most reported as leg ulcers, pressure ulcers, and Diabetic foot ulcers (Wagner grade 1 - 3) 5) Ulcer depth < 0.5 cm	Not reported
21) Ogce 2007[21]	1) Type 1 or Type 2 Diabetes 2) Wagner grade 2 or grade 3 diabetic foot ulcers	Not reported
22) Piagessi 2001[22]	1) All patients presenting to foot clinic in 1998 2) Age 18 - 75 3) Type 1 or Type 2 diabetes > 5 years	1) Active infection: Local signs (purulent discharge, redness, swelling, tenderness, or odor) OR systemic signs (fever, malaise, leukocytosis) + confirmed culture exams 2) Plasma creatinine > 2 mg/dl

	4) Ulcer deeper than 1 cm for 3 weeks 5) Palpable peripheral pulses or ABPI > 0.9 6) Ulcers due to diabetic neuropathy or surgical drainage of previous infection or both.	3) Recent episode of ketoacidosis 4) Malignancies 5) Any therapy of pathology that might interfere with healing process 6) Candidates for a major amputation
23) Piaggesi (1998)[23]	1) All patients newly presenting to the diabetic foot clinic between January - December 1995 2) One or more diabetic neuropathic ulcer 3) Diabetes type 1, type 2, at least 5 years duration uncomplicated.	1) Presence of symptomatic claudication OR absence of foot pulses 2) Recent ketoacidosis 3) Renal Failure Cr > 177 micromole/L 4) Presence of Infection 5) Congenital foot deformities or diabetic neuroarthropathy 6) BMI > 30 7) Clinical history of stroke, cardiac failure, cancer, HIV, Mental Illness 8) ABPI < 0.9 9) Osteomyelitis
24) Rhaiem 1998[24]	1) Diabetic hospitalized patients from 1992 - 1995	Not reported
25) Roberts 2001[25]	1) Type 1 diabetics with neuropathic foot ulcers of the plantar surface. No other inclusion criteria pre-specified.	ABPI < 0.8 No exclusion criteria specified.
26) Shukrimi 2008[26]	1) All NIDDM patients with Wagner grade II ulcers admitted for surgery. 2) Age 35 - 65 3) TcPO2 > 30 mmHg 4) Albumin > 35 g/dl	1) Multiple medical comorbidity 2) Steroid therapy 3) Neutrophil count < 2000/mm^3
27) Singh 2006[27]	1) Diabetic foot ulcers admitted to orthopedic wards. 2) Wagner type 1 and type 2 3) Known cases of DM Type 1 or Type 2 treated medically	1) Wagner grade 3 or grade 4 diabetic foot ulcers 2) Ulcers covered with hard scab 3) Peripheral neuropathy based on modified NDS 4) Patients without at least one of the foot pulses palpable (dorsalis pedis or posterior tibial)

	4) Glycemic control during hospitalization with insulin. 5) Sensate feet based on Modified Neuropathic Disability Score (NDS) 6) At least one of the foot pulses palpable (dorsalis pedis or posterior tibial arteries)	
28) Tallis 2013[28]	1) 18 yrs. or older, any race, either sex 2) Type 1 or Type 2 DM requiring diabetic medications. 3) Full thickness neuropathic ulcers between 0.5 cm^2 - 10 cm^2 4) Ulcer duration 1 month 5) Willing and able to perform daily dressing changes at home. 6) Willing and able to use off-loading 7) Adequate perfusion to target foot ulcer ($TcPO_2$ > 40 mmHg, or toe pressure > 40 mmHg or Doppler waveform consistent with adequate flow) 8) Adequate nutrition (albumin >/= 2.0 g/dL and pre-albumin > 15 mg/dL) 9) No active infection 10) No target wound tunneling 11) Target could not be on heel or over a Charcot deformity	Not reported
29) Vandeputte (1997)[29]: written consent needed	Diabetic wound on foot	Patient receiving systemic antibiotics
30) Whalley (2001)[30]	1) Diabetic neuropathic foot ulcer 2) Type 1 and Type 2 Diabetics	No exclusion criteria specified

Foot notes

TcPo2 – Transcutaneous oximetry in mmHg

ABI – Ankle Brachial Index

Hga1c = Hemoglobin a1c

BMI – Body Mass Index

Supplementary Table 3 ***Table displaying the Study year, sample sizes and study settings of included studies.***

#	[Study ID]	Year	[Total Sample Size]	[Primary Intervention] (# patients preceding)	[Comparator/Control] (# patients preceding)	Study Setting	Country
1	Ali 2013[1]	2013	70	A) Cutimed Sorbact 35 patients	B) Standard Dressing (Saline cleansed povidone-soaked gauze dressing) 35 patients	Hospital	Saudi Arabia
2	Amini 2013[2]	2013	40	A) Low frequency (20-	B) Standard wound care	Clinic	Iran

				60kHz) ultrasound assisted wound therapy + standard wound care 20 patients	alone 20 patients		
3	Apelqvist 1990[3]	1990	44	A) Hydrococolloid 22 patients	B) Adhesive Zinc Oxide tape 22 Patients	Outpatient	Sweden
4	Baker 1993[4]	1993	19	A) Allevyn Hydrocellular dressing ? patients	B) Sorbsan Calcium-Alginate dressings ? patients	Clinic	Unclear
5	Belcaro 2010[5]	2010	66	A) Multivalent silver oxide Ag_4O_4 ointment + elastic compression 34 patients	B) Control group (standard cleaning and elastic compression management methods without silver ointment) 32 patients	Unclear	Italy
6	Blackman 1994[6]	1994	18	A) Polymeric dressing 11 patients	B) Wet to dry saline dressing 7 Patients	Unclear	US
7	Bowling 2011[7]	2011	20	A) Jet lavage debridement with superoxide aqueous solution + hydrogel 10 patients	B) Jet lavage debridement with saline solution + hydrogel 10 patients	Hospital, Outpatient	US, UK
8	Clever 1995[8]	1995	40	A) Hydroactive polyurethane gel dressing Cutinova Hydro + standard therapy* 20 patients	B) Hydrophilic polyurethane foam dressing Allevyn + standard therapy* 20 patients	Outpatient	Germany
9	D'Hemeourt 1998[9]	1998	138	A) Good wound care + Sodium Carboxymethylcelluose Hydrogel 70 patients	B) Good wound care* alone 68 patients	Unclear	USA
10	Donaghue 1998[10]	1998	75	A) Collagen Alginate 50 patients	B) Saline gauze 25 patients	Outpatients	USA
11	EhsanUrRehman 2013[11]	2013	60	A) Honey soaked dressing ? patients	B) Povidone-iodine/normal saline dressing ? patients	Hospital, ED	Pakistan
12	Foster 1994[12]	1994	30	A) Hydrocellular polyurethane foam dressing Allevyn 15 patients	B) Calcium sodium alginate dressing 15 patients	Outpatient	UK

13	Goretti 2008[13]	2008	40	A) Super-oxidized solution (SOS) treatment 20 patients	B) Standard local treatment with povidone iodine 20 patients	Hospital	Italy
14	Hammouri 2004[14]	2004	203	A) Honey/Normal Saline, washed with normal saline post-debridement 100 patients	B) Povidone Iodine/H_2O_2 (3:1) washed with same solution post-debridement 100 patients	Hospital	Jordan
15	Jeffcoate 2009[15]	2009	317	A) Hydrofiber 103 patients B) Iodine Gauze 108 patients	C) Gauze 106 patients	Multidisciplinary Outpatient 9 centers	UK
16	Jensen 1998[31]	1998	31	A) Carrasyn hydrogel wound dressing (CHWD) cleansed with ULTRAKLENZ wound cleanser. 14 patients	B) Wet-to-moist saline gauze cleansed with ULTRAKLENZ wound cleanser 17 patients	Outpatient	USA
17	Lalau 2002[17]	2002	77	A) Calcium Alginate 39 patients	B) Vaseline Gauze 38 patients	Outpatients	France
18	Markevich 2000[18]	1998	140	A) Larval therapy (green bottle fly - Lucilia sericata 6-10 larva per 1 cm^2 of wound surface area) removed after 72 hours 70 patients	B) Hydrogel (no data on frequency of dressing change) 70 patients	Unclear	Europe
19	Mazzone 1993[19]	1993	19	A) Polymeric membrane foam dressing 11 patients	B) Wet to Dry saline gauze mesh dressing 8 patients	Outpatient	USA
20	Munter 2006[20]	2006	619	A) Silver releasing hydrophilic polyurethane foam dressing 326 patients	B) Local Best Practice (study reports that this ranged from gauze, moist wound healing, wound healing products, to antimicrobial treatments) 293 patients	Outpatient	Germany UK Denmark Italy Switzerland Belgium Slovenia

							Brazil Canada
21	Ogce 2007[21]	2007	60	A) Hydrocolloid dressing (combined with paste for wound cavities, and powder for infection) 30 patients	B) Classic wound dressing 30 patients	Hospital	Turkey
22	Piaggesi 2001[22]	2001	24	A) Sodium Carboxy-Methyl Cellulose Hydrofiber (Aquacel) changed every 2nd or 3rd day depending on extent of exudate produced by wound. 10 patients	B) Saline moistened gauze (renewed twice daily with saline to prevent drying) 10 patients	Outpatient	Italy
23	Piaggesi 1998[23]	1998	46	A) Treatment - Surgical debridement 22 patients	B) Control - Non-surgical conservative treatment and pressure relief 24 patients	Outpatient	Italy
24	Rhaiem 1998[24]	1998	80	A) G1: cleaning ulcers with hydrogen peroxide 3% + local applied Jam sugar 16 patients	B) G2: cleaning ulcers with hydrogen peroxide 3% + antibiotic-therapy 24 patients C) G3: cleaning ulcers with hydrogen peroxide 3% + antibiotic-therapy 40 patients	Hospital	Tunisia
25	Roberts 2001[25]	2001	30	A) Allevyn hydrocellular foam dressing 14 patients	B) Saline soaked (low adherent) dressing and standard podiatric care 16 patients	Hospital	UK
26	Shukrimi 2008[26]	2008	30	A) Honey dressing ? patients	B) Standard dressing (Povidone Iodine/Normal saline, 1:10) ? patients	Hospital	Malaysia
27	Singh 2006[27]	2006	60	A) Non-contact Ultrasonic debridement (24 KHz) performed every other day 33 patients	B) Sharp/surgical debridement conducted every other day 27 patients	Hospital	Malaysia
28	Tallis 2013[28]	2013	48	A) Clostridial Collagenase Ointment (CCO) 24 patients	B) Saline Moistened Gauze (SMG) + Selective Sharp Debridement	Outpatient	USA

					24 patients		
29	Vandeputte 1997[29]	1997	29	A) Hydrogel 15 patients	B) Dry gauze (control) 14 patients	Outpatient	Belgium
30	Whalley 2001[30]	2001	66	A) Purilon Hydrogel ? patients	B) Intrasite Hydrogel using Biatain Non-adhesive dressing (Coloplast A/S) as a secondary dressing Dressings changed at least every second day ? patients	Unclear	Europe

Footnotes: G1 = Group 1, G2 = Group 2

Note: The data above was reprinted from the 30 included studies. For referencing see the cited and referencing list for the included studes.

Supplementary Table 4: ***A table displaying the Patient demographics for included studies.***

#	[Study ID]	[Mean Age yrs. +/- SD]	[Gender M/F]
1	Ali 2013[1]	Not reported	48/22
2	Amini 2013[2]	55.2 +/- 9.4	24/16
3	Apelqvist 1990[3]	63 +/- 36	26/20
4	Baker 1993[4]	Not reported	Not reported
5	Belcaro 2010[5]	55.9 +/- 3.8	29/37
6	Blackman 1994	55.9 +/- 13.6	17/1
7	Bowling 2011	53.1 +/- 12.6	12/8

8	Clever 1995	56 +/- 13.13	32/8
9	D'Hemeourt 1998	58.3 +/- 12.13	127/45
10	Donaghue 1998	59.5	54/21
11	EhsanUrRehman 2013	55.3 +/- 3.89	35/25
12	Foster 1994	65.5	20/10
13	Goretti 2008	Not reported	Not reported
14	HammouriJRMS2004	58	112/88
15	Jeffcoate 2009	59.6 +/- 12.6	240/76
16	Jensen 1998	Not reported	Not reported
17	Lalau 2002	62.2 +/- 11.75	45/32
18	Markevich 2000	53.6 +/- 15.4	Not reported
19	Mazzone 1993	Not reported	Not reported
20	Munter 2006	69.3 +/- 13.90	Not reported
21	Ogce 2007	59.85	36/24
22	Piaggesi 2001	62.2 +/- 6.05	Not reported
23	Piaggesi 1998	64.39 +/- 11.67	Not reported
24	Rhaiem 1998	56 +/- 32	59/21
25	Roberts 2001	59.5 Median	23/7
26	Shukrimi 2008	52.1	15/15
27	Singh 2006	56.87 +/- 11/06	33/27
28	Tallis 2013	61 +/- 11.8	32/16
29	Vandeputte 1997	63.95 +/- 14.5	13/16
30	Whalley 2001	Not reported	Not reported

Supplementary Table 5: ***Wagner Wound Grade Classification System.***

Grade					
0	1	2	3	4	5
No ulcer in a high-risk foot	Wound involving full skin thickness	Wound extending to ligament and muscle	Wound with cellulitis or abscess	Localized gangrene	Extensive gangrene involving the whole

					foot

Supplementary Table 6: ***University of Texas Wound Classification System.***

	Grade			
Stage	0 Pre or Post ulcerative lesion completely epithelialized	1 Superficial wound not involving tendon, muscle, or bone	2 Wound penetrating to tendon or capsule	3 Wound penetrating to bone or joint
A No Infection, or Ischemia	0A	1A	2A	3A
B Infection but no ischemia	0B	1B	2B	3B
C Ischemia but no infection	0C	1C	2C	3C
D Infection and ischemia are present	0D	1D	2D	3D

Supplementary Table 7 Baseline wound size and duration characteristics of included studies

Surface Area of wound ** **** Expressed as means +/- SD unless otherwise noted**	**Depth of wound ****	**Wound Staging** **(Wagner Wound Grade 0 - 5 OR Texas classification 1 - 3, A,**	**Duration of ulcer ****

		B, C, or D) **(Staging indicates maximum stage or grade accepted for study.)**	
1) Ali 2013[1] Reported as: < 4 cm^2 4+ cm^2 A) 0 35 B) 8 27	Reported only as: < 3 cm 3+ cm A) 0 35 B) 19 16	Texas 1A -> 2D (Texas 2D)	Total Sample Mean duration of foot ulcers = 9 weeks (1 - 105)
2) Amini 2013[2] A) 6.8 +/- 6 cm^2 B) 9.9 +/- 7.6 cm^2	Not reported	Wagner Grade 3	A) 3.4 +/- 3.5 months (15.6 +/- 16.8 weeks) B) 4.4 +/- 4.7 months (17.6 +/- 18.8 weeks)
3) Apelqvist 1990[3] A) median 2.2 cm^2 (1 - 10.5) B) median 2.2 cm^2 (0.9 - 20.4)	Not reported	Not reported	Not reported
4) Baker 1993[4] No baseline data reported.	Not reported	Not reported	Not reported
5) Belcaro 2010[5] Baseline at 4 weeks	Not reported	Not reported	Not reported

A) 2.22 cm^2 0.24 cm^2 B) 2.18 cm^2 1.66 cm^2 p<0.05 statistically significant difference			
6) Blackman 1994[6] A) 2.67 +/- 1.20 cm^2 B) 1.81 +/- 0.75 cm^2 No statistically significant difference	Not reported.	Wagner Grade 1-2 (Wagner 3)	A) 25 +/- 7 weeks B) 28 +/- 6 weeks
7) Bowling 2011[7] A) 3.0 +/- 3.7 cm^2 B) 1.8 +/- 1.6 cm^2	Not reported	Texas Grade 1-2 (Texas 2)	A) 13.7 +/- 12.0 weeks B) 9.7 +/- 8.1 weeks
8) Clever 1995[8] Initial After 4 weeks A) 2.05 +/- 3.14 cm^2 A) 0.32 ± 0.54 cm^2 B) 2.08 +/- 2.72 cm^2 B) 0.34 ± 0.75 cm^2 (p > 0.2) Not statistically significant	Not reported	Not reported	A) 162.37 +/- 325.55 days (23.2 ± 46.5 weeks) B) 165.00 +/- 318.68 days (23.6 ± 42.5 weeks)
9) D'Hemecourt (1998)[9] A) (Good Wound Care alone) 3.5 +/- 3.53 cm^2 B) (Good Wound Care + NaCMC)	A) 0.4 +/- 0.52 cm B) 0.4 +/- 0.20 cm Full thickness Stage 3 or 4	Wagner Grade 3 - 4 (Wagner 4)	A) 42 +/- 42 weeks B) 52.8 +/- 60.92 weeks

3.2 +/- 2.75 cm^2 Target area 1 cm^2 to 10 cm^2 post-debridement			
10) Donaghue 1998[10] A) 2.6 +/- 0.50 cm^2 B) 2.99 +/- 0.62 cm^2 No statistically significant difference (p=0.6237)	Not reported	Wagner Grade 1 - 3 (Wagner 3)	A) 146 +/- 73 days (20.86 +/- 10.43 weeks) B) 225 +/- 104 days (32.14 +/- 14.86 weeks) No statistically significant difference (p=0.5369)
11) EhsanUrRehman 2013[11] Not reported	Not reported	Wagner Grade 1 - 2 (Wagner 2)	Not reported
12) Foster 1994[12] A) 0.88 cm^2 B) 0.79 cm^2	Superficial Deep A) 12 3 B) 13 2	Not reported	A) 107 days (15.3 weeks) B) 170 days (24.3 weeks)
13) Goretti (2008)[13] Surgical outcomes > 5 cm^2 No other baseline data specified	Not reported	Not reported	Not reported
14) Hammouri 2004[14] Not reported	Not reported	Not reported	Not reported
15) Jeffcoate 2009[15] 0.25-1 cm^2 1.01- 0.25	Not reported	Not reported	Not reported

cm^2 2.5-25 cm^2 A) 53 34 16 B) 48 36 24 C) 50 34 22			
16) Jensen (1998)[31] All ulcers at least 1 cm^2 No other baseline data specified	No other baseline data specified	Wagner Grade 2	A) 8 months (32 weeks) B) 3 months (12 weeks)
17) Lalau 2002[17] A) 8.0 +/- 10.5 cm^2 B) 8.8 +/- 16.0 cm^2	Not reported	Not reported	A) 4.9 +/- 7.8 months (19.6 +/- 31.2 weeks) B) 9.1 +/- 13.1 months (36.4 +/- 52.4 weeks)
18) Markevich (2000)[18] A) 14.90 cm^2 B) 15.14 cm^2	Reported as comparable at baseline, but not otherwise specified	Not reported	Average duration reported for total sample as 15.8 +/- 10.7 years. (821.6 +/- 556.4 weeks) Not reported separately for each intervention group.
19) Mazzone 1993[19] Not reported	Not reported	Not reported	Not reported
20) Munter 2006[20]	Not reported	Wagner Grade 1 - 3 (Wagner grade 3)	Not reported

A) 52.9 +/- 90 cm^2 B) 36.6 +/- 64.4 cm^2			
21) Ogce[21] Not reported	Not reported	Not reported	Not reported
22) Piagessi 2001[22] A) 19.2 +/- 6.4 cm^3 B) 22.6 +/- 8.4 cm^3 No statistically significant difference	A) 2.9 +/- 1.1 cm B) 2.3 +/- 1.4 cm No statistically significant difference	Not reported	A) 5.9 +/- 1.3 weeks B) 6.8 +/- 2.6 weeks No statistically significant difference
23) Piagessi 1998[23] Not reported	A) 1.58 +/- 2.20 cm B) 1.98 +/- 1.07 cm	Wagner Grade 1 - 2 (Wagner Grade 2)	A) 32.74 +/- 19.25 days (4.7 +/- 2.75 weeks) B) 39.43 +/- 18.92 (5.6 +/- 2.7 weeks)
24) Rhaiem 1998[24] Not reported	Not reported	Not reported	Not reported
25) Roberts 2001[25] Sample median 1.23 cm^2 Sample median range (0.21 - 3.50 cm^2) A) Median 1.1 cm^2 B) Median 1.45 cm^2	Not reported	Not reported	Sample 15.2 weeks Range (1 week - 6 years)
26) Shukrimi 2008[26] Not reported	Not reported	Wagner Grade 2	Not reported
27) Singh 2006[32] Not reported	Not reported	Wagner Grade 1 - 2 (Wagner Grade 2)	Not reported

28) Tallis 2013[28] A) 3.0 +/- 2.1 cm^2 B) 2.4 +/- 2.1 cm^2	Not reported	Not reported	Not reported
29) Vandeputte 1997[33] Not reported	Not reported	Not reported	Not reported
30) Whalley 2001[30] A) 2.5 +/- 3.2 cm^2 B) 2.4 +/- 2.9 cm^2	Not Reported	Wagner Grade 1 - 2 (Wagner grade 2)	Not reported

Supplementary Table: 8 Baseline participant complicating risk factors for delayed healing in the included studies

[#]	[Study ID]	[Mean Hgba1c (%)]	[Mean Duration of DM (yrs.)]	[Proportion of sample with baseline PAD/PVD]	[Proportion of sample with baseline Infection]	[Offloading] Reported Y/N	[Proportion with Baseline Immune suppression]	[Nutritional status]	Proportion of sample Smoking	Proportion of sample with Venous Insufficiency
1	Ali 2013[1]	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	0.214	Not reported
2	Amini 2013	8.9 +/- 2.3	14.8 +/- 7.3	0.50	Not reported	Yes	Not reported	Not reported	0.075	Not reported
3	Apelqvist 1990	8.2 +/- 1.75	20.5 +/- 13.5	Not reported	Not reported	Yes	Not reported	Not reported	Not reported	Not reported
4	Baker 1993	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported

5	Belcaro 2010	Not Reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
6	Blackman 1994	8.95 +/- 1	Not reported	Not reported	Not reported	Yes	Not reported	Not reported	Not reported	Not reported
7	Bowling 2011	8.7 +/- 1.8	19.35 +/- 8.1	0	0	Not reported	Not reported	Albumin 40.1 +/- 4.5 grams/Liter	Not reported	Not reported
8	Clever 1995	Not reported	Not reported	Not reported	0.725	Yes	Not reported	Not reported	0.325	Not reported
9	D'Hemeourt 1998	Not reported	Not reported	Not reported	Not reported	Yes	Not reported	Not reported	Not reported	Not reported
10	Donaghue 1998	Not reported	18 Range (30 - 81)	Not reported	0	Yes	Not reported	Alb 3.76 +/- 0.09	Not reported	Not reported
11	EhsanUrRehman 2013	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
12	Foster 1994	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
13	Goretti 2008	Not reported	Not reported	0	1	Not reported	Not reported	Not reported	Not reported	Not reported
14	Hammouri 2004	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
15	Jeffcoate 2009	Not reported	15.7 +/- 10.8	0.196	0	Yes	0	Not reported	0.170	Not reported
16	Jensen 1998	Not reported	Not reported	0	0	Yes	Not reported	Not reported	Not reported	Not reported
17	Lalau 2002	7.75 +/- 1.75	18.05 +/- 10.35	0.22	Not reported	Yes	Not reported	Not reported	Not reported	Not reported
18	Markevich 2000	Not reported	15.8 +/- 10.7	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
19	Mazzone 1993	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
20	Munter 2006	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
21	Ogce 2007	7.73	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
22	Piaggesi 2001	8.5 +/- 2.9	15.45 +/- 7.55	0	0	Yes	Not reported	Not reported	Not reported	Not reported
23	Piaggesi 1998	9.2 +/- 3.0	17.52 +/- 9.51	0	0	Yes	0	Not reported	Not reported	Not reported
24	Rhaiem 1998	Not reported	13 +/- 10.6	Not reported	0.517	Not reported	Not reported	Not reported	0.55	Not reported
25	Roberts 2001	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
26	Shukrimi 2008	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
27	Singh 2006	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
28	Tallis 2013	Not reported	Not reported	0	0	Yes	Not reported	Not reported	Not reported	Not reported
29	Vandeputte 1997	Not reported	Not reported	Not reported	0.069	Not reported	Not reported	Not reported	Not reported	Not reported

30	Whalley 2001	Not reported	Not reported	Not reported	Not reported	Yes	Not reported	Not reported	Not reported	Not reported

Footnotes

Study ID = Study Identification

Hgba1c % = Hemoglobin A1c in percent

Duration of DM = Duration of Diabetes in years

PAD/PVD = Peripheral arterial disease/Peripheral vascular disease

Note: The data above was adapted from the included studies. For referencing, see the cited and reference list for complete details.

Supplementary Table 9: ***Table of industry supported included studies***

[#]	[Study ID]	[Industry support] 0 = No, 1 = Yes, 2 = Unclear
1	Ali 2013[1]	2
2	Amini 2013[2]	0
3	Apelqvist 1990[3]	1
4	Baker 1993[4]	1
5	Belcaro 2010[5]	2
6	Blackman 1994[6]	1
7	Bowling 2011[7]	1
8	Clever 1995[8]	1
9	D'Hemeourt	2

	1998[9]	
10	Donaghue 1998[10]	1
11	EhsanUrRehman 2013[11]	2
12	Foster 1994[12]	2
13	Goretti 2008[13]	1
14	Hammouri 2004[14]	2
15	Jeffcoate 2009[15]	2
16	Jensen 1998[31]	1
17	Lalau 2002[17]	1
18	Markevich 2000[18]	2
19	Mazzone 1993[19]	1
20	Munter 2006[20]	1
21	Ogce 2007[21]	2
22	Piaggesi 2001	0
23	Piaggesi 1998	2
24	Rhaiem 1998	2
25	Roberts 2001	1
26	Shukrimi 2008	2
27	Singh 2006	2
28	Tallis 2013	1
29	Vandeputte 1997	2
30	Whalley 2001	2

Supplementary Table 10 Comparisons that reported on the outcomes of interest

Comparison Number	# of studies included in comparison (reference)	Debridement Type	Comparator	Category of comparison	Outcome(s) reported (95% CI)				
					QoL Score - ordinal scale)	Time to complete healing (days)	Proportion of ulcers healed (%)	Proportion of infections (RR)	Mean difference in Cost using local currency
Comparison 1[23]	1	Sharp Surgical	Nonsurgical	Sharp Surgical vs Autolytic	-2.2 (-3.16 to -1.24)	82 (41.07 to 122.29)			
Comparison 2[13]	1	Superoxide Solution	Autolytic	Chemical vs Autolytic		-6.00 (-6.94 to -5.06)			
Comparison 3[2]	1	Low frequency Ultrasound	Sharp Debridement	Ultrasound vs Sharp Surgical	No pre-specified outcomes of interest reported				
Comparison 4[18]	1	Larvae	Hydrogel	MDT vs Autolytic	No pre-specified outcomes of interest reported				
Comparison 5[30]	1	Hydrogel Purilon	Hydrogel Intrasite	Autolytic vs Autolytic			35% vs. 19%		
Comparison 6[9 31 33]	3	Hydrogel	Gauze	Autolytic vs Autolytic	Pooled in meta-analysis see table 14				
Comparison 7[8]	1	Polyurethane gel	Polyurethane foam	Autolytic vs Autolytic	No pre-specified outcomes of interest reported				
Comparison 8[17]	1	Calcium Alginate	Gauze	Autolytic vs Autolytic		2.8 (1.46 to 4.14)			
Comparison 9[3]	1	Hydrocolloid	Adhesive Zinc	Autolytic vs Autolytic	No pre-specified outcomes of interest reported				
Comparison 10[6 19]	2	Foam dressing	Wet to Dry	Autolytic vs Mechanical debridement	Pooled in meta-analysis see table 14				
Comparison 11[25]	1	Foam dressing	Saline nonadherent	Autolytic vs	No pre-specified outcomes of interest reported				

			gauze	**Autolytic**					
Comparison 12[15]	**1**	**Iodine Impregnated Fiber**	**Gauze**	**Autolytic vs Autolytic**				**1.45 (1.13 to 1.86)**	
Comparison 13[15 22]	**2**	**Hydrofiber**	**gauze**	**Autolytic vs Autolytic**	**Pooled in meta-analysis see table 14**				
Comparison 14[12]	**1**	**Hydrocellular Polyurethane**	**Calcium Alginate**	**Autolytic vs Autolytic**	**No pre-specified outcomes of interest reported**				
Comparison 15[11]	**1**	**Honey-soaked gauze**	**Iodine saline dressing**	**Autolytic vs Autolytic**					
Comparison 16[14]	**1**	**Honey Saline dressing**	**Iodine peroxide saline**	**Autolytic vs Autolytic**					**-334 (374 to -294) Jordanian Dinar**
Comparison 17[24]	**1**	**Sugar Jam Hydrogen peroxide and topical antibiotic**	**Hydrogen peroxide and topical antibiotic**	**Autolytic vs Autolytic**	**No pre-specified outcomes of interest reported**				
Comparison 18[5]	**1**	**Silver dressing**	**Standard dressing**	**Autolytic vs Autolytic**	**No pre-specified outcomes of interest reported**				
Comparison 19[9 10 13 15 17 22 23 25 31 33]	**10**	**Any form of debridement vs autolytic**	**Gauze**	**Any form of debridement vs gauze**	**Pooled in meta-analysis see table 14**				

Supplementary Table 11 Tests for Publication Bias			
Intervention	**Outcome**	**Egger's**	**Begg's**
Any debridement as compared with gauze	**Proportion of Ulcers Healing**	***p = 0.8958**	****p = 0.5858**
Footnote ***2 tailed p-value** *** Beggs performed without continuity correction, 2 tailed p-value.** **Beggs and Eggers test for publication bias performed on outcomes and interventions that included 10 or more studies.**			

Supplementary Table 12: ***Table of Moderators of effect size magnitude for the "Any debridement vs. gauze".***

Outcome(s)	Moderator(s)Characteristic(s)/Level(s)	RR (95% CI)	K[b]	Coefficient	p-value
	Participant-specific demographic characteristics				
Proportion of infections	**Age**	**1.07 (0.76, 1.52)**	**7**	**-0.2132**	**0.0651**
	Risk-specific characteristics				
Proportion of infections	**PAD[c]**	**1.07 (0.76, 1.52)**	**7**	**3.3706**	**0.3023**
Proportion of infections	**Duration of diabetes (yrs.)**	**1.07 (0.76, 1.52)**	**7**	**-0.1528**	**0.5460**
Proportion of infections	**Proportion of females**	**1.07 (0.76, 1.52)**	**7**	**-6.1651**	**0.0264**
	Study-specific characteristics				
Proportion of infections	**Data collection year**	**1.07 (0.76, 1.52)**	**7**	**0.0246**	**0.3890**
Proportion of infections	**Duration of follow up**	**1.07 (0.76, 1.52)**	**7**	**0.0482**	**0.1857**
Proportion of Ulcers healed	**Age**	**1.17 (1.00, 1.36)**	**10**	**-0.0130**	**0.6873**
Proportion of Ulcers healed	**PAD(c)**	**1.17 (1.00, 1.36)**	**10**	**-0.4095**	**0.6191**
Proportion of Ulcers healed	**Duration of diabetes (yrs.)**	**1.17 (1.00, 1.36)**	**10**	**0.0419**	**0.5626**
Proportion of Ulcers healed	**Proportion of females**	**1.17 (1.00, 1.36)**	**10**	**0.2486**	**0.8683**
	Study-specific characteristics				
Proportion of Ulcers healed	**Data collection year**	**1.17 (1.00, 1.36)**	**10**	**0.0013**	**0.9247**
Proportion of Ulcers healed	**Duration of follow up**	**1.17 (1.00, 1.36)**	**10**	**0.0048**	**0.6043**

a. Each moderator listed is evaluated individually without controlling for the other listed moderators. Effect sizes are based on random effects assumptions for the comparison and respective outcome listed in two columns. In this analysis there was 1 comparison ("any debridement" as compared with gauze) and 2 outcomes (proportion of infections, and Proportion of ulcers healed) that approximated a sufficient (number of studies): moderator ratio to facilitate moderator analysis.

b. k = number of studies

c. PAD = proportion with initial baseline peripheral arterial disease.

Supplementary Table 13: ***Non-Significant Moderators***
Non-Significant Moderators
All the following moderators assessed were non-significant.
Age
PAD (Peripheral arterial disease)
Duration of diabetes
Proportion of Females
Data collection year
Duration of follow up
Note: A table displaying non-significant Moderators adapted reported from included studies. See citations and referencing for included studies.

Supplementary Table 14: ***Moderators that were Unable to be analyzed due to lack of Reported Information.***
235 coded variables on our data extraction form 138 of these were non-effect size related variables. These were thoroughly reviewed as candidate variables for regression analysis and most were unable to be analyzed due to lack of reported information as either none of the studies reported certain outcomes or only very few did. Many had as few as 1 or no study reporting information. See Data extraction form Appendix 2.

Supplementary Table 15: *Summary of Finding Tables (SoF). Hydrogel compared to Gauze/Good wound care (gwc) for Diabetic foot ulcers (DFU).*

Hydrogel compared to Gauze/Good wound care (gwc) alone for Diabetic foot ulcer

Patient or population: patients with Diabetic foot ulcer
Settings: Outpatient
Intervention: Hydrogel
Comparison: Gauze/Good wound care (gwc) alone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Gauze/Good wound care (gwc) alone**	Corresponding risk **Hydrogel**				
Number of amputations reported Follow-up: 20 weeks	**Study population**		**RR 0.26** (0.05 to 1.4)	60 (2 studies)	⊕⊕⊖⊖ **low**[1,2,3]	
	19 per 100	**5 per 100** (1 to 26)				
	Moderate					
	20 per 100	**5 per 100** (1 to 27)				
Number of Infections reported Follow-up: 12 - 20 weeks	**Study population**		**RR 0.74** (0.18 to 2.99)	198 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,4,5,6]	
	27 per 100	**20 per 100** (5 to 82)				
	Moderate					
	28 per 100	**21 per 100** (5 to 83)				
Number of ulcers completely healed Follow-up: 12 - 20 weeks	**Study population**		**RR 1.71** (1.16 to 2.52)	198 (3 studies)	⊕⊕⊖⊖ **low**[1,7]	
	26 per 100	**45 per 100** (30 to 66)				
	Moderate					
	35 per 100	**60 per 100** (41 to 89)				

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Many of the risk of bias characteristics were either unclear or high.
[2] The 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit.
[3] 2/3 did not mention whether industry support was sought and the studies yet all had negative findings.
[4] No explanation was provided
[5] Point estimates are far apart and confidence intervals do not overlap.
[6] The 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable harm.
[7] The total (cumulative) sample size is lower than the calculated OIS.

Supplementary Table 16: *Summary of Findings Table. Foam dressing compared with Wet to Dry Saline for DFU.*

Foam dressing compared to Wet to Dry Saline for Diabetic foot ulcer

Patient or population: patients with Diabetic foot ulcer
Settings:
Intervention: Foam dressing
Comparison: Wet to Dry Saline

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Wet to Dry Saline**	Corresponding risk **Foam dressing**				
Number of ulcers completely healed Follow-up: 8 to 24 weeks	**Study population**		**RR 3.56** (0.93 to 13.66)	37 (2 studies)	⊕⊕⊖⊖ **low**[1,2,3]	
	13 per 100	**47 per 100** (12 to 100)				
	Moderate					
	12 per 100	**44 per 100** (12 to 100)				

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Many of the risk of bias characteristics were either unclear or high.
[2] The 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit.
[3] The total (cumulative) sample size is lower than the calculated Optimal Information Size OIS and/or total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878

Supplementary Table 17: *Summary of Findings Table. Hydrofiber compared to Gauze dressing for DFU.*

Hydrofiber compared to Gauze dressing for Diabetic foot ulcers

Patient or population: patients with Diabetic foot ulcers
Settings: Outpatient
Intervention: Hydrofiber
Comparison: Gauze dressing

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk **Gauze dressing**	Corresponding risk **Hydrofiber**				
Number of amputations reported	**Study population**		**RR 1.34** (0.29 to 6.1)	229 (2 studies)	⊕⊕⊖⊖ **low**[1,2,3]	
	3 per 100	**3 per 100** (1 to 16)				
	Moderate					
	6 per 100	**8 per 100** (2 to 36)				
Number of Infections reported Follow-up: 8 - 24 weeks	**Study population**		**RR 0.96** (0.4 to 2.31)	229 (2 studies)	⊕⊕⊖⊖ **low**[1,2,3]	
	44 per 100	**42 per 100** (18 to 100)				
	Moderate					
	38 per 100	**36 per 100** (15 to 87)				
Number of ulcers completely healed Follow-up: 8 - 24 weeks	**Study population**		**RR 1.13** (0.92 to 1.38)	229 (2 studies)	⊕⊕⊖⊖ **low**[1,2,4]	
	43 per 100	**49 per 100** (40 to 59)				
	Moderate					
	64 per 100	**73 per 100** (59 to 89)				
Time to complete healing (days) Scale from: 0 to 295. Follow-up: 8 to 24 weeks	The mean time to complete healing (days) ranged across control groups from **78.3 to 295 days**	The mean time to complete healing (days) in the intervention groups was **53.37 lower** (153.29 lower to 46.56 higher)		229 (2 studies)	⊕⊖⊖⊖ **very low**[1,5,6,7]	

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Many of the risk of bias characteristics were either unclear or high.
[2] The total (cumulative) sample size is lower than the calculated optimal information size OIS) and total number of events is less than 300 (a threshold rule-of-thumb value) (based on: Mueller et al. Ann Intern Med. 2007;146:878-881.
[3] The 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit and appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.
[4] The 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.
[5] There exists widely differing estimates of the treatment effect (i.e. heterogeneity or variability in results) across studies suggesting true differences in underlying treatment effect.
[6] The total (cumulative) sample size is lower than the calculated Optimal Information Size (OIS) and/or total population size is less than 400 (a threshold rule-of-thumb value; using the usual α and β, and an effect size of 0.2 SD, representing a small effect.
[7] The 95% confidence interval includes no effect and the upper or lower confidence limit crosses the minimal important difference (MID), either for benefit of harm (Note: if the MID is not known or the use of different outcomes measures required calculation of an (ES), we suggest downgrading if the upper or lower confidence limit crosses an effect size of 0.5 in either direction).

Supplementary Table 18: *Any debridement compared to Gauze control for Diabetic Foot Ulcers.*

Any debridement compared to Saline gauze for Diabetic Foot Ulcers

Patient or population: patients with Diabetic Foot Ulcers
Settings:
Intervention: Any debridement
Comparison: Saline gauze

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk Saline gauze	Corresponding risk Any debridement	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Number of amputations reported Follow-up: 8 to 24 weeks	**Study population**		**RR 0.48** (0.17 to 1.37)	443 (5 studies)	⊕⊕⊖⊖ **low**[1,2]	
	6 per 100	**3 per 100** (1 to 8)				
	Moderate					
	5 per 100	**2 per 100** (1 to 7)				
Number of Infections reported Follow-up: 4 to 24 weeks	**Study population**		**RR 1.07** (0.76 to 1.52)	659 (7 studies)	⊕⊕⊖⊖ **low**[1,2]	
	30 per 100	**32 per 100** (23 to 46)				
	Moderate					
	29 per 100	**31 per 100** (22 to 44)				
Number of ulcers completely healed Follow-up: 4 to 24 weeks	**Study population**		**RR 1.22** (1.04 to 1.44)	798 (10 studies)	⊕⊖⊖⊖ **very low**[1,2,3]	
	40 per 100	**49 per 100** (41 to 57)				
	Moderate					
	40 per 100	**48 per 100** (41 to 57)				
Number of ulcers completely healed - Any Debridement vs Saline Gauze Follow-up: 4 to 24 weeks	**Study population**		**RR 1.18** (0.99 to 1.41)	728 (8 studies)	⊕⊕⊖⊖ **low**[2]	
	40 per 100	**47 per 100** (39 to 56)				
	Moderate					
	40 per 100	**47 per 100** (39 to 56)				
Number of ulcers completely healed - SA w/o Abstracts Follow-up: 13 to 24 weeks	**Study population**		**RR 1.57** (1.05 to 2.35)	70 (2 studies)	⊕⊕⊖⊖ **low**[1,2]	
	42 per 100	**65 per 100** (44 to 98)				
	Moderate					
	40 per 100	**63 per 100** (42 to 94)				
Quality of life Scale from: 0 to 100. Follow-up: 13 to 24 weeks		The mean quality of life in the intervention groups was **0.01 lower** (0.04 lower to 0.01 higher)		317 (1 study)	⊕⊕⊖⊖ **low**[1,4]	
Time to complete healing (days) Follow-up: 8 to 24 weeks		The mean time to complete healing (days) in the intervention groups was **27.88 lower** (52.53 to 3.23 lower)		458 (4 studies)	⊕⊕⊖⊖ **low**[1,3]	
Recurrence rates	**Study population**		**RR 0.81** (0.25 to 2.58)	357 (2 studies)	⊕⊕⊖⊖ **low**[1,2]	
	88 per 1000	**71 per 1000** (22 to 227)				
	Moderate					
	38 per 1000	**31 per 1000** (9 to 98)				

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Downgraded as substantial risk of bias characteristics were either unclear or high.
[2] Downgraded due to the 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both 1) no effect and 2) appreciable benefit or appreciable harm. GRADE suggests that the threshold for "appreciable benefit" or "appreciable harm" that should be considered for downgrading is a relative risk reduction (RRR) or relative risk increase (RRI) greater than 25%.
[3] Downgraded for asymmetric funnel plot distribution around the null value is observed favoring a positive effect that includes studies with smaller sample sizes.
[4] Downgraded due to total (cumulative) sample size is lower than the calculated optimal information size (OIS) and/or total population size is less than 400 (a threshold rule-of-thumb value; using the usual α and β, and an effect size of less than 0.2 SD, representing a small effect). 95% confidence interval includes no effect, and the upper or lower confidence limit crosses the minimal important difference (MID), either for benefit of harm.
[5] Downgraded due to widely differing estimates of the treatment effect (i.e., heterogeneity or variability in results) across studies suggest true differences in underlying treatment effect.

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