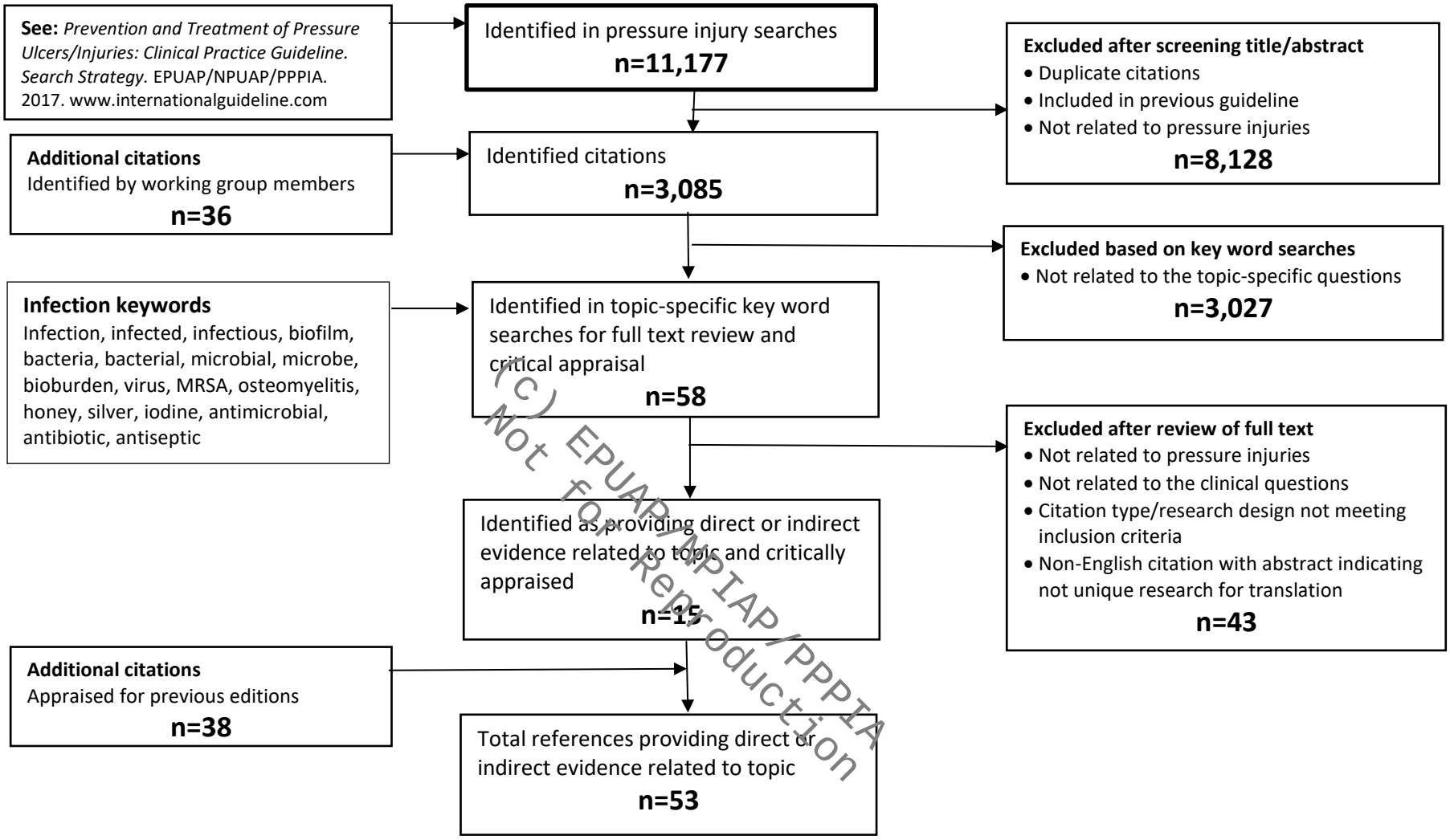
Search results for 2019 International Pressure Injury Guideline: Infection and Biofilm



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

Articles Reviewed for International Pressure Injury Guideline

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

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

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
Clinical question 1 and 2: Assessing and diagnosing the presence of infection and biofilm							
(Nakagami, Schultz et al. 2017)	Prognostic, prospective cohort study investigating **predictive validity of wound blotting and staining for biofilms for identifying future slough formation**	Participants were recruited in one hospital ward in Japan over 18 months (n=83 pressure injuries eligible, n=57 commenced, n=23 pressure injuries analyzed) Inclusion criteria: • Pressure injury Exclusion criteria: • Inaccurate blotting or no blotting conducted • Eschar over wound bed • No digital photography taken Participant characteristics: • Category/stage, size and depth of pressure injuries not reported • Mean age 68 years • Primarily sacral and coccyx pressure injuries • 25% had more than one pressure injury	N/A (management of the wound in between measures is not reported)	• Two consecutive weeks of assessment • One blinded observer determined percent wound covered in slough using a standardized method • Decreased slough was consider to be wound with ≥10% less slough in one week • One clinician did all the wound blots by washing and drying wound tissue, pressing nitrocellulose membrane firmly to wound bed using a reversible protein staining kit that was reverse stained I the lab (validity of method previously tested) •	**Outcomes at 7 days** • 61.4% (of 60 samples from 23 pressure injuries on 16 participants) were positive for biofilm on staining • 38.6% were biofilm negative on staining • In biofilm positive group, 81.4% increased in slough, which was significantly higher than in the biofilm negative group (p=0.002) **Decreased in slough versus increased/not changed in slough at 7 days** • Depth not significantly different (p=0.253) • Size on DESIGN-R scale was not significantly different (p=0.742) • Inflammation/infection was not significantly different (p=0.726) • Wound are in cm 2 was not significantly different (p=0.093) • Slough area was not significantly different (p=0.064) • Percent of area covered in slough was significantly different (p=0.023) • Total DESIGN-R score was significantly different (p=0.042) • Level of exudate was significantly different (p=0.009) **Analysis**	• Large proportion of participants had inadequate follow up data and were not included • Used blinding • Single observer evaluated all wounds, no reporting of intra-rater reliability • Did not include confounders such treatment used on wound, comorbidities • DESIGN-R was measured using unreported method	**Level of evidence: 1 (prognostic study)** **Quality: Low**

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					Odds ratio of biofilm-positive staining increasing in slough by ≥10% at seven days was 9.37 (95% CI 2.47 to 35.5, p=0.001) when adjusted for DESIGN-R, baseline percent slough and age		
(Blanco-Blanco, Gea-Sanchez et al. 2017)	Cross sectional observation study **exploring concordance between classic signs of infection and percutaneous aspiration fluid culture**	Participants were recruited at 2 primary care facilities and 2 long term care facilities in Spain (n=117, n=77 with pressure injuries) Inclusion criteria: • Age ≥ 18 years • Category/Stage 2 or greater pressure injury Exclusion criteria: • Category/Stage 1 pressure injury • Drug anticoagulated Participant characteristics: (not significantly different between groups) • Mean age 78.27±11.07 years • 57.1% males • 48% in acute care hospital, 21% in nursing home, 31% in healthcare center • 44.2% diabetes, 12.3% obesity, 10.4% malignancies, 10.4% renal failure	• Percutaneous aspiration	• Number and type of infective symptoms present: heat, erythema, edema and purulent discharge • Culture results from fluid obtained from percutaneous aspiration • Considered infected if two of 4 classic signs were present (see comments), or is purulent exudate was uniquely present • Data collected by trained nurses	**Pressure injury data** • Mean pressure injury per participant was 1 • 33.3% sacral, 19.7% heel,17.9% malleolus, 11.1% ischial, 9.4% trochanter • 23% Category/Stage 2, 38.5% Category/Stage 3, 38.5% Category/Stage 4 **Classic signs of infection** • 58.1% at least one positive clinical sign • Sacral pressure injury was anatomical location with highest prevalence (27.6%) of positive signs of infection • Category/Stage 4 had the highest prevalence (53.2%) of positive signs of infection • Erythema (p=0.018) and Purulent exudate (p=0.024) were significantly more likely to occur in higher Category/Stage pressure injuries than lower Category/Stage pressure injuries **Cultures** • 50.4% had positive cultures, of which 38.8% were being treated with systemic antibiotics and 22% were receiving topical antibiotics **Inter-rater reliability** • Sensitivity of classic signs against culture was 0.36 • Specificity of classic signs against culture was 0.55 • Positive likelihood ratio was 0.79 • Negative likelihood ratio was 1.17	• No blinding • States the sample size is insufficient for a diagnostic test validation but sufficient for <5% accuracy • Pain was not considered as a sign of infection • Edema was replaced by 'redness' due to difficulty assessing edema – did not explain how erythema and 'redness' were differentiated from each other • Did not consider covert signs of infection • No evaluation of possible presence of biofilm	**Level of Evidence: 1 (diagnostic)** **Quality: High**

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					• Positive predictive value of classic signs was 0.45 • Negative predictive value was 0.46 • Kappa index -0.092 (95% -0.082 to -0.002) **Author conclusion: classic signs of infection have poor ability diagnose a true positive or a true negative compared with the results of the fluid culture from percutaneous aspiration**		

(Braga, Brito et al. 2017)	Prospective cohort study **reporting risk factors for developing bacteremia from a pressure injury colonized with gram negative bacilli (GNB)**	Participants were recruited in a hospital in Brazil (n= 60)
		
		Inclusion criteria:
		• Grade II or greater pressure injury present
		
		Exclusion criteria:
		• Stage/Category 1 pressure injuries
		
		Participant characteristics:
		• 6 subjects were admitted due to infected pressure injury
		• 70% male
		• Mean age 61
		• Mean IP stay 103 days
		• Most common comorbidities: Cardiomyopathy (78.3%) and diabetes mellitus (43.3%).
		• Invasive devices included gastrointestinal catheter (85.0%), central venous catheter (55.0%), mechanical ventilation (45.0%), urinary catheter
			• Swab, culture and isolation/ identification of colonizing and infective organism
			• Blood culture for bacteraemia: isolation/identification of infective organism sp.
				• Colonization of pressure injury based on Giemsa staining
				• Infection of pressure injury defined based on clinical signs and symptoms (i.e., erythema, edema, pain, foul odor, and purulent exudates, fever, delayed healing, discoloration of granulation tissue, friable granulation tissue, and wound breakdown)
				• Bacteremia defined as positive blood culture
				• Pressure injury staging using a system by Santos et. al based on NPUAP
				• Patients followed up for the duration of hospital stay (mean 103 days)
					Microbial profiles
					• 83.3% of the population had pressure injuries colonised with GNB
					• Most common types of GNB were:
					  ○ mixed flora (74.0%).
					  ○ Enterobacteriaceae (49.0%),
					  ○ Escherichia coli (49.0%)
					  ○ Klebsiella pneumoniae (40.8%)
					• Non-fermenting GNB (23.0%), mainly Pseudomonas aeruginosa (78.3%), and Staphylococcus aureus (28.0%).
					• 63% of the isolates were multi-resistant to different antibiotics, including Pseudomonas aeruginosa (100.0%), Proteus spp. (100.0%), Klebsiella spp (85.0%)
					• Most patients had been prescribed 3+ classes of antibiotics (77.9%) These individuals had the highest ratee of mortality.
					
					Relationship between bacteremia and GNB colonization
					• Of those pressure injuries colonized by GNB, 32% developed clinical signs and symptoms of local infection
					• Of those with clinical signs and symptoms of local infection, 62.5% developed bacteremia
						• Observational study with no control
						• Selection of participants is poorly reported
						• No univariate or multivariate analysis that includes potential confounders e.g. frailty, comorbidities, invasive devices
						• No power estimates were made
						• Methods to evaluation of signs/symptoms of infection poorly reported and interrater reliability is not addressed
							Level of evidence: 1 (prognostic)
							
							Quality: Low

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		(40.0%), three or more invasive devices (55.0%),			• Mortality of people with pressure injury infected with GNB bactermia was higher (OR 7.43, 95% CI 1.23 to 45.0, p=0.04) **Author conclusion: Stage II or greater pressure injuries in hospitalized patients are reservoirs of multi-resistant GNB.** **An alternate conclusion: Rather than these patients being a reservoir for GNB, their frailty, complex comorbidities and immobility make them more liable to develop a pressure injury and less able to resist colonization/ infection once the wound is challenged buy GNB.**		
(Tedeschi, Negosanti et al. 2017)	Cross sectional study **evaluating wound swabs as a method for diagnosing wound infection in advanced pressure injuries**	Participants were recruited consecutively in a rehabilitative hospital in Italy over 3 years (n=116) Inclusion criteria: • Spinal cord injury • Pressure injury of Category/stage 3 or 4 undergoing surgical debridement or reconstruction • Not receiving antibiotics prior to surgery Participants characteristics • Primarily male • Primarily post-trauma paraplegia • Mean age 49 years	• Participants received surgery • Immediately prior to surgery all participants received three superficial wound swabs were taken using Levine technique • During surgery all participants had multiple bone and soft tissue specimens taken	Culture of wound swab specimens Culture and histological examination of bone and soft tissue samples	**Bacterial profile** Most common organism in intraoperative specimens were *S. aureus*, *P. mirabilis* and *P aeruginosa* **Comparisons between swab results and culture results** • Concordance between swab and specimen results was 22% of cases • 45% of discordance was due to yielding different microorganism, 34% was due to false negatives (swab negative, specimen positive) and 21% due to false positives (swab positive, specimen negative) **Author conclusions: Superficial wound swab is not a useful diagnostic procedure for diagnosing superinfection or determining bacterial profiles**	• Single site study, results may relate to poor clinical technique	**Level of Evidence: 1 (diagnostic)** **Quality: high**
(Bodavula, Liang et al. 2015)	Retrospective descriptive study **reporting patterns in management**	Retrospective cohort study records review of patients with pressure injury and osteomyelitis admitted in a 5 year period (n=220)	N/A	Reviewed records for: • Demographic information • Comorbidities • Antibiotic therapy history	**Reported signs and symptoms** • Back pain (31%), weakness (74%), fever (43%), weight loss (40%), sensory loss (71%), urine incontinence (71%), fecal incontinence (61%)	• Retrospective study relying on documentation • Single center • Patients were required to have 12	**Level of Evidence: 4 (diagnostic)** **Quality: high**

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	of pressure injury -related osteomyelitis	Inclusion: • Aged ≥18 ears • Admitted with stage IV pressure injury at time of diagnosis of osteomyelitis • 12 months follow up Exclusion: • Stage I-III pressure injury Participant characteristics: • Of 270 patients with pelvic osteomyelitis, 220 (81%) had pressure injury • Mean age 50 ± 18years • 67% male • 52% African American • Median BMI 23.6kg/m^2 (range 12.3 to 48) • 77% patients were para/quadriplegic		• Presenting symptoms • Physical examination and imaging findings • Diagnostic procedures • Microbiology • Medical and surgical management	**Diagnostic investigations** • 41% had pelvic exam, of which 62% were compatible with infection • 37% had CT scan of which 83% were compatible with infection • 18% had a CT scan of which 88% were compatible with infection • 9% had a CT scan of which 79% were compatible with infection **Microbiology** • 29% no growth, 30% mixed growth, 15% MRSA **Management** • 47.7% antibiotics only, 3.2% surgery only, 21.8% mixed medical-surgical approach • mean time from admission to first positive culture was 2.3 days • mean time from admission to empiric antibiotic therapy was 2.1 days **Conclusions: Wound documentation was poor for majority of cases. Microbiology diagnosis is essential for directing antibiotic management.**	months' follow up for inclusion which could have excluded patients with poor outcomes (e.g. death) • Inclusion was determined by ICD-9 coding that may not have reliably captured potential inclusion candidates	
(Brunel, Lamy et al. 2016)	Prospective study **exploring the diagnostic agreement between magnetic resonance imaging (MRI) compared with bone biopsy and culture**	Participants recruited at a university hospital in France (n=34 patients with 44 pressure injuries) Inclusion criteria: • Age ≥ 18 years • Category/Stage III or IV pressure injury • Ischial, sacral or trochanter pressure injury • Worsening or stagnant pressure injury despite optimal treatment	• Bone pelvic MRI performed in the month preceding surgery • 3 to 5 bone samples taken from the same site during surgery for microbiological and pathological examination	• Positive histology was defined as presence of signs of osteomyelitis PLUS either at least one bone culture positive for non-commensal bacteria or at least three bone cultures with the same commensal microorganism of cutaneous flora • Pathologist blinded vor evaluations	**Characteristics of pressure injuries** 55% ischial pressure injuries, 34% sacral pressure injuries 89% Category/Stage IV pressure injuries 30% had previous flap performed Median time from wound to suspected osteomyelitis was 8.8 month (IQR 2.8 to 21.3) **Investigations** • MRI positive for osteomyelitis in 90.9% pressure injuries, with abscess formation in 15.9% and fistula in 61.4%	• Unclear is recruitment is consecutive • Unclear if diagnostic procedure was blinded • Used gold standard reference • Inclusion of more than one pressure injury per participant may influence results	**Level of Evidence: 2 (diagnostic)** **Quality: high**

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		• Indication for surgical debridement • No MRI contraindications • Up to 3 pressure injuries included per person Exclusion criteria: • Antibiotic therapy in 2 weeks before biopsies • Biopsy not performed according to research protocol Participant characteristics: (not significantly different between groups) • Mean age 51 years • 71% males • 100% either paraplegia or tetraplegia • 41% smokers, 24% diabetes, 26% had indwelling catheter, 26% had colostomy • 71% had a previous pressure injury • 47% hospital admission within preceding 3 months, 29% repeated hospital admissions within preceding year • 29% received antibiotic therapy for 15-30 days • 74% had urinary colonization on admission, 18% had fever ≥38.5°C on admission		• Median time between bone culture and sample and MRI was 4.0 days (IQR 3.0 to 7.0)	• Histology was positive in 86.4% of pressure injuries (n=38) • Bone culture was positive for 93.2% pressure injuries (n=41) • 2 pressure injuries had sterile bone culture but histological osteomyelitis • 6 pressure injuries had no histological osteomyelitis but either had positive cultures (n=2) or commensal microorganisms in 1 or 2 samples (n=4) • Agreement between positive microbiology and histology was good (88.6%, κ=0.55) • Agreement between MRI and composite criterion was lower (79.5% , κ=0.20) • MRI sensitivity 94.3%, specificity 22.2%, and negative predictive value 50%. **Quantity and type of organisms** Median isolates per pressure injury: 4.0 (IQR 2.0 to 6.0) Most common organisms: *S. aureus* (77.1%), *Peptostreptococcus spp*. (48.6%), *Bacteroides spp*. (40%) High frequency of anaerobes (51.5%) and MRSA (42.8%) **Author conclusions: A pragmatic diagnostic strategy based on multiple surgical bone biopsies and composite microbio-histological criterion is effective in diagnosing osteomyelitis in pressure injuries.**	• *Enterobacteracea Citrobacter* was reported as being cultured in biopsy, however tables show 0 total cases • This study does not report the relatively high number of un-culturable organisms that are typically found. The best control for this is DNA analysis. • Three cultures where osteomyelitis was diagnosed by histology, cultured as sterile. DNA analysis would identify if MO DNA was present in these samples. • MRI poor agreement with biopsies due to low specificity 22.2%	
(Heiba, Stempler et al. 2017)	Retrospective evaluation **of accuracy of**	Participants were consecutively (retrospective) recruited over 2 years at a	• Final diagnosis was made using:	• Diagnosis was made using dual isotopes bone marrow scans	**Outcomes** • n=19 confirmed osteomyelitis, n=3 soft tissue infection, n=11 no infection	• No blinding • No reference	**Level of Evidence: 1 (diagnostic)**

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	bone scan in diagnosing osteomyelitis versus soft tissue infection	medical imaging center in the US (n=39 recruited, n=33 included) Inclusion criteria: • Referred due to suspected pelvic pressure injury infection • Clinical suspicion of osteomyelitis • Category/Stage 2 or greater pressure injury Exclusion criteria: • Absence of CT imaging • Lack of confirmed diagnosis Participant characteristics: • Mean age 59 to 64 years years • White blood cell count 10 to 11 • C-reactive protein 126 to 134 • 12 pressure injuries were Category/Stage 2 and 21 were indeterminate Category/Stages	○ CT imaging, microbiology and/or pathology (n=21) ○ Clinical imaging followup (n=12) • Dual isotope (DI) step 1 planar, step 1 SPECT/CT, step 2 SPECT/CT, and combined step 1/ step 2 SPECT/CT were reviewed separately for diagnosis and diagnosis confidence	• A scale was used for diagnosis of each scan using a 0 to 5 scale of osteomyelitis • Follow up median 14 months (4mths to 3 years)	• Individuals with and without osteomyelitis did not differ on clinical variable EXCEPT individuals with a sacral pressure injury were more likely to have osteomyelitis **Diagnostic accuracy** • DI step 1 planar: sensitivity 74%, specificity 43%, Area under curve (AUC) 0.63 (95% CI 0.44 to 0.82), positive predictive value (PPV) 64%, negative predictive value (NPV) 55%, diagnostic certainty 3% • DI step 1 SPECT/CT: sensitivity 89%, specificity 50%, AUC 0.84 (95% CI 0.71 to 0.98), PPV 71%, NPV 78%, diagnostic certainty 14% • DI step 2 SPECT/CT: sensitivity 63%, specificity 93%, AUC 0.87 (95% CI 0.75 to 0.99), PPV 92%, NPV 65%, diagnostic certainty 74% • DI step 1/ step 2 SPECT/CT: sensitivity 95%, specificity 93%, AUC 0.93 (95% CI 0.83 to 1.00), PPV 95%, NPV 93%, diagnostic certainty 91% **Author conclusion: DI step 1 is more sensitive and step 2 is more specific. Both step 1 and step 2 DI SPECT/CT images are needed to accurately assess for infection and distinguish osteomyelitis from soft tissue infection.**	• Scale used was not validated • Small sample size • Unclear recruitment	**Quality: Low**
(International Wound Infection Institute (IWII) 2016)	International consensus document on **wound infection and biofilm assessment, diagnosis and management**	Not applicable	Not applicable	Consensus agreement process	**Indicative of biofilm** • Failure of appropriate antibiotics or recurrence after ceasing antibiotics • Recalcitrance to antimicrobials • Delayed wound healing • Increased exudate • Low level inflammation • Low level erythema • Poor granulation • Secondary signs of infection	• Consensus document based on a literature review and formal consensus process • Not specific to pressure injuries	**Indirect evidence (Consensus document for wounds of mixed etiology)**

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					Indicative of local wound infection • Friable, bright red granulation tissue • Increasing malodour • New or increased pain • Epithelial bridging and pocketing in granulation tissue • Delayed wound healing • Wound breakdown and enlargement • New ulceration of the peri-wound **Indication for wound specimen and standard microbiological analysis** • Chronic wound with signs and symptoms of systemic infection (include blood culture) • Infected wound failing to respond to antimicrobials • Individuals with immune incompetency with signs of local wound infection or delayed healing **Topical antiseptics** • Use when there is local wound infection or to prevent infection in individuals at high risk • Use for 2-weeks before reviewing response • Alternate topical antiseptics in 2- or 4-week rotations		
{Sapico, 1986 #378}	Prospective cohort study **investigating types of infection in pressure injuries of different severity and concordance**	Participants had spinal cord injury (n=25 Inclusion criteria: Pressure injury Spinal cord injury Exclusion criteria: None listed	Some patients were receiving antibiotics, 38% of biopsies taken the patient had antibiotics in preceding 72 hours	Biopsies for pressure taken from central area and random peripheral area Wound photography Wound swab cultures Mean colony forming units (CFU) taken between the two biopsies per wound	• Ulcers with necrotic tissue had the most bacteria and the biggest variety of microbes • Mean concordance between swab result and deep tissue biopsy was 74.5% • Mean concordance between central and peripheral biopsy of same wound was 63% **Author observations: Because results can vary from the same wound, consider taking**	• Very small study • Antibiotic use may impact the results • Unclear how close swab and biopsy performed in time • No blinding reported	**Level of evidence: 1** **Quality: low**

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	between swab and biopsy	Characteristics: Primarily males Age rang 19 to 78 years Pressure injuries ranged from 4cm^2 to 225cm^2			**more than one tissue biopsy. Necrotic tissue has most bacteria.**		
(Nery Silva Pirett, Braga et al. 2012)	Prevalence and prognostic retrospective cohort studies **investigating the prevalence of MRSA colonization in pressure injuries and estimating the risk of MRSA-associated bacteraemia**	Participants were recruited over 9 months from a hospital in Brazil for two concurrent cohort studies. Study a): determining the prevalence of MRSA in stage II or greater pressure injuries Study b): in participants detected as having MRSA-colonzied pressure injuries, estimating the risk of MRSA-bacteraemia Data was collected through medical record analysis (n=145). Inclusion: • Stage II or greater pressure injury Characteristics: • 57.2% sample were male • Average age 612±18.4 yrs (range 20 to 101 yrs) • Mean hospital stay 69.6±66.7 days • primarily admitted due to clinical cause (60.1%); 4.1% admitted due to pressure injury infection • 56.5% had used at least 2 classes of antibiotics in the past 30 days	• Following cleansing, a sterile swab moistened with saline solution was rotated over a 1-cm square of granulation tissue with sufficient pressure to force fluid from the wound tissue • The swab was inoculated in Mannitol salt agar and the S. aureus strain was identified as coagulase-positive	• Estimate the prevalence of MRSA colonization • Identify risk factors for colonization of these wounds • Ascertain whether MRSA colonization of pressure injury increases the risk of MRSA bacteremia	• Of the 145 pressure injury participants, 63 (43.5%) had a MRSA colonized pressure injury • 40 (27.6%) participants had presence of infected pressure injury • 12 (8.3%) participants had MRSA bacteremia • There was no statistically significant association between age, gender, cause of admission, length of hospital stay, underlying disease, presence of invasive devices or surgical procedures and having a pressure injury colonized with MRSA • Among the patients with positive blood cultures and MRSA colonized pressure injury: o odds ratio for MRSA bacteremia was 19.0 (95% CI 2.4 to 151.1, p< 0.001) o odds ratio for bacteremia and mortality was 21.9 (95% CI 1.23 to 391.5, p=0.002) • Independent risk factors for MRSA bacteremia were: o ≥2 underlying diseases (OR 6.26, 95% CI 1.01 to 39.1, p=0.04) o prior MRSA infected pressure injury (OR 12.75, 95% CI 1.22 to 132.9, p=0.03)	• Only hospitalized patients, lacks generalizability • Management of the condition and severity of the underlying illness was unavailable • Small sample size • Unclear the duration of pressure injury at time of admission and the prior management techniques • May lack generalizability doe to location	**Level of evidence: 3 (prognostic)** **Quality: low**

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		• 70.3% had at least 2 invasive devices (e.g. mechanical ventilation, IDC, CVC, gastric catheter, endotracheal catheter) • Overall mortality 42.1%pressure injurie					
Gardner et al. (2001)	Cross sectional study to determine **predictive value for clinical signs and symptoms of wound infection**	Participants recruited in three locations - long term care, rehab and a psychiatric inpatient ward in US (n= Participant characteristics: Mixed wounds, but primarily pressure injuries (n=119 eligible, n=36 included) Inclusion criteria: • Non-arterial chronic wound • Aged over 18 years • Biopsy of wound performed within 8 hours of data collection Exclusion: • Declined to participate • Superficial wound • Too close to healing to do a tissue biopsy Participant characteristics: • 53% pressure injuries • Mean size 4.5cm^2	33% of individuals had been treated with topical treatments including growth factors, silver sulfadiazine, topical antibiotics and wound gel	• Checklist was used to evaluation of 12 clinical signs and symptoms of chronic wound infection (i.e., pain, erythema, edema, heat, and purulent exudates) and signs of wound breakdown (i.e., serous drainage with concurrent inflammation, delayed healing, discoloration of granulation tissue, friable granulation tissue, malodor and wound breakdown) • Evaluation performed by blinded health professionals • Wound biopsy and culture • Infection was defined as 10^5 or greater organisms /g	**Predictive validity of swabbing vs biopsy** • Classic signs of infection (increasing pain, heat, erythema, edema and purulent discharge): mean sensitivity 0.38, mean specificity 0.78 • Sensitivity for individual classic signs and symptoms: Heat (0.18), purulent discharge (0.18), edema (0.64), pain (0.36) and erythema (0.55) • Specificity for individual classic signs and symptoms: Heat (0.84), purulent discharge (0.64), edema (0.72), pain (1.00) and erythema (0.68) • Signs of infection specific to wounds: mean sensitivity 0.62, mean specificity 0.76 • Sensitivity for individual wound-specific signs/symptoms: serous drainage plus inflammation (0.55), delayed healing (0.81), discoloration of granulation tissue (0.64), friable granulation tissue (0.82), malodor, (0.36) wound breakdown (0.46) • Specificity for individual wound-specific signs/symptoms: serous drainage plus inflammation (0.72), delayed healing (0.64), discoloration of granulation tissue (0.56), friable granulation tissue (0.76), malodor, (0.88) wound breakdown (1.00) **Wound characteristics infected vs non-infected** • Compared to non-infected wounds, infected wounds had more necrotic tissue and lower mean T_cPO_2 (both p<0.10,	• Inter-rater reliability was reported as 0.52 to 1.00 for individual checklist items • Nonprobability sampling	**Level of evidence: 1 (diagnostic)** **Quality: high**

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					considered significant in this trial due to exploratory design) • There was no difference between infected and non-infected wounds for size, depth, duration and management options **Signs and symptoms specific to wounds are more reliable than classic signs and symptoms of infection in identifying wound infection**		
(De Heredia, Hauptfleisch et al. 2012, Luis, Hauptfleisch et al. 2012, Hauptfleisch, Meagher et al. 2013)	Retrospective record review diagnostic study **investigating inter-rater reliability of MRI scans for identifying osteomyelitis associated with pressure injury**	Participant records from those attending a service in the UK between 2007 and 2011 (n= 37, n= 41 MRI scans) Inclusion: • Adult patients • Diagnosed with SCI • Indication of pressure injury Characteristics: • Primarily male patients (70.2%) • Mean age 52 years (range 22 to 83yrs) • 70.2% of pressure injuries were located in greater trochanter	Analysis of MRI examinations and clinical records collected over a four year period Images were independently assessed by two experiences radiologists for osteomyelitis	Inter-observer agreement for indicative MRI signs of osteomyelitis in complex pressure injuries based on: • Muscle inflammatory change • Deep fluid collection • Corticol bone erosion • Bone marrow edema • Hip effusion • Heterotopic ossification • Presence of sinus tract	• Significant association between an intermediate and high probability of osteomyelitis and cortical bone erosion (sensitivity and specificity 90%, Pearson's *r*=0.84) • Significant association between an intermediate and high probability of osteomyelitis and abnormal bone marrow edema (sensitivity of 81%, Pearson's *r*=0.82) • 88% agreement on likelihood of osteomyelitis (kappa 0.92, 95% CI 0.84 to 1.01, p<0.0001) • Lack of agreement on presence of sinus tract (possibly related to unclear definition of when a pressure injury becomes a sinus) **Study conclusions: there was strong inter-rater agreement in identification of MRI scan signs that may indicate osteomyelitis; however, no comparison was made to a reference standard (e.g. histological confirmation).**	• Retrospective nature of the study • Unclear sample selection • Lack of reference standard including histological confirmation • Raters were given access to the patient's full clinical file to assist in diagnosis	**Level of evidence: 4 (diagnostic)** **Quality: low**
(Larson, Gilstrap et al. 2011)	Retrospective record review diagnostic study **investigating comparing the reliability**	Participant records were recruited from a department of plastic surgery in the USA between 2004 and 2008 (n=44) Inclusion:	• All included participants were treated with surgical debridement of stage IV pressure injuries accompanied by a bone culture, after	• Abstracted data included: o location of ulcer o radiographic imaging obtained before operation	• Sensitivity: percentage of cases with biopsy-proven osteomyelitis identified with imaging was 50% using a computed tomography (CT) scan and 88% using a plain film of the bony area of involvement (overall sensitivity of radiological studies was 61%)	• Small retrospective study • Radiologic studies may or may not have been performed due to	**Level of evidence: 4 (diagnostic)** **Quality: low**

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	of x-ray compared with bone biopsy for identifying osteomyelitis associated with pressure injuries	• Stage IV pressure injury according to NPUAP classification as identified on billing information • Treated with surgical debridement • Bone culture performed after radiologic study of underlying bone • Multiple pressure injuries analysed as separate pressure injuries where at least 6 months passed between treatment Exclusion: • Lacking x-ray imaging or intraoperative bone culture • Pressure injury not treated with surgical debridement	having prior radiographic imaging of the underlying bone were included • Participants were treated in a standard manner preoperatively, intraoperatively and postoperatively	○ data and description of operation ○ results of intraoperative bone biopsy ○ antibiotic received before and after surgical intervention ○ follow-up • Radiographic studies were interpreted by a single musculoskeletal radiologist - who was blind to operative findings	• Specificity: percentage of cases without osteomyelitis identified as not having the condition by imaging was 85% for CT scan and 32% for plain film (overall specificity of radiologic studies was 69%) **Study conclusions: Preoperative radiologic studies for osteomyelitis in pressure injury are far from definitive and might only be of value in defining the extent of disease for surgical planning purpose.**	indications for local osteomyelitis • Radiographic imaging done up to 3 months prior to bone cultures • None of the patients had the complete spectrum of radiologic studies	
(Daniali, Keys et al. 2011)	Retrospective case-controlled study **comparing pre-operative management and post-operative outcomes between pre-operative MRI diagnosis of osteomyelitis and intra-operative bone biopsy**	Participants were recruited from a spinal cord center in the USA between 1996 and 2008 (n=65 had flap reconstruction had osteomyelitis and n=47 had either MRI or bone culture diagnosis). Characteristics: • Mean age 56.2 to 58.7 years • Primarily males with SCI • The preoperative MRI group had a greater percentage of participants with stable pressure injuries of unchanging size win comparison to the	• Data were collected from patient electronic medical records including operative reports, admit notes, daily progress notes and consult and weekly wound care team notes • Participants received either: ○ pre-operative MRI diagnosis of osteomyelitis (n=26) ○ post-operative bone culture diagnosis of	• Recurrence of pressure injury at the same anatomic site • Suture line dehiscence • Significant suture line dehiscence and Time until mobilization by physical therapy	• Patients with a diagnostic preoperative MRI did not differ significantly in rates of pre-operative antibiotic administration compared to those without pre-operative MRI (26.9% versus 23.8% OR 1.2, p=0.81) • There was no significant difference in pressure injury recurrence rates post-surgery between those with osteomyelitis diagnosed by MRI had and those with osteomyelitis diagnosed by bone culture (39% versus 29%,OR 2.4, p=0.22) • There was no significant difference in infection rates post-surgery between those with osteomyelitis diagnosed by MRI had and those with osteomyelitis diagnosed by bone culture (7.7% versus 14.3%,OR 0.50, p=0.44) **Study conclusions: the study concluded that there was no evidence that a preoperative**	● Retrospective chart review subject to Inaccuracies of data recording ● Study cohorts were small potentially limiting the study generalizability.	**Level of evidence: 3 (diagnostic)** **Quality: Moderate**

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		bone culture group (46.2% versus 23.8%, p =0.04) • MRI group had a greater number of patients with a history of peripheral vascular disease (14.3% versus 0%, p=0.05)	osteomyelitis (n=21)		**MRI diagnosis of osteomyelitis significantly alters clinical or surgical management or patient outcomes**		
Clinical question 3: Topical antiseptics for treating infection and biofilm in pressure injuries							
(Dryden, Dickinson et al. 2016)	Observational study exploring the **efficacy of surgical honey in reducing infection and** biofilm in pressure injury	Participants were recruited using unknown methods from UK (hospitals and general practice) and African nations (n=110 participants, n=18 participants with 19 pressure injury) No inclusion or exclusion criteria stated Participant characteristics: (participants with pressure injury only) • Mean age 75 years (range 45 to 97) • Mean number comorbidities 5 • Mean pressure injury duration 5.4 months	• Surgical honey gel (Surgihoney RO) manufactured in a way to enhance the active ingredient (reactive oxygen species including hydrogen peroxide) • Honey gel applied 1mm thick and covered with a sterile secondary dressing selected based on exudate absorption needs • Wound dressings changed 2-3 days at clinician's discretion	• Level of pain on a 3-point verbal scale • Presence of slough, inflammation, healthy granulation tissue or necrosis based on clinician's subjective opinion Wound characteristics were considered presumptive of biofilm but this was never confirmed by testing • Wound swab with semi-quantitative culture • Pressure injuries not graded. • Adverse events • Mean duration of therapy was 7.4 days	**Pain** • 5 pressure injuries rated as mild pain at commencement were rated as no pain at conclusion • I pressure injury rated as mild pain had no change • 1 pressure injury rated as severe pain at commencement was rated as no pain at conclusion **Slough and necrosis** • 5 pressure injuries rated as having lots of slough had no slough at conclusion • 1 pressure injury with mild slough was rated as having lots of slough at conclusion • 1 pressure injury rated as necrotic had no necrosis at conclusion **Wound healing** • 63% of the pressure injuries had reduction in wound size documented • 89% of pressure injuries had improved healing criteria documented **Reduction in bacterial load** Only 47% of the wounds were swabbed and they all showed reduction in bacterial load	• No control, no blinded assessment outcome • Unclear how outcomes were measured, subjective evaluations but no interrater and intrarater reliability reported • No inclusion nor exclusion criteria • Concurrent management not reported and intervention was not standardized • Assessment period was unclear • No statistical analysis • < half pressure injuries were swabbed and none had a formal biofilm evaluation • Potential conflict of interest	**Level of Evidence: 4** **Quality: low**

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(Gawande, Leung et al. 2014)	Laboratory study investigating antibiofilm /antimicrobial activity of **an antibiofilm enzyme (DispersinB®) and broad-spectrum KSL-W peptide and to compare properties to a commercial wound gel (Silver-Sept™ gel) for managing infection and biofilm**	N/A	• One gram of placebo or DispersinB® KSL-W gels were added to each tube and incubated at 37°C for 72 hrs. Samples were removed at 24, 48, and 72 hrs, diluted 10 times to reduce antimicrobial carry-over, and plated on TSA and incubated for 48 h at 37°C. • Colonies were counted and expressed as cfu/ml. Biofilms were grown in 1.5 ml polypropylene microcentrifuge tubes.	Minimal Inhibitory Concentration (MIC) Minimal Bactericidal Concentration (MBC)	**Peptide alone versus peptide in combination with antibiofilm enzyme (experimental gel)** • DispersinB® significantly enhanced antimicrobial activity of KSL-W peptide against biofilm-embedded chronic wound infection associated bacteria, including Gram-positive bacteria MRSA, S. epidermidis, coagulase negative staphylococci (CoNS), and Gram-negative bacteria A. baumannii. • MIC and MBC for experimental gel were <10 µg/ml against test organisms. • Experimental gel showed 50% lower MIC and MBC against MRSA, S. epidermidis, CoNS, and A. baumannii compared to peptide solution alone. • Experimental gel showed sustained broad-spectrum antimicrobial activity against gram-positive bacteria MRSA, S. epidermidis, CoNS, and VRE and Gram-negative bacteria K. pneumoniae, A. baumannii, and P. aeruginosa. **Experimental gel versus commercial gel** • Experimental gel had significantly ($p<0.05$) more antibiofilm activity against all test organisms compared with commercial gel • Commercial gel only moderately effective against S. epidermidis and CoNS biofilm. **Authors concluded the study demonstrated the experimental gel provided antibiofilm and antimicrobial activity and was effective against bacteria embedded in preformed biofilms compared to some commercial gels.**	• The research was supported by the U.S. Army Medical Research and Materiel Command, Award W81XWH-11-P-0321 • Uncertain if this experimental product is available for wound care	**Indirect evidence (laboratory study)**
(Wild, Bruckner et al. 2012)	Prospective RCT **comparing**	Participants were recruited from in and out patients clinics in Switzerland	• Participants were randomly assigned to:	Primary outcome was MRSA eradication assessed on days 7, 14	**MRSA eradication**	• Outcomes for formation of granulation tissue	**Level of evidence: 1**

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	PHMB swabbing to a cellulose dressing impregnated with polyhexa-methylene biguanide (PHMB) in eradicating MRSA from pressure injuries	(n= 30) Inclusion: • MRSA contaminated pressure injury stages II to IV according to EPUAP classification • Pressure injury with MRSA colonization that has been unresponsive to several disinfection attempts during a 2-week wash out period Characteristics: • Groups comparable at baseline • 50% sample female • Mean age 66.5 to 70.9 years • Mean wound area study group 47.67±22.75cm2 and control group 35.80±13.47cm2 • In both groups 7/15 pressure injuries were stage IV sacral pressure injuries	○ Control group: cleansing performed with PHMB swabs for 20 minutes after which a foam dressing was applied (n=15) ○ Study group: cleansed with normal saline and received a PHMB impregnated cellulose dressing with the foam dressing applied as a secondary dressing (n=15) • In both groups, zinc cream was applied to peri-wound skin and dressings were changed second daily for 14 days	and for 3 consecutive days after the treatment period via wound swab and culture Secondary outcome was per cent of non-vital and granulation tissue assessed via wounds photography and planimetry performed weekly	• At day 7 more pressure injuries in the study group had been eradicated of MRSA (40% versus 86.67%) • At day 14 significantly more pressure injuries in the study group had been eradicated of MRSA 66.67% versus 100%, p<0.05)	were not reported in detail • Results for sustained eradication on days 14 to 17 not reported	**Quality: moderate**
(Sipponen, Jokinen et al. 2008)	Prospective, multicentre RCT investigating **effectiveness of resin salves (*Picea abies*) in pressure injury care**	Participants recruited from 11 primary care hospitals in Finland between 2005 and 2007 (n=37, n=22 completed and analysed) Inclusion: • grade II to IV pressure injury • not requiring surgical management of pressure injury	Details of concurrent management strategies were limited. Approximately 22% of control group and 8% of treatment group were managed on a pressure mattress. Participants were randomly assigned to either:	• Primary outcome measure was complete healing of the ulcer within 6 months • Secondary outcome measures included eradication of bacterial strains cultured from ulcers at the study entry • Bacterial cultures were obtained from all	• The resin salve group achieved a higher rate of complete healing at 6 months (92% versus 44%, p=0.003) • The speed of pressure injury healing was significantly faster in the resin than in the control group (p=0.013) • Bacterial cultures from the pressure injury area more often became negative within 1 month in the resin group • 100% of pressure injuries in treatment group were rated fully healed or	• No blinding or intention to treat analysis • Over 40% drop out of study. Although there was no significant difference in baseline characteristics between drop outs in each	**Level of evidence: 1** **Quality: low**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• with or without clinical wound infection Exclusion: • Life expectancy < 6 months • Advanced malignant disease Characteristics: • No significant between group difference on baseline demographics or wound characteristics • Mean age approximately 74 to 80 years • Mean BMI 21.8, mean P-albumin 28.3 to 31.4 gL^{-1} • Primarily bedridden participants • Primarily non-smokers • Primarily stage II and III pressure injuries	• resin salve applied at 1mm thickness between gauze layers with dressing changed third daily or daily for heavily exudating pressure injuries (n=13 with 18 pressure injuries) • sodium caboxymethylcellulose hydrocolloid polymer dressing (Aquacel®) or for clinically infected pressure injuries, hydrocolloid dressing with ionic silver (Aquacel Ag®). Dressing changed third daily, or daily for heavily exudating pressure injury. (n=9 with 11 pressure injuries) • Some participants in both groups received concurrent antibiotics	pressure injuries at baseline and 1 month, but thereafter only as clinically indicated. • pressure injury size measured by digital photography and planimetry	significantly improved versus 91% in the control group (p=0.003) • Drop outs in intervention included participants who required surgical intervention (n=2) and allergic reaction to the product (n=1). Drop outs were not significantly different between groups.	group, more treatment participants dropped out due to deteriorating pressure injuries and had these cases been included in analysis there may not have been statistically significant effect. • Study failed to recruit and maintain sufficient numbers to reach a-priori sample size calculations. • Bacterial eradication analysis is complicated by the concurrent use of antibiotics for some participants	
(Robicsek, Beaumont et al. 2009)	Two retrospective cohort studies **investigating the impact of decolonization therapy on MRSA** **Study 1) evaluating the**	Participants were recruited within three acute care hospitals operated by an organization in the USA. For both studies, retrospective records analysis for all non-neonate patients admitted overnight in a one year period Nov 2006 to Dec 2007 and followed through to March 2008	• Three hospitals with universal surveillance for MRSA colonized patient who could be treated with a 5-day course of nasal mupirocin calcium 2% twice daily plus chlorhexidine gluconate 4% every second day	• MRSA cultures reviewed by microbiology laboratory according to standardized criteria.	**Study 1)** • patients were readmitted for a mean of 76.5±77.2 days after first admission • There was significantly less rate of colonization at readmission in patients who received any dose of mupirocin compared with those who did not receive mupirocin (47.8% versus 63.2%, p=0.007) • In multivariate analysis, independent dependent risk factors for sustained	• Nonrandomized treatment, with patients with a higher risk of infection more likely to receive treatment than those with low risk of infection • Participants who received mupirocin	**Indirect evidence: mixed etiology**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	impact of decolonization therapy in patients who were carrying MRSA and were later readmitted **Study 2) evaluating the impact of decolonization therapy in patients who were carrying MRSA but did not have clinical infection**	Study 1) (n=407) Inclusion: • MRSA surveillance testing performed at time of admission • surveillance test or clinical culture performed within 2 days of admission was positive for MRSA • subsequent readmission in the study period Exclusion: • discharged after first admission with script for mupirocin or chlorhexadine Characteristics: • 69% ≥ 70 years of age • 91% admitted to internal medicine • 41% had diabetes mellitus Study 2) (n=933) Inclusion: • MRSA surveillance testing performed • no clinical culture indicative of MRSA within 30 days prior or 3 days after surveillance testing Exclusion: • discharged after first admission with script for mupirocin or chlorhexidine	• MRSA carriers were later retested for colonization or followed up for development of an MRSA infection		colonization included having pressure injury (OR 2.31, 95%CI 1.22 to 4.35, p=0.010) • Mupirocin at any dose decreased the risk colonization on readmission, particularly during the 30 to 60 day period after therapy (OR 0.48 to 0.56) **Study 2)** • patients were followed for a mean of 271.7±132 days after first admission • 7.4% participants developed MRSA infection during follow-up. • In multivariate analysis, having a pressure injury was not a risk factor for developing a clinical infection. • Receipt of mupirocin did not affect the risk of infection, although there was a trend toward delayed infection among patients receiving mupirocin **Study conclusions: having a** pressure injury pressure injury **is an independent risk factor for MRSA colonization. Treatment of MRSA colonization with a mupirocin-based decolonization regimen leads to only a small reduction in colonization and does not reduce infection rate.**	generally 92.4% also received chlorhexadine • Only performed routine nasal swab surveillance (no wound swabs)	
(Biglari, Vd Linden et al. 2012)	observational case series **reporting on**	Participants were recruited from 9 trauma centres in Germany (n=20)	• All of the participants were treated with Medihoney® approx.	• Weekly photographs, measurement and	• After 1 week of therapy all swabs were void of bacterial growth	• Objective measurement	**Level of evidence: 4**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	Medihoney® for stage III and IV pressure injuries	Inclusion/exclusion: • SCI patients with chronic pressure injuries • No other criteria reported Characteristics: • pressure injuries were at least 12 weeks in duration at entry to study • 65% sample male • Mean age 48.7 years (range 30 to 79) • 5/20 had stage IV pressure injuries • 15/20 had stage III pressure injuries	3mm thickness applied once daily after cleansing with Ringer's solution • Surrounding skin was disinfected with a range of anti-microbial preparations • Treatment was continued for more than 6 weeks	cultured (methods not reported) • Pressure injuries were documented at 3-week intervals	• 90% of participants showed complete wound healing after 4 weeks • No negative effects were noted from the treatment	strategy not reported • Peri-ulcer skin was treated with different antimicrobials that may have influenced culture findings • Pressure injury size and condition at entry not reported • Co-morbidity not reported	**Quality: low**
(Mizokami, Murasawa et al., 2012)	Retrospective **observational study comparing iodoform gauze to povidone-iodine and sugar or sulfadiazine cream** (only data from clinical study is summarised)	Retrospective records analysis of participants with PU treated at geriatric centre in Japan between 2008 and 2010 (n=53 participants with 60 PUs) Inclusion: • All participants with PUs were systematically recorded during a 2-year period and included in the study Characteristics: • Mean age approx. 80 yrs • Participants treated with iodoform gauze had significantly lower albumin (2.8±0.5g/dL versus 3.2±0.6 g/dL, p<0.007) • Participants treated with iodoform gauze had	There was no indication as to how treatment was selected for each participant. Participants were treated with either: • iodoform gauze was applied with a polyurethane top-dressing • The conventional treatment used as a comparison was either silver sulfadiazine cream or povidone-iodine and sugar	Primary outcome was wound-cleaning capacity determined by the % of wound surface area covered in necrotic tissue. The area of necrotic tissue was blindly determined using digitalized images.	• Treatment period was significantly shorter for participants who were treated with iodoform gauze (14.1±9.7 versus 29.0±24.5, p=0.002) • There was significantly greater PUs treated with iodoform gauze classified as having necrotic tissue completely removed after 2 weeks of treatment compared to conventional treatments (60% versus 10%, p<0.001) • By 4 weeks, 80% of PUs treated with iodoform gauze had necrotic tissue completed removed (versus 30%, p<0.001) **Study conclusion: Iodoform gauze is effective in preparing the PU wound bed for healing, but there is no evidence from this study that this leads to complete healing or faster healing**	• Indirect evidence: no relationship between debridement and wound healing outcomes was presented • No randomization, pre-defined outcome measures or clear participant selection • Non-equivalent participants at baseline • Various comparison treatments • Concurrent management strategies not reported	**Level of Evidence: 3** **Quality: low**

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		significantly larger wound surface area (17.6±19.6cm^2 versus 7.7±8.2cm^2, p=0.004) • Participants treated with iodoform gauze had more PUs stage IV (83.3% versus 57%, p=0.009)					
(Chuangsuwanich, Charnsanti et al., 2011)	Prospective randomized clinical trial **comparing silver sulfadiazine cream to a silver dressing**	Participants were recruited from an in and outpatient clinic in Thailand (n=40) Inclusion: PU stage III or IV Characteristics: • Mean age 62.6 to 69.1 years • No significant difference for blood results at baseline, including albumin levels <3.5 in both groups suggesting possible malnutrition • SSD cream group had significantly larger PU at commencement of study (12.17 versus 22.82cm^2)	• All PUs were debrided if required. • Participants were randomly assigned to receive: ○ wound beds covered with silver sulfadiazine (SSD) cream applied daily (n=20) ○ silver mesh dressings applied every 3 days (n=20) • Treatment was for 8 weeks	Data collected at the beginning of the study and every two weeks thereafter: • Wound size (planimetry) • Wound photography • PUSH score • Bacterial wound culture Study period was eight weeks for each participant	• Silver mesh dressing was superior to SSD cream for reduction in wound area at 8 weeks (18.22 versus 7.96 and cm², p=0.093) • There was no significant difference between groups for PU healing rate after 8 weeks (36.95% in the mesh group and 25.06% in the SSD group, p=0.507) • The means of PUSH score were 11.4 (mesh) and 13.4 (SSD cream) at commencement and 7.55 (mesh) and 9.6 (SSD cream) after 8 weeks. • **Study conclusions: considering the significant difference in wound size at commencement of this study, there appears to be no significant difference between a silver dressing and topical SSD cream for healing in PU. There is no placebo group to assess the overall benefit of silver in managing PUs.**	• Small trial, no power study • No placebo control • No blinding • Groups not comparable at baseline • Unclear treatment (e.g. dressing applied over SSD cream?) • Non comparable management (dressing changes at different frequency) • Unclear co-morbidities	**Level of evidence: 1** **Quality: low**
Clinical question 4: Antibacterial wound dressings for treating infection and biofilm in pressure injuries							
(Graham 2014)	Cohort study investigating **the viability of a MRSA wound healing protocol for chronic (non-healing for**	Participants were recruited by unknown methods a wound center and from an office based center (n=40 total, n=7 pressure injuries) (Inclusion criteria:	Debridement every 7–10 days at the wound care center or 10–14 days at the office setting. Daily dressing with an antimicrobial dressing (made from Oakin, a	• Followed for 12 weeks period or until wound closure • Outcomes measured at 30, 60 and 90 days • Wound closure based on wound surface area	• 31 participants healed within 90 days • Approx 70% of pressure injuries healed by 90 days (40% healed in 30 days, further 15% at 60 days and further 15% at 90 days) • Mean healing time for pressure injuries was 34.80±24.40 days) • There was no significant difference in time to healing based on wound etiology	• Methods of recruitment are unclear • Non standardized intervention that different between the two sites • Participants or their families	**Level of evidence:3** **Quality: Low**

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	≥90 days) wounds	• Aged ≥ 18 years Presenting with chronic non-healing lower • extremity wound • Presenting with Celsian signs and symptoms of local wound infection • Wound culture positive for MRSA Exclusion criteria: • Serious wound infection defined as a wound with odor, serous exudate, delayed healing, friable granulation tissue, pocketing or breakdown Participant characteristics: • Primarily diabetic foot ulcer or venous leg ulcers but pressure injuries reported separately	natural tannin harvested from oak extract) Oral antibiotics prescribed		• Statistically significant moderate correlation between time to healing and wound size at baseline (r=0.37, p=0.02) • No adverse effects **While the author concludes that the protocol was effective, there was no formal evaluation of bacterial levels/MRSA after admission not the study, there were a number of aspects to the protocol, debridement protocol was not standardized and there was no control group or blinded evaluation**	performed dressing changes • 10% of participants didn't receive intervention therapy • No control group • No blinded evaluation	
(Ciliberti, De Lara et al. 2014)	Case series evaluating the **efficacy a silver-containing hydrofibre dressing (Aquacel® Ag) that includes carboxymethylated Hydrofibre® technology for treating pressure injuries**	Participants were recruited in home care setting in Italy over 6 months (n=20) Inclusion criteria: • Aged≥ 18 years • Pressure injury Category/stage 3 or 4 • No systemic antibiotic therapy in preceding 7 days Exclusion criteria: • Eschar or necrosis • Anticoagulant therapy	Silver containing hydrofiber dressing for 7 days	• Wound bacterial load change measured by three different tissue biopsies during 1 week of therapy (baseline, 48 hours after commencing therapy, 7 days after commencing therapy)	Bacterial load • At baseline only 1 participant had no bacterial load • After one week, bacterial loads dropped in 84% of the 19/20 participants with bacterial load at baseline • After one week, bacterial loads were negative in 63% of negative in the 19/20 participants with bacterial load at baseline **Author conclusion: Silver containing hydrofiber dressing eliminates need for local or systemic antibiotics**	• Did not evaluate how many wounds with bacterial load at baseline had local signs and symptoms • Unclear if consecutive recruitment • Does not report comorbidities or patient characteristics • Poor description of intervention (uncertain how frequently	**Level of evidence:4** **Quality: Low**

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		• Systemic or local antibiotics or antimicrobial/ antiseptics Participant characteristics: • Wounds did not all show classic signs and symptoms of infection at baseline				dressings changed, or who performed care • No statistical analysis	
(Woo and Heil 2017)	Retrospective, non-randomized study **evaluating methylene blue and gentian violet dressing for management of chronic wounds with local infection**	Participants were recruited from an unknown location using unreported methods (n=29) Inclusion criteria: • ≥ 18 years of age • ≥ one chronic wound ≥1 cm^2 in size that showed signs of localized infection or critical colonization but with good potential for healing. Exclusion criteria: • Systemic antibiotic treatment • Allergy/hypersensitivity to methylene blue or • gentian violet Participant characteristics: • 62% had pressure injuries • Mean age 60.2 years	Participants all received 4 weeks of treatment with the Gentian Violet/methylene blue dressing (Hydrofera Blue Classic dressing)	• Demographics • Changes in Pressure Ulcer Scale for Healing (PUSH) scores PUSH scores • Wound size measurements • Change in percent surface area of devitalized tissue • UPPER and LOWER mnemonic for a wound • infection checklist • Adverse effects • 4 week study period	**Wound infection outcomes at week 4** • Significant 75% reduction in mean UPPER and LOWER wound infection score reduced from 3.6 to 0.9 ($p < 0.001$) **Wound healing outcomes at week 4** • Significant 42.5% reduction in wound surface area from 21.4cm^2 to12.3cm^2 ($p=0.005$) • Significant reduction in mean PUSH score rom 13.3 to 10.7 ($p<0.001$ • Significant decrease in mean wound coverage by devitalised tissue from 52·6% to 11·4% ($p<0.001$) **Adverse effects** None were experience din trial **Author conclusion: Gentian Violet/methylene blue dressing is effective for managing infection and promoting healing in chronic wounds**	• Participants selection biases • No objective evaluation of infection status/bioburden • Does not state who performed evaluations and how interrater reliability was established • Psychometric properties of tools not reported • No control group • Small study	**Indirect evidence (mixed wound etiology)**
(Trial, Darbas et al., 2010)	prospective RCT **comparing anti-microbial effectiveness**	Participants were recruited over 18 months from a wound clinic and inpatient service at a hospital in France	• Participants were randomly assigned to receive either: ○ Study product: An ionic silver alginate	• Assessments on days 1, 8 and 15. • Primary outcome measure was progression or	Participants with pressure injuries • The study group ($p=0.005$) and the control group ($p=0.008$) both had statistically significant improvements in	A priori calculation for sample size was established for the overall study i.e. the findings for PU	**Level of evidence: 2 Quality: low**

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	of an ionic silver alginate dressing to a silver-free alginate dressing for primarily Category/Stage II pressure injuries (includes some Category/Stage III)	(n=42, n=24 with pressure injuries) Inclusion: • One or more symptoms of local infection including local heat, peri-wound erythema, persistent pain, oedema, malodour, fever, pus and heavy ex udate. Exclusion: • Allergy to dressing components • Burn patients • Ulcers associated with infectious disease • Taking anticoagulants • < 18 years or over 80 years Characteristics of pressure injury participants: • Mean age of females 80.9±9.0 and mean age of men 65.5±17.7 • NS between baseline mean clinical infection score (8.7±2.8 treatment group versus 7.9±3.6 control group) • 63% sacral PUs • 46% of PUs were described as having "superficial tissue damage with pus exuding blisters", 33% had "tissue damage not extending to the bone" 79% graded ≥10 on Norton scale and 38% graded ≥ 15 on Norton scale	matrix dressing that is described as providing controlled, sustained delivery of silver ions over 72 hours (Askina® Calgitrol® Ag; n = 20, n=11 with PU) ○ Active control product: A standard alginate dressing (Algosteril® ; n = 22, n=13 with PU) • Treatment was for 15 days. • Concurrent management strategies were not reported	regression of local infection assessed by: ○ an 18-point scale based on presence and intensity of clinical signs (fever, local heat, persistent pain between dressing change, peri-lesion erythema, oedema, pus, exudate) ○ a blinded assessment my a microbiologist categorising wound as deteriorated, unchanged or improved based on bacteriological status • Additional outcomes on 5-point scale were usefulness and acceptance; ease of application and removal; reduction of malodour; reduction of persistent pain; improvement of the periwound skin; dressing comfort; cleansing effect; absorption properties; adherence to the wound. • Adverse events	clinical infection scores between baseline and day 15 • There was no significant difference between the two groups on the clinical infection score at day 15 (3.3±3.1 study group versus 3.2±3.2 control group, p=ns)	participants were underpowered.	

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(Beele, Meuleneire et al. 2010)	Prospective RCT **comparing a silver alginate dressing to silver-free alginate dressing**	Participants were recruited from three centres in Belgium and the Netherlands (n=36 participants, of which n=12 had pressure injuries) Inclusion: • aged over 18 years • chronic wound suitable for treatment (i.e. of size no more than 2cm x 20cm for pressure injuries) • at risk of infection assessed as having at least two characteristics on mASEPSIS tool Exclusion: • target wound showing general or systemic infection based on clinical signs • requiring or already taking systemic antibiotics • known condition or physical/medical state affecting wound healing • systemic corticosteroids, immunosuppressants, radiation or chemotherapy • poor life expectancy Characteristics: • mean age 73.4 to 73.5 years • mean BMI 27.1 to 30.5 • difference in baseline mean wound surface area 20.1cm^2 for study group	Participants were randomized to receive either: • Study group: an ionic silver alginate/ carboxymethylcellulose (SACMC) dressing • control group: a non-sliver calcium alginate fibre (AF) dressing Treatment continued for up to 4 weeks. Concurrent treatments not reported.	The primary study endpoints were: • Prevention of infection (assessed as progress of wound to or away from infection based on mASEPSIS score for wound pain, presence of erythema, oedema, warmth, moderate to heavy exudate, slough, discoloured granulation, pocketing at wound base, malodour, necrosis) • Progression to wound healing based on wound surface area The efficacy was evaluated over a 4-week period	Wound healing • There was a statistically significant difference in the overall wound surface area reduction over time for the treatment wounds (p=0.017) • There was no significant difference at 4 weeks in change in mean surface area from baseline between the two groups (+4.5cm2 control group versus –2.4cm2 study group, p=ns) Prevention of infection • The study dressing was associated with a significantly greater reduction in signs/symptoms associated with infection as rated by mASEPSIS score than the control group (p=0.013) • over the 4-week follow-up period one adverse event (wound maceration) was reported in the study group and five were reported in the control group (two cases of wound infection, one serious sticking of dressing, on rehospitalisation for further wound care).	• sensitive to different definitions of critical colonization • low sample size	**Indirect evidence (mixed aetiology)**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		and 14.2cm^2 for control group • difference in wound duration 15.5 months for study group and 10.2 months					
(Trial, Darbas et al. 2010)	prospective RCT **comparing anti-microbial effectiveness of an ionic silver alginate dressing to a silver-free alginate dressing**	Participants were recruited over 18 months from a wound clinic and inpatient service at a hospital in France (n=42, n=24 with pressure injury) Inclusion: • One or more symptoms of local infection including local heat, peri-wound erythema, persistent pain, oedema, malodour, fever, pus and heavy exudate. Exclusion: • Allergy to dressing components • Burn patients • Ulcers associated with infectious disease • Taking anticoagulants • < 18 years or over 80 years Characteristics of pressure injury participants: • Mean age of females 80.9±9.0 and mean age of men 65.5±17.7 • NS between baseline mean clinical infection score (8.7±2.8 treatment group versus 7.9±3.6 control group)	• Participants were randomly assigned to receive either: ○ Study product: An ionic silver alginate matrix dressing that is described as providing controlled, sustained delivery of silver ions over 72 hours (Askina® Calgitrol® Ag; n = 20, n=11 with pressure injury) ○ Active control product: A standard alginate dressing (Algosteril® ; n = 22, n=13 with pressure injury) • Treatment was for 15 days. • Concurrent management strategies were not reported	• Assessments on days 1, 8 and 15. • Primary outcome measure was progression or regression of local infection assessed by: ○ an 18-point scale based on presence and intensity of clinical signs (fever, local heat, persistent pain between dressing change, peri-lesion erythema, oedema, pus, exudate) ○ a blinded assessment my a microbiologist categorising wound as deteriorated, unchanged or improved based on bacteriological status • Additional outcomes on 5-point scale were usefulness and acceptance; ease of application and removal; reduction of malodour; reduction of persistent pain; improvement of the periwound skin;	Participants with pressure injuries (direct evidence) • The study group (p=0.005) and the control group (p=0.008) both had statistically significant improvements in clinical infection scores between baseline and day 15 • There was no significant difference between the two groups on the clinical infection score at day 15 (3.3±3.1 study group versus 3.2±3.2 control group, p=ns) All participants (mixed aetiology, indirect evidence) • There was no significant difference between the two groups on the clinical infection score at day 15 (3.8±2.9 study group versus 3.8±3.4 control group, p=ns) • Results for the two microbiologists' assessments were not combined. Both microbiologists rated 45% of wounds tested with the study dressing and 27% of positive-control wounds as having improved in biological status (p=ns for both microbiologists) • There was no significant difference between groups for any of the items for acceptability and usefulness except for "adherence to wound for pressure injury", for which the study product showed greater per cent of good/excellent ratings (100% versus 38%, p=0.04)	A priori calculation for sample size was established for the overall study i.e. the findings for pressure injury participants were underpowered.	**Level of evidence: 1 (also some indirect evidence) Quality: low**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• 63% sacral pressure injuries • 46% of pressure injuries were described as having "superficial tissue damage with pus exuding blisters", 33% had "tissue damage not extending to the bone" • 79% graded ≥10 on Norton scale and 38% graded ≥ 15 on Norton scale		dressing comfort; cleansing effect; absorption properties; adherence to the wound. • Bacteriological status rated as deteriorated, unchanged or improved independently by 2 blinded microbiologists • Adverse events	**Study conclusions: The results of this small study indicated that the test dressing appeared to improve the blindly rated bacteriological status of clinically infected wounds over 15 days, but there was no statistically significant difference from the positive control dressing performance.**		
Clinical question 5: Treatment of biofilm							
(Bianchi, Wolcott et al. 2016)	A consensus document by an international inter-disciplinary expert panel evaluating evidence for good clinical practice with respect to **recognizing and managing biofilms in acute and chronic wounds**	Panel of experts convened in Italy (n=17) consisting of wound care experts (n=11) from nursing, dermatology, surgery and pharmacy plus experts in research design (n=5) and one librarian dermatologist	• 37 questions were developed using PICO concerning biofilm relevance diagnosis and treatment, plus 8 additional background questions concerning general aspects of biofilm in wounds • Questions were voted on for inclusion based on relevance and then debated and reformulated	**Not applicable**	**Recommendations for pressure injuries** For people with chronic pressure injuries where biofilm is suspected with or without clinician signs and symptoms, sharp and/or mechanical debridement, antimicrobial wound dressings and antiseptic soaks or cleansing with antiseptics are strongly recommended	• Funding and conflicts of interest are disclosed • Diverse panel experience but subjective opinion • Diversity in opinion might influence the consensus. possibility of intimidation, influence and compromise. • Only one panel member reviewed searches that underpinned the entire process. • Insufficient evidence was found to have more specific recommendations (e.g. which antimicrobial dressings)	**Indirect evidence (consensus document, mixed etiology)**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
Clinical question 6: Emerging diagnosis and treatments for infection							
(Nakagami, Mori et al. 2017)	Cross sectional study **evaluating the reliability of bacterial counts using a rapid bacteria counting system**	Participants were recruited in one facility in japan over a 6 month period (n=13 with n=16 pressure injury U) Inclusion criteria: • Age ≥ 18 years • Category/Stage 2 or greater pressure injury Exclusion criteria: • Category/Stage 1 pressure injury • Drug anticoagulated Participant characteristics: (not significantly different between groups) • Mean age 69.3±16.6 years • Mean pressure injury size 17.6±18.5	• Standardised swabbing method used to collect samples. • A rapid bacterial counting system that used a microelectrode chip on which bacteria are captured by dielectrophoresis to calculate number of bacteria irrespective of presence of biological cells (e.g. host cells) • Bacterial counts measured using a rapid bacteria counting system (Bacteria Counter, DU-AA01NP-H, Panasonic Healthcare Co., Ltd., Tokyo, Japan).	• DESIGN-R assessment tool for wound severity that examines depth, exudate, size, inflammation, granulation tissue, necrotic tissue and undermining • Classification of pressure injury using EPUAP/NPUAP classification system • Standardized swabbing method used by swabbing on longest axis of the wound • Two assessors were used	**Detected bacteria** Inter-rater reliability (n=63 pairs) ICC 0.83, 95 % CI 0.73 to 0.90, p<0.001 Intra-rater reliability (n=57 pairs) ICC 0.89, 95 % CI 0.82 to 0.94, p<0.001 **Undetected bacteria** In 31.0 % of wounds, bacterial levels were less than the detection limit. Interrater reliability ICCs was 0.59 [95 % CI: 0.20 to 0.79, p=0.005] Intrarater reliability 0.82 (0.64 to0.92, p<0.001) (n=30). **Costs** Device costs about 220,000 JPY (£ 1550) and measurement costs about 200 JPY (£ 1.40) per sample which is much lower than quantitative bacterial culture **Conclusion: Device demonstrated high inter- and intra-rater reliability calculated according to the ICCs and using Landis' benchmark criteria.**	• Only one pair used for both • Limited sample of Pressure injuries • The device could not measure 30% of wounds due to insufficient bacteria levels. • Presence of biofilm taken into account when using the rapid bacterial number counting system. However, it is unclear how this was undertaken • Rapid bacterial count device originally developed for the oral hygiene field. Reliability of bacterial counts using this device in wound care settings has not been verified.	**Level of Evidence: 4 (diagnostic)** **Quality: moderate**
(Gomes, Brandino et al. 2015)	Laboratory research exploring **the influence of electrical stimulation on proliferation of bacterial strains**	Samples of *Staphylococcus aureus*, *Pseudomonas aeruginosa*,and *Escherichia coli* at stage of 24 hours' growth	• Two different currents were generated using steel electrodes that were places in saline solution on the surface of petri dishes:	• Bacterial lineage reproduction • pH	**Bacterial reproduction** FD-B current inhibited bacterial growth in a generalised way, presenting an inhibition pattern at the positive pole in all bacteria species studied (p<0.05) HVMP inhibited *P. aerugi-nosa* and *S. aureus* at the two highest voltages, regardless of the polarity (p<0.05). **pH**	• Small in-vitro study • Does not explore the influence of these ES currents on wound tissues	**Indirect evidence** **Primary SWG: included in Biophysical agents**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
			○ FD-B (100 Hz, 10 ms, monophasic, sinusoidal) ○ high voltage monophasic pulsed (HVMP) currents (100 Hz, 15 ms, monophasic, double triangular pulse)		FD-B promoted increase in pH at negative pole and a decrease in pH at positive pole ($p<0.05$) **Study conclusion: FD-B has an inhibitory effect on bacterial reproduction that could have positive implications for managing wound infection.**		
Background information							
{Espejo, 2018 #17482}	Cohort study reporting incidence of bacteremia associated with pressure injuries (BAPI)	Participants were recruited prospectively over 32 years in one hospital in Spain (n= Inclusion: Presentation with episode of blood stream infection with one or more positive blood culture,one or more pressure injuries Positive culture of pressure injry with at least one microorganism isolated in blood culture Exclusion: presentation with same blood stream organism within past 4 weeks Characteristics: Mean age 75.9 years 51.8% had cognitive impairment, 39.3% had diabetes, 19.5% had chronic renal failure	• Chest xray and urinalysis to rule out other sources of infection	• Incidence of BAPI calculated as episodes of bloodstream infection associated with pressure injuries per 10,000 hospital discharges •	• 56 consecutive episodes of BAPUI were identified in 53 patients • Incidence of BAPI was 1.70 episodes per 10,000 adult patient discharges • 35.7% of cases were hospital-acquired, 26.8% health care acquired, 37.5% were community-acquired • Sacral, heel and trochanter were most common anatomical locations • 46.5% *Proteus spp*., 35.7% *Staph aureus* **Suspect bacteremia associated with pressure injury when there is fever but absence of other foci of infection.**	•	**Level of evidence: 3** **Quality: Moderate**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
(Udeani, Onyebuchi et al. 2016)	Cross sectional survey **measuring prevalence of MRSA resistant pressure injury and burns and determine patterns of resistance**	Participants were recruited from a trauma hospital in Nigeria (n=104) Participant characteristics: • Long stay pressure injury patients and burns patients with ≤ 30 days' stay • Previously used antibiotics • Mean age 36.6 ± 20.7 (range 1 to 86)	• Wound surface was cleaned and disinfectant and side tissues were pressed to allow pus excretion	• Swab cultures • Antibiotic susceptibility • Antibiotic Resistance index (MAR)	**Antibiotic sensitivity** • 50% wound swabs had *S. aureus* isolates • 20.2% swabs identified as methicillin resistant *S. aureus* (MRSA) • 29.8% were methicillin sensitive *S. aureus* (MSSA) • Significant association between length of admission and MRSA infection with those having admission ≥ 6mths having prevalence of 14.4%	• Patient recruitment is not described • Wound management strategies not reported • Minimal patient characteristics • pressure injury and burns outcomes not reported individually	**Indirect evidence (mixed etiology)**
(James, Swogger et al. 2008)	Descriptive study reporting **prevalence of biofilm in acute and chronic wounds**	Participants were recruited from a wound care centre in USA. (n= 93 wound specimens) Inclusion: • ≥ 18 years • Requiring sharp wound debridement (chronic wounds) or consenting to wound biopsy (acute wounds) • Characteristics: • 77 subjects with chronic wounds including pressure injuries, diabetic foot ulcers, venous leg ulcers and other (surgical site infections and traumatic wounds) • 16 subjects acute wounds including blisters and skin tears	Wound specimens were obtained from chronic wounds during the debridement process and from acute wounds via wound biopsy	Presence of biofilms	• Significantly more chronic wounds (30/50) than acute wounds (1/16) were characterised via microscopy as containing biofilm (60% versus 0.6%, p<0.001) • Most common isolates in both chronic and acute wounds were: o *Staphylooccus* (65% chronic wounds, 60% acute wound) o *Enterococcus* (62% chronic wounds, 80% acute wound) and o *Pseudomonas* (35% chronic wounds, 20% acute wounds) • **Study conclusions: Biofilms are prevalent in chronic wounds and rare in acute wounds**	Duration and previous treatment of wounds, including previous use of antibiotics, was not reported	**Indirect evidence: mixed wounds**
(Manzur, Gavalda et al. 2008)	Cross-sectional prevalence study **to**	Participants were recruited from nine long term care facilities with in Spain. Prevalence study was	Nasal swabs (n=1337) and 82 decubitus ulcers swabs (n=82)	Microbiological screening for *S. aureus* showing methicillin resistance	• Prevalence of MRSA colonization was 16.8% (95% CI 14.9 to 18.8%)	• Only aged care setting in Spain, might not be generalizable	**Level of evidence: 4** **Quality: low**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
	determine the incidence of MRSA in pressure injuries in long term care facilities	undertaken for all residents present on the day of the study (n=1377 participants) Characteristics: • Comorbidities included dementia (39.8%), diabetes mellitus (23.3%), chronic obstructive pulmonary disease (2315%), solid tumor (14.1%) and hemiplegia (12.3%) • primarily female sample (all facilities have >65% female) • mean age in facilities varied from 76.1 years to 83.9 years • Stay ≥ 6 months varied between facilities from 54.9% to 94.4% • Prior MRSA colonization ranged between facilities from 0 to 21.8% • Prior antibiotic therapy ranged between facilities from 10.3% to 44% • Use of invasive devices ranged between facilities from 0% to 27.6%			• Prevalence of MRSA colonization varied between facilities from 6.7% to 35.8% (p<0.001) • 59% of pressure injuries were colonized with MRSA (63% of these participants also had a positive nasal swab) • Independent factors significantly associated with MRSA colonization: ○ age ≥85 years OR 1.56 (95% CI 1.13 to 2.19, p=0.009) ○ Having a pressure injury OR 2.92 (95% CI 1.73 to 4.93, p<0.001) ○ Previously taking antibiotics OR 2.20 (95% CI 1.56 to 3.13, p<0.001) ○ Medical devices OR 3.05 (95% CI 1.56 to 5.97, p<0.001) • Stay ≥ 6 months was not significantly related to MRSA colonization • **Study conclusions: Prevalence of MRSA colonization in** pressure injuries **in long term care in Spain was 59%**	• wide range of prevalence between different facilities	
(Buck, Goucher et al. 2012)	A retrospective review study **investigating prevalence of MRSA in pressure injuries**	Participants were from a consecutive sample encountered by a single surgeon in USA from 2007 to 2009 (n=56 patients with 115 pressure injuries) Inclusion: • pressure injury Consulting plastic surgery	Demographic data, medical records, culture and laboratory results, and operative details were recorded, and outcomes assessed.	The incidence of MRSA	• 4% of pressure injuries had clinical signs of infection including cellulitis • Seven patients (13%) were positive for MRSA colonization. • Twelve pressure injuries (10%) were positive for MRSA by sterile bedside wound culture • 102 (89%) pressure injuries underwent operative debridement and /or bone biopsy. Intraoperative culture results	• Unclear if the MRSA cases identified during surgery were the same cases as identified by bedside culture • One site study, may not be generalizable;	**Level of evidence: 4** **Quality: low**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		regarding "wound infection" Characteristics: • 82% sample male • Mean age 41.8±14.2 yrs • average of 2.1 pressure injuries per patient • 89% participants had SCI • pressure injuries primarily sacral or ischial • 90% of pressure injuries were classified as stage IV (classification system not reported) • 96% participants had used antibiotics within prior 1 to 2 weeks and 29% were still actively taking antibiotic • 89% presented from a rehabilitation or long term care facility			from these procedures were positive for organism growth in 45 (44%) cases (primarily polymicrobial) including 9 MRSA cases. • **Study conclusions: Rates of antibiotic use may contribute to the incidence of MRSA observed in this single-site study; however confounding factors were not addressed.**	however patients were commenced on antibiotic therapy prior to screening at this service. • Antibiotics commenced in the previous 2 weeks may have influenced the low rate of clinical signs of infection	
(Cataldo, Bonura et al. 2011)	Prevalence study **investigating multidrug-resistant organisms (MDRO) in pressure injuries**	Participants were recruited as a consecutive convenience sample of older adults enrolled in a home care service in Italy in a 3-month period in 2010 (n=32) Characteristics: • It appears that 100% of the patients enrolled in the service over a 3-month period had a pressure injury of at least stage III. • 65.6% sample female • stage III or greater pressure injury • aged 60 to 97 years	Samples for culture were obtained from stage III or greater pressure injuries ulcers by swabbing sterile cotton-tipped applicator sticks	• Colonization as determined by swab and culture • Environmental cultures	• Risk factors for MDRO colonization: ○ 37.5% of participants were on antibiotic therapy ○ 37.5% of participants had taken antibiotic therapy in the preceding 90 days ○ 15.6% of participants had been admitted to hospital for ≥72 hours in the preceding 12 months • Prevalence of MDRO in pressure injuries: ○ Vancomycin-resistant *Enterococcus* (VRE) was found in 1 patient (3%) ○ Methicillin-resistant *Staphylococcus aureus* (MRSA) was found in 5 patients (15%) ○ MDR gram-negative bacilli was identified in 53% patients	• Very small sample size from one service • Duration and severity of the pressure injuries was heterogeneous • Treatment strategies were not reported beyond antibiotic use • Causation was not established	**Level of evidence: 4** **Quality: low**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
		• pressure injuries ranging from 1 to 6 months duration (mean 3.6 months)			• Environmental cultures identified 2 MRSA isolates and 8 MDR gram-negative bacilli isolates from bedroom furniture • **Study conclusions: the authors suggested that** pressure injury **in home care patients could play a role in bringing MDROs in to the community setting; however, there was no confirmation through screening caregivers and family members**		
(Smith, Snow et al. 2010)	Comparative survey **reporting on the biodiversity of bacterial infection in pressure injuries**	Samples from 49 pressure injuries Origin of pressure injury samples was not reported.	• Samples were taken from pressure injury pressure injury wound bed via sharp debridement • Bacterial tag-encoded FLX amplicon pyro sequencing (bTEFAP), a universal bacterial identification method, was used to identify bacterial populations	• Bacteria classified at appropriate taxonomic levels using BLASTn derived sequence identity	• There was considerably large diversity of microflora in pressure injury (228 genera and 487 species over 49 pressure injury samples) • Majority of organisms were most closely related to *Staphylococcus, Enterococcus, Serratia, Pseudomonas, Streptococcus* and *Corynbacterium* • Most pressure injuries contained >10^5 bacteria per mg debridement • The diversity in bacteria in pressure injuries negated global recommendations for targeting microburden in pressure injuries. • **Study conclusions:** pressure injuries **exhibit a diverse range of bacteria. As each** pressure injury **is unique in the range of bioflora treatment of bioburden in** pressure injuries **should be individualized.**	• Unclear from where patients were recruited, their clinical background or their previous treatment (particularly antimicrobial) although this data was collected • Although the researchers report that patient factors (e.g. gender) influence diversity of microflora these characteristics are not reported.	**Level of evidence: 4** **Quality: low**
(Dowd, Delton Hanson et al. 2011)	Retrospective study **investigating the prevalence and diversity of fungal and yeast infection in mixed wound types**	Record review of participants over a 4-month period with a chronic wound (n=609 participants, 915 specimens)	• Samples were obtained by sharp debridement as per standard care • Diagnosis using level I (finite panel of most commonly occurring bacteria and genetic antibiotic resistance factors in chronic wounds) and level II	• Correlation analysis and ANOVA to determine if there were any significant relationships between bacterial and fungal genera and patient demographics	• Of the 915 clinical specimens, 208 (23%) were positive for fungal species • 11.05% of chronic wounds positive for fungal species were pressure injuries (n=23) • The most abundant fungi were yeasts in the genus *Candida* • A notable bacterial/fungal negative correlation was found to be apparent between *Staphylococcus* and *Candida*	• Single site study, potentially site-related factors were associated with the prevalence of fungal infection • Does not report the duration of wounds or previous management	**Indirect evidence: mixed wounds**

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Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
			(comprehensive diagnostic list of bacteria and fungi with capability of >95% sequence identity) wound pathogen diagnostics		• *Candida albicans* was the fungi most observed in pressure injuries	strategies (e.g. have these participants received treatment for wound colonization)	

Additional evidence from systematic reviews to support discussion

Ref	Type of Study	Sample	Intervention(s)	Outcome Measures & Length of Follow-up	Results	Limitations and comments	
Topical antiseptics							
(Norman, Dumville et al. 2016)	Systematic review of **antibodies and antiseptics for healing pressure injuries of Category/Stage II or greater**	The review included only RCTs (n=12 trials, n=437 participants) Of the 11 included studies, 6 are already included or were reviewed for the 2012 guideline. The other 5 studies are pre-2005 publications.			**Author conclusions: There is no consistent evidence of a benefit to using any particular antimicrobial treatment for injuries.**	• Most references already in guideline Additional papers do not add new knowledge. • No meta-analysis due to heterogeneous nature of studies • Most ulcers were not infected at the start of the trials. • The review can be used to support the conclusions in the guideline	**Quality High**

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Table 1: Level of Evidence for Intervention Studies

Level 1	**Experimental Designs** • Randomized trial
Level 2	**Quasi-experimental design** • Prospectively controlled study design • Pre-test post-test or historic/retrospective control group study
Level 3	**Observational-analytical designs** • Cohort study with or without control group • Case-controlled study
Level 4	**Observational-descriptive studies (no control)** • Observational study with no control group • Cross-sectional study • Case series (n=10+)
Level 5	**Indirect evidence**: studies in normal human subjects, human subjects with other types of chronic wounds, laboratory studies using animals, or computational models

Table 2: Levels of evidence for diagnostic studies in the EPUAP-NPUAP-PPPIA guideline update

Level 1	Individual high quality (cross sectional) studies according to the quality assessment tools with consistently applied reference standard and blinding among consecutive persons.
Level 2	Non-consecutive studies or studies without consistently applied reference standards.
Level 3	Case-control studies or poor or non-independent reference standard.
Level 4	Mechanism-based reasoning, study of diagnostic yield (no reference standard). Low and moderate quality cross sectional studies.

Table 3: Levels of evidence for prognostic studies in the EPUAP-NPUAP-PPPIA guideline update

Level 1	A prospective cohort study.
Level 2	Analysis of prognostic factors amongst persons in a single arm of a randomized controlled trial.
Level 3	Case-series or case-control studies, or low quality prognostic cohort study, or retrospective cohort study.

APPRAISAL FOR STUDIES PROVIDING DIRECT EVIDENCE (i.e. ELIGIBLE FOR SUPPORTING AN EVIDENCE-BASED RECOMMENDATIONS

Each criteria on the critical appraisal forms was assessed as being fully met (Y), partially met or uncertain (U), not met/not reported/unclear (N), or not applicable (NA). Studies were generally described as high, moderate, or low quality using the following criteria:

- High quality studies: fully met at least 80% of applicable criteria
- Moderate quality studies: fully met at least 70% of applicable criteria
- Low quality studies: did not fully meet at least 70% of applicable criteria

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CROSS SECTIONAL/SURVEY/PREVALENCE STUDIES/OBSERVATIONAL

Endnote ID	Author/year	Focussed question	Sampling method	Representative sample	States number invited participants	Clear outcome measures	Valid reliable outcome measurement	Comparable results for multiple sites	Confounders identified and accounted for	Minimal bias	Reliable conclusions	Level of evidence	Quality
9577	(Bodavula, Liang, Wu, VanTassell, & Marschall, 2015)	Y	Y	Y	Y	Y	U	NA	Y	Y	Y	4 (diagnostic)	high
13200	(Dryden et al., 2016)	Y	N	N	Y	Y	N	U	N	N	U	4	Low
14548	(Nakagami, Mori, et al., 2017)	Y	N	U	Y	Y	Y	NA	U	Y	Y	4 (diagnostic)	Moderate

CASE SERIES

	Author/year	Focussed question	Participant characteristics reported	Inclusion criteria defined	Consecutive recruitment	Participants entered at same disease stage	Intervention clearly reported	Outcomes relevant and defined apriori	Valid, reliable outcome measurement	Per cent drop out reported and acceptable	Estimates of random variability	Comparable results for multiple sites	Minimal bias	Reliable conclusions	Level of evidence	Quality
2994	(Ciliberti et al., 2014)	Y	N	Y	U	U	N	Y	N	N	N	NA	Y	U	4	Low

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COHORT STUDIES

	Author/year	Focussed question	Comparable source populations	States number invited	Likelihood of outcome at enrolment considered	Per cent drop out in study arms is reported	Comparison btw drop outs and participants	Clear outcome measures	Assessment blinded, or discuss potential bias	Valid, reliable assessment with supporting reference	More than one measure of exposure	Confounders identified and accounted for	Provides confidence intervals	Minimal bias	Reliable conclusions	Level of evidence	Quality
3255	(Graham, 2014)	Y	N	N	N	N	N	Y	U	Y	N	N	N	Y	N	3	Low
17482	{Espejo, 2018 #17482}	Y	NA	Y	Y	N	N	Y	Y	Y	N	Y	N	Y	Y	3	Moderate

PROGNOSTIC STUDIES

	Author/year	Adequate description of baseline characteristics	Satisfactory study attrition	Clear outcome measures/prognostic factors	Range of prognostic factors/confounders measured and identified	Method of measuring prognostic factor is reported, valid and reliable	Same method of measure of prognostic factor for all	Continuous variables or appropriate cut offs	Percent participants with complete data acceptable	Appropriate imputation method	Confounders/prognostic factors accounted for in analysis	Selective reporting avoided	Adequate sample size (10 PIs per factor)	Level of evidence	Quality
14339	(Braga, Brito, Filho, Filho, & Ribas, 2017)	Y	U	Y	N	Y	Y	N	Y	NA	N	Y	N	1 (prognostic)	Low
14228	(Nakagami, Schultz, et al., 2017)	N	N	Y	N	Y	N	Y	Y	NA	N	Y	N	1 (prognostic)	Low

DIAGNOSTIC STUDIES

	Author/year	True diagnostic test – a test is compared to another test	Selection is either consecutive enrolment or	No case-control methods	No inappropriate exclusion of participants	Independent interpretation of test and standard (i.e. without knowing results of other test)	Any threshold is pre-determined	Reference standard test is likely to correctly identify condition	Appropriate interval of time between index and standard tests	All participants receive same reference standard	All recruited participants are included in analysis	Minimal bias	Level of evidence	Quality
14604	(Blanco-Blanco et al., 2017)	Y	Y	Y	Y	Y	NA	Y	Y	Y	U	Y	1 (diagnostic)	High
10871	(Brunel et al., 2016)	Y	N	Y	Y	Y	NA	Y	Y	Y	Y	Y	2 (diagnostic)	High
15254	(Heiba, Stempler, Sullivan, Kolker, & Kostakoglu, 2017)	Y	N	Y	N	N	U	Y	U	N	N	N	1 (diagnostic)	Low
13982	(Tedeschi et al., 2017)	Y	Y	Y	Y	U	Y	Y	U	Y	Y	Y	1 (diagnostic)	High

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SYSTEMATIC REVIEWS FOR DISCUSSION

RATING CRITERIA:
1 Partial yes: states review question, search strategy, in/exclusion criteria and risk of bias were a-priori; full yes: meta-analysis/synthesis plan, investigation of heterogeneity and justification for protocol deviation
2 Partial yes: At least 2 databases, provides keywords and search, justifies publication restrictions; full yes: searched reference lists of included studies, searched trial registries, consulted experts in field, searched grey literature, search within 24 months of review completion
3 At least two reviewers independently agreed on selection of studies to include or reviewers achieved 80% agreement on a sample of studies
4 Either two reviewers did data extraction and had >80% agreement, or two reviewers reached consensus on data to extract
5 Partial yes: list of all relevant studies that were read and excluded; full yes: every study that was excluded is independently justified
6 Partial yes: described populations, interventions, comparators, outcomes and research design; full yes: detailed descriptions of same plus study setting and timeframe for follow-up
7 FOR RCTS Partial yes: appraised risk of bias from unconcealed allocation and lack of blinding; full yes: appraised risk of bias on true randomisation, selection of reported result from multiple measurements/analyses
FOR non randomised studies: Partial yes: appraised confounding and selection bias; full yes: appraised methods to ascertain exposures and outcomes, selection of reported result from multiple measurements/analyses
8 Must include reporting of the source of funding of individual studies, or reports that the reviewers considered this even if individual funding sources aren't listed in review

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Endnote ID	Author/year	PICO research question and inclusion criteria	Explicitly states a-priori protocol[1]	Rationale for selection of study designs	Comprehensive search[2]	Duplicate study selection[3]	Duplicate data extraction[4]	Excluded studies listed[5]	Adequate description of included studies[6]	Risk of bias assessed[7]	Source of funding reported[8]	Appropriate meta-analysis including weighting and adjustment for heterogeneity	Meta-analysis considers risk of bias of studies	Discussion consider risk of bias of studies	Assessment of publication bias if quantitative analysis is done	Potential conflicts of interest of authors reported and managed	Review Quality	Type of evidence included in review
10814	(Norman et al., 2016)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	NA	NA	Y	NA	Y	High	RCTs –12 studies at moderate to high risk of bias
9524	(Jull et al., 2015)				Y			Y		Y		N		Y	NA		Exclude	Only one RCT in pressure injuries

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