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

- **Identified in pressure injury searches**: n=11,177
- **Excluded after screening title/abstract**
  - Duplicate citations
  - Included in previous guideline
  - Not related to pressure injuries
  - n=8,128
- **Identified in topic-specific key word searches for full text review and critical appraisal**: n=58
- **Excluded based on key word searches**
  - Not related to the topic-specific questions
  - n=3,027
- **Identified as providing direct or indirect evidence related to topic and critically appraised**: n=15
- **Excluded after review of full text**
  - Not related to pressure injuries
  - Not related to the clinical questions
  - Citation type/research design not meeting inclusion criteria
  - Non-English citation with abstract indicating not unique research for translation
  - n=43
- **Total references providing direct or indirect evidence related to topic**: n=53

**Additional citations**
- Identified by working group members: n=36
- Identified as providing direct or indirect evidence related to topic and critically appraised: n=15
- Additional citations: n=38

**Infection keywords**
- Infection, infected, infectious, biofilm, bacteria, bacterial, microbial, microbe, bioburden, virus, MRSA, osteomyelitis, honey, silver, iodine, antimicrobial, antibiotic, antiseptic


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Data Tables: 2019 Guideline Update: Assessment and Treatment of Infection and Biofilms in Pressure Injuries © EPUAP/NPIAP/PPPIA

Page 1
**Assessment and Treatment of Infection and Biofilms: data extraction and appraisals**

**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 resource and are not for reproduction.


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**Ref** | **Type of Study** | **Sample** | **Intervention(s)** | **Outcome Measures & Length of Follow-up** | **Results** | **Limitations and comments**
---|---|---|---|---|---|---
(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) | 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 in 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 intrarater 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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## Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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| (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) | • Percutaneous aspiration | • Number and type of infective symptoms present: heat, erythema, edema and purulent discharge | 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 | • No blinding | Level of Evidence: 1 (diagnostic) 
Quality: High |

**Inclusion criteria:**
- Age ≥ 18 years
- Category/Stage 2 or greater pressure injury

**Exclusion criteria:**
- Category/Stage 1 pressure injury
- Drug anticoagulated

**Participant characteristics:**
- 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

**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

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### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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| (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 bacteremia: 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) | • 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 to diagnose a true positive or a true negative compared with the results of the fluid culture from percutaneous aspiration | 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, morbidities, invasive devices  
• No power estimates were made  
• Methods to evaluate of signs/symptoms of infection poorly reported and interrater reliability is not addressed | Level of evidence: 1 (prognostic)  
Quality: Low
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<td>(Tedeschi, Negosanti et al. 2017)</td>
<td>Cross sectional study evaluating wound swabs as a method for diagnosing wound infection in advanced pressure injuries</td>
<td>Participants were recruited consecutively in a rehabilitative hospital in Italy over 3 years (n=116) &lt;br&gt; Inclusion criteria: &lt;br&gt; - Spinal cord injury &lt;br&gt; - Pressure injury of Category/stage 3 or 4 undergoing surgical debridement or reconstruction &lt;br&gt; - Not receiving antibiotics prior to surgery &lt;br&gt; Participants characteristics &lt;br&gt; - Primarily male &lt;br&gt; - Primarily post-trauma paraplegia &lt;br&gt; - Mean age 49 years</td>
<td>Participants received surgery immediately prior to surgery all participants received three superficial wound swabs were taken using Levine technique &lt;br&gt; During surgery all participants had multiple bone and soft tissue specimens taken</td>
<td>Culture of wound swab specimens &lt;br&gt; Culture and histological examination of bone and soft tissue samples</td>
<td>Bacterial profile &lt;br&gt; Most common organism in intraoperative specimens were <em>S. aureus</em>, <em>P. mirabilis</em> and <em>P. aeruginosa</em> &lt;br&gt; Comparisons between swab results and culture results &lt;br&gt; - Concordance between swab and specimen results was 22% of cases &lt;br&gt; - 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)</td>
<td>Single site study, results may relate to poor clinical technique</td>
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<td>(Bodavula, Liang et al. 2015)</td>
<td>Retrospective descriptive study reporting patterns in management</td>
<td>Retrospective cohort study records review of patients with pressure injury and osteomyelitis admitted in a 5 year period (n=220)</td>
<td>N/A</td>
<td>Reviewed records for: &lt;br&gt; - Demographic information &lt;br&gt; - Comorbidities &lt;br&gt; - Antibiotic therapy history</td>
<td>Reported signs and symptoms &lt;br&gt; - Back pain (31%), weakness (74%), fever (43%), weight loss (40%), sensory loss (71%), urine incontinence (71%), fecal incontinence (61%)</td>
<td>Retrospective study relying on documentation &lt;br&gt; Single center &lt;br&gt; Patients were required to have 12</td>
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- Mortality of people with pressure injury infected with GNB bacteremia was higher (OR 7.43, 95% CI 1.23 to 45.0, p=0.04) <br>

Author conclusion: Stage II or greater pressure injuries in hospitalized patients are reservoirs of multi-resistant GNB. <br> 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.
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| of pressure injury-related osteomyelitis | Inclusion:  
- Aged ≥18 years  
- 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 ± 18 years  
- 67% male  
- 52% African American  
- Median BMI 23.6kg/m² (range 12.3 to 48)  
- 77% patients were para/quadriplegic | 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 | 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 | 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 |  
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  
- 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) | 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) | 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 |
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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| (Heiba, Stempler et al. 2017) | Retrospective evaluation of accuracy of | Participants were consecutively (retrospective) recruited over 2 years at a | • Indication for surgical debridement  
• No MRI contraindications  
• Up to 3 pressure injuries included per person | • 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%. | • *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 unculturable 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% |

**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  

**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 microbiological criterion is effective in diagnosing osteomyelitis in pressure injuries.
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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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) | o CT imaging, microbiology and/or pathology (n=21)  
- 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% | • Scale used was not validated  
• Small sample size  
• Unclear recruitment |
| (Internatio nal Wound Infection Institute (IWII) 2016) | International consensus document on wound infection and biofilm assessment, diagnosis and management | 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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| {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 | 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 | 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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| (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-colonized pressure injuries, estimating the risk of MRSA-bacteraemia. Data was collected through medical record analysis (n=145). | - 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:  
    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 due to location. | Level of evidence: 3 (prognostic) Quality: low |
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| 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=119 eligible, n=36 included) | 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) | 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) | Inter-rater reliability was reported as 0.52 to 1.00 for individual checklist items  
- Nonprobability sampling |

Wound characteristics infected vs non-infected:  
- Compared to non-infected wounds, infected wounds had more necrotic tissue and lower mean T-PO2 (both p<0.10, |

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| 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=119 eligible, n=36 included) | 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) | 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) | Inter-rater reliability was reported as 0.52 to 1.00 for individual checklist items  
- Nonprobability sampling |

Wound characteristics infected vs non-infected:  
- Compared to non-infected wounds, infected wounds had more necrotic tissue and lower mean T-PO2 (both p<0.10, |
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</thead>
</table>
| (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) | 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  
• Cortical 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) |  
• 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 |
| (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) | All included participants were treated with surgical debridement of stage IV pressure injuries accompanied by a bone culture, after | Abstracted data included:  
• Location of ulcer  
• 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 |

Signs and symptoms specific to wounds are more reliable than classic signs and symptoms of infection in identifying wound infection.
### Ref: Daniali, Keys et al. (2011)

**Type of Study:** Retrospective case-controlled study comparing pre-operative management and post-operative outcomes between pre-operative MRI diagnosis of osteomyelitis and intra-operative bone biopsy

**Sample:** 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 than comparison to the

**Intervention(s):** 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:
  - o pre-operative MRI diagnosis of osteomyelitis (n=26)
  - o post-operative bone culture diagnosis of

**Outcome Measures & Length of Follow-up:**
- Recurrence of pressure injury at the same anatomic site
- Suture line dehiscence
- Significant suture line dehiscence
- Time until mobilization
  - by physical therapy

**Results:**
- 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 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 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

**Limitations and comments:**
- Retrospective chart review subject to inaccuracies of data recording
- Study cohorts were small potentially limiting the study generalizability.
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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<tbody>
<tr>
<td>(Dryden, Dickinson et al. 2016)</td>
<td>Observational study exploring the efficacy of surgical honey in reducing infection and biofilm in pressure injury</td>
<td>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</td>
<td>Surgical honey gel (Surgihoney RO) manufactured in a way to enhance the active ingredient (reactive oxygen species including hydrogen peroxide) Honey gel applied 2mm thick and covered with a sterile secondary dressing selected based on exudate absorption needs • Wound dressings changed 2-3 days at clinician’s discretion</td>
<td>• 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</td>
<td>MRI diagnosis of osteomyelitis significantly alters clinical or surgical management or patient outcomes</td>
<td>• 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 • &lt; half pressure injuries were swabbed and none had a formal biofilm evaluation • Potential conflict of interest</td>
</tr>
</tbody>
</table>

### Clinical question 3: Topical antiseptics for treating infection and biofilm in pressure injuries

- **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)

- **Clinical question 3: Topical antiseptics for treating infection and biofilm in pressure injuries**

  - **Observational study**
  - **Sample**
    - 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)
    - 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 2mm thick and covered with a sterile secondary dressing selected based on exudate absorption needs
    - Wound dressings changed 2-3 days at clinician’s discretion
  - **Intervention(s)**
    - Surgical honey gel (Surgihoney RO)
    - Manufactured in a way to enhance the active ingredient (reactive oxygen species including hydrogen peroxide)
    - Honey gel applied 2mm thick and covered with a sterile secondary dressing selected based on exudate absorption needs
  - **Outcome Measures & Length of Follow-up**
    - 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
  - **Results**
    - Pain
      - 5 pressure injuries rated as mild pain at commencement were rated as no pain at conclusion
      - 1 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
  - **Limitations and comments**
    - 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

- **MRI group**
  - Had a greater number of patients with a history of peripheral vascular disease (14.3% versus 0%, p=0.05)

- **MRI diagnosis of osteomyelitis**
  - Significantly alters clinical or surgical management or patient outcomes

- **Ref**
  - Dryden, Dickinson et al. 2016
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<tr>
<td>(Gawande, Leung et al. 2014)</td>
<td>Laboratory study investigating antibiofilm/antimicrobial activity of an antibiofilm enzyme (Dispersin®) and broad-spectrum KSL-W peptide and to compare properties to a commercial wound gel (Silver-Sept™ gel) for managing infection and biofilm</td>
<td>N/A</td>
<td>One gram of placebo or Dispersin® 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.</td>
<td>Minimal Inhibitory Concentration (MIC) Minimal Bactericidal Concentration (MBC)</td>
<td>Peptide alone versus peptide in combination with antibiofilm enzyme (experimental gel)</td>
<td>• Dispersin® 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.</td>
<td>• 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</td>
</tr>
<tr>
<td>(Wild, Bruckner et al. 2012)</td>
<td>Prospective RCT comparing</td>
<td>Participants were recruited from in and out patients clinics in Switzerland</td>
<td>Participants were randomly assigned to:</td>
<td>Primary outcome was MRSA eradication assessed on days 7, 14</td>
<td>MRSA eradication</td>
<td>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.</td>
<td>Level of evidence: 1</td>
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</table>

Indirect evidence (laboratory study)
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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<th>Quality</th>
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<tr>
<td>(Sipponen, Jokinen et al. 2008)</td>
<td>Prospective, multicentre RCT investigating effectiveness of resin salves (Picea abies) in pressure injury care</td>
<td>Participants recruited from 11 primary care hospitals in Finland between 2005 and 2007 (n=37, n=22 completed and analysed)</td>
<td>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:</td>
<td>• 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</td>
<td>• 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</td>
<td>• 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</td>
<td>Level of evidence: 1 Quality: low</td>
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<td>PHMB swabbing to a cellulose dressing impregnated with polyhexamethylene biguanide (PHMB) in eradicating MRSA from pressure injuries</td>
<td>(n= 30)</td>
<td>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</td>
<td>o Control group: cleansing performed with PHMB swabs for 20 minutes after which a foam dressing was applied (n=15) o Study group: cleansed with normal saline and received a PHMB impregnated cellulose dressing with the foam dressing applied as a secondary dressing (n=15)</td>
<td>• 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&lt;0.05)</td>
<td>were not reported in detail • Results for sustained eradication on days 14 to 17 not reported</td>
<td>Quality: moderate</td>
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<td>• with or without clinical wound infection</td>
<td>• resin salve applied at 1mm thickness between gauze layers with dressing changed third daily or daily for heavily exuding pressure injuries (n=13 with 18 pressure injuries)</td>
<td>pressure injuries at baseline and 1 month, but thereafter only as clinically indicated.</td>
<td>significantly improved versus 91% in the control group (p=0.003)</td>
<td>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.</td>
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<td>Exclusion:</td>
<td>• sodium carboxymethylcellulose 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 exuding pressure injury. (n=5 with 11 pressure injuries)</td>
<td>• pressure injury size measured by digital photography and planimetry</td>
<td>• 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.</td>
<td>Study failed to recruit and maintain sufficient numbers to reach a-priori sample size calculations.</td>
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<td>Characteristics:</td>
<td>• Some participants in both groups received concurrent antibiotics</td>
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<td>Bacterial eradication analysis is complicated by the concurrent use of antibiotics for some participants</td>
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<td>• No significant between group difference on baseline demographics or wound characteristics</td>
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<td></td>
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<td>• Mean age approximately 74 to 80 years</td>
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<td>• Mean BMI 21.8, mean P-albumin 28.3 to 31.4 gL⁻¹</td>
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<td>• Primarily bedridden participants</td>
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<td></td>
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<td>• Primarily non-smokers</td>
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<td></td>
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<td>• Primarily stage II and III pressure injuries</td>
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<td>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</td>
<td>• 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</td>
<td>• MRSA cultures reviewed by microbiology laboratory according to standardized criteria.</td>
<td>Study 1)</td>
<td>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</td>
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<td>(Robicsek, Beaumont et al. 2009)</td>
<td>Two retrospective cohort studies investigating the impact of decolonization therapy on MRSA</td>
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<td>Indirect evidence: mixed etiology</td>
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<tr>
<td></td>
<td>Study 1) evaluating the</td>
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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 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 chlorhexidine

**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**

**Results**
- 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 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 chlorhexidine
- 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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<tr>
<td>Medihoney® for stage III and IV pressure injuries</td>
<td>Inclusion/exclusion:  • SCI patients with chronic pressure injuries  • No other criteria reported</td>
<td>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</td>
<td>3mm thickness applied once daily after cleansing with Ringer’s solution  • Surrouding skin was disinfected with a range of anti-microbial preparations  • Treatment was continued for more than 6 weeks</td>
<td>cultured (methods not reported)  • Pressure injuries were documented at 3-week intervals</td>
<td>• 90% of participants showed complete wound healing after 4 weeks  • No negative effects were noted from the treatment</td>
<td>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</td>
</tr>
<tr>
<td>(Mizokami, Murasawa et al., 2012)</td>
<td>Retrospective observational study comparing iodoform gauze to povidone-iodine and sugar or sulfadiazine cream (only data from clinical study is summarised)</td>
<td>Retrospective records analysis of participants with PU treated at geriatric centre in Japan between 2008 and 2010 (n=53 participants with 60 PUs)</td>
<td>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</td>
<td>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.</td>
<td>• 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&lt;0.001)  • By 4 weeks, 80% of PUs treated with iodoform gauze had necrotic tissue completely removed (versus 30%, p&lt;0.001)</td>
<td>• 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</td>
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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
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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</table>
| (Charnsantiwanich, 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) | ● 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 dressing 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 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 comorbidities |

### Clinical question 4: Antibacterial wound dressings for treating infection and biofilm in pressure injuries

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| (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) | 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 |
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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<tr>
<td>≥90 days) wounds</td>
<td></td>
<td>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</td>
<td>natural tannin harvested from oak extract Oral antibiotics prescribed</td>
<td>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)</td>
<td>Statistically significant moderate correlation between time to healing and wound size at baseline (r=0.37, p=0.02) No adverse effects</td>
<td>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</td>
</tr>
<tr>
<td>(Ciliberti, De Lara et al. 2014)</td>
<td>Case series evaluating the efficacy a silver-containing hydrofibre dressing (Aquacel® Ag) that includes carboxymethylated Hydrofibre® technology for treating pressure injuries</td>
<td>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</td>
<td>Silver containing hydrofibre dressing for 7 days</td>
<td>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</td>
<td>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</td>
<td>Level of evidence:4 Quality: Low</td>
</tr>
</tbody>
</table>
### Ref: Woo and Heil (2017)

**Type of Study:** Retrospective, non-randomized study evaluating methylene blue and gentian violet dressing for management of chronic wounds with local infection

**Sample:** Participants were recruited from an unknown location using unreported methods (n=29)

**Inclusion criteria:**
- ≥ 18 years of age
- ≥ one chronic wound ≥1 cm² 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

**Intervention(s):** Participants all received 4 weeks of treatment with the Gentian Violet/methylene blue dressing (Hydrofera Blue Classic dressing)

**Outcome Measures & Length of Follow-up:**
- 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

**Results:**

- **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 21.4 cm² to 12.3 cm² (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)

**Limitations and comments:**
- 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

**Author conclusion:** Gentian Violet/methylene blue dressing is effective for managing infection and promoting healing in chronic wounds

---

### Ref: Trial, Darbas et al. (2010)

**Type of Study:** Prospective RCT comparing anti-microbial effectiveness

**Sample:** Participants were recruited over 18 months from a wound clinic and inpatient service at a hospital in France

**Intervention(s):** Participants were randomly assigned to receive either:
- Study product: An ionic silver alginate

**Outcome Measures & Length of Follow-up:**
- Assessments on days 1, 8 and 15.
- Primary outcome measure was progression or

**Results:**

- Participants with pressure injuries
  - The study group (p=0.005) and the control group (p=0.008) both had statistically significant improvements in

**Limitations and comments:**
- A priori calculation for sample size was established for the overall study i.e. the findings for PU

**Level of evidence:** Low

**Quality:** Low
## Data Tables: 2019 Guideline Update: Assessment and Treatment of Infection and Biofilms in Pressure Injuries

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### Ref

1. **Type of Study**: of an ionic silver alginate dressing to a silver-free alginate dressing for primarily Category/Stag e II pressure injuries (includes some Category/Stag e III)

   **Sample**
   
   (n=42, n=24 with pressure injuries)

   **Intervention(s)**
   
   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)

   **Outcome Measures & Length of Follow-up**
   
   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 by a microbiologist categorising wound as deteriorated, unchanged or improved based on bacteriological status

   **Results**
   
   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)

   **Limitations and comments**
   
   participants were underpowered.

   **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

   **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.**
| Ref                                      | Type of Study                                                                 | Sample                                                                 | Intervention(s)                                                                 | Outcome Measures & Length of Follow-up                          | Results                                                                                                                                                                                                 | Limitations and comments                                                                 |
|-----------------------------------------|-----------------------------------------------------------------------------|----------------------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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) | Participants were randomized to receive either: Study group: an ionic silver alginate/carboxymethylcellulose (SACMC) dressing control group: a non-silver 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 | 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 |

Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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<td>(Trial, Darbas et al. 2010)</td>
<td>prospective RCT comparing anti-microbial effectiveness of an ionic silver alginate dressing to a silver-free alginate dressing</td>
<td>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)</td>
<td>• Participants were randomly assigned to receive either:  o 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)  o Active control product: A standard alginate dressing (Algosteril®; n = 22, n = 13 with pressure injury)  • Treatment was for 15 days.</td>
<td>• Assessments on days 1, 8 and 15.  • Primary outcome measure was progression or regression of local infection assessed by:  o 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 by 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;</td>
<td>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)</td>
<td>A priori calculation for sample size was established for the overall study i.e. the findings for pressure injury participants were underpowered.</td>
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<td></td>
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<td>Exclusion:</td>
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<td>• Allergy to dressing components  • Burn patients  • Ulcers associated with infectious disease  • Taking anticoagulants  • &lt; 18 years or over 80 years</td>
<td>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)</td>
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Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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<td>dressing comfort; cleansing effect; absorption properties; adherence to the wound.</td>
<td>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.</td>
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Clinical question 5: Treatment of biofilm

(Bianchi, Wolcott et al. 2016)

A consensus document by an international interdisciplinary 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)
### Clinical question 6: Emerging diagnosis and treatments for infection

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</table>
| (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) | - 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 bacterial 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 | Only one pair used for both  
Limited sample of Pressure injuries  
The device could not measure 30% of wounds due to insufficient bacteria levels.  
The 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. |
| (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. aeruginosa and S. aureus* at the two highest voltages, regardless of the polarity (p<0.05).  
\( \text{pH} \) | 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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<td>{Espejo, 2018 #17482} Cohort study reporting incidence of bacteremia associated with pressure injuries (BAPI)</td>
<td>Participants were recruited prospectively over 32 years in one hospital in Spain (n=53)</td>
<td></td>
<td>FD-B (100 Hz, 10 ms, monophasic, sinusoidal) high voltage monophasic pulsed (HVMP) currents (100 Hz, 15 ms, monophasic, double triangular pulse)</td>
<td>FD-B promoted increase in pH at negative pole and a decrease in pH at positive pole (p&lt;0.05)</td>
<td>Study conclusion: FD-B has an inhibitory effect on bacterial reproduction that could have positive implications for managing wound infection.</td>
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#### Background information

- **Inclusion:** Presentation with episode of blood stream infection with one or more positive blood culture, one or more pressure injuries

- **Positive culture of pressure injury 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.**

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| (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:  
- *Staphylococcus* (65% chronic wounds, 60% acute wound)  
- *Enterococcus* (62% chronic wounds, 80% acute wound)  
- *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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<td>determine the incidence of MRSA in pressure injuries in long term care facilities</td>
<td>undertaken for all residents present on the day of the study (n=1377 participants)</td>
<td>Demographic data, medical records, culture and laboratory results, and operative details were recorded, and outcomes assessed.</td>
<td>The incidence of MRSA</td>
<td>• Prevalence of MRSA colonization varied between facilities from 6.7% to 35.8% (p&lt;0.001)</td>
<td>• wide range of prevalence between different facilities</td>
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<tr>
<td>characteristics</td>
<td>Characteristics:  • Comorbidities included dementia (39.8%), diabetes mellitus (23.3%), chronic obstructive pulmonary disease (23.15%), solid tumor (14.1%) and hemiplegia (12.3%)  • primarily female sample (all facilities have &gt;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%</td>
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<td>(Buck, Goucher et al. 2012)</td>
<td>A retrospective review study investigating prevalence of MRSA in pressure injuries</td>
<td>Participants were from a consecutive sample encountered by a single surgeon in USA from 2007 to 2009 (n=56 patients with 115 pressure injuries)</td>
<td>Consulting plastic surgery</td>
<td>• 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</td>
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<td>Inclusion:  • pressure injury</td>
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<td>• Unclear if the MRSA cases identified during surgery were the same cases as identified by bedside culture  • One site study, may not be generalizable;</td>
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| (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) | 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 | 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 | 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 |

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  

However 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.

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  

Environmental cultures  

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
<table>
<thead>
<tr>
<th>Ref</th>
<th>Type of Study</th>
<th>Sample</th>
<th>Intervention(s)</th>
<th>Outcome Measures &amp; Length of Follow-up</th>
<th>Results</th>
<th>Limitations and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith, Snow et al. 2010</td>
<td>Comparative survey reporting on the biodiversity of bacterial infection in pressure injuries</td>
<td>Samples from 49 pressure injuries Origin of pressure injury samples was not reported.</td>
<td>▪ Samples were taken from pressure injury pressure injury wound bed via sharp debridement ▪ Bacterial tag-encoded FLX amplicon pyrosequencing (bTEFAP), a universal bacterial identification method, was used to identify bacterial populations</td>
<td>▪ Bacteria classified at appropriate taxonomic levels using BLASTn derived sequence identity</td>
<td>▪ 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 into the community setting; however, there was no confirmation through screening caregivers and family members</td>
<td></td>
</tr>
<tr>
<td>Dowd, Delton Hanson et al. 2011</td>
<td>Retrospective study investigating the prevalence and diversity of fungal and yeast infection in mixed wound types</td>
<td>Record review of participants over a 4-month period with a chronic wound (n=609 participants, 915 specimens)</td>
<td>▪ 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</td>
<td>▪ Correlation analysis and ANOVA to determine if there were any significant relationships between bacterial and fungal genera and patient demographics</td>
<td>▪ 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</td>
<td>▪ 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.</td>
</tr>
</tbody>
</table>
### Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

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

### Additional evidence from systematic reviews to support discussion

<table>
<thead>
<tr>
<th>Ref</th>
<th>Type of Study</th>
<th>Sample</th>
<th>Intervention(s)</th>
<th>Outcome Measures &amp; Length of Follow-up</th>
<th>Results</th>
<th>Limitations and comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Norman, Dumville et al. 2016)</td>
<td>Systematic review of antibodies and antiseptics for healing pressure injuries of Category/Stage II or greater</td>
<td>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.</td>
<td></td>
<td>Author conclusions: There is no consistent evidence of a benefit to using any particular antimicrobial treatment for injuries.</td>
<td>• 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</td>
<td>Quality High</td>
</tr>
</tbody>
</table>
### Table 1: Level of Evidence for Intervention Studies

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

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

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

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

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level 1</td>
<td>A prospective cohort study.</td>
</tr>
<tr>
<td>Level 2</td>
<td>Analysis of prognostic factors amongst persons in a single arm of a randomized controlled trial.</td>
</tr>
<tr>
<td>Level 3</td>
<td>Case-series or case-control studies, or low quality prognostic cohort study, or retrospective cohort study.</td>
</tr>
</tbody>
</table>

### 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
### CROSS SECTIONAL/SURVEY/PREVALENCE STUDIES/_OBSERVATIONAL

<table>
<thead>
<tr>
<th>Endnote ID</th>
<th>Author/year</th>
<th>Focussed question</th>
<th>Sampling method</th>
<th>Representative sample</th>
<th>States number invited</th>
<th>Participants clearly defined</th>
<th>Intervention clearly defined</th>
<th>Outcomes measured and defined apriori</th>
<th>Outcomes measured</th>
<th>Valid, reliable outcome measurement</th>
<th>Confounders identified and accounted for</th>
<th>Minimal bias</th>
<th>Reliable conclusions</th>
<th>Level of evidence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>9577</td>
<td>(Bodavula, Liang, Wu, VanTassell, &amp; Marschall, 2015)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>NA</td>
<td>4 (diagnostic)</td>
</tr>
<tr>
<td>13200</td>
<td>(Dryden et al., 2016)</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
<td>N</td>
<td>N</td>
<td>U</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>U</td>
<td>4</td>
</tr>
<tr>
<td>14548</td>
<td>(Nakagami, Mori, et al., 2017)</td>
<td>Y</td>
<td>N</td>
<td>U</td>
<td>Y</td>
<td>Y</td>
<td>NA</td>
<td>U</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>4</td>
</tr>
</tbody>
</table>

### CASE SERIES

| Endnote ID | Author/year | Focussed question | Participant characteristics reported | Inclusion criteria defined | Consecutive recruitment | Participants entered at same disease stage | Intervention clearly defined | Outcomes relevant and defined apriori | Valid, reliable outcome measurement | Comparison between drop outs and participants | Clear outcome measures | Assessment blinded, or discuss potential bias | Valid, reliable outcome measurement supporting reference | More than one measure of exposure | Confounders identified and accounted for | Minimal bias | Reliable conclusions | Level of evidence | Quality |
|------------|-------------|-------------------|--------------------------------------|---------------------------|-------------------------|------------------------------------------|-----------------------------|-----------------------------------|----------------------------------|-------------------------------|------------------------|-----------------------------|------------------------------------------|--------------------------|-----------------------------|------------------|--------|
| 2994       | (Ciliberti et al., 2014)                        | Y                 | N                             | Y                       | U                       | U                          | N                           | Y                  | N               | N                           | N                           | N                     | N               | N               | NA              | Y        | U               | 4                | Low     |

### COHORT STUDIES

<table>
<thead>
<tr>
<th>Endnote ID</th>
<th>Author/year</th>
<th>Focussed question</th>
<th>Comparable source populations</th>
<th>States number invited</th>
<th>Likelihood of outcome at enrolment considered</th>
<th>Per cent drop out in study arms reported</th>
<th>Comparison between drop outs and participants</th>
<th>Clear outcome measures</th>
<th>Assessment blinded, or discuss potential bias</th>
<th>Valid, reliable outcome measurement</th>
<th>Confounders identified and accounted for</th>
<th>Minimal bias</th>
<th>Reliable conclusions</th>
<th>Level of evidence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>3255</td>
<td>(Graham, 2014)</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
<td>U</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>17482</td>
<td>(Espejo, 2018 #17482)</td>
<td>Y</td>
<td>NA</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
</tbody>
</table>
## PROGNOSTIC STUDIES

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

## DIAGNOSTIC STUDIES

<table>
<thead>
<tr>
<th>Author/year</th>
<th>True diagnostic test - a test is compared to another test</th>
<th>Selection is either consecutive enrolment or no case-control methods</th>
<th>No inappropriate exclusion of participants</th>
<th>Unbiased, independent interpretation of index and standard test results (i.e., without prior knowledge of results of other test)</th>
<th>Any threshold is pre-determined</th>
<th>Reference standard test is likely to correctly identify condition</th>
<th>Appropriate interval of time between index and standard tests</th>
<th>All participants receive same reference standard test</th>
<th>All recruited participants are included in analysis</th>
<th>Minimal bias</th>
<th>Level of evidence</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>14604</td>
<td>(Blanco-Blanco et al., 2017)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
</tr>
<tr>
<td>10871</td>
<td>(Brunel et al., 2016)</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
<td>NA</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>15254</td>
<td>(Heiba, Stempler, Sullivan, Kolker, &amp; Kostakoglu, 2017)</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
<td>N</td>
<td>U</td>
<td>Y</td>
<td>U</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>13982</td>
<td>(Tedeschi et al., 2017)</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
<td>Y</td>
<td>Y</td>
<td>U</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>
Assessment and Treatment of Infection and Biofilms: data extraction and appraisals

### 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 | 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 |

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


Assessment and Treatment of Infection and Biofilms: data extraction and appraisals


