ConvaTec

AQUACEL® Ag+ Dressings
The Evidence

BIOFILM ERADICATION REQUIRES MORE THAN ANTIMICROBIAL ACTION ALONE.[1]

In their 2014 guideline on the diagnosis and treatment of biofilm infections the European Society for Clinical Microbiology and Infectious Diseases:

- Recognise biofilm is a principle cause of chronic wound infection and discuss the persistent nature of these infections, despite appropriate use of antibiotics and normal functioning of the host immune system.
- Express an urgent need for research to improve prevention and treatment of biofilm infections, including research into biofilm degrading enzymes and chelators that break down that biofilm and change the biofilm organisms into the planktonic, more susceptible cells, making them more amenable to antibiotic treatment.

MORE THAN SILVER™ – THE DEVELOPMENT OF A BREAKTHROUGH ANTIBIOFILM DRESSING.[2,3]

- A wide range of antibiofilm agents in combination with ionic silver were tested in a rapid throughput in vitro biofilm model:[2]
  - ~250,000 potential combinations were identified and ~60,000 were tested
- A combination (Ag+ Technology) of the metal chelator Ethylenediaminetetraacetic (EDTA), surfactant Benzethonium chloride (BEC), together with ionic silver was identified as the optimal formulation to enhance performance:[2]
  - Tested in dressing format in a simulated wound biofilm model.
  - Demonstrated superior efficacy compared to other silver dressings*.
- The synergistic action of EDTA and BEC disrupting the biofilm, combined with the antimicrobial action of ionic silver give the dressing superior performance:[3]
  - When AQUACEL® Ag+ Extra™ dressing was tested *in vitro* versus non-silver dressing and silver only-containing dressing the biofilm was only reduced in the presence of AQUACEL® Ag+ Extra™ dressing. (Fig 1).
  - Control *in vitro* experiments showed that the combination of only EDTA and BEC does not have a bactericidal effect. (Fig 2).

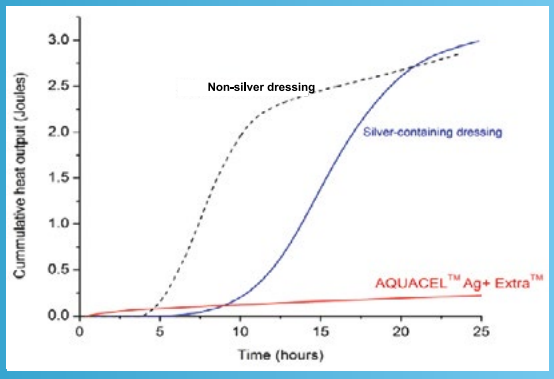

Figure 1. Growth curves for biofilms in the presence of AQUACEL® Extra™ (non-silver), AQUACEL® Ag Extra™ (silver only) and AQUACEL Ag+ Extra™ (silver combined with EDTA and BEC) dressings

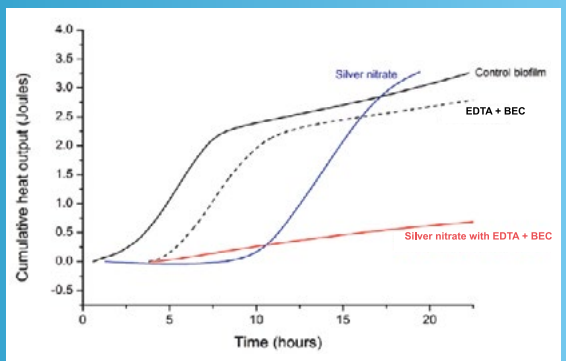

Figure 2. Growth curves for biofilm alone and in the presence of AgNO3, EDTA+BEC, and AgNO3+EDTA+BEC

*As compared to AQUACEL® Ag Extra™ dressing, SILVERCEL™ NA dressing and ACTICOAT™ 7 dressing

MORE THAN SILVER™ ENABLES BIOFILM DISRUPTION AND SUPERIOR EFFECTIVENESS

AQUACEL® Ag+ Extra™ dressing's unique, antibiofilm mode of action is supported by an extensive range of testing carried out on both single and mixed-species *in vitro* biofilms of increasing complexity against a range of challenge organisms to demonstrate the enhanced antimicrobial effectiveness achieved when Hydrofiber™ Technology with ionic silver is combined with EDTA and BEC.[4]

- A biofilm-disrupting effect was demonstrated by a significantly greater reduction ($p<0.05$) in metal ions within the biofilm (that give biofilm strength and structure) by AQUACEL® Ag+ Extra™ dressing compared to Hydrofiber™ Technology with ionic silver, or Hydrofiber™ Technology alone.
- AQUACEL® Ag+ Extra™ dressing was the only dressing* to significantly reduce ($p=0.000$) the thickness of biofilms protective, extracellular, polysaccharide matrix. (Fig. 3)
- The testing also demonstrated a greater susceptibility of the exposed microorganisms to the killing action of the ionic silver. AQUACEL® Ag+ Extra™ dressing induced a statistically significant greater silver uptake ($p=0.014$) by the biofilms than Hydrofiber™ Technology with ionic silver alone.
- This resulted in AQUACEL® Ag+ Extra™ dressing outperforming the other dressings (including those with higher silver concentrations) in killing biofilm cells.

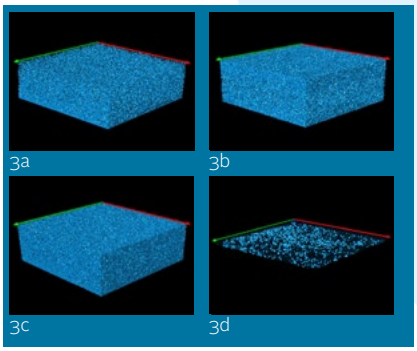

Figure 3. Staining of biofilm polysaccharides and confocal microscope images show neither a nanocrystalline silver (Fig 3b) nor silver alginate (Fig 3c) dressings resulted in any reduction of this protective biofilm component compared to the initial biofilm (Fig 3a), while bulk reduction by AQUACEL® Ag+ Extra™ dressing was evident (Fig 3d).

* When compared to AQUACEL® Extra™ dressing, AQUACEL® Ag Extra™ dressing and other silver-only competitor dressings: ACTICOAT™ 7 and SILVERCEL™ Non-Adherent dressings.

MORE EFFECTIVE AGAINST ANTIBIOTIC-RESISTANT *PSEUDOMONAS AERUGINOSA IN-VITRO* BIOFILM[5]

In a 48 hour simulated *in-vitro Pseudomonas aeruginosa* biofilm wound model:

- AQUACEL® Ag+ Extra™ dressing rapidly killed the challenging bacterial population resulting in no viable bacteria after 96 hours. (Fig 4)
- After the re-inoculation of fresh, living pseudomonas cells the AQUACEL® Ag+ Extra™ dressing continued to work - rapidly killing the organisms and preventing any re-growth.
- The speed of action and the ability to prevent re-growth was superior with AQUACEL® Ag+ Extra™ dressing compared to AQUACEL® Ag Extra™ dressing.

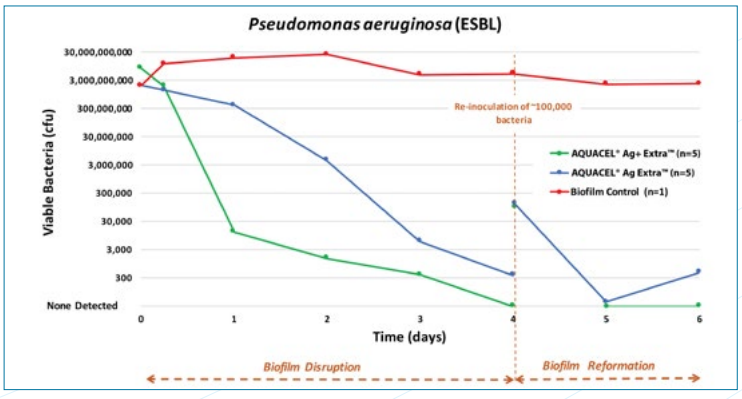

Figure 4. AQUACEL® Ag+ Extra™ dressing vs *Pseudomonas aeruginosa* ESBL in a biofilm model

ESBL = Extended Spectrum Beta-Lactamase

SAFE AND EFFECTIVE IN WIDESPREAD CLINICAL EVALUATIONS[7]

112 patients, required to have challenging wounds with a range of aetiologies that were failing to progress towards healing, were included from 60 centres across the UK and Ireland. After using AQUACEL® Ag+ Extra™ dressing as part of the protocol of care:

- 78% of wounds progressed towards healing of which 13% healed completely during an evaluation period ranging from 1-16 weeks, average 3.9 weeks. (Fig 10)
- 83% of the wounds progressed in key wound healing parameters (exudate, suspected biofilm and wound healing status). (Fig 11)
- Suspected biofilm, more common than any other clinical sign of infection at baseline, was reduced from 54% of cases to 27% after management with AQUACEL® Ag+ Extra™ dressing.
- AQUACEL® Ag+ Extra™ dressing was rated as more effective than the previously used primary dressing in at least 72% of cases.
- Overall AQUACEL® Ag+ Extra™ dressing was well tolerated, there were only 3 adverse events related to the use of the dressing.

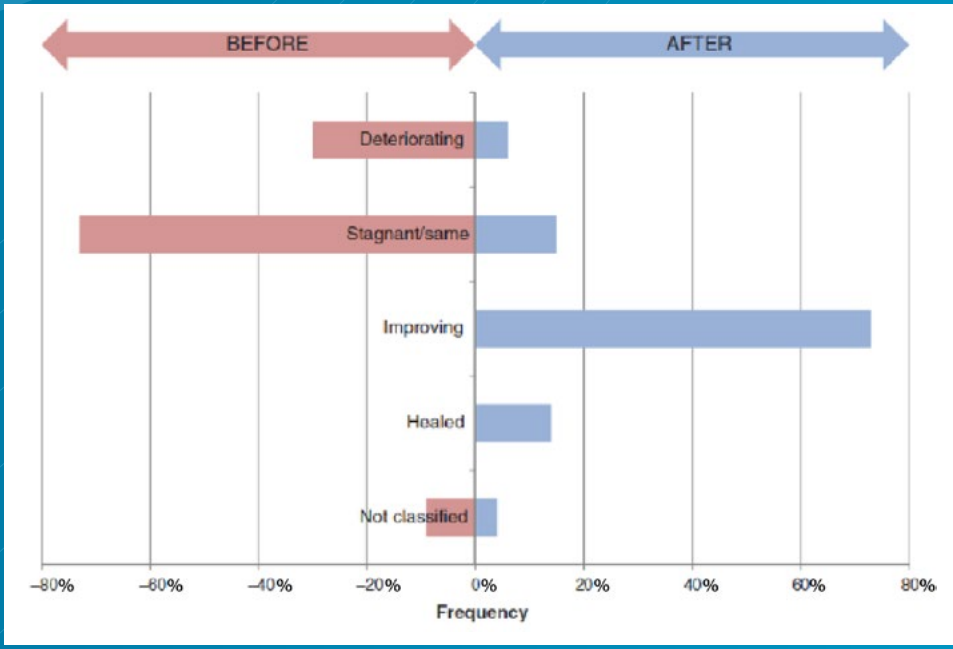

Figure 10. Wound status at baseline ( ) and after evaluation ( ).

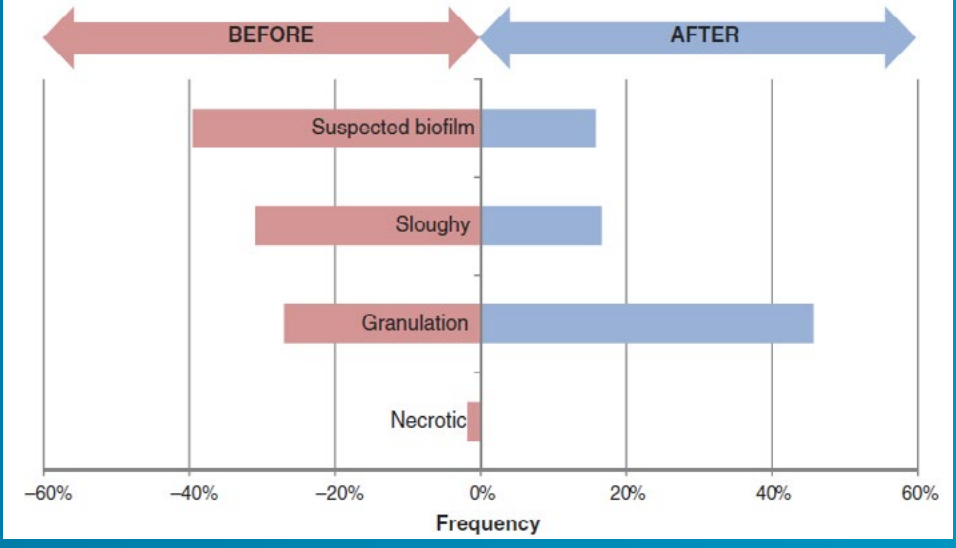

Figure 11. Average estimated wound bed coverage as a percentage of different tissue types at baseline ( ) and after evaluation ( ).

CLINICALLY EFFECTIVE IN NON-HEALING, CHRONIC WOUNDS[8]

AQUACEL® Ag+ Extra™ dressing was shown in practice to manage exudate, infection, biofilm and improve wound and skin health on stagnating, deteriorating and long-standing wounds (n = 29)

- 90% of wounds reduced in size or were completely healed at final assessment. Median dressing usage was 4.5 weeks. (Figure 12)
- 34% of wounds healed completely after management with AQUACEL® Ag+ Extra™ dressings.
- On average wounds showed 57% granulation/epithelialisation after management with AQUACEL® Ag+ Extra™ dressing.

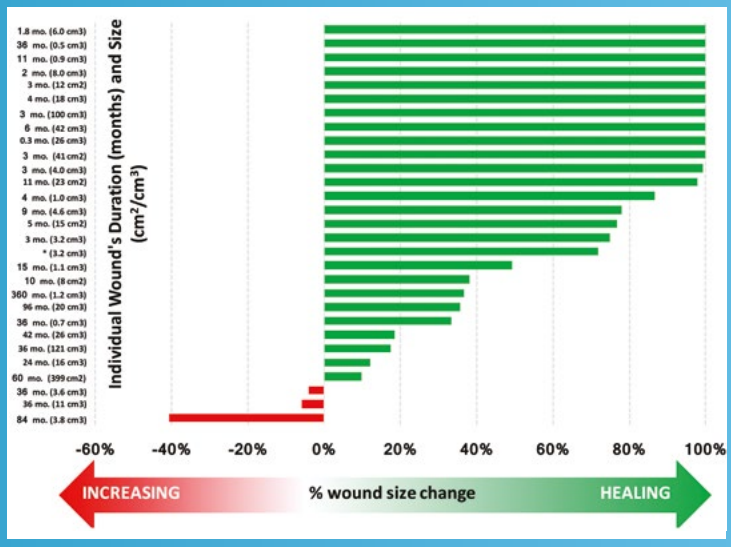

Figure 12. Percentage decrease (green) or increase (red) in wound size for each wound in the evaluation, as judged by change in wound volume/area. Note that each wound is labelled with its initial duration (months) and size (cm² or cm³)

EFFECTIVE IN PATIENTS WHERE TOPICAL ANTIMICROBIAL THERAPIES HAD PREVIOUSLY FAILED[7]

In a widespread evaluation of 112 patients with challenging wounds from a range of aetiologies a wide variety of antimicrobial wound care products had been used prior to switching to AQUACEL® Ag+ Extra™ dressing as part of the protocol of care. (Fig. 13)

- 92% of wounds were stalled or deteriorating at baseline.
- Alongside systemic antibiotics, Hydrofiber™ dressings with silver and iodine based dressings were the most frequently prescribed at baseline. (Fig. 13)
- 78% of wounds shifted to improved or healed following evaluation of AQUACEL® Ag+ Extra™ dressing.
- AQUACEL® Ag+ Extra™ dressing was rated as being more effective than the previous dressing used by the majority of clinicians.

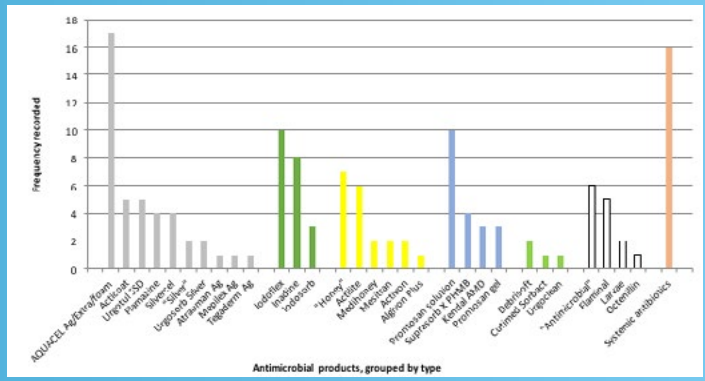

Figure 13. Antimicrobial products used prior to the AQUACEL® Ag+ Extra™ dressing evaluations grouped by type.

MORE EFFECTIVE AGAINST COMMUNITY-ACQUIRED METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS IN VITRO* BIOFILM[5]

In a 48-hour simulated *in-vitro* Methicillin-Resistant *Staphylococcus aureus* biofilm wound model:

- AQUACEL® Ag+ Extra™ dressing rapidly killed all viable bacteria within 120 hours. AQUACEL® Ag Extra™ was not effective against CA-MRSA. (Fig 5)
- After re-inoculation at 120 hours, AQUACEL® Ag+ Extra™ dressing again rapidly killed all viable bacteria and prevented re-growth.

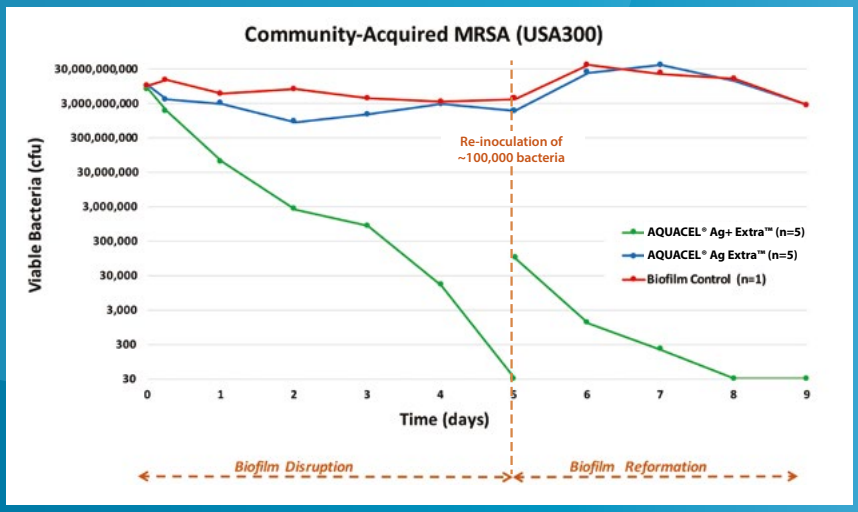

Figure 5. AQUACEL® Ag+ Extra™ dressing vs community-acquired Methicillin-Resistant *Staphylococcus aureus* in an *in vitro* model

MRSA = Methicillin-Resistant *Staphylococcus aureus*

ANTIBIOFILM AND HEALING EFFICACY PROVEN IN SCIENTIFICALLY CONTROLLED WOUNDS

AQUACEL® Ag+ dressing* demonstrated rapid reduction of wound biofilm and subsequent progression towards wound healing in an independently validated *in vivo* wound model with *Pseudomonas aeruginosa*:[6]

- Significant reduction ($p<0.05$) in wound biofilm after 24 hours compared to antimicrobial (PHMB, polyhexamethylene biguanide, gauze dressing) and non-antimicrobial controls (Hydrofiber™ dressing).
- Significant improvement ($p<0.05$) in epithelialisation and granulation tissue measurements.
- Wounds managed with AQUACEL® Ag+ dressing visually showed improvements in wound healing relative to antimicrobial control dressed wounds through POD18. (Fig. 9)

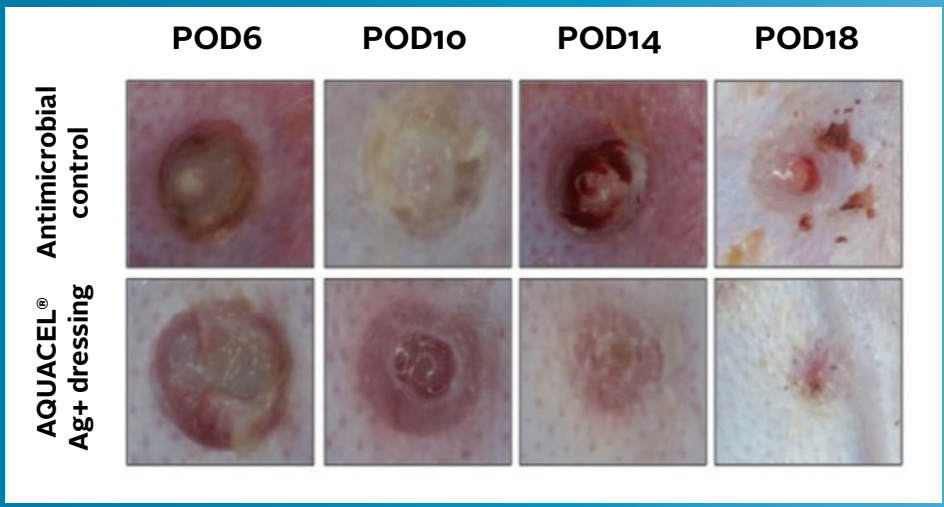

Figure 9. Photographs of polybacterial wounds treated with antimicrobial control or AQUACEL® Ag+ dressing over time. AQUACEL® Ag+ dressing wounds showed visual improvement in healing over time relative to antimicrobial control wounds at each photographed time point.
(POD = post-operative day)

* Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing

EFFECTIVE EVEN WHERE SYSTEMIC ANTIBIOTICS HAD FAILED[9]

Sixteen patients with wounds where thirteen were recorded as stalled or deteriorating at baseline were receiving systemic antibiotics as part of their protocol of care. After an average management of 4.7 weeks with AQUACEL® Ag+ Extra™ dressing:

- 13 (81%) of these wounds improved or healed (Fig. 14).
- 2 remained the same, and only 1 deteriorated.

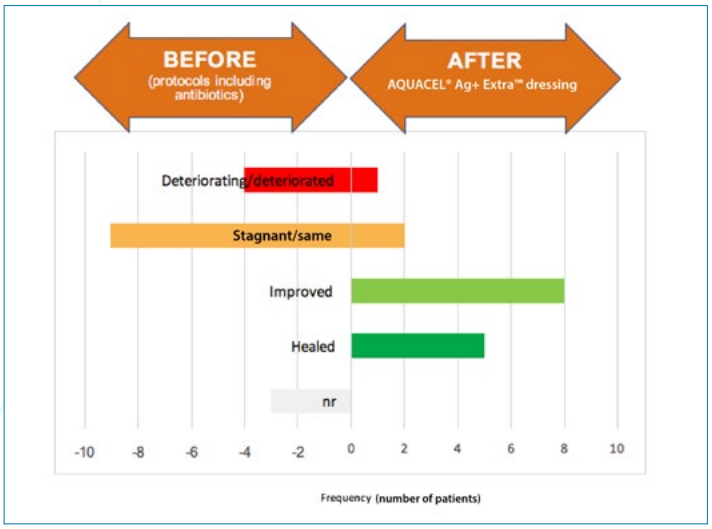

Figure 14. Clinical impact of AQUACEL® Ag+ Extra™ dressing in non-healing wounds previously managed with antibiotics.

CLINICALLY EFFECTIVE IN CHRONIC VENOUS LEG ULCERS[10]

In a prospective, multi-centre, non-comparative study on 42 chronic leg ulcer patients with at-risk or infected wounds Hydrofiber™ with Ag+ Technology* was used for the first 4 weeks followed by AQUACEL™ Extra™ dressing for the next 4 weeks:

- There was a 54% reduction in ulcer area in all wound types. (Figure 15)
- There was a 70% reduction in ulcer area in a subset of 10 wounds thought to be clinically infected.

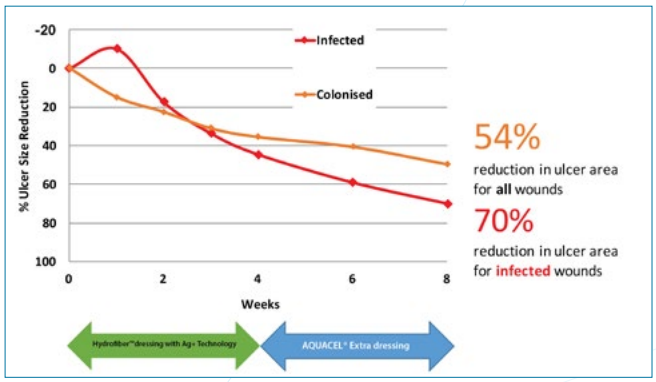

Figure 15. Mean percentage reduction in ulcer area was measured at each treatment visit for patients with clinically infected ulcers (n=10, red line) or all ulcers (n=42, orange line).

* Dressing did not contain strengthening yarn or have the additional absorptive capacity of AQUACEL™ Ag+ Extra™ dressing

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