Recommendations for the management of biofilm: A consensus document

Article *in* Journal of Wound Care · June 2016

DOI: 10.12968/jowc.2016.25.6.305

CITATION
1

READS
1,303

20 authors, including:

Angela Peghetti
Policlinico S.Orsola-Malpighi
6 PUBLICATIONS **7** CITATIONS
SEE PROFILE

Keith Cutting
Hertfordshire
124 PUBLICATIONS **980** CITATIONS
SEE PROFILE

Andrea Bellingeri
Policlinico San Matteo Pavia Fondazione IRCCS
35 PUBLICATIONS **54** CITATIONS
SEE PROFILE

Giovanni Pomponio
Università Politecnica delle Marche
55 PUBLICATIONS **582** CITATIONS
SEE PROFILE

Recommendations for the management of biofilm: a consensus document

The potential impact of biofilm on healing in acute and chronic wounds is one of the most controversial current issues in wound care. A significant amount of laboratory-based research has been carried out on this topic, however, in 2013 the European Wound Management Association (EWMA) pointed out the lack of guidance for managing biofilms in clinical practice and solicited the need for guidelines and further clinical research.

In response to this challenge, the Italian Nursing Wound Healing Society (AISLeC) initiated a project which aimed to achieve consensus among a multidisciplinary and multiprofessional international panel of experts to identify what could be considered part of 'good clinical practice' with respect to the recognition and management of biofilms in acute and chronic wounds. The group followed a systematic approach, developed by the GRADE working group, to define relevant questions and clinical recommendations raised in clinical practice.

An independent librarian retrieved and screened approximately 2000 pertinent published papers to produce tables of levels of evidence. After a smaller focus group had a multistep structured discussion, and a formal voting process had been completed, ten therapeutic interventions were identified as being strongly recommendable for clinical practice, while another four recommendations were graded as being 'weak'.

The panel subsequently formulated a preliminary statement (although with a weak grade of agreement): 'provided that other causes that prevent optimal wound healing have been ruled out, chronic wounds are chronically infected'. All members of the panel agreed that there is a paucity of reliable, well-conducted clinical trials which have produced clear evidence related to the effects of biofilm presence. In the meantime it was agreed that expert-based guidelines were needed to be developed for the recognition and management of biofilms in wounds and for the best design of future clinical trials. This is a fundamental and urgent task for both laboratory-based scientists and clinicians

Declaration of interest: David Leaper was a paid lecturer/consultant advisor within the last two years for Johnson and Johnson, CareFusion and Pfizer. Andrea Bellingeri, consultant advisor in the last two years for Coloplast, Angelini. Keith Cutting: has received honoraria as a member of speakers bureaus and advisory boards and received travel and accommodation expenses from a number of wound products companies. All the other authors have no conflict of interest to declare.

biofilm • consensus • wound healing • wound infection • ulcer

Treatment of non-healing, or hard-to-heal, wounds is a critical issue which is being addressed by health-care systems worldwide. This affects a considerable number of the population of the Western World, requires expensive investigation, intervention and treatment, and accounts for 2–4% of health-care budgets.[1]

Overt infection, or an increasing colonising bioburden, are the most common complications of chronic wounds which lead to prolonged treatment and increased the use of resources. In the last 40 years the use of products with an antimicrobial activity to prevent and treat increasing bioburden and infection has dramatically increased.

On the other hand, there is an increasing need to reduce the non-appropriate use of antibiotics, to tackle antimicrobial resistance and to avoid adverse or tissue toxic effects caused by topical antimicrobial agents.

Published studies have associated the development from the classically cultured planktonic growth microorganism phenotype to a complex, diverse biofilm phenotype in chronic wounds which leads to impairment of wound healing.[2]

Biofilms have been defined as coherent clusters of bacterial cells embedded in a biopolymer matrix, which, compared with planktonic cells, show increased tolerance to topical (antiseptics) and systemically

T. Bianchi,[1]; **R.D. Wolcott**,[2] **A. Peghetti**,[3] **D. Leaper**,[4] **K. Cutting**,[5] **R. Polignano**,[6] **Z. Rosa Rita**,[7] **A. Moscatelli**,[8] **A. Greco**,[9] **M. Romanelli**,[10] **S. Pancani**,[11] **A. Bellingeri**,[12] **V. Ruggeri**,[13] , **L. Postacchini**,[15] **S. Tedesco**,[1] **L. Manfredi**,[15] **Maria Camerlingo**,[16] **S. Rowan**,[17] **A. Gabrielli**,[15] **G. Pomponio**,[18]

E-mail: tommaso.b.bianchi@gmail.com;

1 UO Dermatologia AUSL Bologna – Istituto delle scienze neurologiche Bellaria, Bologna, Italy. **2** Southwest Regional Wound Care Center, Lubbock, Texas, USA. **3** Casa Di Cura Solatrix Rovereto, AISLeC Membership, Italy. **4** University of Newcastle upon Tyne, Institute of Skin Integrity and Infection Prevention, University of Huddersfield, Huddersfield, UK. **5** Wound Care 4 Heroes and Perfectus Biomed, UK. **6** IOT Hospital Cardiovascular Rehabilitation, Florence, Italy. **7** Ambulatorio Infermieristico ASS 1 Trieste, AISLeC Membership, Italy. **8** Lesioni Cutanee e Ambulatori Infermieristici Lesioni Cutanee SITRA, A.O. Legnano e Abbiategrasso, AISLeC Membership, Italy. **9** Outpatient Wound Care Centre, Local Health Care System Frosinone, Italy. **10** Division of Dermatology, Dept. of Clinical and Experimental Medicine, University of Pisa, Pisa Italy. Burns Unit, Department of Neonatal and Emergency Surgery, "Meyer" Children's Hospital, Florence (Italy). **12** Ambulatory vascular and wound care centre, Policlinic San Matteo, Pavia, Italy. **13** Wound Care Centre - AOU Careggi, Firenze, AISLeC Membership, Italy. **14** Ospedale 'M. Bufalini' – AUSL Cesena, Italy. **15** Università Politecnica delle Marche, Istituto di Clinica Medica, AOU Ospedali Riuniti di Ancona, Italy. **16** Regione Emilia-Romagna, Library - Bologna, Italy. **17** University of Modena, C3S – Lecturer - Clinical Scientific Support Services, Italy. **18** Istituto di Clinica Medica, AOU Ospedali Riuniti di Ancona, Italy

(antibiotics) administered antimicrobials and resist the antimicrobial properties of host defences.[3]

Biofilms have been recognised in dental plaque and the water industry for many years, more recently they have been found in sutures and staples from healed surgical wounds[4] and later also found in chronic wounds.[5,6] Bacteria in their biofilm phenotype are extremely difficult to remove, other than by surgical or sharp and/or mechanical wound debridement. The definition of sharp, surgical and mechanical wound debridement according to EWMA document 2013 are as follows:[7]

- Mechanical wound debridement consist of the use of dry gauze dressings, wet to dry gauze dressings, impregnated gauze/tulle dressings or a monofilament fibre pad to remove non-viable tissue from the wound bed.
- Sharp debridement is a minor surgical bedside procedure, involving cutting away tissue with a scalpel or scissors while 'surgical debridement' is defined as a procedure performed under general anaesthesia, using various surgical instruments.

Review

There is more published evidence on the effectiveness of debridement in diabetic foot ulcers (DFUs) than for venous leg ulcers (VLUs) and pressure ulcers (PUs).[8] After debridement, systemic antibiotics, if appropriate, and topical antimicrobial agents are more effective at treating infected wounds, critical colonisation and in avoiding the reformation of microbial biofilm.[9,10]

A 2013 EWMA document posed several questions and states controversies which exist surrounding the significance of wound bioburden, wound infection and biofilm. In particular, the document stated:

> *'no specific indications for the treatment of biofilms have been established in non-healing wounds and may have differing outcomes in differing circumstances. This is an emerging area of research'.*[7]

Purpose

The purpose of this document was to agree on recommendations for clinical practice in the management of biofilm in chronic wounds, where consensus was achievable.

The lack of reliable evidence from controlled, clinical studies prevents scientific societies or other authoritative associations from formulating recommendations for clinical practice. To bridge this gap, Italian Nursing Wound Healing Society (AISLeC) brought together an informed group of scientists and practicing clinicians to achieve a consensus on the optimal or presumptive methods for recognition and management of biofilm to enhance the effectiveness of treatment of hard-to-heal chronic wounds.

The rationale of this consensus was therefore to provide practical guidance for clinical management of biofilm when its presence is suspected.

Methods

The wide variety of clinically, non-healing wounds were categorised as acute (dehisced surgical wounds, burns) and chronic (arterial, venous, diabetic and pressure ulcers). Management of these hard-to-heal wounds was coupled with different management decisions (surgical debridement, use of antimicrobial dressings, antimicrobial soaks/cleansing with antiseptics). The scenarios coupled with management decisions were matched together to generate several questions concerning biofilm presence and its treatment.

This project was designed and implemented by the AISLeC which organised a steering committee to provide methodological expertise and organisational support. In 2009 the National Institute of Health (NIH) of the United States published guidelines (Consensus Development Program) for the formation and conduct of a consensus panel.[11] In the current project this systematic approach, recommended by NIH and by the analogous Italian National System for Guidelines, was used.[12]

A group of 17 people from three different countries (US, UK and Italy) participated in the expert panel. The participants were from the following fields of expertise: 11 were experts in wound care of whom four were nurses, three dermatologists, one plastic surgeon, one paediatric surgeon, one angiologist, one pharmacist, five experts in trial design and statistics and one librarian.

Phase 1: identifying the questions

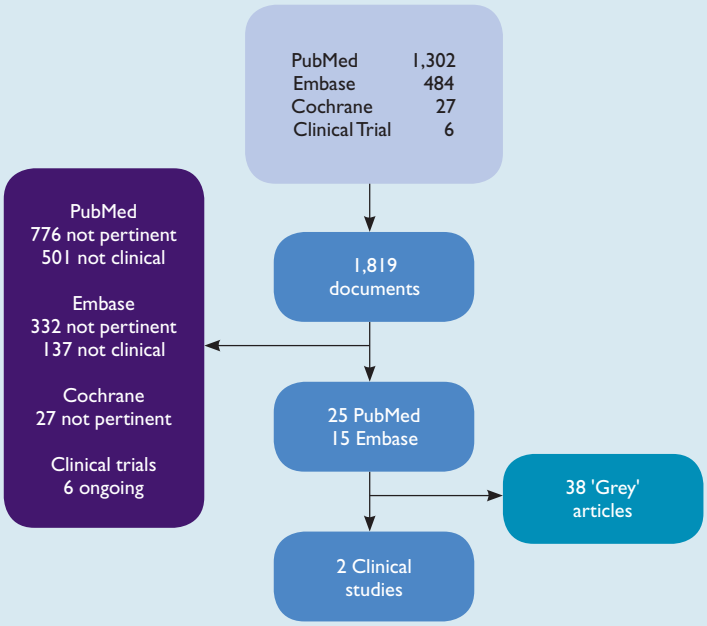
The participating clinicians of the steering committee identified six clinical areas of interest (PUs, venous and arterial ulcers, surgical wounds, DFUs and burns). We formulated 37 questions concerning biofilm relevance, diagnosis and treatment using the patient, intervention, comparison, outcome (PICO) format. In addition, eight background questions concerning basic aspects of biofilm in wound healing were considered. The generated questions were sent to the whole panel by email to confirm their importance and to comment on the exact wording and meaning. Particular attention was given to the clinical relevance of the optimal clinical outcome(s). The expert group was also asked to vote whether they accepted or rejected the question as being relevant and useful.

First meeting of the panel took place in November 2014 (Milan, Italy) where each question, together with pertinent comments and criticisms, underwent a critical analysis through a structured discussion. All the questions were reformulated based on the debate and voted for relevance.

Phase 2: systematic review of the literature

Based on the questions, agreed by the panel, an independent librarian carried out a literature search. Electronic databases (MEDLINE, EMBASE, CINHAL, CENTRAL) were explored with a comprehensive group of terms without limitations in terms of data or language using the following words (March 2015): PubMed (1302 documents): Biofilm*[all fields],

Fig 1. Literature search flow-chart



wound*[all fields] OR damage*[all fields] OR injur*[all fields]; Embase (1854 documents): 'biofilm'/exp AND ('wound care'/exp OR 'injury'/exp OR 'wound'/exp OR 'wound infection'/exp OR 'wound healing'/exp OR 'wound dressing'/exp OR 'surgical infection'/exp OR 'surgical stapling'/exp); #1 AND ([article]/lim OR [article in press]/lim OR [conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [erratum]/lim OR [review]/lim OR [short survey]/lim) AND [humans]/lim AND [Embase]/lim; Cochrane (27 documents): wound*[all fields] OR damage*[all fields] OR injur*[all fields].

Related articles were identified and a manual search was also performed from retrieved articles. Panel experts were asked to comment and identify any missed relevant publications. Finally, trial registries (for example clinicaltrials.gov) were searched for on-going or non-published relevant trials. One investigator (AP) read all the abstracts. If a study was identified as being potentially eligible for inclusion, the full study report was retrieved. All pertinent articles were classified as:

- 'Grey' literature (editorials, comments, consensus-based position papers, narrative reviews, etc.)
- Clinical studies
- Basic/laboratory-based science report.

Clinical studies were critically appraised and rated by using the GRADE Working Group method and scales.[12] Evidence tables were built for the clinical trials. Very few clinical studies were found. Therefore, any evidence that was pertinent was included. The articles were then divided according to the corresponding questions set by the panel.

Phase 3: the formulation of recommendations for practice

Based upon the results of the literature search a preliminary list of recommendations was made and then sent by email to the panel together with retrieved evidence. A large number of further suggestions and criticisms were suggested and included.

A second panel meeting took place in May 2015 (Arezzo, Italy), where each recommendation was examined, debated and finally voted on.

Voting process and attribution of grade of strength

In both the meetings the experts voted by using a scale ranging from 0 (absolutely not recommended) to 9 (strongly recommended). Interquartile ranges (IQR) and medians (M) were calculated to integrate results and the level of agreement. In line with the GRADE method, an intervention was defined as being

- 'Strongly recommended' (in a specific population for a specific outcome) if the median was ≥8 and the lower level of the IQR was >5
- 'Weakly recommended' if the median was 6 or 7 and the lower boundary of the IQR was >5
- 'Not recommended' in the case when median was <5 and the upper boundary of IQR was ≤5
- 'Uncertain' in the remaining situations (median=5; median >5 but lower quartile <5; median <5 but upper quartile >5).[13]

Management of potential conflicts of interest

The Consensus Conference was mainly supported by AISLeC. However, some companies which market products used in wound care (mostly antiseptic-based products and medical devices) made donations to this initiative (for practical organisation of the consensus and travel expenses of the participants, which are shown in the disclosure). No fees were received by any member of the panel or the steering committee. None of the sponsors participated actively in any aspect of the consensus nor did they provide articles or other material of any kind. This paper solely reflects the opinions of the participating experts.

Results

Questions

From Phase 1 46 questions emerged (Table 1 presents the final rewording of these questions). In particular, the panel judged five background questions and eight foreground questions as being not relevant.

A preliminary statement concerning the relationship between chronic infection and the wound healing process was added (see below).

Literature research

Fig 1 summarises the results of the literature search. There were no randomised controlled trials, exploring the impact of therapeutic or diagnostic intervention on biofilm. Only two clinical trials[14,15] were retrieved. However, a large number of articles containing

Table 1. The 46 questions identified by the steering committee in their final re-wording. The results of the voting process (median, interquartile range)* and the voting interpretation (R=relevant, NR=not relevant, U=uncertain) are shown. The black shading represents the refused questions

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
1	Is it relevant to investigate the presence and features of biofilm in post burn wounds which not have clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in post burn wounds which do not have clinical signs and/or symptoms of infection?	5 (4, 8)	NR
2	Is it relevant to investigate the presence and features of biofilm in patients with skin wounds which are not healing after surgery, without clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in patients with a skin wound which is not healing after surgery, without clinical signs and/or symptoms of infection?	7 (6, 7.5)	R
3	Is it relevant to investigate the presence and features of biofilm in patients who have chronic venous leg ulcers, without clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in patients who have chronic venous leg ulcers, without clinical signs and/or symptoms of infection?	6 (5.5, 7)	R
4	Is it relevant to investigate the presence and features of biofilm in patients who have chronic arterial ulcers of the lower limb, without clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in patients who have chronic arterial ulcers of the lower limb, without clinical signs and/or symptoms of infection?	6 (5, 7)	U
5	Is it relevant to investigate the presence and features of biofilm in patients who have chronic pressure ulcers, without clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in patients who have chronic pressure ulcers, without clinical signs and/or symptoms of infection?		
6	Is it relevant to investigate the presence and features of biofilm in patients who have chronic diabetic foot ulcers, without clinical signs and/or symptoms of infection?	Is it relevant to investigate the presence and features of biofilm in patients who have chronic diabetic foot ulcers, without clinical signs and/or symptoms of infection?	7 (6, 8)	R
7	Is wound biopsy the optimal method for sampling and analysis of biofilm in wounds without clinical signs and/or symptoms of infection?	Is wound biopsy the optimal method for the sampling and analysis of biofilm in wounds without clinical signs and/or symptoms of infection?	4 (3.5, 7.5)	NR
8	What is the optimal method for analysing biofilm in wounds without clinical signs and/or symptoms of infection?	What is the optimal method for analysis of biofilm in wounds without clinical signs and/or symptoms of infection?	5 (5, 6.5)	U
9	In patients who have wounds without clinical signs and/or symptoms of infection, would the swab for quantitative culture be sufficiently reliable for the detection of biofilm and its features?	In patients who have wounds without clinical signs and/or symptoms of infection, would the swab for quantitative culture be sufficiently reliable for the detection of biofilm and its features?	5 (2.5, 6)	NR
10	In patients who have wounds without clinical signs and/or symptoms of infection, can the investigation of metalloproteases by doing specific tests be sufficiently reliable for the detection of biofilm and its features?	In patients who have wounds without clinical signs and/or symptoms of infection, can the investigation of metalloproteinases by doing specific tests be sufficiently reliable for the detection of biofilm and its features?	5 (3, 5.5)	NR
11	In patients with chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6.5, 7.5)	R
12	In patients who have chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients who have chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6.5, 8)	R

Table 1. (Continued)

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
13	In patients with chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection of infection?	In patients with chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6, 8)	R
14	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (5, 7)	U
15	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (5.25, 7)	R
16	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6, 7)	R
17	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (5.5, 8)	R
18	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7.75)	R
19	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 8)	R
20	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7.75)	R
21	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6, 7.75)	R

Table 1. (Continued)

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
22	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with chronic pressure ulcers without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7.75)	U
23	In patients with burn wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with burn wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (5.25, 7.75)	R
24	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7)	R
25	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7)	R
26	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of debridement reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (5, 7.75)	U
27	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antimicrobial dressings reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	7 (6.25, 7)	R
28	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, can the use of antiseptic soaks or cleansing with antiseptics reduce the wound surface area and/or prevent the onset of clinical signs and/or symptoms of infection?	6 (6, 7)	R
29	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, is the use of debridement associated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	6 (6, 7.75)	R
30	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antiseptics more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of Biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5.25, 7.75)	R

Table 1. (Continued)

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
31	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with antiseptic soaks or cleansing with antiseptics?	In patients with surgically dehisced wounds without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5.25, 7)	R
32	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement assocated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	7 (5, 8)	U
33	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antiseptics more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5, 8)	U
34	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressing more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with antiseptic soaks or cleansing with antiseptics?	In patients with a burn wound without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressing more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5, 6.75)	U
35	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	7 (5.5, 8)	R
36	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antiseptics more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	7 (6.25, 8)	R
37	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with antiseptic soaks or cleansing with antiseptics?	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5.25, 7.75)	R

Table 1. (Continued)

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
38	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	7 (6.25, 8)	R
39	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antiseptics more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	7 (6.25, 8)	R
40	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with antiseptic soaks or cleansing with antiseptics?	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (6, 7)	R
41	In patients with a chronic venous leg ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a chronic venous leg ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	6 (5, 7.75)	U
42	In patients with a chronic venous leg ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antiseptics more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with a chronic venous leg ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5.25, 7.75)	R
43	In patients with a chronic venous leg ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with antiseptic soaks or cleansing with antiseptics?	n patients with a chronic venous leg ulcer without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5, 7.75)	U
44	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antimicrobial dressings more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antimicrobial dressings?	6 (5, 7.75)	U

Table 1. (Continued)

Question Number	Initial wording	Final re-wording	Voting process results*	Voting interpretation
45	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement associated to antiseptic soaks or cleansing with antisepticsmore effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared with the two interventions alone?	In patients with lower limb arterial ulcers without clinical signs and/or symptoms of infection, but where the presence of biofilm is suspected, is the use of debridement more effective in reducing the wound surface area and/or preventing the onset of clinical signs and/or symptoms of infection, when compared to antiseptic soaks or cleansing with antiseptics?	6 (5, 6.75)	U

information about the basic scientific aspects of biofilm-wound interaction, or discussing its potential clinical consequence on the wound healing process, emerged from the search.

Preliminary Statement

The European Clinical Microbiology and Infectious Disease Society guidelines unequivocally state that chronic infections (including the clinical behaviour of chronic infections) are caused by biofilm and describe chronic wounds as being chronic infections.[6] Therefore a preliminary statement was formulated:

> *'provided that other causes that prevent optimal wound healing have been ruled out, chronic wounds are chronically infected'.*

The purpose was to seek consensus that chronic wounds represent chronic infections or presence of biofilms. This preliminary statement was added and voted, achieving the majority of votes without unanimous agreement. In fact three out of 11 experts voted against the statement with a median score of 7 and IQR of 5.5–8.8. Consequently, the grade of strength was rated as being weak (WR).

Recommendations

Recommendations have been grouped by type of intervention and by wound type (see Table 2).

By type of intervention:

- Biofilm detection and investigation is relevant in patients affected by diabetic foot ulcers (strongly) and in patients affected by chronic dehisced surgical wounds (strongly).
- Sharp and/or mechanical debridement is recommended in all wound types except in patients affected by arterial-deficiency, ischaemic wounds.
- The use of antimicrobial dressings is recommended for all wound types.
- The use of antiseptic soaks or cleansing with antiseptics is recommended for all wound types.

By wound type:

- In patients affected by burns surgical, sharp and/or mechanical debridement, the use of antimicrobial dressings and the use of antiseptic soaks or cleansing with antiseptics is strongly recommended.
- In patients affected by chronic dehisced surgical wounds sharp and/or mechanical debridement and the use of antimicrobial dressings is weakly recommended. The use of antiseptic soaks or

Table 2. Clinical recommendations for biofilm detection and treatment

	Type of wound					
	Burns	**Dehisced surgical wounds**	**Arterial ulcers**	**Venous leg ulcers**	**Pressure ulcers**	**Diabetic foot ulcers**
Need for biofilm investigation	*	Strongly relevant	Not relevant	*	*	Strongly relevant
Treatment Procedure						
Mechanical debridement	SR	WR	NR	SR	SR	SR
Use of antimicrobial dressings	SR	WR	SR	WR	SR	SR
Use of antiseptic soaks /cleansing with antiseptics	SR	SR	SR	WR	SR	SR

*question considered not eligible by panel experts
SR–strongly recommended; WR–weakly recommended; NR–not recommended; U–uncertain

Table 3. The 10 clinical recommendations rated strongly by the panel experts

Recommendations voted as strongly recommended	
SR	In patients with surgically dehisced wounds without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the use of proper antimicrobial dressings.
SR	In patients with surgically dehisced wounds without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics.
SR	In patients with surgically dehisced wounds without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the proper use of antimicrobial dressings is recommended to promote wound healing, but does not exclude the use of antiseptic soaks or cleansing with antiseptics.
SR	In patients with a chronic venous leg ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics
SR	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the use of proper antimicrobial dressings.
SR	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics.
SR	In patients with a chronic pressure ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the proper use of antimicrobial dressings is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics
SR	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the proper use of antimicrobial dressings.
SR	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the use of debridement is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics.
SR	In patients with a diabetic foot ulcer without clinical signs and/or symptoms of exacerbation, but where the presence of biofilm is suspected, the proper use of antimicrobial dressings is recommended to promote wound healing, but does not exclude the proper use of antiseptic soaks or cleansing with antiseptics.

cleansing with antiseptics is strongly recommended. Investigation of biofilm presence is strongly relevant.

- In patients affected by lower limb arterial ulcers the use of antimicrobial dressings and the use of antiseptic soaks or cleansing with antiseptics is strongly recommended.
- In patients affected by chronic VLUs sharp and/or mechanical debridement is strongly recommended whereas the use of antimicrobial dressings and the use of antiseptic soaks or cleansing with antiseptics is weakly recommended.
- In patients affected by PUs sharp and/or mechanical debridement, the use of antimicrobial dressings and the use of antiseptic soaks or cleansing with antiseptics are strongly recommended.
- In patients affected by DFUs surgical, sharp and/or mechanical debridement, the use of antimicrobial dressings and the use of antiseptic soaks or cleansing with antiseptics are strongly recommended. Investigation for the presence of biofilm is strongly relevant.

The panel board decided, with 90% agreement, that clinical intervention which includes the use of other types of interventions cannot be considered as definitely inappropriate. Table 3 shows the recommendations which were voted for as being strongly recommended.

Discussion

The aim of this work was to shed light on those areas in which little or no evidence exists to support guidance of clinical behaviours in biofilm recognition/diagnosis and treatment. The evaluation of clinical indicators of wound biofilm was proposed in an algorithm that was published in 2008, which still needs to be validated.[16]

The results which emerged from the consensus agreement underline the important role of biofilm which should be considered in the pathophysiology of progression of wounds to non-healing. Therefore, the panel recommends the following treatment paths: sharp and/or mechanical debridement to remove biofilm in all wound types except arterial-related ulcers; and the use of antimicrobial dressings and of antiseptic soaks/cleansing in all clinical settings. Selection of appropriate debridement technique should be carefully made taking in account clinical setting and the possibility to minimise disconfort to patients. The use of antimicrobials should be accompanied by adjunct strategies when possible, following guidelines and safe use of antiseptics.[17]

Assessing practical recommendations, the board was surprised by the number of occasions on which a high degree of strength had been reached despite little evidence in the literature, thereby demonstrating that there is a lot of experience in favour of these clinical interventions. Management of chronic wound types, such as PUs and DFUs reached a wider agreement, whereas wound types, such as dehisced surgical wounds, arterial disease-related ulcers and VLUs, reached a narrower agreement. Despite this, it was recommended that good quality clinical research is needed to justify these clinical recommendations.

The formulated recommendations could be considered too vague because they treat interventions of the same type as being equal: a good example being the use of different antimicrobials with different mechanisms of action. However, this is not to say that different interventions are equivalent, but that the

panel did not consider that there was sufficient shared evidence and experience to agree and suggest specific interventions. This is seen as the most urgent topic for future research.

Acceptance of the statement that provided that other causes that prevent healing have been ruled out, non-healing chronic wounds should be perceived as being chronically infected or affected by biofilm presence is a starting point that could lead to a different clinical treatment paradigm. This could empower clinicians, who manage chronic wounds, to use all the diagnostics, therapeutic agents and therapeutic methods already used by clinicians who successfully treat other chronic infections, such as chronically infected cystic fibrosis (CF) patients, chronic otitis media and chronic conjunctivitis which are known to be related to biofilm presence. **JWC**

Acknowledgements
The project was mainly supported by AISLeC. Donations from industries have been used for organizational purposes. The list of contributing Industries follows: BBraun, Bsn, Coloplast, Convatec, Plurogen, Smith & Nephew . None of the sponsor had a role in the study design, data collection and analysis, or writing of the anuscript. This article totally reflects the opinion of the Authors and it was not contingent upon the approval of any of the sponsors. AISLeC warmly acknowledges all the sponsors for the transparent and unconditioned support

References

1 Posnett, J., Gottrup, F., Lundgren, H., Saal, G. The resource impact of wounds on health-care providers in Europe. J Wound Care 2009; 18: 4, 154–161.

2 Trengove, N.J., Stacey, M.C., McGechie, D.F., Mata, S. Qualitative bacteriology and leg ulcer healing. J Wound Care 1996; 5: 277–280.

3 Burmolle, M., Thomsen, T.R., Fazli, M. et al. Biofilms in chronic infections—a matter of opportunity - monospecies biofilms in multispecies infections. FEMS Immunol Med Microbiol 2010; 59: 324–336.

4 Gristina, A.G., Price, J.L., Hobgood, C.D. et al. Bacterial colonization of percutaneous sutures. Surgery 1985; 98: 1, 12–19.

5 Percival, S.L., Bowler, P.G. Biofilms and their potential role in wound healing. Wounds 2004; 16: 7, 234–240.

6 Høiby, N., Bjarnsholt, T., Moser, C. et al. ESCMID guideline for the diagnosis and treatment of biofilm infections 2014. Clin Microbiol Infect 2015; 21 Suppl: S1–S25.

7 Gottrup, F., Apelqvist, J., Bjarnsholt, T. et al. Antimicrobials and Non-Healing Wounds. Evidence, controversies and suggestions-key messages. J Wound Care 2014; 23: 10, 477–482.

8 Lebrun, E., Tomic-Canic, M., Kirsner, R.S. The role of surgical debridement in healing of diabetic foot ulcers. Wound Repair Regen 2010; 18: 433–438.

9 Caputo, W.J., Beggs, D.J., DeFede, J.L. et al. A prospective randomised controlled clinical trial comparing hydrosurgery debridement with conventional surgical debridement in lower extremity ulcers. Int Wound J 2008; 5: 2, 288–294.

10 Rhoads, D.D., Wolcott, R.D., Percival SL. Biofilms in wounds: management strategies. J Wound Care 2008; 17: 11, 502–508

11 National Institutes of Health. Consensus Development Program. http://consensus.nih.gov/ABOUTCDP.htm#intro, 2009.

12 GRADE. Available at: http://www.gradeworkinggroup.org (accessed June 2016).

13 Jaeschke, R. et al. Use of GRADE grid to reach decisions on clinical practice guidelines when consensus is elusive. BMJ 2008; 337: a744.

14 Beele, H., Meuleneire, F., Nahuys, M,. Percival, S.L. A prospective randomised open label study to evaluate the potential of a new silver alginate/carboxymethylcellulose antimicrobial wound dressing to promote wound healing. Int Wound J 2010; 7: 4, 262–270.

15 Romanelli, M., Dini, V., Barbanera, S., Bertone, M.S. Evaluation of the efficacy and tolerability of a solution containing propyl betaine and polihexanide for wound irrigation. Skin Pharmacol Physiol 2010; 23 Suppl: 41–44.

16 Metcalf, D., Bowler, P.G., Hurlow, J. Clinical algorithm for wound biofilm identification. J Wound Care 2014; 23: 3, 137–142.

17 Gottrup, F., Apelqvist, J., Bjarnsholt, T. et al. EWMA document: Antimicrobials and non-healing wounds. Evidence, controversies and suggestions. J Wound Care. 2013; 22: 5 Suppl, S1–S89.