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Use of a TLC-Ag dressing on 2270 patients with wounds at risk or with signs of local infection: an observational study

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Objective: A description of wounds treated with a poly-absorbent silver dressing (with technology lipido-colloid with silver ions, TLC-Ag), and evaluation of the short-term clinical impact of the dressing on the wound healing process, under real-life conditions.
Method: A large, prospective, multicentre, observational study of patients in 81 centres in Germany, presenting with an exuding wound at risk or with clinical signs of local infection for whom the evaluated TLC-Ag dressing (UrgoClean Ag, Laboratoires Urgo, France) has been prescribed. Main outcomes included: reduction in number of wound infections diagnosed and clinical signs of local infection, wound healing rate, clinical assessment of wound healing progression, relative wound area reduction (RWAR), local tolerability, handling and acceptance of the dressing.
Results: A total of 2270 patients with acute and chronic wounds of various aetiologies were treated with the evaluated dressing for a mean duration of 22±13 days. All clinical signs of local infection and the diagnosed wound infections were substantially reduced at two weeks after the treatment initiation. All wound infection parameters continued to reduce until the last visit. In the meantime, clinical improvement in wound healing was reported in 98.9% of acute wounds, with a wound closure rate of 68.5%. In chronic wounds, a median RWAR of 57.4% was achieved, with an improvement in healing process documented by clinicians in 90.6% of cases, stabilisation in 6.1% and worsening in 3.2%. Similar results were reported, regardless of exudate level and proportion of sloughy and granulation tissues in the wound bed at baseline. The dressing was well tolerated and well accepted by both patients and health professionals.
Conclusion: These results, documented in a large cohort of patients treated in current practice, support and complete the clinical evidence on the healing properties and safety profile of the TLC-Ag dressing in the management of wounds at risk or with clinical signs of local infection, regardless of wound and patient characteristics.
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acute wounds • chronic wounds • observational study • poly-absorbent fibres • TLC-Ag • wound infection

Wound infections are associated with delayed wound healing and increased risk of complications, and can, in extreme cases, lead to systemic infection or amputation.[1–4] Wound infections increase patients' anxiety and reduce their quality of life (QoL).[5] They are also responsible for increasing the economic burden related to wound management, and the number and duration of hospital stays.[3,4] Most wound infections are diagnosed by health professionals in the community where their treatment is initiated.[5]

Understanding the risk factors and signs and symptoms of wound infection is crucial for early detection and timely treatment. Diagnosis of wound infection is principally based on the heath professionals assessment of the patient, inflammatory responses, wound and periwound tissue.[6] Effective wound infection management requires optimisation of the individual host response and the wound healing environment, the reduction in microbial load, and regular assessment of the clinical situation.[6] For wounds at risk or with clinical signs of local infection, standard of care (SoC) usually includes wound cleansing, debridement and the selective use of an appropriate topical antimicrobial and dressing.[6]

Increasing occurrence of antibiotic resistance has generated a search for alternative solutions and development of various antimicrobial agents, such as silver, PHMB (polyhexamethylene biguanide) or honey.[6,7] Silver dressings are globally well accepted, despite some controversy, notably due to clinical evidence disparity related to inappropriate use.[6–8] According to a recent meta-analysis of clinical studies from 2000 to 2015, clinical evidence shows that, used selectively and for a limited period of time, silver

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dressings can provide, in addition to their antimicrobial effects, improved QoL for patients and good cost-effectiveness.[9] In particular, use of dressings including the technology lipido-colloid with silver ions (TLC-Ag) has been supported by high-quality clinical evidence in the management of wounds at risk or with clinical signs of local infection, and these TLC-Ag dressings have been commonly used in this indication since 2006. Their superior efficacy in reducing wound bioburden and promoting wound healing has been demonstrated compared with dressings without silver in a randomised controlled trial (RCT) on chronic leg ulcers.[10,11] TLC-Ag dressings have also been proven to be well tolerated and accepted both by health professionals and patients, notably due to their atraumatic and painless removal at dressing changes in various clinical studies conducted in the management of acute and chronic wounds.[11–14]

More recently, in order to optimise the usefulness of TLC-Ag dressings in the management of wounds regardless of their level of exudate or healing stage (debridement or granulation), a new TLC-Ag dressing with cohesive poly-absorbent fibres was developed. Poly-absorbent fibres ensure the absorption of exudate and the trapping of sloughy residues.[15–17] The autolytic properties of these poly-absorbent fibres have been demonstrated compared with a hydrofiber dressing in a European RCT involving 159 patients.[17] After six weeks of treatment, a significantly higher reduction of sloughly tissue was reported in the group of patients treated with the poly-absorbent fibre dressing compared with the group of patients treated with hydrofiber, while the safety profile of both dressings were demonstrated to be similar. *In vitro* investigations have also established a synergic action of the TLC-Ag matrix and the poly-absorbent fibres against meticillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* biofilms.[18,19] The clinical efficacy and safety profile of the new TLC-Ag dressing with poly-absorbent fibres has been evaluated in a prospective, open-label study, conducted in dermatology and vascular medicine hospital departments and in private-practice of specialised physicians, on 37 patients with chronic leg ulcers.[20] After four weeks of treatment, reductions of all clinical signs of local infection were reported and wound healing progression was evident based on a substantial reduction in sloughy tissue, an increased in granulation tissue, a decrease in wound surface area and an improvement of periwound skin. The dressing also presented a good safety profile associated with a high level of acceptability, noted by both patients and nursing staff. However, to our knowledge, the performance of this dressing had yet to be assessed in an observational study on a cohort of patients treated according to daily routine practice.

We aimed to evaluate the TLC-Ag dressing with poly-absorbent fibres in a large, unselected cohort of patients with wounds at risk or with clinical signs of local infection, under real-life conditions.

Methods

Study design and patients

This observational study was a prospective, non-interventional, multicentre study. It was conducted with physicians (general practitioners and specialists), located across all German federal states to ensure a representative cohort of patients and physicians.

Any patient with an exuding wound at risk or with clinical signs of local infection that the physician had decided to treat with the evaluated dressing was eligible. In the case of patients presenting with multiple eligible wounds, the wound with the largest area was selected for the study. Patients were followed up in the outpatient setting or during home visits, for a maximum duration of four weeks and with a maximum of three documented visits. All decisions with regard to diagnosis and therapy were made by the treating physician and the therapeutic procedure was not influenced by the study. No specific education or training on the dressing was given to the participating physicians and patients before commencing the study. Clinical best practices were assumed, for example with compression therapy for venous leg ulcers (VLUs) or appropriate offloading for diabetic foot ulcers (DFUs) and differences in care protocols were expected between clinical settings, for example use of antibiotics as per institutional protocols. The participating physicians could discontinue the use of the evaluated dressing and the patient's participation in the study at any point.

Study wound dressing

The evaluated wound dressing, UrgoClean Ag (Laboratoires URGO, France) is a sterile, non-woven pad of cohesive poly-absorbent fibres, coated with a soft adherent healing matrix impregnated with silver (3.5% silver sulfate; TLC-Ag). According to the manufacturer's instructions, it is recommended to change the dressing every 1–2 days during the wound desloughing phase. Thereafter, the dressing should be changed as often as required, depending on the exudate volume and clinical status of the wound and at least once a week.

Outcomes and assessments

At the initial visit, relevant demographic information and medical history of the patient were recorded along with the wound characteristics (aetiology, duration, wound area, clinical signs and risk factors for infection, exudate level, wound bed tissue, condition of the periwound skin) and the previous and current wound treatment, including previous dressings used, current antibiotic treatment and local wound care.

The assessment of the first application of the evaluated dressing (ease of application, conformability and patient's acceptance) was also documented. At the interim visit, the wound characteristics and wound healing progression and the presence of clinical signs of local infection or of a wound infection were documented.

Outcomes related to the final assessment visit included:

- Treatment and evaluation duration (in days)
- Overall wound healing progression ('wound healed', 'greatly improved', 'slightly improved', 'unchanged', 'slightly deteriorating' or 'greatly deteriorating')
- Relative reduction of wound area (%)
- Reduction of the proportion of diagnosed wound infection and of the clinical signs of infection (pain, erythema, oedema, malodorous wound, friable granulation tissue)
- Reduction of the percentage of sloughy tissue on the wound bed
- Change in the exudate level ('improved', 'stabilised', 'worsened')
- Change in the periwound skin condition ('improved', 'unchanged', 'deteriorating'), based on a five-point scale (1='healthy skin' to 5='greatly impaired')
- Frequency of dressing changes and acceptability of the dressing (ease of application, ease of handling, conformability, patient's acceptance)
- Identification of the main reasons for having selected the evaluated dressing
- Overall opinion of physicians ('better,' 'identical' or 'worse') on the characteristics of the evaluated dressing (antimicrobial efficacy, desloughing properties, application, conformability, handling of the dressing, tensile strength, patient's pain, acceptance by the patient) compared with their previous experience with commonly used silver dressings.

Throughout the study period, the occurrence of local adverse events were documented and the local tolerance of the dressing was assessed by the physicians at the final visit according to the following definitions: 'very good' (no local adverse event related to the device during the observation period), 'good' (not more than one temporary event of mild or moderate intensity) and 'poor' (more than one event or at least one severe temporary event or one persistent event).

Table 1. Aetiologies of treated wounds (n=2270)

Wound aetiology	n	(%)
Chronic wounds	**1050**	**(46.3)**
Diabetic foot ulcer	545	(24.0)
Venous leg ulcer	229	(10.1)
Pressure ulcer	118	(5.2)
Mixed aetiology ulcer	95	(4.2)
Arterial ulcer	33	(1.5)
Lymphatic ulcer	28	(1.2)
Neoplastic wound	2	(0.1)
Acute wounds	**876**	**(38.6)**
Abrasion	291	(12.8)
Postoperative wound	264	(11.6)
Burn/scald	134	(5.9)
Contusion	83	(3.7)
Intruding foreign body wound	60	(2.6)
Bite	39	(1.7)
Iatrogenic wound	5	(0.2)
Wounds with another aetiology (unclassified)	**339**	**(14.9)**
Unspecified aetiologies	**5**	**(0.2)**

Data management

An electronic data entry system with a standardised electronic case report form (eCRF) was used in this clinical study. All participating physicians received specific access codes to enable them to enter their data. The electronic system performed automatic checks for data completeness and inconsistent data. The data management and quality assurance of the study was carried out by an independent contract research organisation (INPADS GmbH, Germany) in accordance with the recommendations on planning, conducting and analysing of post-marketing surveillance studies of the Federal Institute for Drugs and Medical Devices/Paul Ehrlich Institute (BfArM/PEI, 2010). The patients included in the study were informed about the processing of their personal and health data by their participating physicians, and gave their explicit and written consent in processing their individual data in the study. In the case of minors (<18 years of age), written consent was given by their parents or guardians.

Statistical analysis

The estimation of the cohort size required for this observational study was based on the literature and on experience from previous observational studies, in order to allow a pragmatic evaluation of the dressing's performance in a sufficiently diverse cohort of patients and physicians.[13,14,20,21] Statistical analyses were performed according to the statistical analysis plan, by an independent contract research organisation (INPADS), using SAS 9.1.3 for windows (Statistical Analysis System, SAS Institute, US). The biometric analyses and dressing performance evaluations were merely descriptive, and no statistical tests were used. Values were reported as mean±standard deviation (SD); median and inter-quartile range (IQR), or count and percentage. Efficiency and safety analyses included all patients for whom the initial visit and the final visit were documented. Missing values were not replaced.

Subgroup analyses were intended and performed based on the classification of pre-identified aetiologies:

- 'Chronic' wounds: diabetic foot ulcers (DFUs), leg ulcers, pressure ulcers (PUs), and neoplastic wounds
- 'Acute' wounds: abrasions, postoperative wounds, burns, contusions, intruding foreign body wounds, bites and iatrogenic wounds
- 'Unclassified' wounds: wounds of any other aetiology.

Table 2. Demographics and medical history of treated patients

	Chronic wounds (n=1050)		Acute wounds (n=876)		Unclassified wounds (n=339)	
Demographics						
Male/female, n (%)*	541 (51.5)	508 (48.4)	463 (52.9)	413 (47.1)	194 (57.2)	145 (42.8)
Age (years), mean±SD	72.4±13.6		53.2±23.0		54.0±22.7	
BMI (kg/m²), mean±SD†	30.7±23.7		26.8±11.4		27.5±6.5	
Comorbidities, multiple answers possible, n (%)						
Diabetes type 2	718	(68.4)	182	(20.8)	47	(13.9)
Cardiac insufficiency	337	(32.1)	192	(21.9)	50	(14.7)
Limited mobility	299	(28.5)	139	(15.9)	34	(10.0)
Confirmed peripheral neuropathy	273	(26.0)	58	(6.6)	15	(4.4)
Renal insufficiency	216	(20.6)	75	(8.6)	16	(4.7)
Obesity: body mass index (BMI) ≥30 kg/m²	176	(16.8)	120	(13.7)	37	(10.9)
Respiratory insufficiency	94	(9.0)	80	(9.1)	18	(5.3)
Malnutrition	39	(3.7)	73	(8.3)	19	(5.6)
Immunodeficiency	12	(1.1)	63	(7.2)	15	(4.4)
Current infectious problem independent of the wound	19	(1.8)	65	(7.4)	18	(5.3)
Chemotherapy	23	(2.2)	80	(9.1)	5	(1.5)
Other disorders	182	(17.3)	141	(16.1)	19	(5.6)
Missing data	*29*	*(2.8)*	*223*	*(25.5)*	*181*	*(53.4)*
Multiple wounds, n (%)	**161**	**(15.3)**	**81**	**(9.2)**	**10**	**(2.9)**
Missing data	8	(0.8)	3	(0.3)	1	(0.3)
Recurrence of the wounds, n (%)	**264**	**(25.1)**	**16**	**(1.8)**	**11**	**(3.2)**
Missing data	8	(0.8)	13	(1.5)	3	(0.9)

*One gender value missing for a patient with lymphatic ulcer; SD—standard deviation; †The mean BMI is given for the cohorts of patients ≥17 years old; The data from the five patients with unspecified wounds are not reported here

Post-hoc analyses were also performed according to an analysis plan in order to determine the performances of the dressing depending on exudate level and wound bed tissue proportion at initiation of the treatment. Wounds were considered to be in 'debridement stage' when the wound bed was covered by <50% granulation tissue, and in 'granulation stage' when the wound bed was covered by ≥50% granulation tissue.

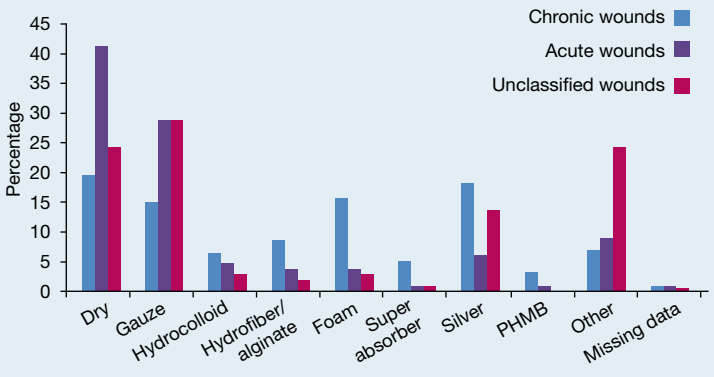
Ethical approval

The study was conducted in accordance with the German Medical Devices Act and Federal data protection law (Bundesdatenschutzgesetz, 2009). Due to the non-interventional design of this study performed on a CE-marked device, and used according to the manufacturer's instructions, no ethics

Table 3. Conditions at risk of wound infection reported in the subgroup of patients with neither a diagnosed wound infection nor one of the five pre-identified clinical signs of wound infection

Individual conditions	n=642	(100%)
Immunosuppressive condition	263	(41.0)
Contaminated or dirty wound	141	(22.0)
Extreme age/older patients	69	(10.7)
Extreme age/young patients	1	(0.2)
Prolonged hospitalisation/postoperative wounds	66	(10.3)
Critical wound surface or depth, possibly with direct contact with organ	57	(8.9)
Haematological or cancer affection	36	(5.6)
Worsening or stagnating wound	144	(22.4)

Fig 1. Dressings used on the wounds before poly-absorbent silver dressing



PHMB—polyhexamethylene biguanide

committee or authorities approval were required.

Results

Baseline characteristics of included patients

Between September 2016 and September 2017, a total of 2297 patients with wounds at risk or with clinical signs of local infection, treated with the evaluated dressing, were included by 81 active centres in Germany.

Median number of patients recruited per centre was 10 (IQR: 5–25). Due to incomplete documentation, 27 patients (1.2%) were excluded, and the evaluations of 2270 patients were considered in the analyses. Patients were followed on average for 22±13 days. An interim visit, performed after 11±8 days of treatment, was documented for 2244 patients (98.9%). The remaining patients had only an initial and final visit.

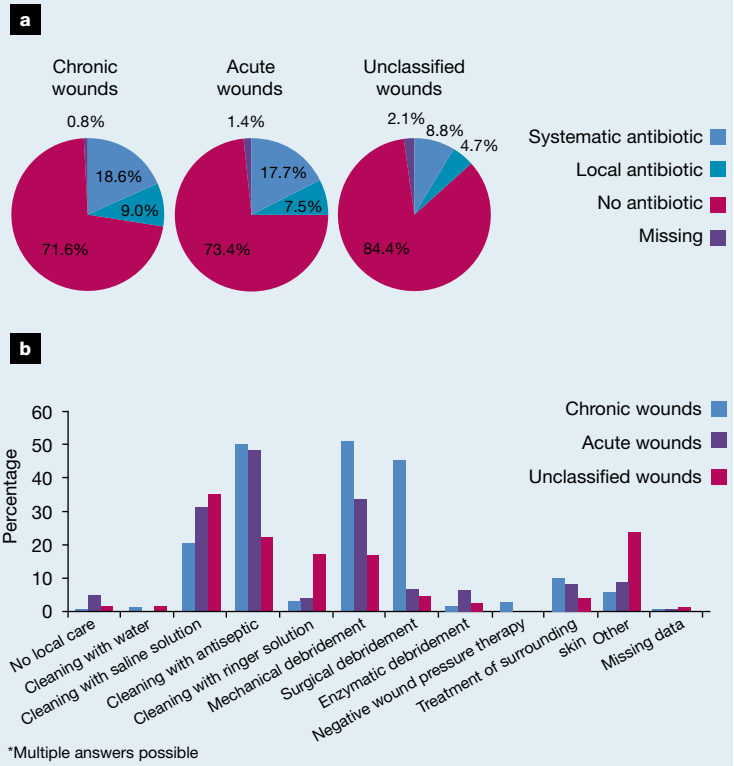
As reported in Table 1, all types of wound aetiologies were included in this observational study. Among the chronic wounds (n=1050 patients; 46.3%), the most frequent aetiologies were DFUs (n=545; 24.0%), VLUs (n=229; 10.1%) and PUs (n=118; 5.2%). Abrasions (n=291; 12.8%), postoperative wounds (n=264; 11.6%) and burns (n=134; 5.9%) were the most frequently treated acute wounds (n=876; 38.6%). Other wounds had a different aetiology than the ones pre-identified as 'chronic' or 'acute' and were gathered in an 'unclassified wounds' subgroup (n=339; 14.9) or were of an unspecified aetiology (n=5; 0.2%).

Gender by wound aetiology was consistent with the literature. The age of the included patients ranged between two years old and 97 years old. Patients with PUs were on average the oldest subgroup of patients (77.7±14.8 years old) while patients with bites were the youngest (35.3±20.6 years old). A total of 77 patients were <18 years old. Most had acute wounds (abrasions n=21, burns n=15, bites n=10, wounds caused by an intruding foreign body n=8, contusions n=7, postoperative wounds n=7), eight patients had an unclassified type of wound, and one patient had a PU.

Patients with chronic wounds had on average a higher body mass index (BMI, 30.7±23.7kg/m^2) than patients with acute (26.8±11.4kg/m^2) or unclassified wounds (27.5±6.5kg/m^2).

Due to the high number of DFUs in the study (n=545, 24%), the proportion of patients with type 2 diabetes and confirmed peripheral neuropathy were particularly high in the chronic wound cohort (68.4% and 26.0%, respectively) (Table 2). Patients with chronic wounds often also had cardiac insufficiency (32.1%), immobility (28.5%), renal insufficiency (20.0%) and obesity (16.8%). These comorbidities were also reported in the subgroup of patients with acute or unclassified wounds but to a much lesser extent. Respiratory insufficiency, malnutrition, immunodeficiency, current infection not related to the wound and chemotherapy were reported with frequencies ranging between 7.2% and 9.1% in patients with acute wounds at risk or with clinical signs of local infection. Multiple wounds and recurrent wounds were respectively documented in 15.3% and 25.1% of the patients with a chronic wound (versus 9.2% and 1.8% in the cohort of patients with an acute wound and 2.9% and 3.2% in patients with an unclassified wound).

Fig 2. Antibiotic therapy (**a**) and local wound care* (**b**)



*Multiple answers possible

Baseline characteristics of the wounds, previous and current treatments and local care

Treatment with the evaluated silver dressing was initiated after a median wound duration of 30.5 days for chronic wounds, five days for acute wounds and two days for unclassified wounds. Among chronic wounds,

Table 4. Wound characteristics at baseline

	Chronic wounds (n=1050)		Acute wounds (n=876)		Unclassified wounds (n=339)	
Median wound area, cm² (IQR)	4.7	(1.6–11.0)	6.3	(3.1–13.7)	6.3	(3.1–9.4)
Wound healing stage						
Granulation stage, n (%)	226	(21.5)	268	(30.6)	92	(27.1)
Debridement stage, n (%)	757	(72.1)	512	(58.4)	231	(68.1)
Missing	67	(6.4)	96	(11.0)	16	(4.7)
Level of exudate						
High/moderate exudate, n (%)	564	(53.7)	435	(49.7)	95	(28.0)
Little/no exudate, n (%)	484	(46.1)	435	(49.7)	242	(71.4)
Missing	2	(0.2)	6	(0.7)	2	(0.6)
Periwound skin condition score						
Healthy skin (1)	108	(10.3)	174	(19.9)	97	(28.6)
(2)	323	(30.8)	250	(28.5)	92	(27.1)
(3)	365	(34.8)	285	(32.5)	127	(37.5)
(4)	183	(17.4)	131	(15.0)	19	(5.6)
Greatly impaired skin (5)	63	(6.0)	26	(3.0)	4	(1.2)
Missing	8	(0.8)	10	(1.1)	0	(0.0)

IQR—interquartile range

the shortest wound durations were reported for PUs and lymphatic ulcers (median duration: 14.0 and 17.5 days, respectively), and neoplastic wounds presented the longest duration (50.5 days). With regard to acute wounds, the treatment was initiated after three days in burns and iatrogenic wounds, and it was started after 10 days in postoperative wounds (median values).

At baseline, 318 patients (14.0%) already had a diagnosed wound infection and 1310 (57.7%) had at least one of the five pre-suggested clinical signs of infection (malodour, spontaneous pain, localised oedema, erythema and friable tissue granulation). When only one sign was present (n=808), the most current sign was malodour (n=299; 37.0%), followed by spontaneous pain (n=227; 28.1%) and the presence of a localised oedema (n=210; 26.0%). Periwound erythema (n=45, 5.6%) and friable granulation tissue (n=27, 3.3%) were more rarely reported as a unique clinical sign of local infection.

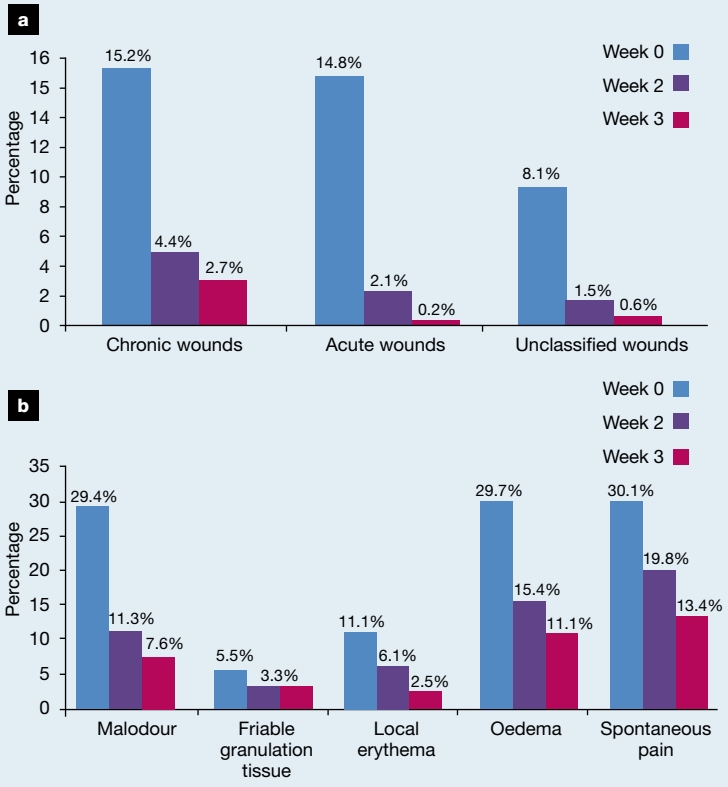
As to the patients in whom no wound infection had been diagnosed and none of the five pre-suggested clinical signs of local infection had been identified (n=642; 28.3%), almost half of them had an immunosuppressive condition (n=263; 41.0%), 141 (22.0%) had a contaminated or dirty wound and 144 (22.4%) had a stagnated or worsening wound. The other conditions reported as at risk of infection in these patients are presented in Table 3.

As illustrated in Fig 1, previous dressings included mainly dry dressings (n=648; 28.5%) or gauze (n=512; 22.6%), especially for acute wounds and unclassified wounds. Dressings with antimicrobial properties were previously used in 335 (14.8%) of the cases. Most patients did not receive antibiotics at baseline (n=1685; 74.2%); 381 (16.8%) were under systemic antibiotic therapy and 177 (7.8%) were receiving local antibiotic therapy; the remaining 27 (1.2%) had missing data (Fig 2). Most frequently, the wounds were cleaned with antiseptic solutions (n=1026; 45.2%). Mechanical wound cleaning and surgical debridement were also performed in 877 (38.6%) and 557 (24.5%) of the cases, respectively.

The median wound area of the chronic wounds was 4.7cm² (IQR: 1.6–11.0cm²), ranging between 2.1cm² (IQR: 1.1–7.1cm²) for DFUs and 11.0cm² (IQR: 3.0–23.6cm²) for lymphatic ulcers (Table 4). The median area of the acute wounds was larger with a value of 6.3cm² (IQR: 3.1–3.7cm²), ranging between 0.9cm² (IQR: 0.8–1.6cm²) for iatrogenic wounds to 11.0cm² (IQR: 4.0–21.2cm²) for burns. The median area of the unclassified wounds was 6.3cm² (IQR: 3.1–9.4cm²).

All patients considered, wound beds were covered, on average, by 48±26% of sloughy tissue, by 39±28% of granulation tissue and by 13±20% of necrotic tissue. At baseline, 588 wounds (25.9%) were in the granulation stage of the wound healing process, i.e. with a wound bed covered by more than 50% of granulation tissue. Wounds with high or moderate exudate levels (n=1124;

Fig 3. Evolution of the diagnosed wound infection (**a**) and of the clinical signs of local infection (**b**) under the poly-absorbent silver dressing treatment

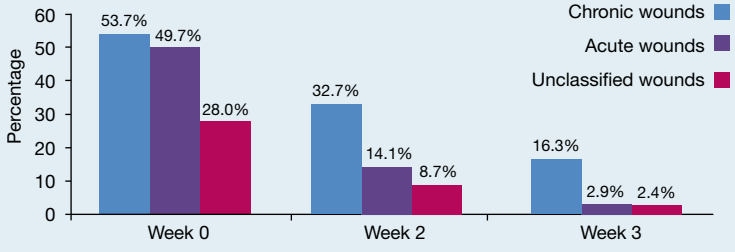


49.5%) and those with little or no exudate (n=1161; 51.1%) were similarly represented in the overall patient population. The majority of patients (n=1873; 82.5%) presented at baseline with an impaired condition of their periwound skin.

Reduction of diagnosed wound infection and clinical signs of infection throughout the treatment period

The number of diagnosed wound infections sharply reduced from 318 (14.0%) at baseline, to 70 (3.1%) after two weeks of treatment (at the interim visit) and to 32 (1.4%) at the final visit. Similar results were obtained for all types of wounds. As illustrated in Fig 3, the proportion of clinical signs of local infection also decreased drastically between the initiation of the treatment and the interim visit and continued to decrease until the final visit at week three, whatever the clinical sign. An antibiotic therapy was no longer required in 80.6% of those patients who had it prescribed at baseline (450/558). At the final visit, 59 patients (2.6%) were under systemic antibiotic therapy (compared with 381 at baseline, 16.8%).

Fig 4. Evolution of wounds with high or moderate exudate levels during the treatment period



As reported in Fig 4, the proportion of wounds with a high or moderate level of exudate continuously decreased during the treatment period, in all types of wounds. At two weeks after the initiation of the treatment with the poly-absorbent silver dressing, the level of exudate was reduced in 997 patients (44.4%), stabilised in 1130 patients (50.5%) and still increasing in 100 patients (4.5%). This improvement in exudate levels compared to baseline in the global cohort was prolonged the following week with a reduction of the exudate level in 1454 patients (64.1%). A stabilised level was also reported in 677 patients (29.8%) and an increased level in 57 patients (2.5%).

Meanwhile, at the final visit, the periwound skin condition improved in 1399 patients (61.6%), remained unchanged in 803 patients (35.4) and worsened in 42 patients (1.9%). The proportion of patients with a healthy skin condition rose from 16.7% (n=380) at baseline to 50.8% (n=1153) by the third week of treatment.

Wound healing progression under the TLC-Ag dressing treatment

Around two weeks after the TLC-Ag treatment was initiated, wound closure or an improvement in the wound healing was reported in 83.4% (868/1041) of chronic wounds, in 97.1% (838/863) of acute wounds and in 96.7% (324/335) of unclassified wounds (Fig 5). At the final visit, wound closure rates were 68.5% (n=600/876) in acute wounds, 49.6% (n=168/339) in unclassified wounds and reached 21.5% (n=226/1050) in chronic wounds, despite the underlying causes of the chronicity of the wounds and the risk factors or clinical signs of local infection at the initiation of treatment. In acute wounds, closure rate ranged from 64.9% (n=155/264) in postoperative wounds to 89.7% (n=35/39) in bites. Among chronic wounds, the highest closure rate by week three was reported in PUs (33.1%; n=39/118) and the lowest in DFUs (17.8%; n=97/545). Improvement of the wound was reported in the large majority of patients resulting in >90% of patients experiencing positive wound healing outcomes, whatever the type of wound.

The wound surface area substantially decreased throughout the treatment period. In the group of chronic wounds, a median relative wound area reduction (RWAR) of 21.0% (IQR: 0.0–50.0%) was reported at the interim visit and the good healing progression pursued with a median RWAR of 57.4% (IQR: 21.6–95.4%) after three weeks of treatment with the poly-absorbent silver dressing, ranging between 38.8% in DFUs (IQR: 15.0–89.6%) and 81.6% in PUs

(36.0–100.0%). In acute wounds, the median RWAR was of 54.0% (IQR: 22.3–77.2%) after two weeks of treatment and reached 100.0% (IQR: 93.8–100.0%) by week three. In unclassified wounds, the median RWAR was 50.0% at the interim visit (IQR: 0.0–75.5%) and 99.1% (IQR: 75.0–100.0%) at the final visit.

All wound types showed a reduction of sloughy tissue and an increase of granulation tissue. Overall, the proportion of sloughy tissue decreased from 48±26% at baseline to 22±23% at the final visit.

Performance of the dressing depending on wound healing stage at treatment initiation

In the group of patients for whom the treatment had been initiated at the granulation stage (n=588) of the wound healing process (granulation tissue ≥50%), the median RWAR reached 100.0% (IQR: 50.0–100.0%) at the final visit (Fig 6). By week three, 53.4% of the wounds had healed and 41.8% had greatly or slightly improved. Positive healing outcomes were similarly reported in those patients whose treatment had been initiated in the debridement stage, especially considering the negative impact that sloughy tissue usually has on the wound healing process. In addition to the 39.1% of wound that had healed, 55.1% of wounds had been judged by physicians as 'improving' in terms of their wound healing progression. In total, the healing process of 94.2% of wounds had improved. This improvement is also illustrated by a median RWAR of 90.6% (IQR: 45.3–100.0%) by week three. In both granulation and debridement subgroups, the proportion of worsening wounds was similar and low (1.6% and 2.0%, respectively), demonstrating the positive healing performance of the poly-absorbent silver dressing, regardless of the stage of wound healing at treatment initiation.

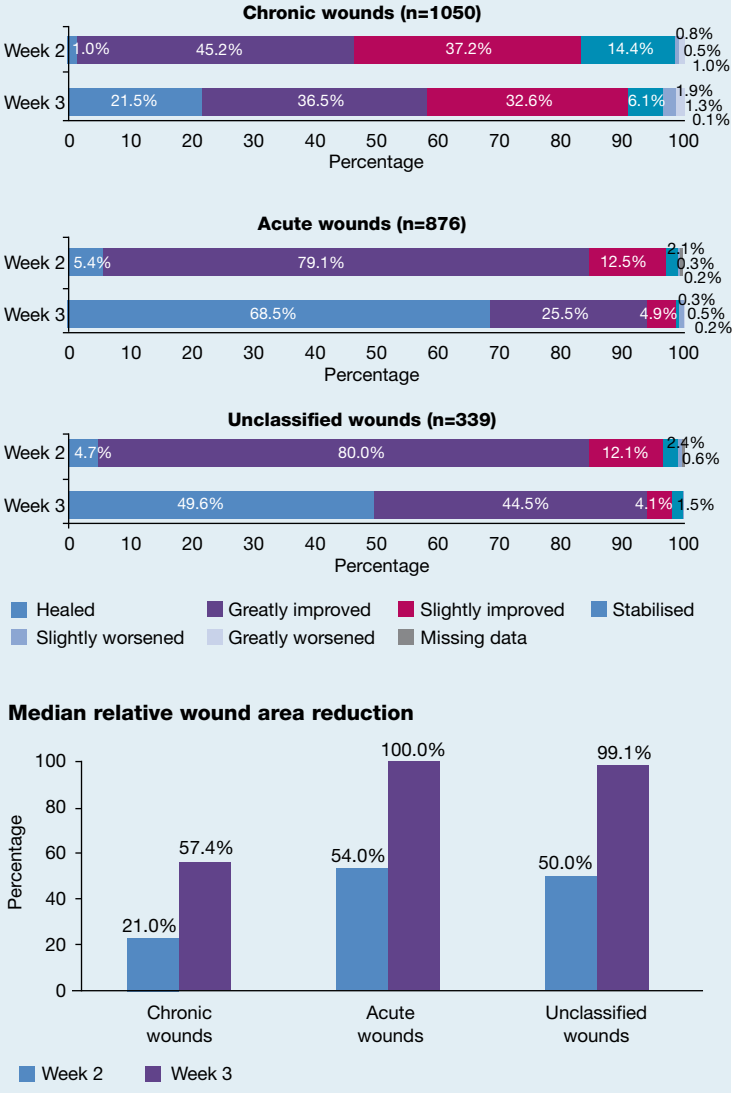
Performance of the dressing depending on the level of exudate at treatment initiation

As represented in Fig 7, similar results were achieved in both groups of wounds that had a 'high or moderate level of exudate' and 'little or no exudate' at baseline in terms of RWAR 93.3% (IQR: 53.0–100.0) versus 93.8% (IQR: 40.0–100.0) respectively), wound healing rate (43.9% versus 43.7%, respectively, and proportion of improved wounds (51.1% versus 51.2%, respectively), demonstrating the positive effect of the poly-absorbent silver dressing on the wound healing process, regardless of the level of exudate at treatment initiation.

Safety assessment: local tolerance

The local tolerance of the dressing was assessed by the physicians as 'very good' in 1869 patients (82.3%) and 'good' in 398 patients (17.5%). 'Poor' local tolerance was reported in two cases (0.1%) and the data was missing for one patient. No intolerance to the dressing was documented during the observation period. The good safety profile of the dressing was similarly reported in all patients, including patients <18 years old, patients at risk of local infection and patients with clinical signs of local infection, and regardless of the level of exudate at baseline (data not shown).

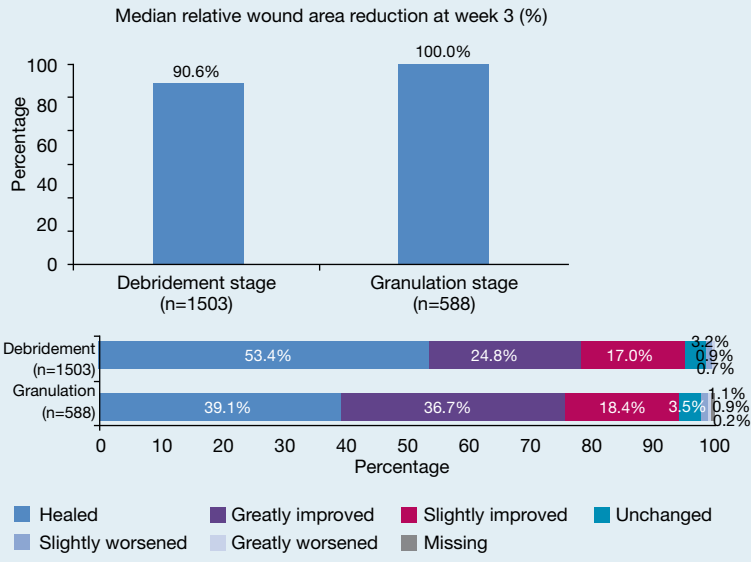
Fig 5. Wound healing progression under the TLC-Ag dressing treatment



Acceptability, handling and overall assessment of the TLC-Ag dressing performance compared with other antimicrobial dressings

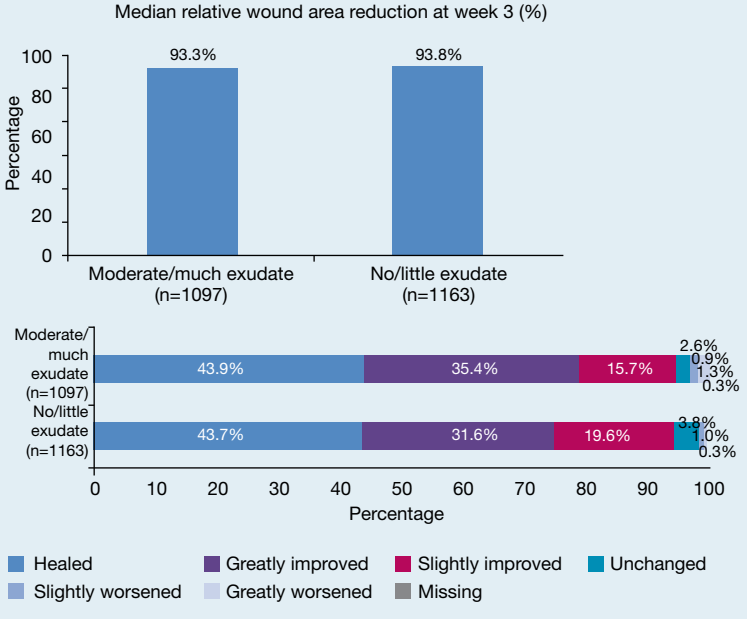
Throughout the course of the study, the evaluated dressings were changed on average 2.5±0.2 times a week. The most frequently applied size of dressing was 6x6cm^2, especially at the final visit (80.1%); larger sizes (10x12cm^2, 15x15cm^2 and 15x20cm^2) had been changed for smaller ones during the treatment period, in correlation with wound area reduction. The physicians of the 81 centres involved in this study concluded the dressing had, in the majority of cases, been 'very easy' or 'easy' to apply since its first application (n=2232; 98.3%), 'very conformable' or

Fig 6. Final wound healing assessment, depending on the wound healing stage at baseline (debridement versus granulation)



'conformable' (n=2229; 98.2%) and 'very easy' or 'easy' to handle (n=2251; 99.2%). At both the initial and final visits, the patients' acceptance of the dressing was also documented as 'very good' or 'good' in 96.8% (n=2198) and 98.9% (n=2246) of the cases, respectively. Of note, the investigators have specified that they had selected the evaluated dressing, among the other options of antimicrobial absorbent dressings available, for an important part due to its painless dressing changes in 54.6% of the cases (n=1240 patients), due to the pain history of the patient in 24.3% of the cases (n=552 patients) or directly due to a specific request from the patient in 24.9% of the cases (n=566 patients).

Fig 7. Final wound healing assessment, depending on the wound exudate level at baseline (much or moderate exudate versus no or few exudate)



At the last evaluation, and based on their global experience with the dressings, the physicians expressed their preference towards the evaluated dressing compared with their previous experience with other absorbent antimicrobial dressings commonly used in this indication (Fig 8), in particular in terms of antimicrobial efficacy, desloughing properties, conformability and tensile strength, pain management and patient acceptance. These preferences were similarly reported, whatever the level of exudate at treatment initiation ('none/little' or 'moderate/high').

Discussion

This clinical study is the first to assess the performance of the TLC-Ag dressing, with poly-absorbent fibres, under real-life conditions in a large, unselected cohort of patients with acute and chronic wounds at risk or with clinical signs of local infection. The results demonstrate a use for this new dressing in a variety of wound aetiologies, at different wound healing stages and with different exudate levels. Furthermore, in addition to the clinical signs of local infection classically reported in the literature, various conditions at risk of local infection have been identified as important for clinicians in current practice, such as immunosuppressive conditions, extreme age, critical surface or depth of wounds, presence of soiling or contaminating agents.

Wound infection is commonly regarded as a continuum: from contamination to local infection, to spreading and systemic infection that is associated with a higher risk of severe sepsis and septic shock, which can lead to organ failure and death.[6] Early diagnosis, and timely and appropriate treatment is essential to avoid the severe progression of a wound infection, which would then require systemic antibiotic treatment. Local infection is usually suspected from the appearance of those first subtle clinical signs such as delay in wound healing progression, new or increasing pain, malodour or friable granulation. Overt signs include erythema, local warmth, oedema or swelling, and purulent discharge.[6] However, these signs may be not present or detected due to some underlying comorbidities, such as diabetes which can suppress or conceal the signs of inflammation and make it difficult to identify infection.[7,22–24] Therefore, assessment of wounds for infection should incorporate a full evaluation of the patient and consider how immune status, comorbidities, wound aetiology/status and other factors will affect the risk, severity and likely signs of infection.[6,23,25] In the case of chronic wounds especially, a thorough and expert surveillance of the patient and wound progression using a multidisciplinary team approach is recommended.[23,24]

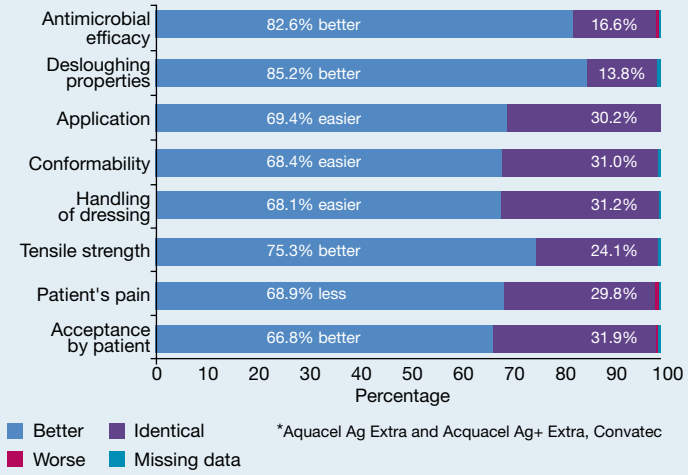
In this observational study, the antimicrobial effect of the dressing was detected since the interim visit (after

the first two weeks of treatment), with a substantial reduction in all clinical signs and diagnosed wound infections. Regular reassessment is strongly recommended in the management of wound infection and for the appropriate use of antimicrobial dressings.[6,7]

Based on the results of this study, the 'two-week challenge' usually recommended by current guidelines to evaluate the relevance and need to pursue an antimicrobial treatment,[6,7] is widely complied with in real-life practice. The additional week of treatment with the evaluated dressing achieved a greater reduction in wound infection-related parameters, while the wound healing progression was already greatly improved. It is sometimes argued that antimicrobial dressings may delay wound healing.[26] The good efficacy and safety profile of the TLC-Ag healing matrix has previously been demonstrated in the management of wounds at risk or with clinical signs of local infection through an RCT and interventional clinical trials.[11,12,20] According to the results of this observational study, the TLC-Ag dressing promoted the wound healing process, with a substantial wound healing rate in acute wounds and considerable wound area reduction in chronic wounds. These results were consistent regardless of the wound aetiology, level of exudate or healing stage at initiation of the treatment. Exudate, slough and devitalised tissue are known to provide a favourable environment for microbial proliferation, inflammatory response exacerbation and wound healing hindrance. In particular, the presence of >50% of sloughy tissue has be shown to significantly slow down the healing process and increase the risk of wound closure failure.[27,28] The positive clinical outcomes reported in this study, on both wounds at granulation and debridement stage, are consistent with the clinical evidence previously published on dressings with these poly-absorbent fibres.[15–17,20] The superior capacity to manage exuding wounds with sloughy tissue compared with hydrofibers has been demonstrated in a RCT.[17] The good performance on wound healing and safety profile of the dressings were also similarly established, both in debridement and at granulation stage, through the analysis of various cohort studies.[15,16,20] This observational study confirms that this is also the case with wounds at risk or with clinical signs of local infection.

Of note, it is also likely that the antimicrobial efficacy of the TLC-Ag healing matrix is enhanced by the action of the poly-absorbent fibres. Based on *in vitro* studies, the ability of the poly-absorbent fibres to disrupt a biofilm matrix improves diffusion of silver ions and their bactericidal activity against sessile cells. The synergic combination of the poly-absorbent TLC-Ag dressing resulted in a reduction of both the volume and thickness of the tested biofilms.[18,19]

Fig 8. Characteristics of the TLC-Ag dressing compared with the ones of absorbent silver dressings* commonly used in this indication, according to the physicians' point of view



Finally, the results achieved within this study in terms of local infection management and wound healing were associated with a good tolerance and a high acceptance of the treatment in the large cohort of patients and physicians involved. These results support a universal profile of the evaluated dressing in the management of wounds at risk or with clinical signs of local infection, regardless of the characteristics of the wounds and patients, which may facilitate wound care.

Limitations

A limitation of non-interventional studies is that no additional assessments, such as measurement of bacterial load in wounds, could be requested; however, this type of study offers a picture of real-life practices. Considering the study's large cohort size, the variety of patients treated, wound care performed and wound infection management carried out, the German community is adequately represented.

Conclusion

The clinical evidence presented in this paper, based on a large cohort of 2270 patients treated under real-life conditions, supports and completes the efficacy and safety profile of the TLC-Ag dressing with poly-absorbent fibres.

The dressing reduced the clinical signs of infection,

Reflective questions

- What are the key elements to provide for an optimal management of wound at risk or with clinical sign of local infection?
- What other benefits than antimicrobial effects can be expected from a poly-absorbent antimicrobial dressing?
- Which type of wounds can be treated with the TLC-Ag poly-absorbent dressings?

promoted wound healing in acute and chronic wounds at risk or with clinical signs of infection, regardless of their level of exudate or their wound healing stage. The dressing was well tolerated and accepted, and rated highly by physicians and patients. Based on their previous experience, the physicians expressed their preference for this new dressing, compared with other antimicrobial dressings currently used in this indication. **JWC**

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References

1 Armstrong DG, Boulton AJ, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med 2017 Jun;376(24):2367–2375. https://doi.org/10.1056/NEJMra1615439
2 Norbury W, Herndon DN, Tanksley J et al. Infection in burns. Surg Infect (Larchmt) 2016; 17(2):250–255. https://doi.org/10.1089/sur.2013.134
3 Badia JM, Casey AL, Petrosillo N et al. Impact of surgical site infection on healthcare costs and patient outcomes: a systematic review in six European countries. J Hosp Infect 2017; 96(1):1–15. https://doi.org/10.1016/j.jhin.2017.03.004
4 Nussbaum SR, Carter MJ, Fife CE et al. An economic evaluation of the impact, cost, and medicare policy implications of chronic nonhealing wounds. Value Health 2018; 21(1):27–32. https://doi.org/10.1016/j.jval.2017.07.007
5 Cutting KF. The current burden of infected wounds. British Journal of Healthcare Management 2016; 22(9):436–438. https://doi.org/10.12968/bjhc.2016.22.9.436
6 International Wound Infection Institute. Wound infection in clinical practice. Principles of best practice. Wounds International 2016. https://tinyurl.com/y2jzft6w (accessed 11 February 2020)
7 International Consensus. Appropriate use of silver dressings in wounds. An expert working group consensus. Wounds International, 2012. https://tinyurl.com/uyouo6r (accessed 11 February 2020)
8 Wounds Australia. Standards for wound prevention and management (3rd edition). Cambridge Media, 2016
9 Dissemond J, Böttrich JG, Braunwarth H et al. Evidence for silver in wound care - meta-analysis of clinical studies from 2000-2015. JDDG: Journal der Deutschen Dermatologischen Gesellschaft 2017; 15(5):524–535. https://doi.org/10.1111/ddg.13233
10 Lazareth I, Meaume S, Sigal-Grinberg ML et al. The role of a silver releasing lipido-colloid contact layer in venous leg ulcers presenting inflammatory signs suggesting heavy bacterial colonization: results of a randomized controlled study. Wounds 2008; 20(6):158–166
11 Lazareth I, Meaume S, Sigal-Grinberg ML et al. Effcacy of a silver lipidocolloid dressing on heavily colonised wounds: a republished RCT. J Wound Care 2012; 21(2):96–102. https://doi.org/10.12968/jowc.2012.21.2.96
12 Lazareth I, Ourabah Z, Senet P et al. Evaluation of a new silver foam dressing in patients with critically colonised venous leg ulcers. J Wound Care 2007; 16(3):129–132. https://doi.org/10.12968/jowc.2007.16.3.27015
13 Schäfer E, Le Guyadec T, Senet P et al. [Use of an evaluation scale for risk of infection and application of Lipidocolloid-dressings with silver – results of a binational observational study including 4960 patients]. Z Wundheilung 2008; 13(2):74–87
14 Allaert FA. [Observational study on the efficacy of TLC-Ag and TLC-NOSF on chronic wounds]. Soins 2014; 785(785):15–18
15 Meaume S, Perez J, Rethore V et al. Management of chronic wounds with an innovative absorbent wound dressing. J Wound Care 2012; 21(7):315–322. https://doi.org/10.12968/jowc.2012.21.7.315
16 Sigal ML, Addala A, Maillard H et al. Evaluation of TLC-NOSF dressing with poly-absorbent fibres in exuding leg ulcers: two multicentric, single-arm, prospective, open-label clinical trials. J Wound Care 2019; 28(3):164–175. https://doi.org/10.12968/jowc.2019.28.3.164
17 Meaume S, Dissemond J, Addala A et al. Evaluation of two fibrous wound dressings for the management of leg ulcers: results of a European randomised controlled trial (EARTH RCT). J Wound Care 2014; 23(3):105–116. https://doi.org/10.12968/jowc.2014.23.3.105
18 Desroche N, Dropet C, Janod P, Guzzo J. Antibacterial properties and reduction of MRSA biofilm with a dressing combining polyabsorbent fibres and a silver matrix. J Wound Care 2016; 25(10):577–584. https://doi.org/10.12968/jowc.2016.25.10.577
19 Desroche N, Dropet C. [Biofilm and association of poly-absorbent fibres and silver ions]. [Article in French] Escarre 2017;74:9–13
20 Dalac S, Sigal L, Addala A et al. Clinical evaluation of a dressing with poly absorbent fibres and a silver matrix for managing chronic wounds at risk of infection: a non comparative trial. J Wound Care 2016; 25(9):531–538. https://doi.org/10.12968/jowc.2016.25.9.531
21 Münter KC, Meaume S, Augustin M et al. The reality of routine practice: a pooled data analysis on chronic wounds treated with TLC-NOSF wound dressings. J Wound Care 2017; 26 Sup2:S4–S15. https://doi.org/10.12968/jowc.2017.26.Sup2.S4
22 Siddiqui AR, Bernstein JM. Chronic wound infection: facts and controversies. Clin Dermatol 2010; 28(5):519–526. https://doi.org/10.1016/j.clindermatol.2010.03.009
23 Schaper NC, van Netten JJ, Apelqvist J et al; International Working Group on the Diabetic Foot (IWGDF). IWGDF practical guidelines on the prevention and management of diabetic foot disease, 2019. https://tinyurl.com/wf5h96q (accessed 11 February 2020)
24 Lipsky BA, Senneville E, Abbas ZG et al; International Working Group on the Diabetic Foot (IWGDF). IWGDF guideline on the diagnosis and treatment of foot infection in persons with diabetes, 2019. https://tinyurl.com/u5soagt (accessed 11 February 2020)
25 World Union of Wound Healing Societies (WUWHS). Principles of best practice: wound infection in clinical practice. An international consensus. MEP Ltd, 2008
26 Storm-Versloot MN, Vos CG, Ubbink DT, Vermeulen H. Topical silver for preventing wound infection. Cochrane Database Syst Rev 2010; 3(3):CD006478
27 Margolis DJ, Berlin JA, Strom BL. Risk factors associated with the failure of a venous leg ulcer to heal. Arch Dermatol 1999; 135(8):920–926. https://doi.org/10.1001/archderm.135.8.920
28 Milic DJ, Zivic SS, Bogdanovic DC et al. Risk factors related to the failure of venous leg ulcers to heal with compression treatment. J Vasc Surg 2009; 49(5):1242–1247. https://doi.org/10.1016/j.jvs.2008.11.069