

Le Medicazioni Vecchie e Nuove: dalla Disinfezione alla Terapia Locale

Dr. Alessia Scatena

Direttore UOC Diabetologia

Ospedale San Donato, Arezzo



SID Società Italiana di Diabetologia
AMD ASSOCIAZIONE MEDICI DIABETOLOGI

ASSISI (PG)
15/17
GIUGNO 2023
Grand Hotel Assisi

Congresso Nazionale
PIEDE DIABETICO
GDS SID-AMD

La **S**indrome del **piede diabetico**: competenze in azione con uno sguardo al futuro

La sottoscritta Alessia Scatena dichiara ai sensi dell'art. 3.3 sul Conflitto di Interessi dell'Accordo Stato-Regione del 19 Aprile 2012 che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

- Novo-Nordisk
- Emoled
- Urgo
- Molteni
- Eli Lilly

BURDEN OF WOUNDS IN THE UNITED KINGDOM

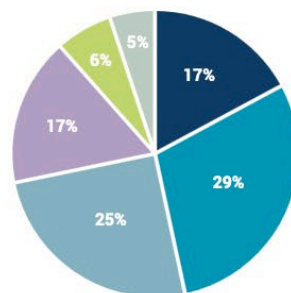


Reference: Guest JF, Fuller GW, Vowden P. Cohort study evaluating the burden of wounds to the UK's National Health Service in 2017/2018: update from 2012/2013. BMJ Open 2020;10:e045253. doi:10.1136/bmjopen-2020-045253

£8.3
Billion

Total annual cost of wound management
Of which 67% was spent on managing unhealed wounds

Over 70% of cost is associated with Nurse, Doctor, or Healthcare Assistant visits



Wound Products account for only 6% of costs

- Hospital admissions, day case and outpatients
- District/community nurse visits
- GP and Practice nurse visits
- Healthcare assistant visits
- Wound care products
- Other



The UK's NHS managed

3.8 million patients

with a wound in 2017/2018, equivalent to 7% of the adult population

25% of all wounds lacked a recorded differential diagnosis

The annual prevalence of wounds
increased by 71%

between 2012/2013 and 2017/2018.

Patient management cost
increased by 48%

in real terms.

Annual levels of resource use attributable to wound management included:

> **54.4 million**
district/community nurse visits

> **53.6 million**
healthcare assistant visits

> **28.1 million**
practice nurse visits

Between 2012 and 2017, there was an estimated 30% decline in the number of district nurses employed in front-line patient care.

81%

Of the total annual NHS cost was incurred in the community.

Average duration of chronic wounds

4
months

Wounds that healed during study period

32
months

Wounds that remained unhealed during study period

Julian Guest, Editorial, Wounds UK, Vol 17, No 1: 2021



Diabetic Foot Ulcers: Appraising Standard of Care and Reviewing New Trends in Management

Paola C. Aldana¹ · Amor Khachemoune^{2,3}





Practical
guidelines



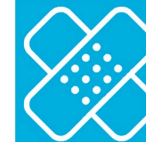
Offloading



Peripheral
Artery Disease



Infection



Wound healing
interventions

Controllo Glicometabolico

Controllo dell'Edema

Gestione Malnutrizione

Trattamento dei Fattori di
rischio CV

Gestione Depressione &
Difficoltà psico-sociali

Local Ulcer Care (IWGDF 2019=2023)

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- Select dressings to control excess exudation and maintain moist environment.
- Do not soak the feet, as this may induce skin maceration.
- Consider negative pressure to help heal postoperative wounds.

Local Ulcer Care

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- Select dressings to control excess exudation and maintain moist environment.
- Do not soak the feet, as this may induce skin maceration.
- Consider negative pressure to help heal postoperative wounds.

Riparazione Tissutale

1. Fase Flogistica

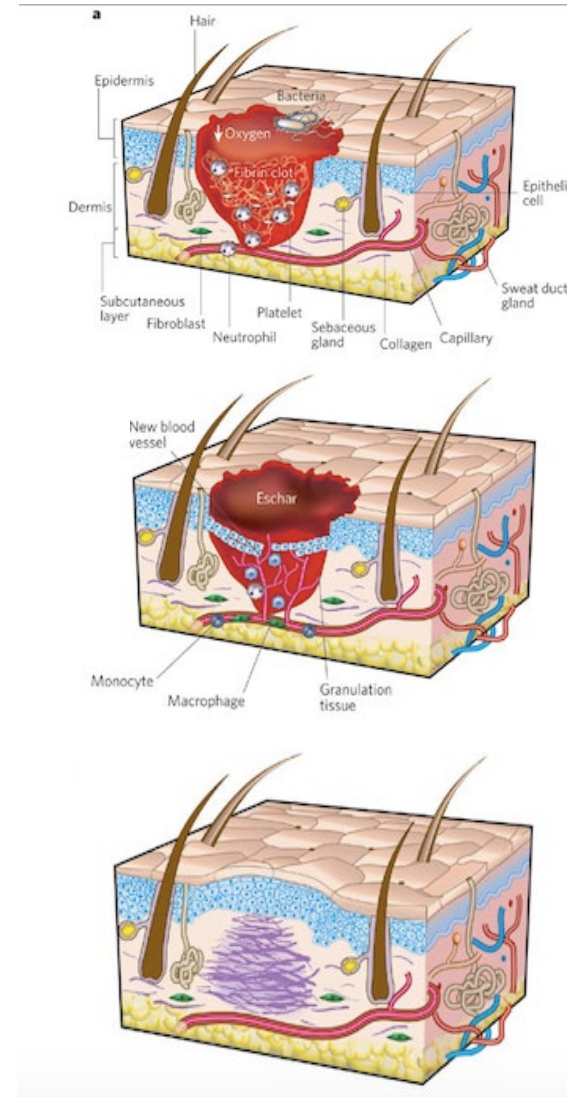
- Trauma
- Coagulazione, Tappo di Fibrina
- Chemiotassi dei macrofagi e PMN

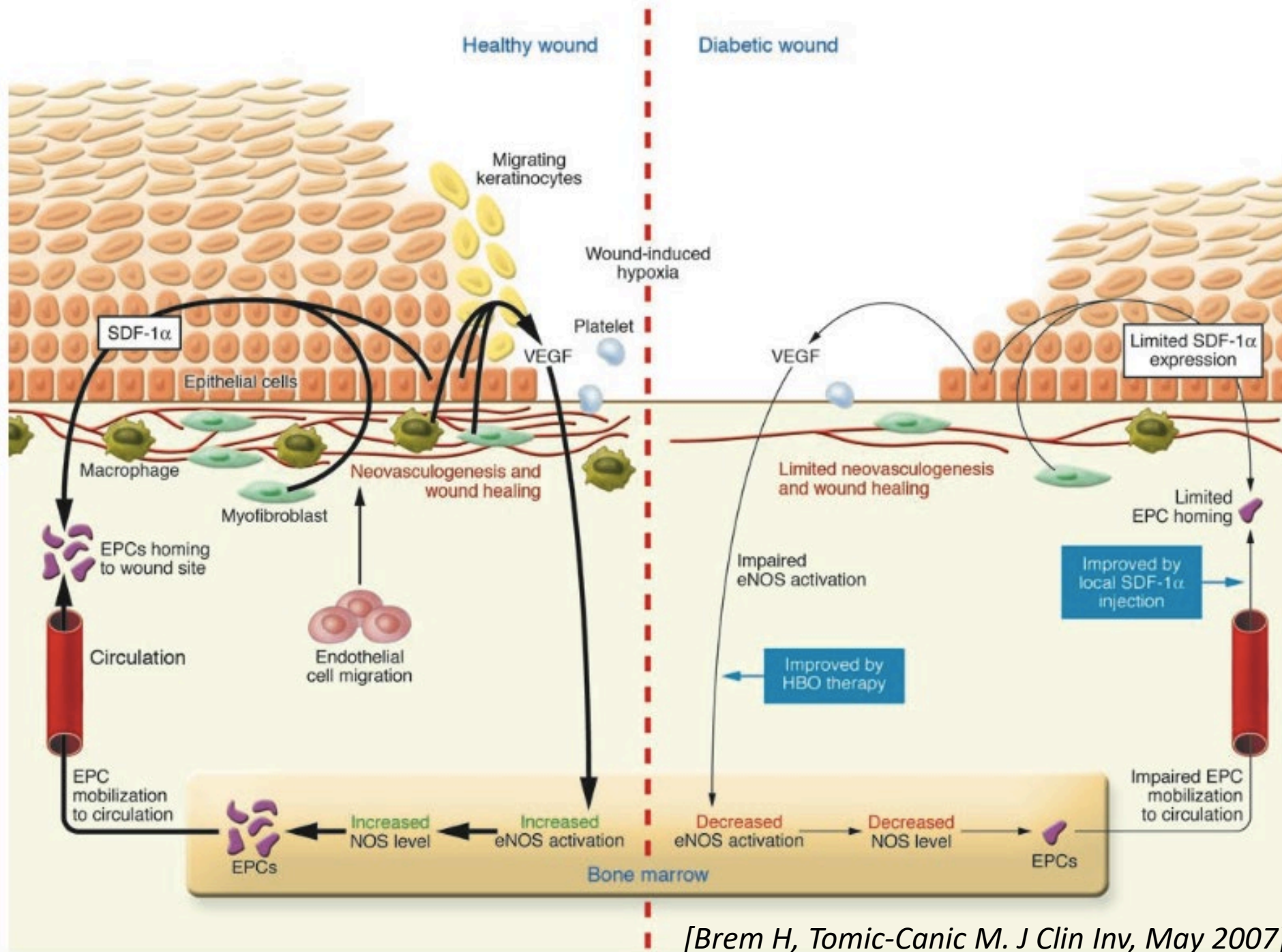
2. Fase Proliferativa

- Proliferazione dei Fibroblasti
- Deposizione del Collagene
- Formazione del tessuto di Granulazione
- Contrazione

3. Fase di Rimodellamento

- Formazione del Tessuto di Granulazione
- Neoangiogenesi
- Riepitelizzazione





[Brem H, Tomic-Canic M. J Clin Inv, May 2007]

Wound Bed Preparation

CHRONIC WOUND

'stuck' in the inflammatory and proliferative stages of healing
Epidermis fails to migrate at the wound margins

Over-production of matrix molecules, Fibrinogen and Fibrin.

Chronic wound fluid slows down, and can block the proliferation of cells.



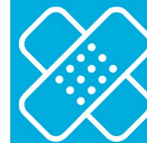
ACUTE WOUND

*[Falanga V, 2000,
Ennis and Menses, 2000
Schultz, 2003]*



Local Ulcer Care

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- Select dressings to control excess exudation and maintain moist environment.
- Do not soak the feet, as this may induce skin maceration.
- Consider negative pressure to help heal postoperative wounds.



Wound healing
interventions

Debridement

- Riduce la pressione
- Permette la chiara ispezione di tutta l'estensione della lesione
- Facilita il drenaggio delle secrezioni
- Stimola la guarigione
- I pazienti con ulcere neuropatiche che vengono regolarmente sottoposti a debridement chirurgico hanno un'evoluzione migliore rispetto agli altri.

[Steed DL, J Am Coll Surg 1996; 183:61-64]

- Rimuovere lo slough, il tessuto necrotico e l'ipercheratosi perilesionale preferibilmente per via chirurgica (bisturi), ad eccezione dei casi di estrema dolorabilità o di ischemia severa.

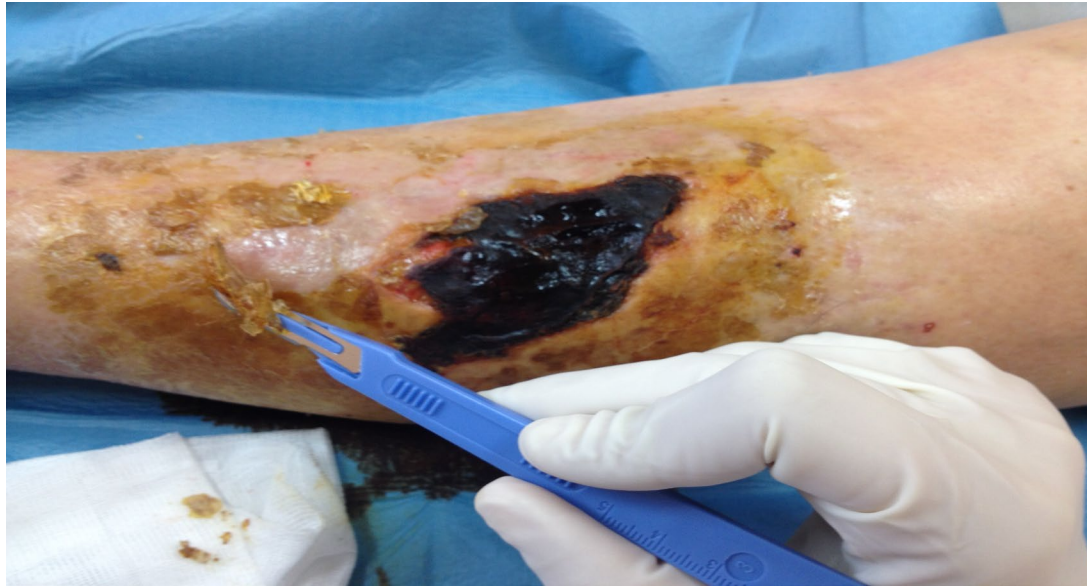
GRADE strength of recommendation:strong; quality of evidence: low



Sharp Debridement - *Gold Standard*



Sharp Debridement - *Gold Standard*



DEBRIDEMENT PERFORMANCE INDEX

0=debridement needed but not done

1=debridement needed and done

2=debridement not needed



I pz con uno score tra 3 e 6 avevano una probabilità di guarigione 2,4 volte maggiore

Debridement Autolitico

Hydrogel dressings for healing diabetic foot ulcers (Review)

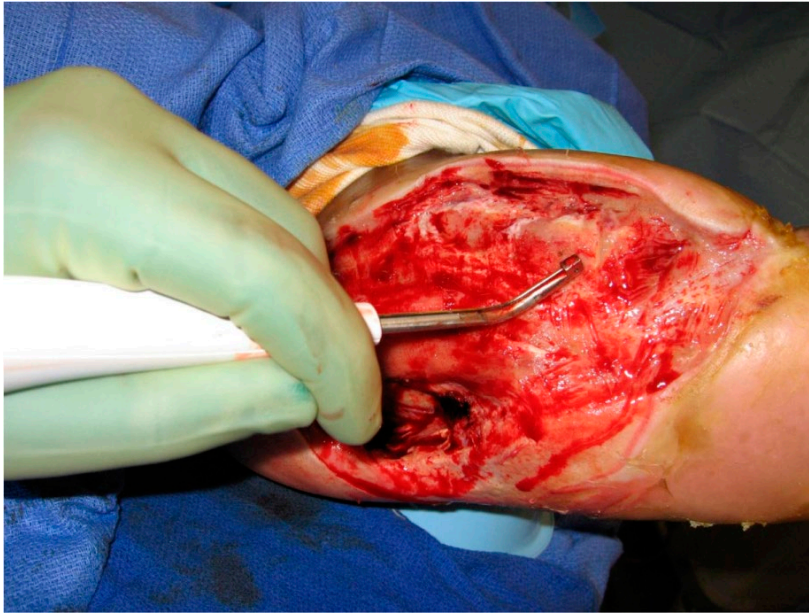
Dumville JC, O'Meara S, Deshpande S, Speak K



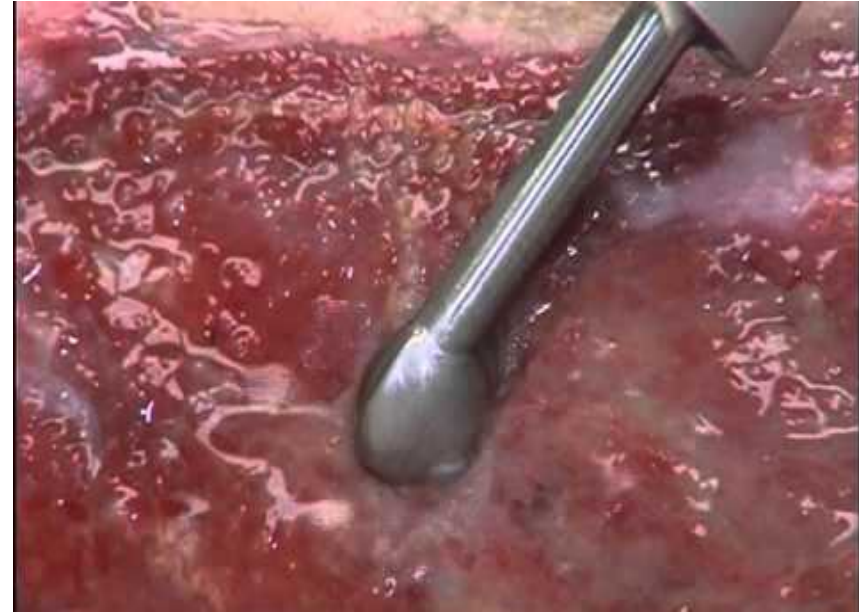
Hydrogel migliori rispetto alle
medicazioni di contatto in termini di
guarigione.
Non evidenze rispetto ad altre
medicazioni.
GRADE: basso

Mechanical Debridement

Pressurized Irrigation



Ultrasound



Do not use agents reported to have an effect on wound healing through alteration of the physical environment including through the use of electricity, magnetism, ultrasound and shockwaves, in preference to best standard of care. (Strong; Low)

A prospective randomised controlled clinical trial comparing hydrosurgery debridement with conventional surgical debridement in lower extremity ulcers

Wayne J Caputo, Donald J Beggs, Jessica L DeFede, Lisa Simm, Hussein Dharma

RCT

Saving Debridement Time (36%) ($p < 0,008$)

No differences between the two groups in term of healing time or number of healed

Biodebridement- Maggots

In one study there was a significantly longer antibiotic-free time period in patients who received maggot therapy than in those who did not, but in two studies the proportion of antibiotic use was similar for those who did and did not receive maggot therapy.

[Sun X, Int J Infect Dis 25:32-37, 2014]

[Edwards J, Cochrane Database Syst Rev Jan 20:CD003556, 2010]



IWGDF Wound Healing Guideline



Do not use autolytic, biosurgical, hydrosurgical, chemical or laser debridement over standard of care (i.e. sharp debridement). (Strong; Low)

Do not routinely use enzymatic debridement as opposed to standard of care (i.e. sharp debridement) to improve wound healing outcomes in people with diabetes and a foot ulcer. (Strong; Low)

2a. In specific situations where the availability of sharp debridement may be limited by access to resources and/or availability of skilled personnel, consider using enzymatic debridement. (Conditional; Low)

Do not use surgical debridement in those for whom sharp debridement can be performed outside a sterile environment. (Strong; Low)

We recommend the frequency of sharp debridement should be determined by the clinician based on clinical need. (Strong; Low)

Disinfezione

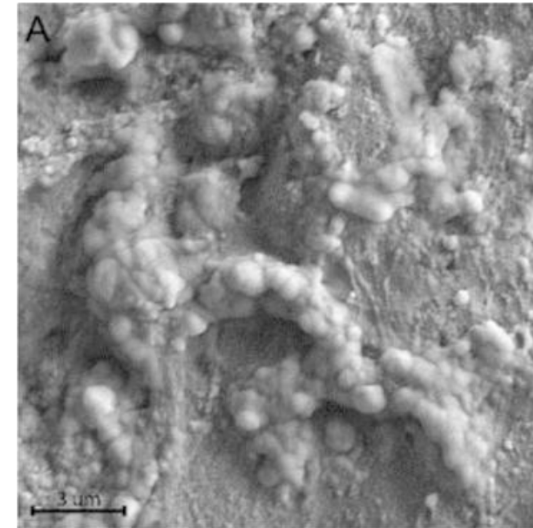


La crescente antimicrobico-resistenza rende necessario un utilizzo appropriato di tutti i prodotti antimicrobici:

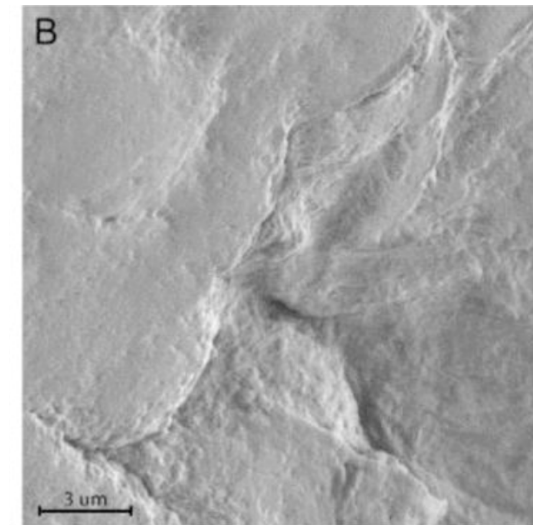
- Disinfettanti
- Antisettici
- Antivirali
- Antifungini
- Antiparassitari
- Antibiotici

Biofilm

- Le ulcere croniche sono universalmente colonizzate da batteri, che per sopravvivere formano un biofilm, che conferisce loro l'abilità di resistere all'attacco macrofagico dell'ospite e agli antimicrobici.
- I microrganismi ivi presenti sono protetti da una barriera meccanica, la sostanza esopolimerica (EPS), che respingendo la risposta immune, provoca effetti collaterali nel tessuto perilesionale e ritarda la guarigione della lesione.



A. Ulcera murina inoculata con *St. Aureus* incassato nella sostanza esopolimerica a formare il biofilm



B. Ulcera murina non inoculata e senza biofilm

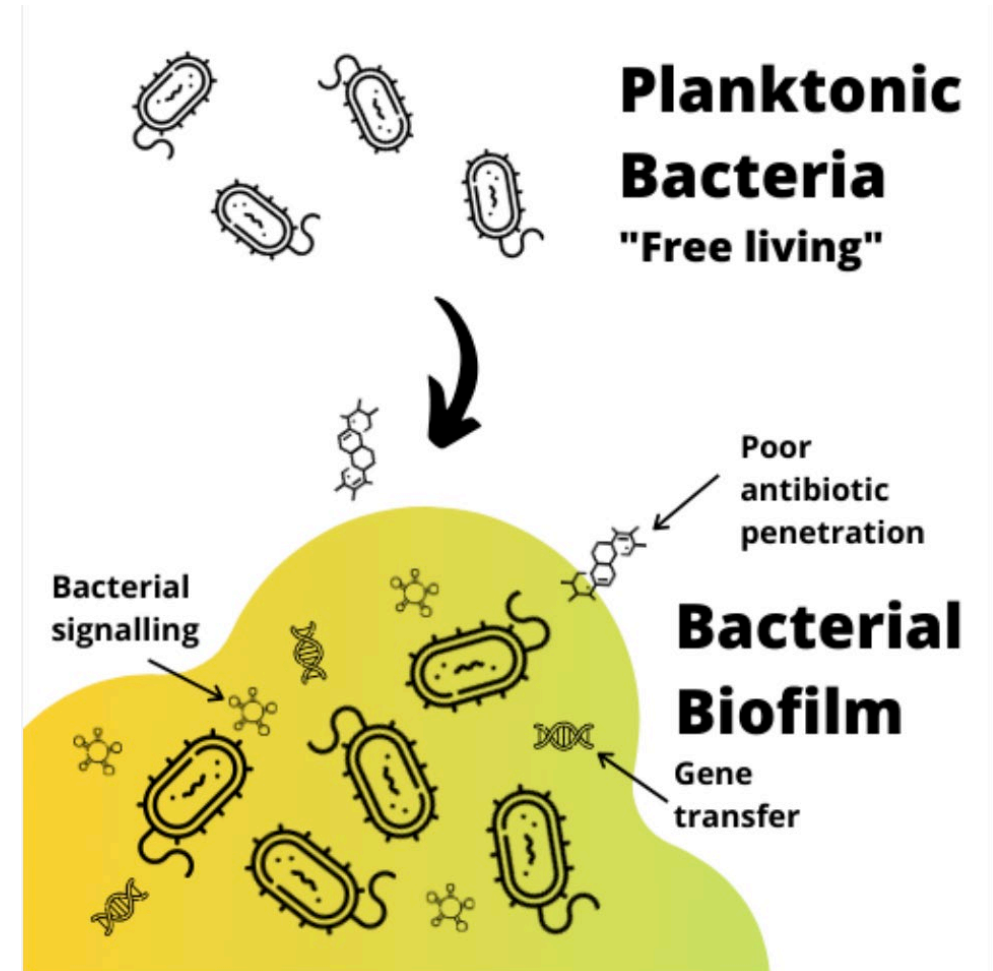
Biofilm

- Il biofilm è presente nel 60-80% delle lesioni.
- E' responsabile della resistenza antibiotica e agli agenti topici.
- Il biofilm prodotto varia da una specie batterica all'altra, ad esempio quello prodotto dallo *Ps. Aeruginosa* ha una densità molto alta e inibisce il movimento dei neutrofili, liberando una sostanza chiamata ramnolipide.
- Il biofilm prodotto dallo *St. Aureus* è in grado di bloccare la migrazione dei cheratinociti per effetto citotossico diretto.

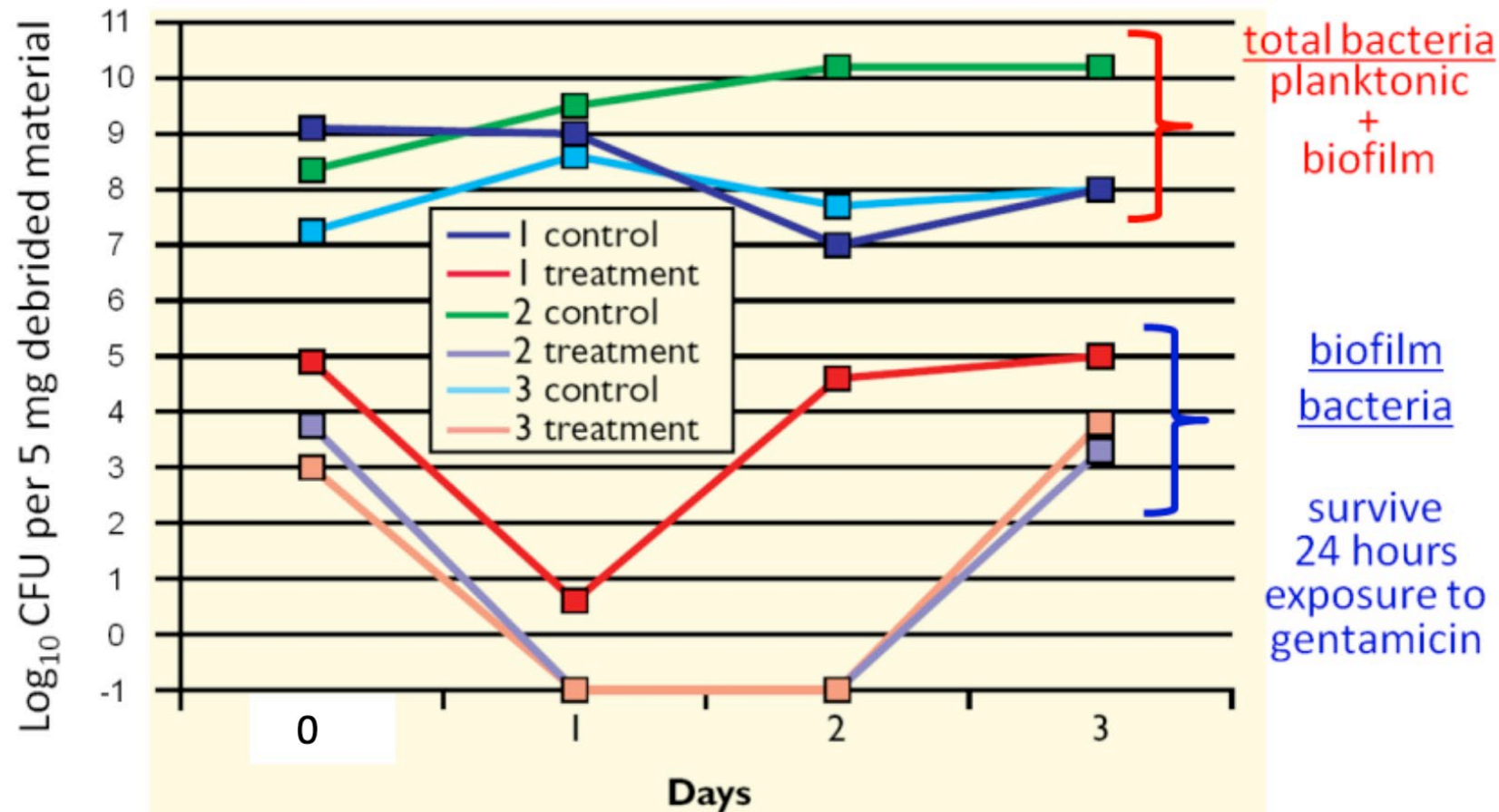


Biofilm

- Sebbene in passato si pensasse che i batteri in forma planctonica generassero infezioni acute, mentre il biofilm fosse responsabile di infezioni croniche, adesso sappiamo che l'acuzie dipende dal livello di attività del metabolismo batterico.
- I batteri «tolleranti» in vitro sono dormienti e protetti dall'antibiotico rimanendo non interagenti e quindi vitali.



Debridement e Biofilm



Window of Opportunity

Le biopsie condotte in 3 pz con ulcere venose mostrano una riduzione della carica batterica subito dopo il debridement chirurgico, per poi aumentare nuovamente. La finestra temporale, seppur breve offre un'opportunità di attacco alla terapia antibiotica e alle difese immunitarie.

ANTIMICROBIALS AND NON-HEALING WOUNDS: AN UPDATE

INCLUDING A CONCISE
APPROACH TO
TREATING POTENTIALLY
INFECTED WOUNDS



Q10: Is there any antimicrobial agent that is not expected to select for resistance or tolerance in bacteria in the wound?

It is likely that resistance will develop against any topical antimicrobial. Careful use and pro-active monitoring for resistance is the key. In laboratory experiments, bacteria treated with chlorhexidine, silver nitrate, silver sulfadiazine, polyhexanide, and silver nanoparticles have not been shown to develop resistance.

Antibiotics

Scars are a common complication of wound healing. Scar formation is influenced by many factors, including the use of antibiotics. Scar formation is a complex process involving many factors, including the use of antibiotics. Scar formation is a complex process involving many factors, including the use of antibiotics.

Antisettici

I batteri hanno un'innata capacità di sopravvivere e sovrattivare meccanismi di estrusione di anti-farmaco quando a contatto con prodotti topici. Tale sovraespressione è aspecifico e può coinvolgere antibiotici e metalli pesanti.

ANTIMICROBIALS AND NON-HEALING WOUNDS: AN UPDATE

INCLUDING A CONCISE
APPROACH TO
TREATING POTENTIALLY
INFECTED WOUNDS



Q1: Which type of antimicrobials agents should clinicians choose to treat wound infections, while minimizing the risk of AMR?

Gli antimicrobici devono essere limitati per l'utilizzo nelle lesioni infette.

Non vi sono evidenze che gli antimicrobici possano prevenire l'infezione o accelerare la guarigione.

Si raccomanda invece un adeguato debridement per prevenire o trattare le infezioni.

IWGDF Wound Healing Guideline



INTERVENTION: DRESSINGS

Clinical question 2: In people with diabetes-related foot ulcers, are dressings or applications with surface antimicrobial properties, honey or those that influence chronic wound biology more effective for achieving wound healing compared to basic contact dressings and best standard of care?

TOPICAL ANTIMICROBIAL OR ANTISEPTIC DRESSINGS

Recommendation 6: Do not use topical antiseptic or antimicrobial dressings for wound healing of diabetes-related foot ulcers (Strong; Moderate)

Local Ulcer Care

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- **Select dressings to control excess exudation and maintain moist environment.**
- Do not soak the feet, as this may induce skin maceration.
- Consider negative pressure to help heal postoperative wounds.

Healing of Skin Wounds and the Influence of Dressings on the Repair Process

G D Winter

Department of Biomedical Engineering, Institute of Orthopaedics (University of London), Royal National Orthopaedic Hospital, Stanmore, Middlesex

The surgical dressing is a therapeutic agent; its purpose the provision of the best possible environment for the healing of wounded skin. Historically dressings have been introduced and improved largely on an empirical basis. The purpose of this paper is to examine how far recent knowledge of cutaneous wound healing and data from experiments with dressings can help to solve some of the problems in the development, standardisation and use of dressings.

NORMAL PATTERN OF HEALING

Firstly, it should be noted that wound healing, like other bodily functions, has been subjected to biological evolution and has become modified to suit the needs of species with different integuments and different habitats. Man has inherited and adapted a pattern of repair suited to his own peculiar skin and dressings have played no part in this. Surgical dressings are not found in nature. Wounds under dressings heal in artificial conditions and this is important when drawing conclusions about the effect of dressings on healing.

Wounds vary enormously, depending on the site of the body, severity of injury, type of agency inflicting the damage, degree of contamination with dirt or micro-organisms and other things. For the purpose of study, to reduce complications to a minimum, we use a standard shallow wound in the skin of young domestic pigs made with a sharp scalpel blade, taking full aseptic precautions. This is roughly the same degree of injury as a graze and is similar to a Thiersch graft donor site. Potentially, the most serious consequences follow from the loss of epidermal layer of the surface of the skin and the protection it affords the underlying tissue. Water vapour can escape and the tissue beneath becomes dehydrated, dirt can get in and bacteria can invade the deeper tissues through the breach in the outer barrier. The ideal dressing will temporarily perform the protective functions of the epidermis, while the living layer is being replaced.

Any wound penetrating the epidermis into the underlying tissues disrupts blood vessels and causes

bleeding, which is efficiently dealt with by the biochemically complex blood clotting mechanism. Dressings have to be absorbent enough to contain the blood loss without 'strike through', meaning that the blood should not penetrate to the upper surface of the dressing and create a moist passageway down which bacteria can proliferate to the tissues underneath. Contrary to common belief, it is not the blood clot which causes dressings to stick to wounds, nor does it play a significant part in healing. More important in these respects is the protein-rich filtrate of blood, which begins to escape from venules within minutes of the injury and later percolates through the walls of capillaries also. Abnormal vascular permeability is mediated by a number of substances released by injured tissues, among them bradykinin and histamine, and the flow of a serous exudate into the tissues is one of the first events in the inflammatory reaction. The exudate causes the tissues to swell and it oozes on to the surface of the wound, where it gradually dries to produce a serous scab. This is nature's dressing which temporarily performs some of the functions of the epidermis. It is not water vapour proof, as one can easily demonstrate by holding a cooled glass slide over a scab when it will rapidly cloud over with condensed water passing through the scab. It does, however, protect the wound surface underneath from contamination and shelters the cells which shortly start to replace the lost tissue.

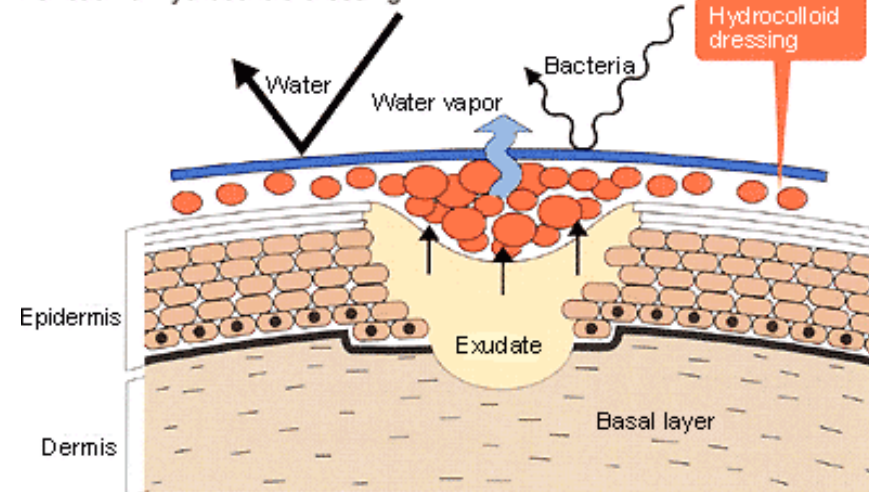
Another event in the inflammatory reaction is the movement of granular leukocytes out of the blood stream through the vessel walls into the surrounding tissues. The polymorphonuclear cells, joined later by mononuclear cells, mop up micro-organisms that have gained access to the wound and clear away dead cells and damaged tissue fibres. This 'demolition phase' takes place in the first 24 hours after injury and varies in intensity in proportion to the amount of trauma and of contamination of the wound.

Nel 1962 GD Winter Ha postulato la teoria della "Medicazione in ambiente umido", dimostrando che la riepitelizzazione era due volte più veloce in un ambiente umido vs secco.

La disidratazione causa un ritardo nella migrazione cellulare.

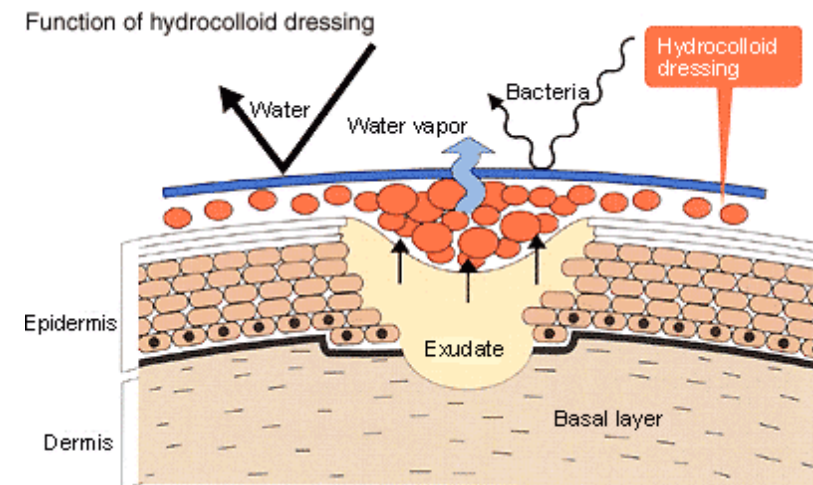
L'eccesso di fluidi (essudato) è responsabile della macerazione dei margini.

Function of hydrocolloid dressing



Bilancio dei Fluidi nella Gestione dell'Ulcera

- **Tp diretta:** bendaggi, medicazioni assorbenti, NPWT.
- **Tp indiretta:** tp dell'infezione, dell'edema.
- **Medicazioni che contrastano la disidratazione:**
 - Hydrogel
 - Idrocolloidi
- **Medicazioni che contrastano l'essudato:**
 - Schiume
 - Idrofibre
 - Alginati
 - Poliacrilati



La frequenza di cambio
della medicazione
dipende dall'essudato

Medicazioni

```
graph LR; A[Medicazioni] --- B[Di Base]; A --- C[Avanzate]; A --- D[Antimicrobiche]; B --- B1[✓ Garze non aderenti]; B --- B2[✓ Garze assorbenti]; C --- C1[✓ Alginati]; C --- C2[✓ Hydrogel]; C --- C3[✓ Films]; C --- C4[✓ Hidrocolloid]; C --- C5[✓ Schiume]; C --- C6[✓ TLC-NOSF]; D --- D1[✓ Miele]; D --- D2[✓ Iodio]; D --- D3[✓ Argento]; D --- D4[✓ Polyhexamethylene]
```

Di Base

- ✓ Garze non aderenti
- ✓ Garze assorbenti

Avanzate

- ✓ Alginati
- ✓ Hydrogel
- ✓ Films
- ✓ Hidrocolloid
- ✓ Schiume
- ✓ TLC-NOSF

Antimicrobiche

- ✓ Miele
- ✓ Iodio
- ✓ Argento
- ✓ Polyhexamethylene

A Comparative Study Between Honey and Povidone Iodine as Dressing Solution for Wagner Type II Diabetic Foot Ulcers

A Shukrimi (MMed Ortho*), A R Sulaiman (MMed Ortho)**, A Y Halim (MMed Ortho)**, A Azril (MMed Ortho)*
*Department of Orthopaedics, Kuliyah of Medicine, International Islamic University Malaysia, 25710 Kuantan, Pahang,
**Department of Orthopaedics, School of Medical Sciences, University Sains Malaysia, 16150 Kota Bharu, Kelantan, Malaysia

Group A #15; Group B #15
Tempo di guarigione: n.s.

COMPARISON OF CONVENTIONAL PYODINE DRESSING WITH HONEY DRESSING FOR THE TREATMENT OF DIABETIC FOOT ULCERS

JPMI 2012 VOL. 26 NO. 04 : 402 - 407
Waqar Alam Jan¹, Habibullah Shah², Mansoor Khan³,
Mohammad Fayaz⁴, Naeem Ullah⁵

Group A #50; Group B #50
Tempo di guarigione: minore nel gruppo trattato con il miele (p<0.0001)
Tasso di guarigione: n.s.
Tasso di Amputazioni: n.s.

Manuka honey-impregnated dressings in the treatment of neuropathic diabetic foot ulcers

Alexandros V. Kamaratos¹, Konstantinos N. Tzirogiannis¹, Stella A. Iraklianiou¹,
Georgios I. Panoutsopoulos², Ilias E. Kanellos¹ & Andreas I. Melidonis¹
1 Diabetes Center, Tzanio General Hospital, Piraeus, Greece
2 Department of Nursing, University of Peloponnese, Orthias Artemidos and Plateon, Sparta, Lakonia, Greece

Group A #31; Group B #32
Tempo di guarigione: minore nel gruppo trattato con il miele (p<0.5)
Tasso di sterilizzazione: maggiore nel gruppo trattato con il miele

A Randomized, Controlled Clinical Trial of Honey-Impregnated Dressing for Treating Diabetic Foot Ulcer

Muhammad Imran¹, Muhammad Barkaat Hussain², Mukhtiar Baig³

Group A #179; Group B #169
Tempo di guarigione: minore nel gruppo trattato con il miele (p < 0.001)
Tasso di guarigione: maggiore nel gruppo trattato con il miele (p =0.001)

Cochrane review del 2015 ha compreso solo 2 studi, ritenendoli non dirimenti

Sodium carboxyl-methyl-cellulose dressings in the management of deep ulcerations of diabetic foot

A. Piaggese, F. Baccetti, L. Rizzo, M. Romanelli*, R. Nevalesi and L. Benzi

Department of Endocrinology and Metabolism,
University of Pisa, Pisa, Italy

*Department of Dermatology, University of Pisa,
Pisa, Italy

Accepted 29 November 2008

Abstract

Aims To test the safety and effectiveness of carboxyl-methyl-cellulose dressing (Aquacel™; ConvaTec, UK) in the management of deep diabetic foot ulcers, a group of consecutive out-patients attending the foot clinic of the Department of Metabolic Diseases was studied.

Methods Patients were selected according to the following inclusion criteria: a foot ulcer deeper than 1 cm for >3 weeks, good peripheral blood supply (palpable peripheral pulses or ABPI > 0.9). Exclusion criteria were as follows: active infection, as evident from clinical signs (purulent discharge, redness, swelling, tenderness) and confirmed by culture exams, plasma creatinine > 2 mg/dl, recent episodes of ketoacidosis, malignancies, and any therapy or pathology which might interfere with the healing process. Twenty patients were enrolled in the study and having obtained their informed consent, their lesions were surgically debrided with the complete elimination of all necrotic tissue and debris up to the bleeding healthy tissue; then ulcers were staged and measured, and patients were randomly assigned to two different treatment groups. Patients in group A were dressed with saline-moistened gauze, while patients in group B were dressed with Aquacel™ according to the manufacturer's instructions. All patients in both groups received special post-operative shoes (Pedibates; Zeno Bonatto, Treviso, Italy) and crutches until complete re-epithelialization. Ulcers were all left to heal by secondary intent. After 8 weeks patients were blindly evaluated for the rate of reduction of lesional volume (RLV), rate of granulation tissue (GT), number of infective complications (IC), Intersessional (ILTC) and perilesional (PLTC) temperatures were also recorded with a thermocouple surface digital thermometer, and the difference between the two values (DTC) was calculated. Healing time (HT, days), was then compared between the two groups. Data were compared by analysis of variance (ANOVA), linear regression, Kaplan-Meier survival analysis and Fisher's exact test.

Results HT was significantly shorter in Group B than in Group A ($P < 0.001$). RLV was significantly ($P < 0.01$) higher in Group B patients compared with Group A, as well as GT ($P < 0.05$). IC were in 1/10 Group B and in 3/10 Group A ($P = 0.582$). In addition, both ILTC and ATC were higher in Group B compared with Group A ones ($P < 0.01$).

Conclusions Carboxyl-methyl-cellulose dressings were shown to be safe, effective and well tolerated in the management of non-ischaemic, non-infected deep diabetic foot ulcers.

Lo studio ha valutato l'efficacia di una medicazione a base di sodio-carbossil-metil-cellulosa in confronto con una garza inerte: la medicazione avanzata si è dimostrata sicura ed efficace e ben tollerata nella gestione della lesioni non ischemiche e non infette.

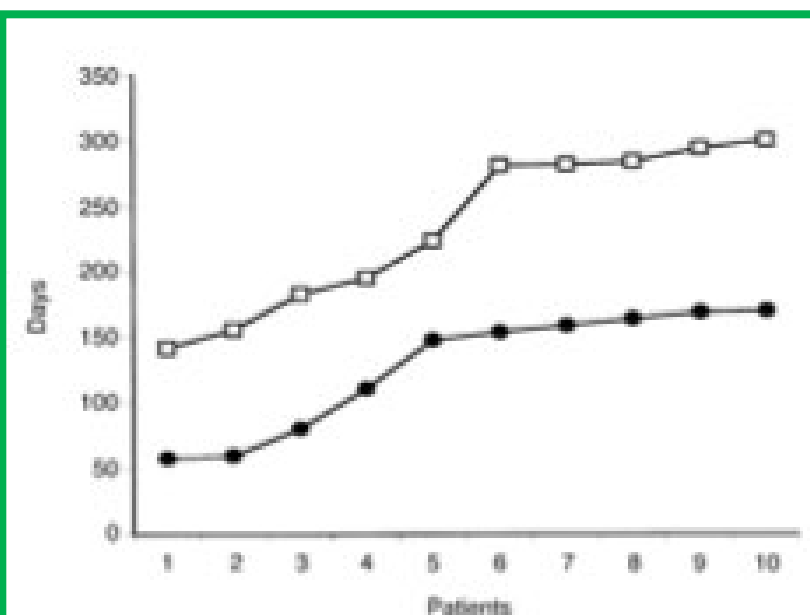


Figure 1 Healing time of patients of both groups during the course of the study (log rank Mantel-Cox $P < 0.001$). □, Group A; ●, Group B.

Randomised controlled trial of the use of three dressing preparations in the management of chronic ulceration of the foot in diabetes

WJ Jeffcoate, PE Price, CJ Phillips, FL Game, E Mudge, S Davies, CM Amery, ME Edmonds, OM Gibby, AB Johnson, GR Jones, E Masson, JE Patmore, D Price, G Rayman and KG Harding

317 pz



Garza grassa

Garza
betadinata

Idrofibra

Più drop-out nel primo gruppo,
Il costo elevato di Idrofibra era bilanciato dalla minor frequenza di cambio

senze sui
tempi di
guarigione o di
recidive.

Local Ulcer Care

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- Select dressings to control excess exudation and maintain moist environment.
- **Do not soak the feet, as this may induce skin maceration.**
- Consider negative pressure to help heal postoperative wounds.

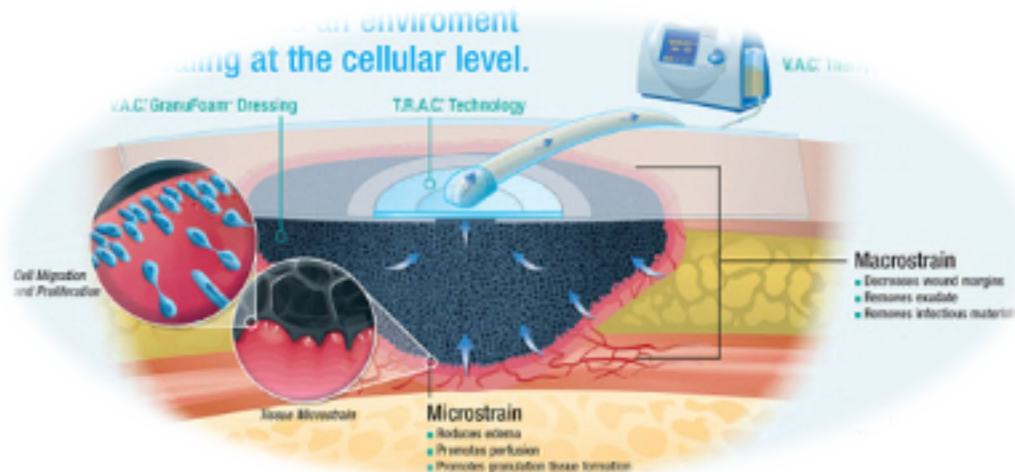
Local Ulcer Care

- Regular inspection of the ulcer by a trained health care provider is essential; its frequency depends on the severity of the ulcer and underlying pathology, the presence of infection, the amount of exudation, and wound treatment provided.
- Debride the ulcer and remove surrounding callus (preferably with sharp surgical instruments), and repeat as needed.
- Select dressings to control excess exudation and maintain moist environment.
- Do not soak the feet, as this may induce skin maceration.
- Consider negative pressure to help heal postoperative wounds.



28. Consider the use of Negative Pressure Wound Therapy as an adjunct therapy to standard of care for the healing of postsurgical diabetes-related foot wounds. (Conditional; Low)
- 28a. Do not use Negative Pressure Wound Therapy as an adjunct therapy to standard of care for the healing of non-surgically related diabetes foot ulcers. (Strong; Low)

- La Negative pressure wound therapy (NPWT) crea una pressione controllata subatmosferica (negative pressure) che facilita il processo di guarigione in ambiente umido.
- Essa migliora la perfusione tissutale, stimola il tessuto di granulazione, riduce l'edema e controlla l'eccesso di secrezioni, riduce l'area della lesione, aiuta a migliorare il tasso di formazione del tessuto di granulazione e la migrazione epiteliale.



Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial

David G Armstrong, Lawrence A Lavery, for the Diabetic Foot Study Consortium

Pz con amputazioni minori open fino al livello transmetatarsale
e buona perfusione periferica

77 pts NPWT

85 pts standard
dressing

Healing rate
43 [56%] vs 33 [39%],
($p=0.040$)

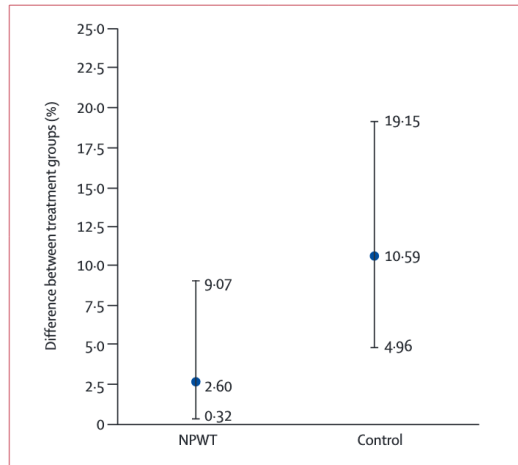


Figure 4: Incidence of re-amputation during active assessment period
Data show percentages with 95% binomial CIs.

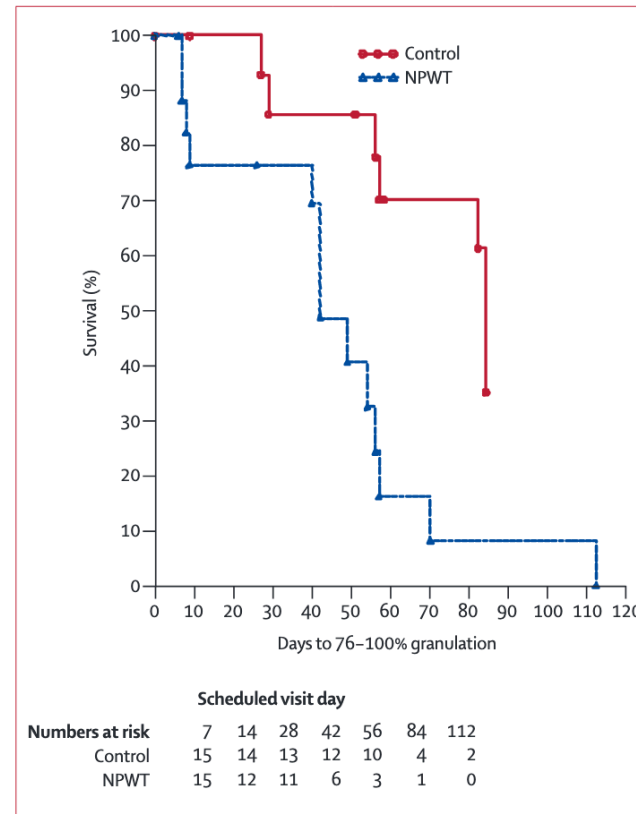


Figure 3: Kaplan-Meier estimates for time to 76-100% granulation (days)
Number at risk at conclusion of treatment period; control 5, NPWT 1.

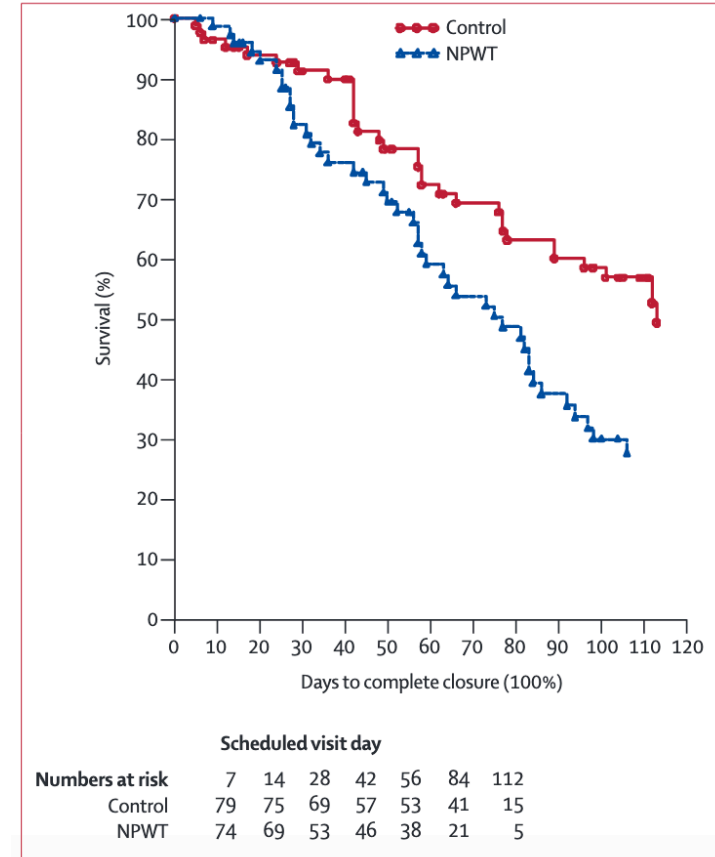


Figure 2: Kaplan-Meier estimates for time to complete wound closure
Number at risk at conclusion of treatment period; control 15, NPWT 12.

Comparison of Negative Pressure Wound Therapy Using Vacuum-Assisted Closure With Advanced Moist Wound Therapy in the Treatment of Diabetic Foot Ulcers

A multicenter randomized controlled trial

PETER A. BLUME, DPM¹
JODI WALTERS, DPM²
WYATT PAYNE, MD³

JOSE AYALA, DPM⁴
JOHN LANTIS, MD⁵

169 pts
NPWT

166 pts
hydrogel o
alginati

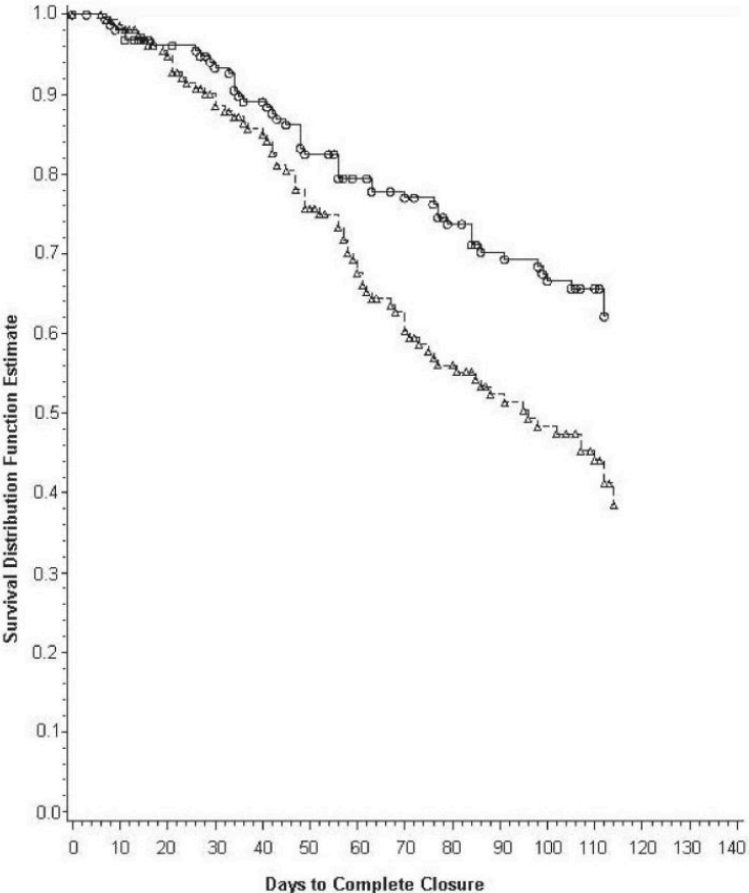
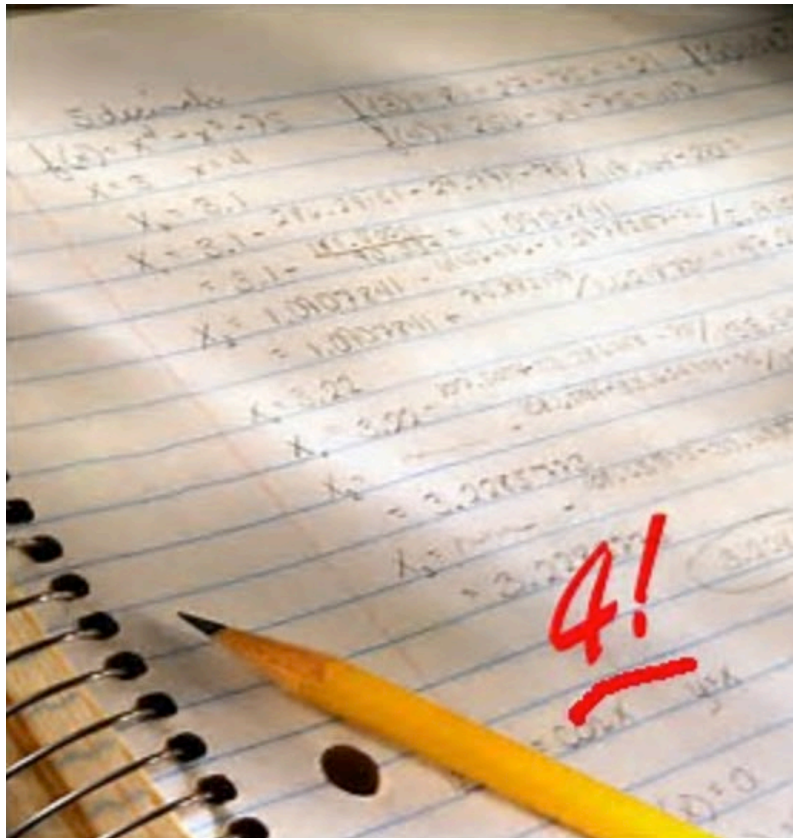


Figure 2—Kaplan-Meier estimates for time to complete ulcer closure ($P = 0.001$). Δ , NPWT; $\circ$, AMWT.

Healing rate
43.2% vs 28.9% ($p=0.007$)

no significant difference between the groups was observed in treatment-related complications such as infection, cellulitis, and osteomyelitis at 6 months.



Altri studi considerati
metodologicamente
non dirimenti.

IWGDF Wound Healing Guideline

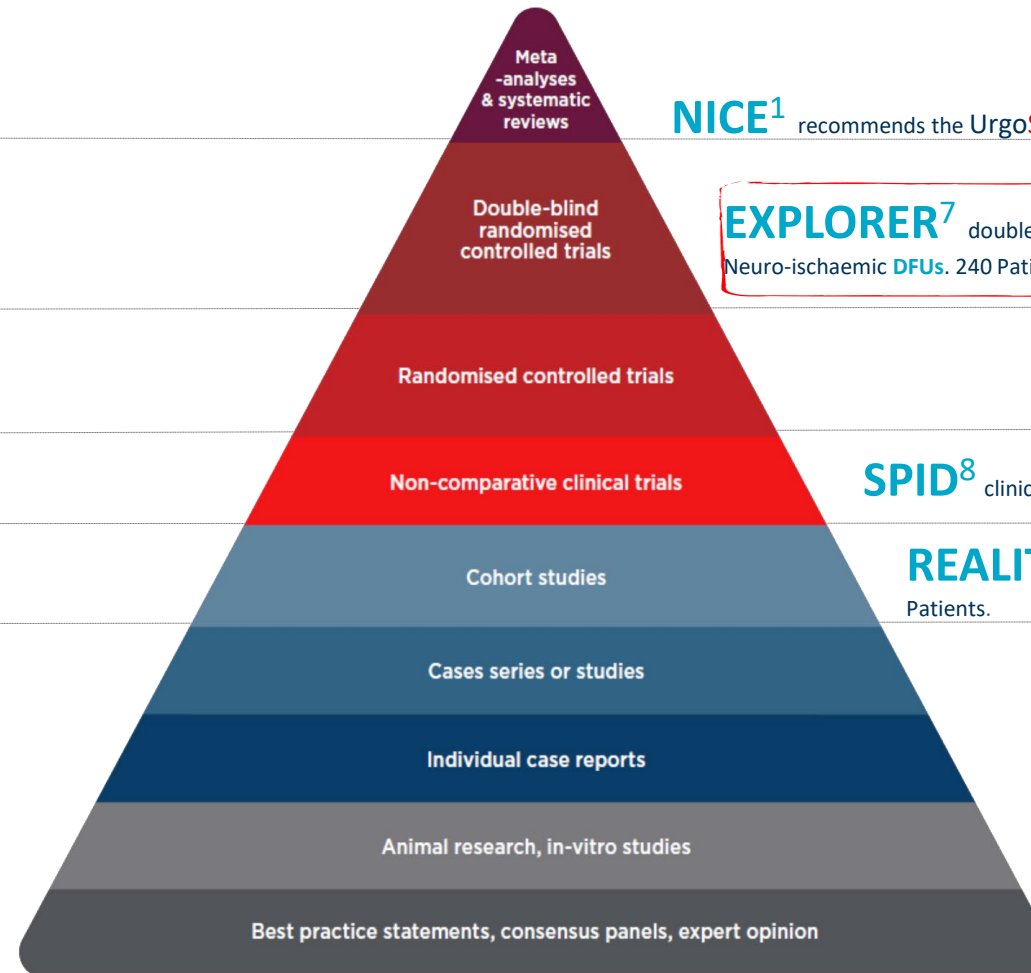


6. Do not use topical antiseptic or antimicrobial dressings for wound healing of diabetes-related foot ulcers. (Strong; Moderate)
7. Do not use honey (or bee related products) for the purpose of wound healing in diabetes-related foot ulcers. (Strong; Low)
8. Do not use collagen or alginate dressings for the purpose of wound healing of diabetes-related foot ulcers. (Strong; Low)
9. Consider the use of the sucrose-octasulfate impregnated dressing as an adjunctive treatment, in addition to the best standard of care, in non-infected, neuro-ischaemic diabetes-related foot ulcers which have had insufficient change in ulcer area with best standard of care including appropriate offloading for at least 2 weeks. (Conditional; Moderate)

UrgoStart (Matrice TLC- NOSF /medicazione con matrice saccarosio octasolfato): Il più alto livello di evidenza nel wound care

Fibre poliassorbenti in Poliacrilato associate ad una matrice di guarigione TLC-NOSF:

- Azione di **modulazione dei processi infiammatori** (MMPs) grazie al NOSF (saccarosio octasolfato)
- Azione di **detersione continua** dimostrata in RCT grazie alle fibre di poliacrilato
- **Guarigione accelerata** grazie alla combinazione delle due caratteristiche dimostrata su oltre 12.000 pazienti



NICE¹ recommends the UrgoStart treatment range for **DFUs** & **VLUs**.

EXPLORER⁷ double-blind RCT (vs neutral dressing).
Neuro-ischaemic **DFUs**. 240 Patients.

SPID⁸ clinical study. Neuropathic **DFUs**. 33 Patients.

REALITY⁶ pooled data analysis **DFUs**, **LUs** & **PU**s. 10220 Patients.



In **DFUs**



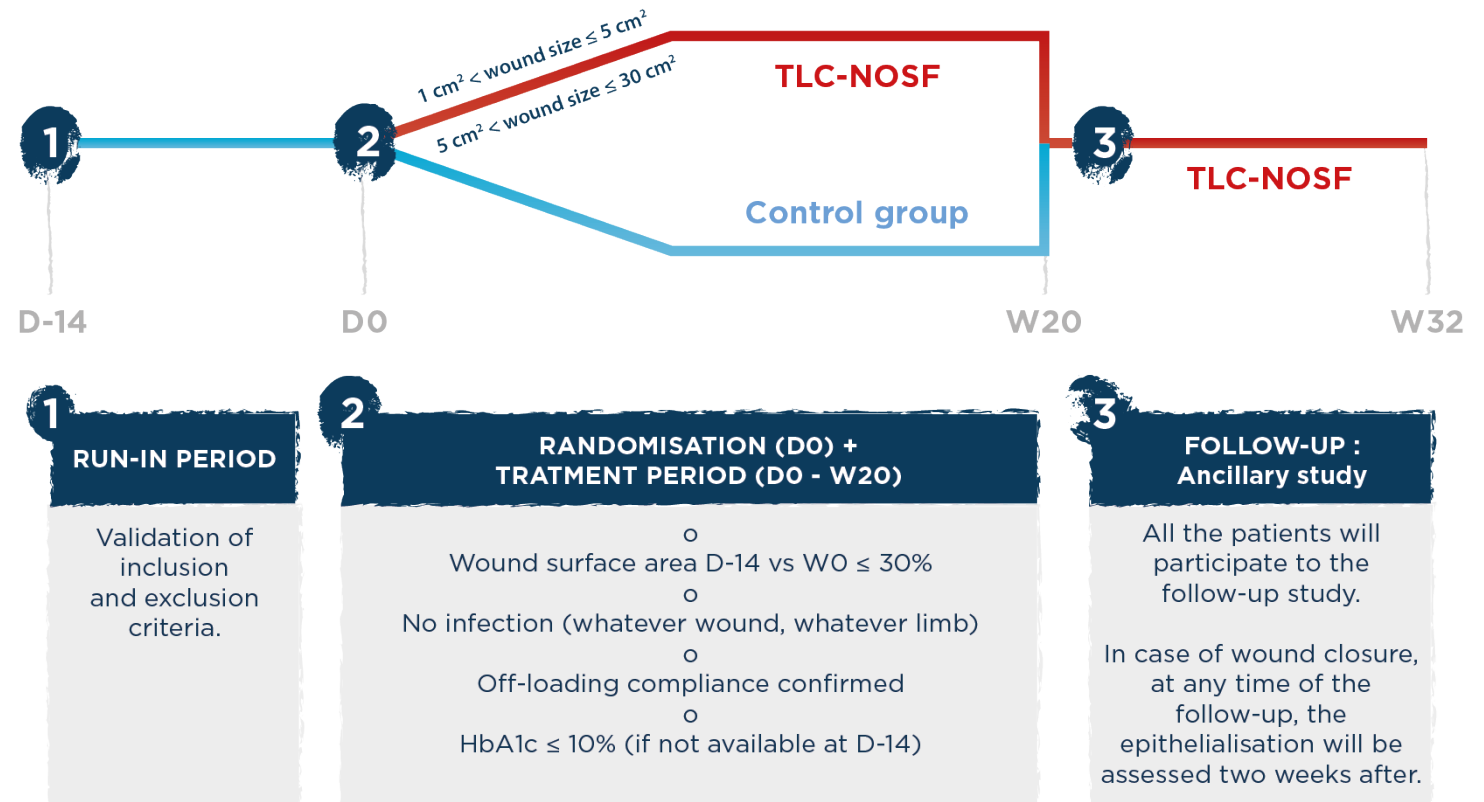
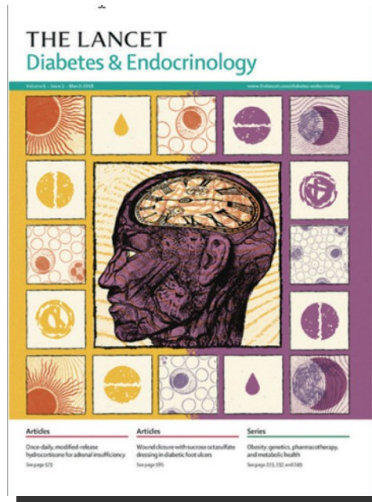
1- UrgoStart for treating leg ulcers and diabetic foot ulcers, <https://www.nice.org.uk/guidance/mtg42>, January 2019. 2- Meaume S, Truchetet F, Cambazard F et al. A randomized, controlled, double-blind prospective trial with a Lipido-Colloid Technology-Nano-oligosaccharide Factor wound dressing in the local management of venous leg ulcers. Wound Repair Regen. 2012; 20(4):500-511. 3- Meaume S, Domp Martin A, Lazareth I, Sigal M, Truchetet F, Sauvadet A, Bobbot S. Quality of life in patients with leg ulcers: results from CHALLENGE, a double-blind randomized controlled trial. Journal of Wound Care. 2017; 26 (7): 368-379. 4- Schmutz J-L, Meaume S, Fays S, Ourabah Z, Guillot B, Thirion V, Collier M, Barrett S, Smith J, Bobbot S, Domp Martin A et al. Evaluation of the nano-oligosaccharide factor lipido-colloid matrix in the local management of venous leg ulcers: results of a randomised, controlled trial. International Wound Journal 2008, 5(2), 172-182. 5- Sigal ML, Addala A, Maillard H, Chahim M, Sala F, Blaise S, Dalac S, Meaume S, Bobbot S, Tumba C, Tacca O. Clinical evaluation of a new TLC-NOSF dressing with poly-absorbent fibers for the local management of exuding leg ulcers, at the different stages of the healing process: Results from two multicentric, single-arm, prospective, open-label clinical trials. J Wound Care 2019; 28(3) :164-175. 6- Münter KC, Meaume S, Augustin M, Senet P, Kerihuel J.C. The reality of routine practice: a pooled data analysis on chronic wounds treated with TLC-NOSF wound dressings. J of Wound Care. 2017 Feb, 26 (Sup2):S4-S15. Erratum in J Wound Care. 2017 Mar 2; 26(3): 153. 7- Edmonds M, Lázaro-Martínez JL, Alfayate-García JM, Martini J, Petit JM, Rayman G, Lobmann R, Uccioli L, Sauvadet A, Bobbot S, Kerihuel JC, Piaggese A. Sucrose octasulfate dressing versus control dressing in patients with neuroischaemic diabetic foot ulcers (Explorer): an international, multicentre, double-blind, randomised, controlled trial. Lancet Diabetes Endocrinol. 2018 Mar;6(3):186-196. 8- Richard J.L., Martini J, Bonello Farail M.M., M'Bemba J, Lepeut M, Truchetet F, ehrler S, Schuldtner S, Sauvadet A, Bobbot S. Management of diabetic foot ulcers with a TLC-NOSF wound dressing. Journal of Wound Care Vol 21. No 3, March 2012.

Studio Explorer: RCT che dimostra un'efficacia senza precedenti in DFU con medicazioni a base di Sucralosio Octasulfato (TLC-NOSF)

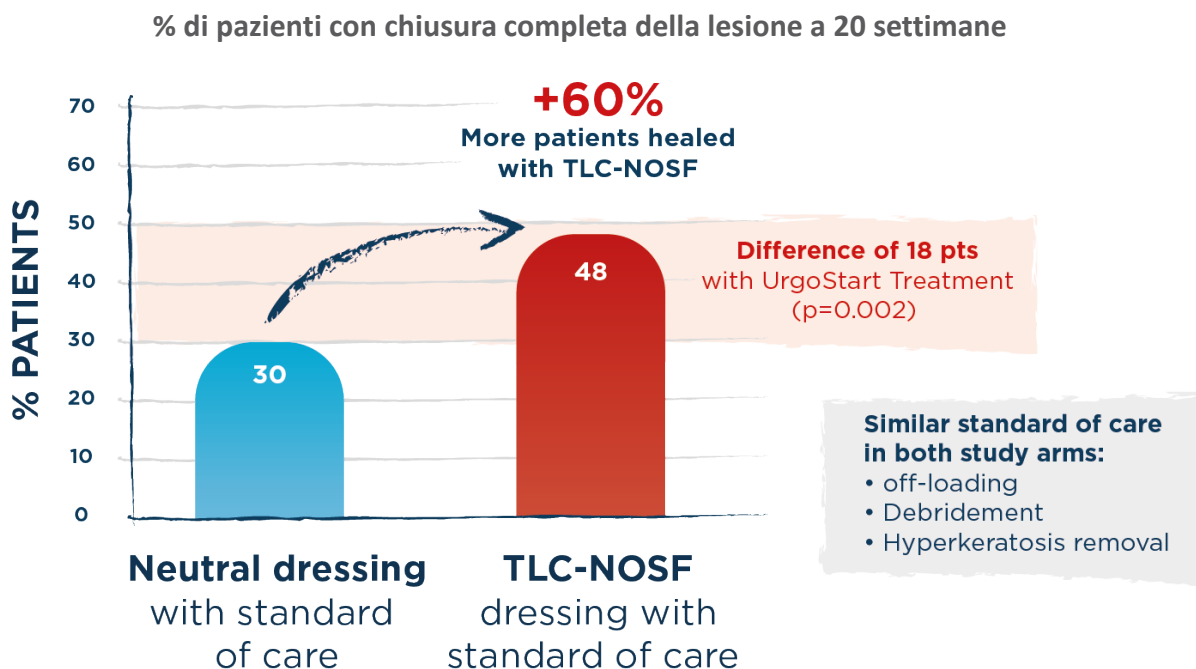


Studio randomizzato, in doppio cieco, controllato e stratificato, condotto su 2 gruppi paralleli

- 240 pazienti
- Con DFU neuroischemica
- Trattamento con **TLC-NOSF** vs medicazione neutra
- Standard of care in entrambe i gruppi



Studio Explorer: riduzione dei tempi di guarigione di 60 giorni nel gruppo TLC-NOSF vs medicazione neutra



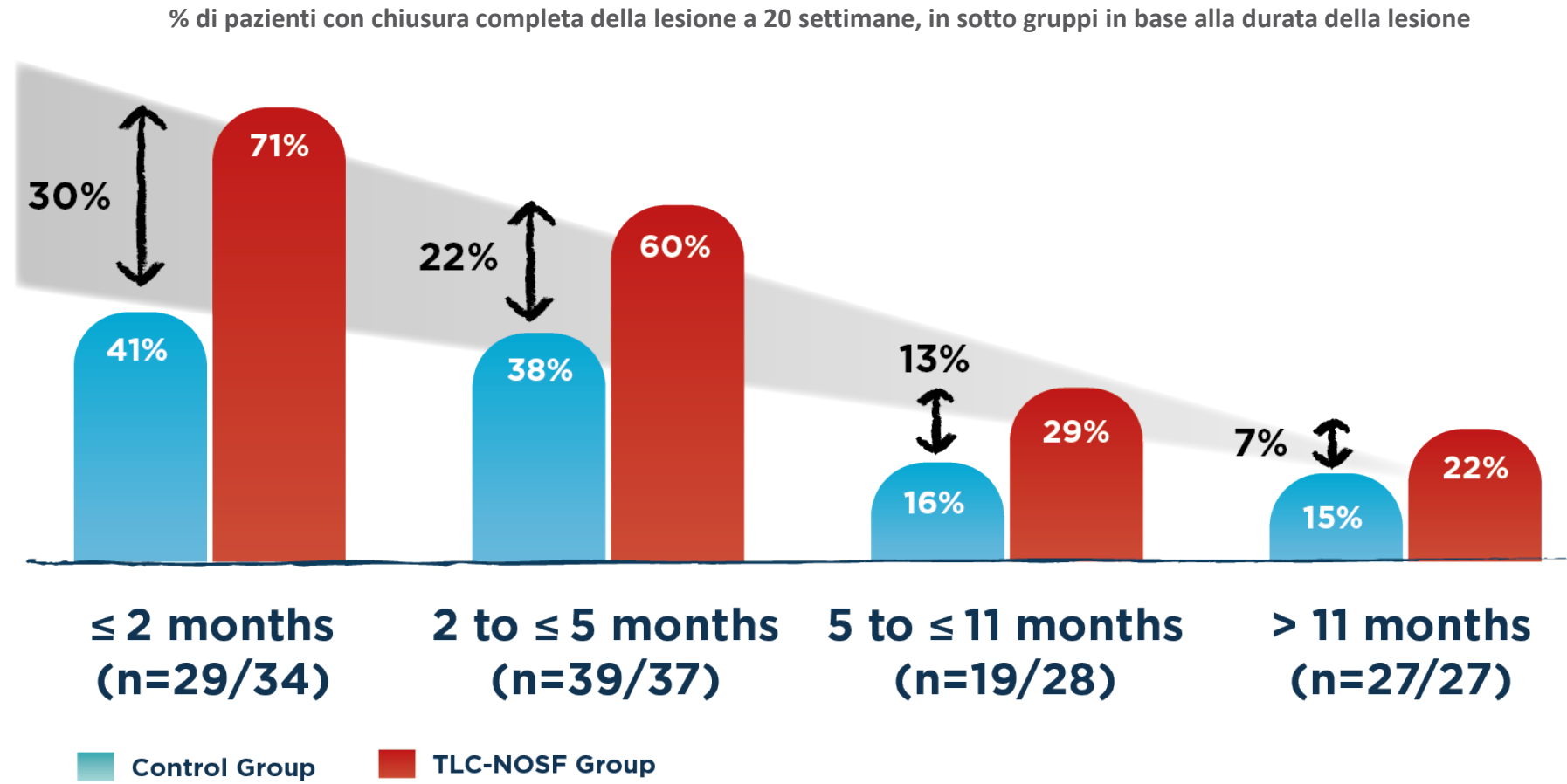
L'utilizzo della medicazione TLC-NOSF ha confermato un **tasso significativamente alto di chiusura completa della lesione in DFU** vs il solo standard of care

	Control group (n=114)	TLC-NOSF group (n=126)	Time to closure Difference (Control-Treatment)	Log rank (Mantel-Cox)
ITT Analysis	180,5 ± 8,7 (163,4 - 197,7)	119,7 ± 4,7 (110,5 - 128,9)	60 days	p= 0.029



Tempo di guarigione con chiusura completa della lesione avviene 60 giorni prima con TLC-NOSF

Trattamento di prima intenzione: PRIMA si utilizza TLC-NOSF, MIGLIORE l'outcome del paziente



Terapia Iperbarica

12. Consider the use of hyperbaric oxygen as an adjunct therapy in neuro-ischemic or ischemic diabetes-related foot ulcers where standard of care alone has failed and where resources already exist to support this intervention. (Conditional; Low)
13. Consider the use of topical oxygen as an adjunct therapy to standard of care for wound healing in people with diabetes-related foot ulcers where standard of care alone has failed and resources exist to support this intervention. (Conditional; Low)

L'utilizzo dell'HBO nel piede diabetico non ha ancora evidenze forti:

- Un RCT ha dimostrato un tasso di guarigione a 12 mesi maggiore nel gruppo trattato*.
- Un grosso studio osservazionale non ha dimostrato benefici rispetto alla terapia standard.
- 2 RCT hanno dimostrato efficacia in termini di guarigione.

** Il gruppo era composto da pazienti con buona perfusione periferica e da pazienti con no-CLI.*





14. Do not use other gases (e.g. cold atmospheric plasma, ozone, nitric oxide, CO₂) in comparison to standard of care for wound healing in people with diabetes-related foot ulcers. (Strong; Low)
15. Do not use any interventions reported in the field of physical therapies for wound healing in the management of diabetes-related foot ulcers. (Strong; Low)
16. We suggest not using cellular skin substitute products as a routine adjunct therapy to standard of care for wound healing in patients with diabetes-related foot ulcers. (Conditional; Low)
17. We suggest not using acellular skin substitute products as a routine adjunct therapy to standard of care for wound healing in patients with diabetes-related foot ulcers. (Conditional; Low)
18. Do not use autologous skin graft skin substitute products as an adjunct therapy for wound healing in patients with diabetes-related foot ulcers. (Strong; Low)
19. With the exception of the autologous leucocyte, platelet and fibrin patch we suggest not using autologous platelets therapy (including blood bank derived platelets) as an adjunct therapy to standard of care. (Conditional; Low)
20. Consider the use of autologous leucocyte, platelet and fibrin patch for diabetes-related foot ulcers as an adjunctive therapy to standard of care, where best standard of care alone has been ineffective, and where the resources and expertise exist for the regular venepuncture required. (Conditional; Moderate)

~~Gas, terapie fisiche,
sostituti cellulari,
sostituti acellulari,
innesti omologhi di
cute, PRP.~~



Platelet based application

7 studi inclusi, con buoni risultati in termini di guarigioni e tempi di guarigione ma con inclusione di lesioni di piede e di gamba, di diabetici e non diabetici, di analysis per protocol, di volume di sangue richiesto, di frequenza di applicazione.

Costi elevati.

Recombinant platelet derived growth factor

Degli 8 studi riportati, alcuni non hanno dimostrato significative differenze in termini di guarigione o tempi di guarigione vs SoC, altri hanno problemi metodologici o di analisi statistica (analysis per protocol).

Autologous combined leucocytes, platelets and fibrin

l'utilizzo di patch arricchiti con leucociti, piastrine e fibrina autologhi è stato valutato in uno studio multicentrico randomizzato non in cieco in ulcere difficili che non guarivano dopo 4 settimane vs SoC (34% vs. 22%).

La terapia richiede applicazioni settimanali ed elevati costi.

IWGDF Wound Healing Guideline



21. We suggest not using other cell therapy as an adjunct therapy to standard of care for wound healing in people with diabetes-related foot ulcers. (Conditional; Low)
22. We suggest not using growth factor therapy as an adjunct therapy to standard of care for wound healing in people with diabetes-related foot ulcers. (Conditional; Low)
23. Consider the use of placental derived products as an adjunct therapy to standard of care for wound healing in people with diabetes-related foot ulcers where standard of care alone has failed. (Conditional; Low)
24. Do not use pharmacological agents promoting perfusion and angiogenesis to improve wound healing outcomes over standard of care. (Strong; Low)
25. Do not use pharmacological agents that supplement vitamins and trace elements to improve wound healing outcomes over standard of care. (Strong; Low)
26. Do not use pharmacological agents that stimulate red cell production or prostaglandin synthesis to improve wound healing outcomes over standard of care. (Strong; Low)
27. Do not use other pharmacological agents to improve wound healing over standard of care. (Strong; Low)

Gli studi condotti su LMWH, iloprost, pentossifillina non mostrano significativa efficacia.

- *«However, the rising incidence and costs of diabetes-related foot ulcer management necessitates that interventions promoted to enhance wound healing of chronic diabetes-related foot ulcers are adequately supported by high quality evidence promoting efficacy and cost-effectiveness, when used in conjunction with established aspects of gold-standard multidisciplinary care».*

«Dressings do not heal wounds. Property selected dressings enhance the body's ability to heal the wound»

Garza inerte,
Captazione
batterica, iodio,
Argento, etc.

Fase flogistica

Sostituti
dermici

POST-OP

TLC-NOSF, idrofibra,
alginati, poliacrilati,
idrogel, idrocolloidi,
schiume di
poliuretano,
collagene

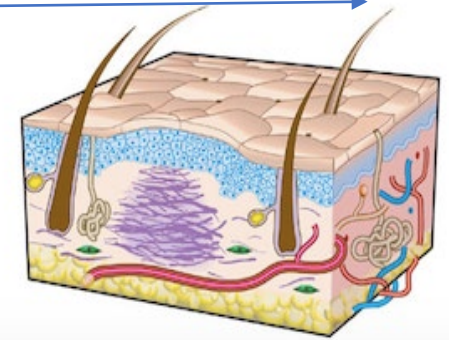
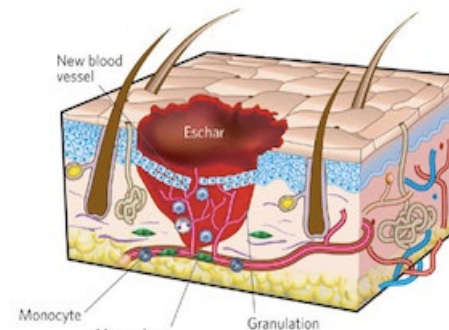
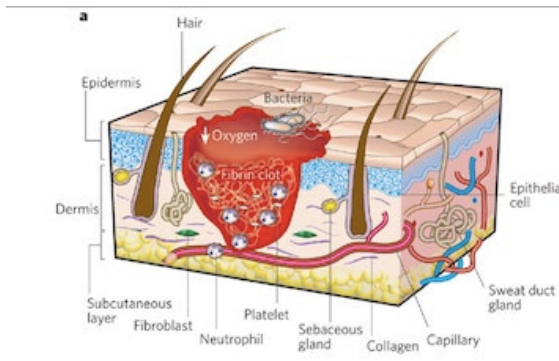
Fase proliferativa

Innesti
autologhi

POST-OP

Garze grasse,
tulle, TLC-NOSF,
idrofibra,
schiume di
poliuretano

Fase riparativa



Emad Naseri, et al. *European Polymer Journal*,
Volume 173,2022,111293,ISSN 0014-3057,
<https://doi.org/10.1016/j.eurpolymj.2022.111293>.

Di che cosa abbiamo bisogno?

- Disegno dello studio
- Recidive
- SoC e Caratteristiche dei pazienti
- Studi indipendenti
- Costo-Efficacia
- Combinazioni di terapie e timing di utilizzo

Panel: 21-point scoring system for reports of clinical studies of the prevention and management of disease of the foot in diabetes

The desired answer for each question is intended to be “yes”, and each scores one point.

Study design

- 1 Are appropriate definitions included for the terms “ulcer”, “healing”, and all other required aspects of the population and the outcomes?
- 2 Was the choice of study population appropriate for the chosen intervention and the stated conclusions?
- 3 Was there a control population that was managed at the same time as those in the intervention group or groups?
- 4 Is the intervention sufficiently well described to enable another researcher to replicate the study?
- 5 Are the components of other aspects of care described for the intervention and comparator groups?
- 6 Were the participants randomised into intervention and comparator groups?
- 7 Were the participants randomised by an independent person or agency?
- 8 Was the number of participants studied in the trial based on an appropriate sample size calculation?
- 9 Was the chosen primary outcome of direct clinical relevance?
- 10 Was the person who assessed the primary outcome or outcomes blinded to group allocation?
- 11 Were either the clinical researcher who cared for the wound at research visits or the participants blinded to group allocation?

Study conduct

- 12 Did the study complete recruitment?
- 13 Was it possible to document the primary outcome in 75% or more of those recruited?
- 14 Were the results analysed primarily by intention-to-treat analysis?
- 15 Were appropriate statistical methods used throughout?

Outcomes

- 16 Was the performance in the control group of the order that would be expected in routine clinical practice?
- 17 Are the results from all participating centres comparable? Answer “yes” if the study was done in only one centre.

Study reporting

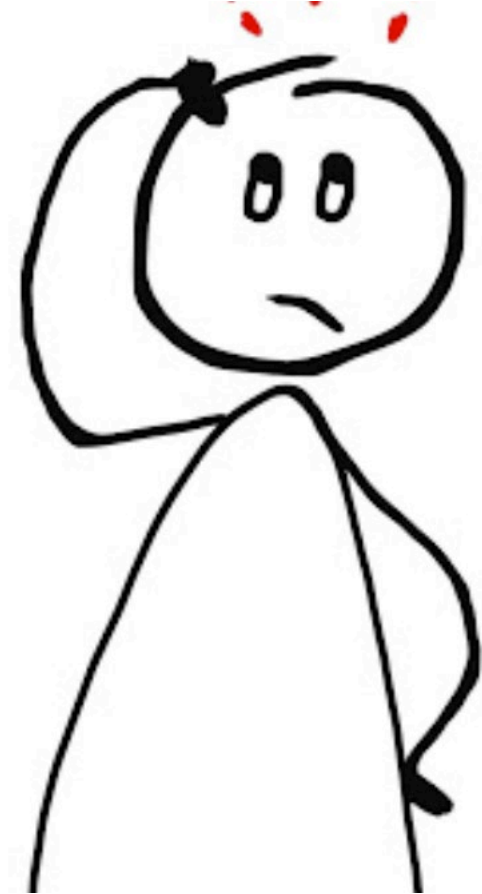
- 18 Is the report free from errors of reporting—eg, discrepancies between data reported in different parts of the report?
- 19 Are the important strengths and weaknesses of the study discussed in a balanced way?
- 20 Are the conclusions supported by the findings?
- 21 Is the report free from any suggestion that the analysis or the conclusions could have been substantially influenced by people with commercial or other personal interests in the findings?

Efficacia della Terapia Standard

- Solo il 30% delle DFU guariscono con la SOC

**There's
always
room for
improvement.**

Grazie per l'attenzione



[Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Healing diabetic neuropathic foot ulcers: are we getting better? Diabet Med. 2005].



Grazie per l'attenzione