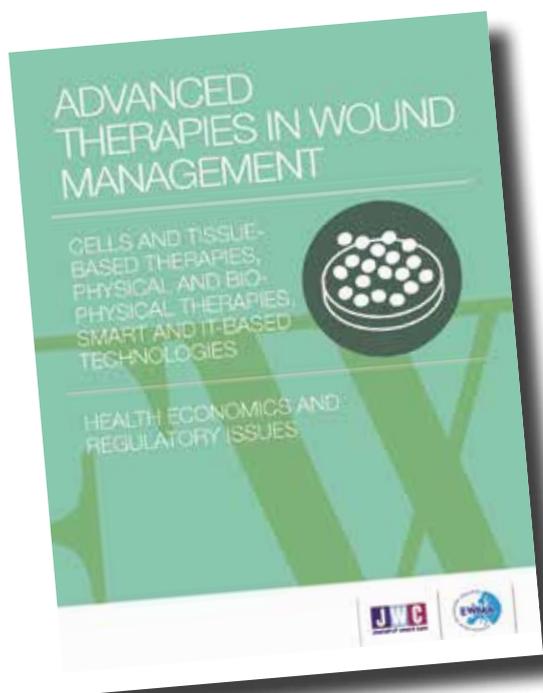


New EWMA document:

Advanced therapies in wound management



Presentation of the "Advanced Therapies in Wound Management" document is the main topic of a key session at EWMA 2018 scheduled for Wednesday, 9 May in "Wisla Session Room".

This article introduces a new document from the European Wound Management Association (EWMA), aiming to outline the current situation, challenges and opportunities related to the introduction of new advanced therapies in wound management in the clinic. Here, the document contents and structure are briefly presented to the potential readers of the full document. This will be published as an online supplement to the Journal of Wound Care in May 2018.

Backgrounds and aims

With this document, the European Wound Management Association (EWMA) aims to investigate the barriers and possibilities of advanced therapies in next-generation wound management, including technologies based on cellular therapies, tissue engineering and tissue substitutes, which are all associated with the clinical discipline of regenerative medicine. The document also describes new treatments based on physical therapies and the potential of sensors, software and internet technologies. EWMA wishes to be on the forefront of the development of new, sustainable, cost-effective advanced therapies and to examine further how these may support the continuous improvement of wound management with regard to patients' quality of life while also providing a more effective and efficient approach to wound management.

The objectives of this document are to:

- Review and discuss clinical experiences and the scientific evidence where this is available;
- Provide an objective and exhaustive overview of the available therapies and their potential roles in clinical practice and make recommendations for the implementation of these therapies in the different areas of wound management;
- Analyse and debate cost-effectiveness issues related to the included therapies; and
- Discuss the regulatory framework for advanced therapies in Europe, providing a point of referral for future discussions and negotiations with health care providers and payers. ▶



Alberto Piaggese,
Document Editor

MD, Prof. Director of the Diabetic Foot Section of the Pisa University Hospital, Department of Endocrinology and Metabolism, University of Pisa, Italy

EWMA Scientific Recorder

Correspondence:
ewma@ewma.org

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Due to the general lack of scientific documentation for many of these emerging therapies, the document is based on the available literature and experts' opinions. It includes an evaluation of the potentials for future use in clinical practice and a call for research in recommended areas.

Definition of advanced therapies

The group of authors responsible for this document agreed on the following definition for the term 'advanced therapies'. It has been adopted as a basis for selecting relevant technologies for inclusion in this publication.

The therapies related to chronic wound management can be defined as 'advanced' when they are based on novel principles and technologies, or when they refer to a novel application of consolidated principles and technologies, including either a singular mechanism of action or a strategy with different levels of action, given that some evidence has been produced in a measurable and comparable way by the manufacturers/developers. For the sake of this document, advanced therapies will be grouped according to their nature in four different categories: materials, cell and tissue engineering, physical and bio-physical, and sensors and IT-related.

Document contents

The document is organised into six sections; four of them deal with the different areas of advanced therapies and are, in order of position in the document, dedicated to:

Materials:

This section describes advanced therapies based on films, foams, hydrocolloids, hydrogels, alginates and acellular matrices, including their previous, current and future uses.

Cell- and tissue-based therapies:

This section includes a chapter highlighting advanced therapies based on cells, including:

- Stem cells, including bone marrow stem cells, keratinocytes and fibroblasts, adipose-derived stem cells and other cells
- Scaffolds, including carrier systems
- Skin substitutes, including cellular non-living allografts, placental-based allografts, bioengineered skin substitutes and skin substitutes for in-vitro and in-vivo applications
- Tissue-based therapies, including autologous blood derivatives for wound care and advanced cell therapies;

- Epidermal substitutes, dermal substitutes and dermo-epidermal substitutes

- Melanocytes, vessels and genetic manipulation, and automation.

Physical therapies:

This section describes advanced therapies using shock waves (ESWT), electro-magnetic fields (EMF), photobiomodulation (PMB) and nanotechnologies (NT).

Smart technologies:

This section describes the wearables and applications available to manage chronic ulcers 'smartly', including:

- Wearable devices;
- Wearable wound therapy;
- Modern wound dressings, including sensors;
- Mobile health (m-health); and
- The 'Internet of Things' in the remote management of wounds.

The document also includes two sections dedicated to the economic and regulatory aspects of advanced therapies in wound management. The aim of these sections is to provide a different perspective on this complex and fast-evolving field, bridging the gap between the technologies and their inception in the real world of wound healing.

The document is concluded with a "wish list"; a separate concise section including ten points that highlights crucial aspects to be addressed with regards to supporting proper evaluation and potential implementation of relevant advanced therapies in wound management. This final section is included as a potential tool for addressing future issues and controversies in this challenging and promising field. This tool targets health care professionals as well as administrators, decision makers and regulators. The list is followed by a paragraph in which EWMA describes the potential role of a European clinical and scientific association with regards to supporting the realisation of the promises that advanced therapies makes to wound healing. The authors hope that reading this document will be not only interesting for scientists and clinicians, but also helpful for all the stakeholders in the field of wound management, assisting them in building a better future for our patients.

The wish list - for a better future

Based on an extensive review and critical reappraisal of the existing evidence, and of the problems related to the

implementation of new technologies in wound healing, the authors responsible for this EWMA position document agree on the following recommendations for future developments:

1. Development of new technologies: As the development of new technologies is a time- and resource-consuming process, often lasting several years, companies interested in developing and introducing both new technologies and medical devices for wound healing are advised to consult preliminarily with an interdisciplinary team of stakeholders, including basic scientists, bioengineers and clinicians with a specific expertise in wound healing, in order to test the originality and applicability of their ideas/projects.

2. Health technology assessments (HTAs): The limited financial resources in all health care systems across Europe (which are typically financed via a taxpayer system) emphasise the need for an adequate allocation of resources based on updated evidence and principles of cost-effectiveness. HTAs have become the standard approach whenever new technologies are proposed for introduction in the field. The fact is that HTA procedures vary from country to country, or, in some cases, from region to region within a country. As part of a rationalisation process, which should be promoted and endorsed by the EU in the framework of legislative action, HTA procedures should be defined and standardised across the EU. This would simplify the process of bringing new technologies from the lab to the patients. It would also reduce the amount of resources that companies must invest in these procedures, eventually saving them further research activities.

3. Implementation of new technologies in clinical practice: In order to bridge the gaps that almost unavoidably develop between the realisation of new technologies and their implementation in clinical practice, it is important to define minimum standard requirements for testing/implementation in clinical practice. These requirements must be related to Items 1 and 2 in this list, tested under controlled conditions and following the recommendations of good clinical research. RCTs are the preferred approach. However, due to the cost- and method-related difficulties linked with the organisation of an RCT, prospective observational trials may be considered, if they are independent and relevant for wound management.

4. Translational science: Despite the increasing number of options in terms of the variety and quality of technologies available for clinical use in wound management, there is a diffuse underuse of new technologies the moment they become available to clinicians. Often, the implementation in clinical practice does not meet the expectations of the manufacturers. One major component of this bias is

related to poor knowledge of the basic principles of the new technologies and their materials among health care professionals. Their level of knowledge may eventually be improved by translational science initiatives aimed at bridging the technological gap.

5. The need for investments in research: Important economic resources are needed to sustain the growth of research and the development of new technologies for wound management. Beyond the commercial interests of the industries in the field, institutions at the European level must also recognise the importance of investing in a field that will interest one out of four EU citizens over the next decades.

6. Access to new technologies in the EU: The possibility of accessing new technologies varies significantly across the different countries in the EU, not only for the reasons described below in Items 7 and 8 in this list. Another key factor in ensuring the accessibility of new technologies is that the companies are willing to market the new technologies in all European countries, despite the economic arguments for targeting certain countries before others. When new technologies are not available across the European health care systems, this creates idiosyncrasies in the actual possibility of patients being treated with new technologies. Companies are thus advised to extend their diffusion of new technologies across Europe to the extent that it is possible.

7. Regulatory controversies: Regenerative medicine is on the rise and about to shift the focus from replacing and repairing tissue to regenerating it. Although regenerative medicine is not yet a reality in wound management, the on-going development of activities in the field of Advanced Therapy Medicinal Products (ATMPs) holds the realistic promise of revolutionising standard treatment. Gene therapies producing wound-healing factors may soon become a reality and open new horizons for treatments. Most regenerative medicines are classed as ATMPs and are thus confronted with high product and development standards. Thus, their development can be very challenging for companies due to the inherent complexity of the products. In particular, detailed EU guidance related to emerging gene editing technologies is available, but it is missing, so far, for wound management-related endeavours. It would be advisable to engage with regulatory authorities in the future, in order to make them aware of the challenges related to the development of medical products for wound management, and this lack of guidance. This will hopefully lead to the development of specific guidelines from which product developers can benefit in the future.



8. Definition of outcomes, direct and indirect costs: Cost studies vary in approach and quality. The wide variety of outcome measures and costs hinder comparisons of interventions and progress. Thus, there is an increasing need to define outcomes, direct costs and indirect costs that should be included in the economic evaluations clearly. Promoting research and clinical trials on advanced therapies, and involving health economists and health statisticians in the planning, execution and analysis of the studies, is essential for ensuring the appropriate economic assessment of the impact of these interventions. Moreover, given the paucity of studies on the quality of life of patients, more analyses focusing on this dimension should be performed.

9. The growth of a wound care-centred research field within the telemedicine and wearables milieus: Technologies such as telemedicine and wearables enable the reduction of in-person visits and allow physicians to check on patients remotely, track patient adherence to prescribed therapies, detect the early stages of serious medical conditions and triage those who need immediate supervised care. While the application of such technology for effectiveness of diabetic foot care is still in its infancy, and its cost-effectiveness is still debated, it is anticipated that general healthcare and chronic wound care delivery will change dramatically in the near future. Thus, more research is recommended in this field to translate these telehealth technologies into better management of chronic wounds and improve patient-centred outcomes, including the number of in-person visits.

10. Evaluation of outcomes: A major challenge for a fair comparison between new technologies and conventional therapies is the lack of consensus and guidelines for the standardisation of reporting of outcomes. In addition, new outcomes that are more sensitive to new technologies should be defined and standardised (e.g., number of in-person visits for telehealth applications, levels of restriction in mobility during the wound healing phase, etc.). Moreover, most research in the area of chronic wound management is currently focused on wound outcomes during the wound-healing phase, not taking into consideration the high rate of recurrences. It is recommended that the time to recurrence of ulcers, as well as their frequency, also be taken into consideration when examining the effectiveness of new technologies. ■

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