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Review article

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Wound management materials and technologies from bench to bedside and beyond

Canran Wang[1], Ehsan Shirzaei Sani[1], Chia-Ding Shih[2], Chwee Teck Lim[3,4,5], Joseph Wang[6], David G. Armstrong[2] & Wei Gao[1]

Abstract

Chronic wounds represent a major global health problem, causing staggering economic and social burdens. The pursuit of effective wound healing strategies demands a multidisciplinary approach, and advances in material sciences and bioengineering have paved the way for the development of novel wound healing biomaterials and technologies. In this Review, we provide an overview of the history and challenges of wound management and highlight the current state of the art in wound healing biomaterials alongside the emerging technologies poised to transform the landscape of chronic wound treatment and monitoring. Moreover, we discuss the clinical and commercial considerations associated with wound healing strategies, including the regulatory pathways and key steps in the translational process. Furthermore, we highlight existing translational gaps and offer a nuanced understanding of the challenges that persist in translating innovative concepts into mainstream clinical practices. Continued innovations and interdisciplinary collaboration will pave the way for better wound care outcomes and potentially markedly improved quality of life for a steadily increasing and ageing population.

Sections

[1]Andrew and Peggy Cherng Department of Medical Engineering, California Institute of Technology, Pasadena, CA, USA. [2]Southwestern Academic Limb Salvage Alliance (SALSA), Department of Surgery, Keck School of Medicine of University of Southern California, Los Angeles, CA, USA. [3]Institute for Health Innovation & Technology, National University of Singapore, Singapore, Singapore. [4]Department of Biomedical Engineering, National University of Singapore, Singapore, Singapore. [5]Mechanobiology Institute, National University of Singapore, Singapore, Singapore. [6]Department of Nanoengineering, University of California San Diego, La Jolla, CA, USA.
e-mail: weigao@caltech.edu

Introduction

Wound healing is an intricate and dynamic process crucial for preserving the integrity and functionality of the skin and the adjacent tissues. Acting as a protective barrier, the efficient healing of the skin is essential in preventing infections and maintaining homeostasis. Wounds, categorized into acute and chronic, present considerable challenges to the health-care system. Acute wounds typically follow a predictable sequence of inflammation, proliferation or repair and remodelling. Conversely, chronic wounds, often associated with conditions such as diabetes, vascular diseases or pressure injuries, frequently linger in the inflammatory stage, leading to prolonged healing times, heightened infection risks, increased morbidity and even mortality[1–3] (Fig. 1).

The burden of wounds on health-care systems is substantial, affecting millions annually with associated costs estimated to be more than US$28 billion[4,5]. A recent update suggests that 40–60 million people worldwide are affected by diabetic foot ulcers (DFUs), with prevalence rates fluctuating owing to variations in surveillance methods, definitions and access to care. DFU prevalence in North America is 13% and lower in Europe (5.1%), with a global average of 6.4%. Increasing rates have been reported in Africa and South America (15%), with males and patients with type 2 diabetes more frequently affected[4,6]. Surgical wounds, pressure injuries and burns contribute extensively to this burden, underscoring the need for effective wound management strategies. The current standard of care involves preparing a viable wound bed through practices such as debridement, irrigation and closure techniques. However, continuous innovation is evident in wound care, ranging from advanced wound dressings to technologies targeting specific pathophysiological factors[7].

Chronic wounds pose a mortality risk greater than commonly appreciated. For instance, the 5-year mortality rates among individuals contending with diverse forms of chronic wounds, such as diabetic chronic ulcers, stand at a considerable 70%. This statistic notably exceeds the 5-year mortality rates observed in patients with conditions such as colorectal, breast and prostate cancers. Unlike cancer treatments, there exists a conspicuous gap in education and awareness about wound care among health-care professionals, patients and the general population. Strengthening community engagement and patient advocacy efforts is crucial for addressing such educational gaps and promoting preventive measures for more effective wound management.

Commercial wound care products are not limited to passive biomaterial-based wound dressings, and smart wound dressings capable of real-time monitoring and active intervention have also been developed. Chronic wounds often involve bacterial infections, excessive inflammation, poor perfusion and vascularization. The limitations of conventional wound dressings in providing real-time information on the complex wound microenvironment impede the attainment of optimal wound healing. A promising solution to overcome this constraint lies in the integration of wearable sensors into smart wound dressings. Furthermore, the advent of smart bioelectronic systems presents great potential for personalized wound care, owing to their advantages such as wearability, cost–effectiveness and rapid and simple application[8–16].

Although numerous wound care products have been developed, each follows a distinct clinical and regulatory pathway, and only a limited number of them have received clinical approval, with many failing during the translation process. According to the FDA guidelines, a fundamental understanding of the pathophysiological processes driving injury is crucial for developing targeted therapies. Multidisciplinary collaboration efforts and early engagement with clinicians are imperative for identifying unmet clinical needs and creating evidence-based target product profiles. Additionally, preclinical models that accurately represent human tissue responses are also critical for successful translation from bench to bedside[7]. The notable increase in wound care technologies since 2017 reflects the convergence of factors that have collectively accelerated advancements in this field (Fig. 2). This surge can be largely attributed to the fusion of multidisciplinary technologies, including biotechnology, nanotechnology and digital health, which have paved the way for the development of innovative wound care solutions such as smart dressings and bioactive materials. Additionally, there has been a marked increase in funding for wound care research from both governmental and private sources. This uptick in investment is motivated by a growing awareness of the challenges posed by chronic wounds and the expanding wound care market, which was valued at US$20.18 billion in 2022 and is expected to reach US$30.52 billion by the end of 2030 (refs. 17–20). Advancements in material science have introduced novel biomaterials that enhance wound healing more effectively. Wearable technologies have transformed wound monitoring and management by enabling real-time data analysis. Furthermore, regulatory bodies have optimized their approval processes for medical devices and therapeutic products, accelerating the commercialization of new innovations. Additionally, global collaborations among researchers, clinicians and industry stakeholders have improved the distribution and adoption of these advanced technologies. This multifaceted progression underscores the dynamic evolution of wound care methodologies, marking a leap in therapeutic approaches and product development in recent years.

In this Review, we present the design principles for wound care technologies tailored to specific clinical applications, aiming to bridge the gap between applied research and translational outcomes. Our assessment of wound care encompasses various aspects of material design principles derived from diverse fields, such as tissue regeneration, wound dressing, smart bandages and cell or drug delivery in the context of wound care applications. We then delve into recent advances in chronic wound management, emphasizing the importance of a multidisciplinary approach and capitalizing on breakthroughs in material science and bioengineering to enable personalized chronic wound assessment. The integration of novel materials facilitates controllable and sustainable delivery of therapeutic agents to the wound site while preserving physiological microenvironments. Furthermore, we explore recent strides in diagnostic medical devices, particularly wearable biosensors, which empower non-invasive, real-time monitoring and analysis of the wound condition to enable timely intervention and enhance patient compliance. The imperative development of such materials and technologies has become evident to address the unmet needs of chronic wound care. Additionally, we describe the translational process and regulatory pathways indispensable for the effective development of wound management strategies. Last but not the least, we provide an illustrative overview of the various classifications of wound care products, offering a comprehensive perspective on the evolving landscape of wound care technologies.

Emerging materials for advanced wound management

Wound management integrates a diverse array of materials designed to modulate the wound microenvironment, thereby orchestrating essential facets of the healing process. These materials play pivotal roles in fostering fibroblast growth, re-epithelization, vascularization, collagen

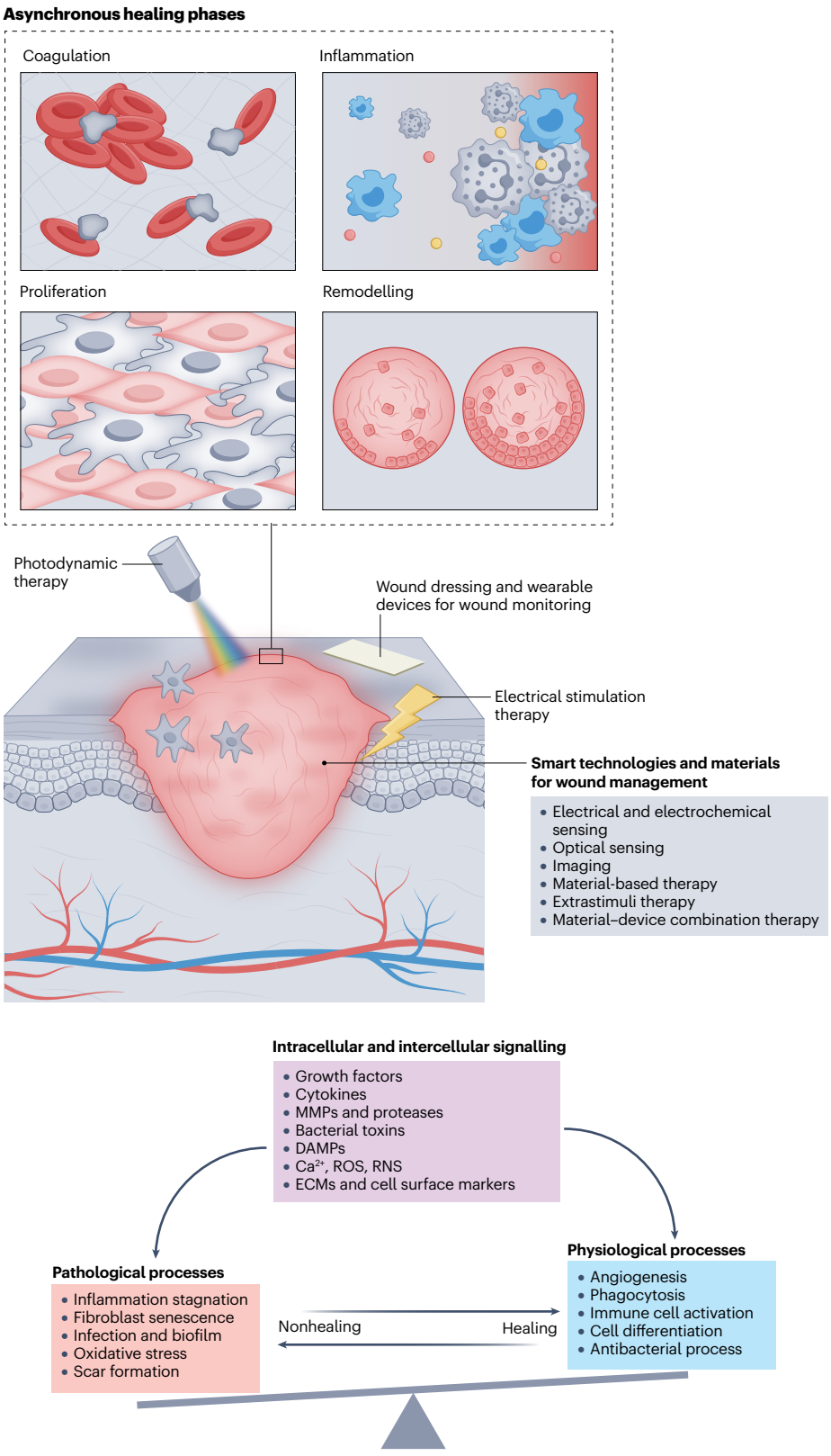

Fig. 1 | Chronic wound healing and management process. Schematic illustrates the process of healing in chronic wounds. Chronic wounds exhibit a complex and protracted healing trajectory, marked by the occurrence of various healing phases in a nonlinear and unpredictable fashion. Addressing the distinct challenges posed by each phase within the same wound necessitates diverse therapeutic approaches tailored to specific areas. Wound healing is facilitated by physiological activities such as angiogenesis and phagocytosis, which are driven by positive intracellular and intercellular communication involving growth factors and cytokines. Conversely, pathological conditions, including chronic inflammation, fibroblast ageing and oxidative stress, arise from disrupted signalling mechanisms. These conditions are often worsened by elements such as matrix metalloproteinases (MMPs), damage-associated molecular patterns (DAMPs) and bacterial toxins, leading to wounds that do not heal. Therefore, therapeutic efforts should aim to modulate these biochemical pathways and signals to promote a shift towards healing by addressing the specific challenges that impede recovery in pathological wound healing scenarios. Advanced smart technologies and materials have been innovatively designed to tackle this complexity and provide a personalized and dynamic strategy for optimal wound management. ECM, extracellular matrix; RNS, reactive nitrogen species; ROS, reactive oxygen species. Adapted from ref. 41, Springer Nature Limited.

deposition, immunomodulation and mitigating complications such as infection, pain, bleeding and tissue scar formation. Tailored materials and methodologies are crucial across the four stages of wound healing (Fig. 1), although their linear sequence may not correspond with the healing process of chronic wounds. Initially, hydrogels and chitosan contribute to clotting and offer antimicrobial benefits. As healing progresses, smart dressings facilitate the release of anti-inflammatory agents during the inflammation phase. In the proliferative phase, biodegradable scaffolds, such as collagen, foster new tissue formation. During the remodelling phase, the focus shifts towards minimizing scarring, with silicone sheets and biomimetic materials being preferred options. Given that chronic wounds may deviate from this orderly progression, the selected materials must be adaptable, capable of simultaneously addressing various aspects of healing to effectively manage the intricate dynamics of chronic wound care.

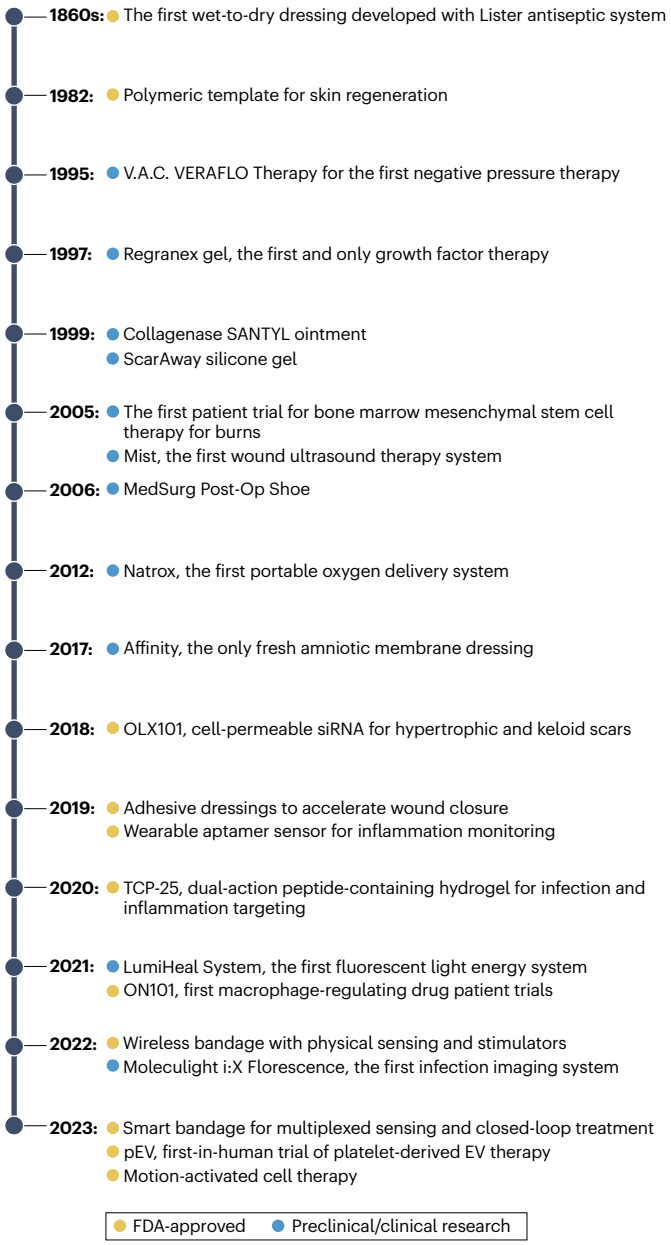

Fig. 2 | A timeline of technology development in chronic wound management. The history of wound care devices, encompassing the FDA-approved innovations and those currently undergoing preclinical or clinical research. The history of wound care products spans from cellular-level topical ointment, sophisticated therapy, to cutting-edge biosensors and portable diagnostic devices, illustrating the forward-moving trajectory of key advancements in wound management technologies. EV, extracellular vesicle; siRNA, small interfering RNA.

Rational material and technology design for clinical applications

Achieving effective wound care necessitates the strategic development of materials and technologies tailored specifically to the nuanced requirements of clinical applications. The rational design of biomaterials for wound healing entails meticulous considerations to uphold the physiological microenvironment and therapeutic functionality[9,21,22] (Fig. 3a,b).

Mechanical properties. The mechanical properties of materials have a pivotal role in minimizing secondary damage and promoting the healing process. The maximum strain rate of human epidermis, ~15%, underscores the importance of proper elasticity to ensure adherence and prevent damage to both tissue and device[23]. The strength, elasticity and adaptability of materials not only safeguard wounds but also exert a profound influence on cellular behaviours. The mechanical attributes of wound dressings and scaffolds can severely impact tissue regeneration, inflammation and even scar formation. For instance, a substrate stiffness of 10 kPa and a dressing length of 7–9 cm to promote force transmission proves ideal for fibroblast proliferation because it closely mirrors the mechanical environment of cutaneous tissues[24,25]. Materials endowed with adjustable mechanical properties are promising, demonstrating improved healing by offering controlled and sustained contraction on moist wound surfaces[26].

Porosity, breathability and transparency. The porosity of the scaffold plays a critical role in governing cellular infiltration and supporting the vascularization, as interconnected pore networks enhance the transport of elements such as nutrients, oxygen and waste products[27]. Beyond porosity, the breathability of wound dressing is crucial, allowing the penetration of oxygen towards the wound while simultaneously serving as an effective barrier against bacterial contamination[28,29]. Additionally, material transparency proves invaluable, facilitating real-time monitoring and visualization of the healing progress of the wound. When using transparent wound devices, integrating layers that shield against ultraviolet radiation is crucial. This measure prevents possible changes in skin pigmentation and ensures both the material durability and sustained functionality of its embedded components.

Wettability. The wettability of wound dressings greatly influences the behaviour of biofluids in the proximity of wounds. Although a moisture-retentive feature is essential, an excess of biofluids at wound sites can lead to infections and impede the healing process[30]. To address this, self-pumping dressings are ingeniously designed to drain excess biofluids from their hydrophobic side to their hydrophilic side, effectively preventing the wound from becoming excessively wet[31]. Achieving a delicate balance between retaining moisture and facilitating evaporation is key to avoiding fluid build-up, which can cause maceration and infection. The water vapour transmission rate (WVTR) is an important

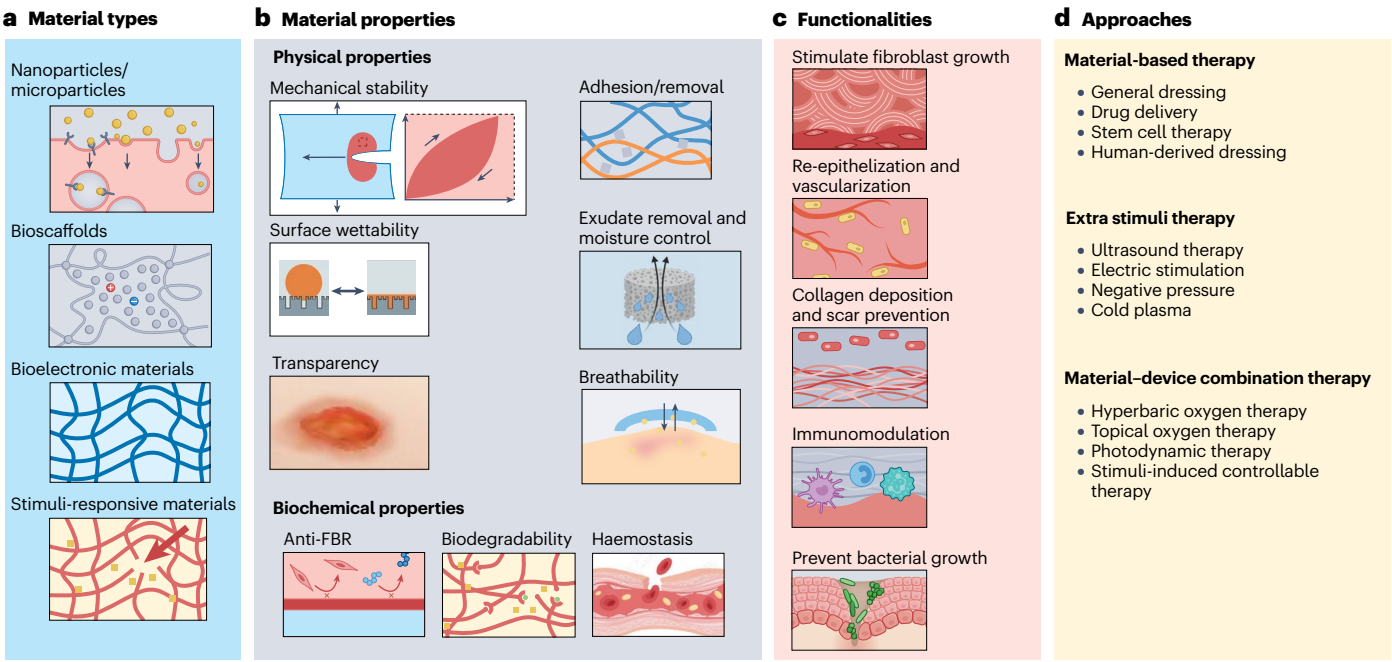

Fig. 3 | Translational materials for wound treatment. a, Various material types employed for chronic wound treatment, including nanoparticles/microparticles, bioscaffolds, bioelectronic materials and stimuli-responsive materials. **b**, Physical properties including mechanical stability, adhesion, wettability, moisture control, transparency and breathability, as well as biochemical properties such as anti-foreign body response (FBR), biodegradability and haemostasis. These characteristics can control a range of cellular functions and therapeutic efficiency. **c**, The materials designed to realize functionalities such as fibroblast growth stimulation, re-epithelization, vascularization, collagen deposition, scar prevention, immunomodulation and infection prevention. **d**, Currently, available therapeutic approaches could be categorized as material-based therapy, extra stimuli therapy or material–device combinational therapy.

metric that varies with the type and stage of the wound; for instance, normal skin has a WVTR range of 204–278 g m^{-2} per day, whereas first-degree burns and granulating wounds exhibit a substantially higher rate of 5,138 ± 202 g m^{-2} per day (ref. 32). A dressing is considered to have adequate moisture-retentive properties if its WVTR is less than 840 g m^{-2} per day (ref. 33). Dressings with high water vapour permeability may dry out the wound too quickly, leading to scarring, whereas those with low permeability may cause exudate accumulation, slowing the healing process and increasing infection risk.

Adhesion. Adhesive dressings are gaining prominence in wound care owing to their direct application, eliminating the need for cutting and attaching surgical tapes. This not only ensures secured wound coverage but also maintains a stable interface between the wound and the dressing material[34]. However, it is crucial to note that excessive adherence to the wound can lead to removal of substantial layers of the stratum corneum, either from the newly formed epithelium or from the healthy skin surrounding the wound.

Haemostasis. Retaining wound haemostatic constituents on the dressing material is paramount, as they can contribute to haemostasis and provide a scaffold for incoming cells and growth factors. This retention potential holds promise for enhancing wound regeneration[35,36]. For example, the application of laponites, a synthetic nanoclay with inherent haemostasis capacity, can improve shear-thinning properties, making it a widely utilized material for the 3D printing of wound dressing[37,38].

Biochemical properties. The biochemical properties of wound biomaterials encompass critical factors such as biocompatibility, the interaction between biomaterials and the wound microenvironment, scaffold degradation and the release of entrapped therapeutic agents. Following application, dressings and devices will quickly accumulate a layer of adsorbed proteins, triggering the immune system recognition and dictating the foreign body response process. Anti-foreign body response properties become imperative to mitigate inflammation and complications, optimize device performance and enhance overall functionality. The degradation of biomaterials is intricately linked to the local microenvironment. For example, chronic wounds are characterized by a high level of proteases, which can accelerate the degradation of peptide-derived matrix[39]. Conversely, the release of signalling ions from biomaterials can positively alter the local microenvironment. For example, calcium ions released from alginate can serve as both haemostatic and fibroblast proliferation signals[40].

Therapeutic strategies in wound management can be intricately customized to align with the distinct characteristics and demands of diverse wound types. Essential to this approach is a profound understanding of the underlying causes of the wound, such as pressure, diabetes, venous insufficiency or arterial disease, as this knowledge is crucial to judiciously select appropriate materials. For instance, addressing venous leg ulcers typically involves the application of compression bandages to enhance circulation, whereas the treatment of DFUs often prioritizes meticulous debridement and safeguarding the wound from further injury[41]. Moreover, individual patient considerations, such as pain levels, can influence dressing selection and the

frequency of dressing changes and may necessitate the incorporation of pain management interventions. Additionally, the selection of a wound care strategy is shaped not only by clinical considerations but also by economic factors and the availability of qualified care providers. These factors underscore the paramount importance of adopting a holistic and adaptable approach to wound care that not only caters to the specific needs of the wound but also addresses the broader context of patient well-being.

Advanced materials for wound treatment

Cutting-edge materials play a pivotal role in supporting the healing process and mitigating complications associated with wounds. Acting as protective shields, they redistribute pressure and shield against external contaminants. In situations demanding wound stabilization, immobilization or precise pressure distribution, medical devices incorporating rigid materials present specialized solutions such as negative pressure therapy, orthotic device for wound prediction and prognosis and casts for fractures. These tailored devices contribute to optimal wound recovery by addressing individual patient needs.

Nevertheless, conventional materials, although they provide essential support, often fall short in conforming to the contours of the body and lack breathability. These factors can result in discomfort, potential skin complications and the need for frequent adjustments during the healing process. There is a growing interest in developing novel materials that are more adaptable, comfortable and conducive to the overall healing trajectory.

Emerging materials-based treatments have shown great potential in wound healing applications[42]. Unlike conventional rigid materials that offer passive wound support, many of these materials are flexible and wearable, enhancing user comfort and enabling responsive, personalized treatment for faster tissue regeneration and reduced infection risks (Fig. 3c). Leveraging materials such as hydrocolloids, hydrogels, nanofibres and other functionalized materials, these treatments exhibit promising biocompatibility and the ability to maintain and modulate the physiological microenvironment of the wound[21,35,43,44]. Various technologies for wound healing, including targeted and controlled drug delivery[45,46], bioelectronics stimulation[11], photodynamic therapy[47,48], negative pressure wound therapy (NPWT)[49], hyperbaric oxygen therapy[50] and gene and cell therapy[51], have progressed substantially, facilitated by these novel materials. The integration of these innovative material-based therapies has the potential to revolutionize wound management, improving healing outcomes and reducing health-care costs. The focus on patient-centric care is evident in the drive to enhance patient comfort, minimize the risk of complications and improve overall treatment outcomes in wound care (Fig. 3d).

Microparticles and nanoparticles. Microparticles and nanoparticles possess immense potential for direct treatments and functioning as carriers for delivering therapeutic agents owing to their tailorable characteristics, including a high surface area, tunable properties and the ability to encapsulate therapeutic agents. Microparticles and nanoparticles, including metallic, ceramic, polymeric, self-assembling, composite and hydrogel-embedded nanoparticles, have versatile functionality, rendering them invaluable tools for advancing wound healing processes. To mitigate skin irritation and multisystemic complications, as well as to maintain their functional integrity, nanoparticles can be stabilized using materials such as metal shells, polymers or surfactants and coated with low-sensitization substances[52].

Microparticles and nanoparticles can directly influence cellular behaviour and physiological balance. For example, zinc oxide (ZnO) nanoparticles impact inflammatory responses, enhance epithelialization and facilitate the restoration of skin haemostasis. Nanoparticles can influence the wound healing process by modulating the activity of various cells engaged in regeneration and immune response. Notably, wounds treated with microporous-annealed particle revealed a de novo regenerated appearance, enhanced myeloid cell recruitment, improved tissue architecture and increased vascularization, indicating a return to a healthier, more normal state of the skin[43].

Metal-based nanoparticles, including metallic and metal oxide varieties, as well as quantum dots, offer substantial advantages for antimicrobial activity and reactive oxidative species scavenging, particularly against multidrug-resistant organisms[53–55]. Among these, silver nanoparticles are increasingly incorporated into commercial wound dressings, playing a crucial role in preventing and combating infections in wound care[56]. Certain nanoparticles can be externally controlled for drug releases with responsiveness to wound features such as the levels of pH or metabolites, offering utility in precisely directing them to a wound site or for remote activation.

Microparticles and nanoparticles are extensively employed for target delivery of drugs directly to the wound site in a controlled manner. Various therapeutic agents, including antibiotics, anti-inflammatory drugs, growth factors and genetic material such as DNA or RNA, can be incorporated into these particles for efficient delivery. The sustained release capability of these particles proves crucial for prolonged therapeutic effects, particularly in wound healing scenarios in which a consistent drug supply maintains the optimal healing environment. Additionally, the encapsulation of therapeutic agents in microparticles or nanoparticles can protect drugs from premature degradation caused by the enzymatic and pH conditions in the wound environment. However, utilizing microparticles–nanoparticles in wound healing and monitoring presents several challenges that must be addressed. One primary concern is the risk of cytotoxicity, as certain materials used in nanoparticles such as metals and metal oxides can elicit adverse cellular responses, potentially compromising the healing process. Another challenge lies in the precise control of particle delivery and retention at the wound site, as inadequate localization may reduce therapeutic efficacy and increase the risk of off-target effects. Furthermore, the complex wound microenvironment, characterized by varying pH levels, enzymes and fluid exudates, can affect the stability and functionality of nanoparticles, necessitating robust particle design and surface modification strategies. Addressing these challenges requires comprehensive preclinical testing and the development of innovative engineering solutions to fully exploit the capabilities of microparticles and nanoparticles in advancing wound care.

Bioelectronic materials. The discovery that cutaneous cells can generate and respond to bioelectrical signals has sparked a wave of innovation in techniques aimed at electrically assessing and modulating wounds. Specifically, the pursuit of refined ways to augment the bioelectrical signal at the wound site has led to the evolution of materials and methodologies that seamlessly integrate electronics into wound care and tissue repair processes.

Electroactive materials, possessing the ability to generate or respond to electrical signals, introduce a dynamic dimension to wound management strategies. Made from conductive matrices or by encapsulating conductive components, these materials exhibit excellent electron–ion interconversion efficiency, which is independent of

voltage and frequency. Their notable capacitive characteristics and their ability to operate effectively across a broad frequency range, all the while maintaining their electrical conductivity, strength, flexibility and biocompatibility, are attributes crucial for achieving optimal performance[57]. For instance, low-frequency (<10 Hz) monophasic pulsed microcurrents lead to enhanced fibroblast proliferation and migration, whereas high-frequency (>1 kHz) therapy is used for pain reduction and antibacterial treatment[58–61]. Electric field generated by nanogenerators is also employed to facilitate healing progress[21,62].

The integration of electronic conductors, such as carbon nanotubes, metal nanoparticles and graphene oxides, into biomaterials could enable better electrical signal transmission[63]. Challenges, however, arise from the uneven dispersion of the conductive materials, leading to interruptions or irregularities in the electrical signals transmitted through it. In addition, long-term safety of these materials needs to be assessed owing to concerns about their potential toxicity. Alternatives such as conductive organic polymers, notably polyaniline, polypyrrole and poly(3,4-ethylenedioxythiophene):polystyrene sulfonate, have shown promise in creating stretchable electrodes capable of accommodating the movement of wound tissues[64–66].

Ion-conductive hydrogels, characterized by their high water content and malleability, are ideal candidates for direct application to wound sites. Despite appearing solid at the macroscopic level, these hydrogels exhibit liquid-like properties at the microscopic scale, facilitating ion migration and contributing to the charge conversion between ion-conductive hydrogels and tissues. They can serve multiple purposes, including maintaining wound moisture and aiding electric field-driven healing processes[67–69]. Ion-conductive hydrogels, although exhibiting lower electrical conductivity and electrochemical properties than their conductive nanomaterial-infused hydrogels or conducting polymers counterparts, still offer great potential for wound healing applications. In therapeutic settings, particularly in which the objective is to apply low-level electrical stimulation to facilitate healing, the safety and biocompatibility of ion-conductive hydrogels take precedence over achieving the highest possible conductivity.

Harnessing electrical cues, bioelectronic materials can facilitate cell migration, enhance tissue regeneration and modulate inflammation. Furthermore, electroactive materials have the potential for controllable drug delivery, real-time monitoring of wound healing progress and creation of electrically stimulated environments that expedite the overall healing process. Employing electroactive materials in wound care requires the meticulous consideration of several key factors: biocompatibility, precise adjustment of electrical characteristics and a careful balance of mechanical durability and appropriate degradation rates. Moreover, incorporating electroactive materials into current medical devices and ensuring their scalability for clinical applications pose major engineering challenges. Overcoming these challenges necessitates a multidisciplinary approach to ensure that these materials are safe, effective and compatible with bodily dynamics and existing medical technologies.

Natural and synthetic bioscaffolds. Bioscaffolds, inspired by the natural extracellular matrix, offer a platform that fosters the intrinsic healing processes of the body, redefining the realm of wound management. Natural bioscaffolds, such as collagen, chitosan, silk and alginate, closely emulate the own extracellular matrix of the body, creating a conducive environment for tissue regeneration[70–73]. In addition to their high biocompatibility, these natural scaffolds provide receptors essential for cell migration and proliferation, neo-angiogenesis support and scar-free healing[74]. Multiple studies and clinical trials have explored products from xenogenous sources (such as porcine and bovine) and human tissues as scaffolds for wound dressing[7], with some of these products also containing growth factors from the donor[75,76]. However, the inherent variability in composition of natural bioscaffolds, stemming from differences in their biological sources, can result in inconsistent properties that may influence the healing outcomes. Furthermore, these natural scaffolds pose a risk of immunogenic reactions or disease transmission, requiring stringent purification procedures to ensure their safety and effectiveness.

Conversely, synthetic bioscaffolds such as polyethylene glycol, poly(lactic-co-glycolic acid) and polycaprolactone offer precise control over properties such as porosity, degradation rate and mechanical strength[77–79]. This versatility enables the customization of the scaffold to meet specific wound care requirements. By providing mechanical support, promoting cell attachment and modulating biochemical cues, these scaffolds accelerate wound healing while minimizing scar formation. Additionally, these scaffolds can also be finely tuned to realize controllable release of bioactive molecules and therapeutic drugs entrapped inside. For example, polyacrylamide hydrogels can be designed with varying stiffness, ranging from 0.1 kPa to 25 kPa, with the stiffness crucially influencing stem cell differentiation[80]. However, their biocompatibility and bioactivity might not rival those of natural scaffolds, possibly requiring surface modifications such as their coating with cell adhesin molecules to enhance cell interactions[81,82].

Stimuli-responsive materials. Stimuli-responsive materials, also known as smart materials, have garnered a lot of interests for wound healing owing to their ability to respond to internal changes within the wound microenvironment (such as temperature, pH, metabolites and enzymes) or external stimuli fields (such as force, electrical, magnetic and ultrasound fields).

Responsive wound care products can be devised by harnessing the physical properties of materials, such as a low critical solution temperature, strategically aligning with the pathological conditions typically observed in wound environments. For example, drugs can be evenly dispersed throughout a liquid-state hydrogel, whereas its solidification transition under body temperature prevents the rapid release of the drug, thereby ensuring the prolonged delivery. Additionally, these materials can dynamically adjust their size in response to temperature changes and provide contractile force, which accelerates the healing process. Alternatively, responsive materials can be engineered using scaffold and crosslinkers that are susceptible to digestion by biochemicals present in the wound for therapeutic agent release[83,84]. For example, a DNA-crosslinked hydrogel was designed to degrade in response to deoxyribonuclease (DNase) secreted by pathogens and release neutrophils[85].

Nanogenerators, capable of converting mechanical energy from body movements or external pressure into electrical energy, present an innovative approach for wound care[62,66,86]. For example, piezoelectric materials produce electrical signals in response to mechanical stress, which can be harnessed to stimulate cellular processes vital for tissue repair and regeneration. This property is particularly useful in dynamic wound dressings designed to provide continuous electrical stimulation directly to the wound site, thus promoting healing in an active, non-invasive manner.

Photodynamic therapy is a strategy that has been used to achieve antibacterial properties, in which light is used to locally elevate temperature, inducing bacteria mortality. This method is effective against

antibiotics-resistant bacteria while minimizing side effects[87–90]. Using stimuli fields to control scaffold degradation is a prevalent approach to realize drug or cell therapy. For example, by incorporating magnetic particles in wound dressing scaffolds, magneto-induced dynamic mechanical stimulation can enable controlled drugs and cutaneous cell release, accelerating the healing process[91,92]. Despite these strides, challenges, including the longevity of these materials, ensuring precision in controlled drug release dosages and maintaining consistent therapeutic effectiveness over time, persist.

Direct applications of stimuli fields have also been leveraged for wound treatment. For instance, applying ultrasound to induce cavitation, leading to the breakdown and erosion of devitalized tissue[93], shows promise for debriding wounds, a process of removing dead, damaged or infected tissue to improve the healing potential of the remaining healthy tissue. This can be a critical step in the management of chronic wounds, particularly those with necrotic tissue.

Emerging technologies for wound monitoring

Traditional methods of wound assessment, primarily relying on visual inspection and subjective evaluation, are undergoing a transformation as sophisticated technologies emerge to provide objective, real-time and precise data. These advances are shaping a new paradigm in which wound care becomes increasingly predictive, personalized and efficient. The integration of wearables and imaging tools is at the convergence of engineering and clinical practice, paving the way for a future in which wounds can be monitored and managed with unprecedented precision. This approach not only reduces complications but also accelerates the healing process, marking a significant leap forward in the field of wound care. Advanced wound care monitoring technologies cater to various wound conditions and multiplexed biomarkers through signal transduction techniques and system integration, providing a comprehensive platform for the development and application of smart wound management (Fig. 4).

Biomarkers for wound healing

Emerging biosensors and imaging devices have shown promising capabilities to characterize wound features and monitor versatile biomolecules including metabolites (such as glucose, uric acid and lactate), electrolytes (such as pH, Na^+, Ca^{2+} and NH_4^+), nutrients (such as vitamins, amino acids and fatty acids), proteins (such as cytokines and C-reactive protein) and therapeutic drugs (such as growth factors, plasmids and antibiotics)[85,94–100]. These biomarkers are associated with physiological and pathological conditions, such as infection and inflammation[101–103]. Notably, analytes of interest can be detected directly at the wound site, eliminating the need for blood tests or invasive tissue biopsies. Blood tests typically reflect systemic conditions that may differ from the local wound environment, whereas tissue biopsies, being invasive, can exacerbate wound damage and typically require weeks to produce results. Additionally, certain crucial wound biomarkers, such as reactive oxidative species and reactive nitrogen species, exhibit high reactivity and short half-lives. In situ monitoring addresses these challenges by providing real-time analysis, yielding results that are otherwise unattainable with current approaches[104–106].

The detection of crucial proteins plays a pivotal role in assessing the healing process and guiding treatment. These proteins include growth factors and cytokines such as platelet-derived growth factor, transforming growth factor-β, epidermal growth factor, vascular endothelial growth factor and interleukins, which regulate cell functions essential for repair. Matrix metalloproteinases (MMPs) such as MMP2 and MMP9 are involved in extracellular matrix remodelling, with elevated levels indicating chronic wounds. Structural proteins such as collagen, elastin and fibronectin contribute significantly to tissue formation and integrity. Inflammatory markers, including C-reactive protein and procalcitonin, signal inflammation stages.

Monitoring these biomarkers provides a comprehensive view of wound healing phases and potential complications. For instance, the presence of virulence factors such as pyocyanin and bacteria DNA fragment could serve as early sign of infection. Timely treatment based on such insights could enhance therapeutic efficacy. These wound monitoring devices not only contribute to our understanding of the wound environment, classifications and healing process but could also assist in drug screening and prognosis prediction[107,108].

Wound sampling

Efficient and precise sampling of wound exudate is crucial in wound care research and management, given that wound exudate is a valuable source of biomarkers. Ensuring the precision and relevance of data derived from biomarkers necessitates the careful collection of samples in which fresh and old wound exudate must be separated. Old exudate, potentially laden with degraded substances, may not accurately convey the current condition of the wound, contrarily to fresh exudate, which provides immediate insights into the state of the wound. The ability to efficiently collect and promptly transfer fresh exudate to analysis modules is crucial for reliable wound assessment. Adopting continuous and effective in situ sampling techniques, aimed at isolating fresh exudate through a singular extraction process, offers a promising avenue. However, the practical implementation and success of such a strategy remain areas for future demonstration and refinement.

Dressings with enhanced exudate absorption capacity and a self-pumping feature were developed for efficient exudate sampling[31]. However, there are challenges associated with this approach, such as potential contamination from the biomaterials and difficulties in extracting fluid from the dressing scaffolds without losing critical information. Alternatively, NPWT and microneedles are capable of extracting fluid from deeper tissue layers, providing a more comprehensive overview of the wound environment. However, this approach may not solely represent surface conditions. The methods used for measuring wound exudate can yield disparate results. A comparative study of 14 patients revealed significant differences in exudate collection between methods: 0.17–0.21 g cm^{-2} per day with dressing and 1.3 g cm^{-2} per day with NPWT[109]. The inconsistencies in wound analysis methods and sample collection pose a crucial challenge, hindering accurate characterization of the wound healing process and impeding effective results comparison across studies. To address these challenges, microfluidic-based sampling has been introduced for on-site intermittent storage and precise management of wound exudate. This approach effectively reduces the likelihood of dilution, mixing or cross-contamination[96,110]. However, one main challenge of such microfluidic sampling is the limited volume of collected wound extrudate, typically 0.05–0.4 g cm^{-2} per day (ref. 111). Despite numerous reports on microfluidics for wound sampling, none has demonstrated direct wound exudate collection from animals or patients. The limited volume of wound exudate, coupled with its high content of solid components (such as proteins, dead cells and debris), reduces the available liquid portion for analysis. Furthermore, the drainage rate also varies across patients with different chronic wound types, depths, positions, circulations and other underlying health issues.

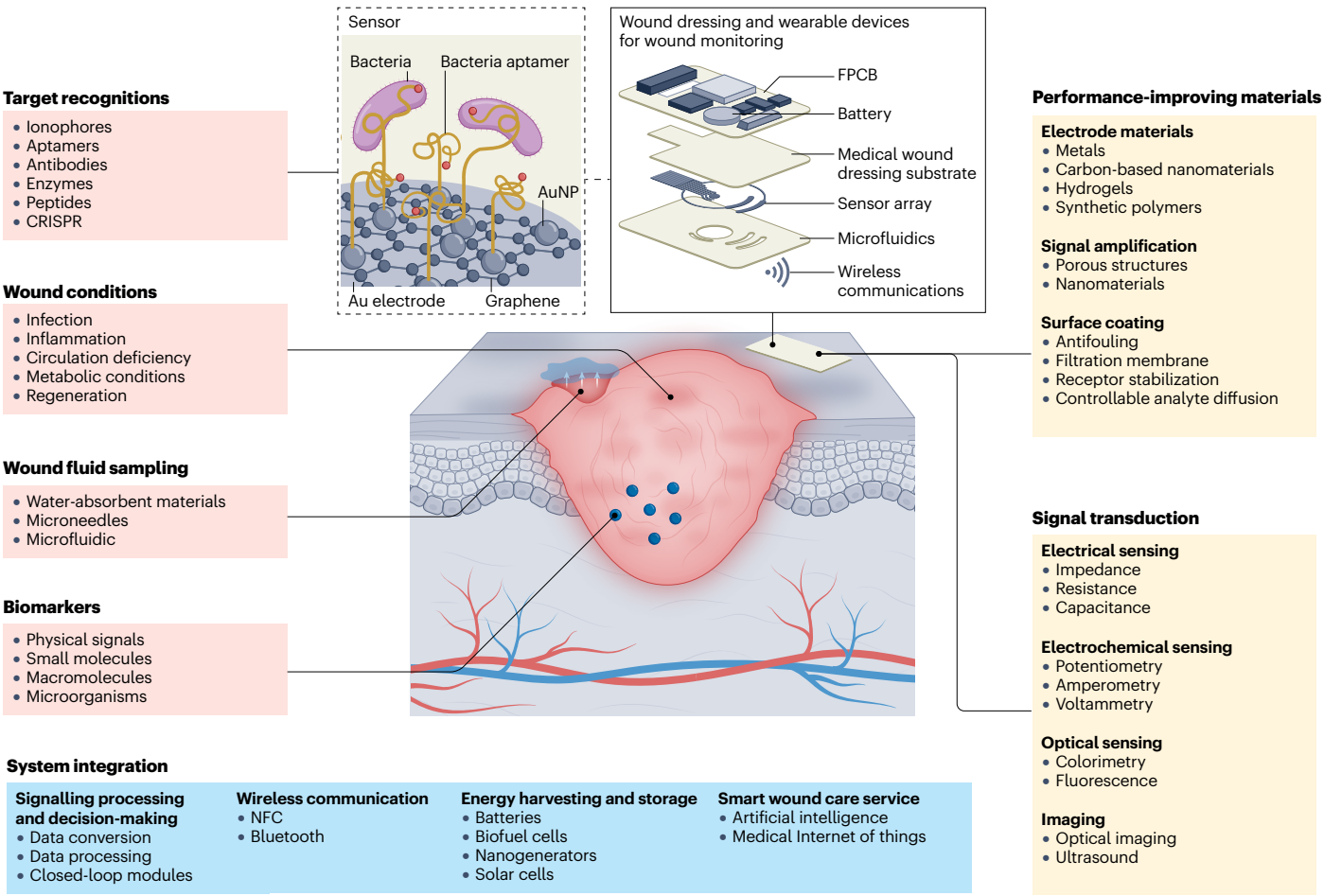

Fig. 4 | Materials and technologies for wound analysing and monitoring. Overview of the integrated components and processes involved in advanced wound monitoring systems. This overview includes a holistic representation of key elements such as wound conditions, biomarkers, signal transduction, performance-enhancing materials, system integration and strategies for wound fluid sampling and target recognition. FPBC, flexible printed circuit board; NFC, near field communication; NP, nanoparticle. The detail of the 'wound dressing and wearable devices for wound monitoring' schematic is adapted from ref. 98, Springer Nature Limited.

For example, a cross-sectional study of 41 patients with pressure ulcers exhibited a mean exudate volume of 6 ml per day with a wide range of 0.0–47.0 ml per day (ref. 112). These variations underscore the complexity of wound exudate dynamics, emphasizing the need for standardized and efficient sampling methods to advance our understanding of wound healing processes.

Sensors

Sensors are devices capable of translating biomarker levels into measurable signals. The real-time insights into specific biomarkers obtained by wearable sensors have the potential to address the critical demand for personalized monitoring and timely intervention in various medical conditions. Achieving selective biomarker detection in the wound environment often requires the integration of specific target-recognition materials or receptors such as ionophores, enzymes, antibodies, aptamers and molecularly imprinted polymers. In the realm of wound care, many reported sensors rely on either electrochemical or optical principles for their signal transduction mechanisms.

Electric and electrochemical sensors. Electric sensors typically utilize impedimetry to detect variations in electrical signals prompted by changes in physical parameters such as temperature and skin impedance, providing crucial indicators of infection, hydration and inflammation. Conversely, electrochemical sensors leverage techniques including amperometry, potentiometry and voltammetry, to precisely quantify alterations in electrical signals at the sensor interface, facilitating detailed analysis of chemical and biological processes. For ions (such as Na^+, Ca^{2+} and NH_4^+) and pH monitoring, potentiometry is primarily employed, utilizing ion-selective electrodes modified with ionophores (such as valinomycin) that selectively and reversibly bind to ions or ion-sensitive materials (such as polyaniline for pH sensing)[113,114]. The measured voltage difference between the ion-selective electrode and the reference electrode shows a log-linear relationship with the analyte concentration. The detection of metabolites such as glucose, uric acid and lactate can be achieved using amperometric enzymatic electrodes immobilized with a specific enzyme (such as glucose oxidase, uricase and lactate oxidase) to catalyse the oxidation

of the target analyte. Redox mediators such as Prussian blue are often used to enable low-potential and efficient signal transduction with mitigated interferences from other electroactive molecules[95]. The measured current signals in this case are linearly correlated with the concentration of the target analyte. The detection of protein-based wound healing biomarkers, such as transforming growth factor-β and interleukins, often necessitates the use of antibody or aptamer receptors coupled with tagged electrochemical redox probes or field-effect transistors. Continuous monitoring of these biomarkers remains challenging owing to their low concentration and difficulties in in situ sensor regeneration[96,115]. When selecting biomarker measurement methods, it is essential to consider their physiological concentration ranges. For instance, glucose levels in wound exudate can range into the tens of millimolars, whereas uric acid concentrations might hover around 100 μM (ref. 95). The presence and concentration of specific biomarkers are influenced by the wound healing stage and the type of wound. For example, as wounds advance towards the proliferative and remodelling phases, the pH level typically decreases. Animal studies have shown that lactate concentration, a crucial indicator of cellular metabolism and hypoxia, peaks within the first 3 days post-injury. In diabetic wounds, lactate levels can surpass the 5–15 mM range typical for non-diabetic wounds, indicating the distinct metabolic challenges in diabetic wound healing[116]. Techniques such as square wave voltammetry and differential pulse voltammetry offer greater sensitivity compared with linear sweep voltammetry, particularly owing to their sampling methodology that effectively reduces the charging current associated with non-faradaic processes[117]. This greater sensitivity makes square wave voltammetry and differential pulse voltammetry particularly effective for detecting biomarkers within their precise concentration ranges in the wound environment, leading to more accurate and dependable readings. Additionally, the choice of recognition mechanism between receptors and targets can substantially influence the sensitivity range. For example, some aptamer or antibody-based biosensors can detect concentrations down to the picomolar level, whereas enzyme-based sensors are typically utilized for identifying biomarkers at micromolar levels or above, showcasing the importance of sensing method selection and specific wound context to ensure accurate and effective wound monitoring[16,118].

Optical sensors. Optical sensors function by leveraging chemical or biological reactions that induce changes in optical signals of specific molecules or materials. These changes manifest as shifts in light absorbance (exemplified by colour alterations), or as modifications in light emission (exemplified by changes in fluorescence or luminescence). Notably, these alterations are directly associated with the levels of analyte molecules.

In the realm of wound care, optical sensors, predominantly colorimetric ones, have been developed to monitor crucial parameters including temperature, pH and small molecules such as oxygen and amino acids[119]. The benefits of employing colorimetric sensors in wound care include direct visual detection, design simplicity, cost–effectiveness and ease of operation. Nevertheless, when compared with electrochemical sensors, colorimetric sensors exhibit a slower response time and require an external readout system to achieve quantitative measurements. Their dependence on visual colour transformations resulting from chemical reactions requires a duration to gather observable alterations, which must subsequently be quantified by an external system. This stands in contrast to electrochemical sensors, which provide a more rapid, real-time electronic conversion of data. These characteristics pose challenges, particularly in scenarios requiring high-frequency continuous data collection. Additionally, the sensitivity and selectivity of this method can be influenced by environmental factors such as ambient light conditions and the optical properties of the wound matrix.

Imaging sensors. Various imaging modalities can provide visual and quantitative insights into critical wound characteristics such as size, depth, volume and tissue composition. Conventional digital photography is commonly used for surface visualization of wounds, facilitating the monitoring of changes in size and appearance over time.

Infrared thermography is a powerful technique for mapping wound temperature, with elevated temperatures serving as reliable markers of inflammation, which is a predictive risk of ulceration, infection and potential amputation. Conversely, decreased temperatures may indicate insufficient blood supply, signalling potential ischaemia[120].

Fluorescence imaging devices, strategically deployed at the point-of-care, enable real-time, non-contact visualization of tissue and bacterial fluorescence within wounds. Tissues typically emit green fluorescence, whereas bacteria exhibit red or cyan fluorescence under violet excitation light. Red fluorescence indicates the presence of porphyrins (by-products of bacterial haem production), whereas cyan signals the presence of pyoverdines, particularly in *Pseudomonas aeruginosa*[121–123]. These distinct fluorescence signals, derived from natural bacterial processes, aid in the early identification and treatment of wound infections. Clinical trials of MolecuLight i:X (MolecuLight Inc.), a portable, point-of-care device for bacteria imaging, have demonstrated a 100% positive predictive value for the detection of bacteria in wounds, highlighting its effectiveness in identifying wound pathogens[124,125].

Ultrasound imaging surpasses superficial wound assessment by effectively measuring wound depth and volume, key factors in ascertaining the severity and healing stage. It also aids in detecting underlying structures, such as bone involvement or sinus tracts, essential for devising appropriate and targeted treatment plans[126].

Materials for enhanced in situ wound monitoring

Advanced materials have a crucial role in the development of sensors for enhanced in situ wound biomarker analysis. Metals, carbon nanomaterials, hydrogels or polymers are commonly chosen in the sensor matrix owing to their unique properties, including high conductibility, biocompatibility, electrochemical stability and the ability to host biorecognition and signal transduction elements.

Given that wound healing biomarkers are often present at extremely low concentrations, achieving the desired sensitivity requires in situ signal amplification strategies. Nanomaterials or porous structures are frequently employed to increase the sensor surface area, thereby enhancing the functionalization of recognition elements and facilitating electron transfer. Emerging materials such as quantum dots and pyranine offer advantages such as intense brightness and high resistance to photobleaching compared with traditional fluorescent dyes[127,128].

The intricate interactions between the wound environment and electrodes present challenges such as biofouling, impacting sensor longevity and performance. To address this, antifouling coatings, such as polyethylene glycol, hydrogels, Nafion and chitosan, are commonly utilized[129–132]. These protective coatings introduce desired surface hydrophilicity, charge or porosity to minimize protein adsorption and

cell adhesion, ensuring the functionality of the sensors in complex wound fluids. Additionally, filtration membranes made from materials such as polyvinylidene fluoride or polytetrafluoroethylene are used to selectively permit the passage of target analytes while excluding larger interfering substances[86,133]. The stability of receptors, such as antibodies or enzymes, is often addressed through receptor stabilization coatings such as silica-based materials and polyvinyl alcohol and crosslinking agents such as glutaraldehyde or carbodiimide that protect these sensitive elements from the harsh conditions of the wound environment[118,134,135]. Furthermore, coatings, including hydrogel-based coatings for adjustable permeability, regulate the rate at which analytes reach the sensor, ensuring consistent and controlled detection[136]. These coating elements are integral to developing advanced wound sensors, providing reliable and precise data for effective wound management and treatment.

For reliable in situ biomarker monitoring with conformal sensor–skin contact, stretchable biosensors can be developed. This typically involves incorporating metallic or carbon-based nanomaterials into elastomers, such as polydimethylsiloxane or styrene–butadiene–styrene[137,138]. This approach enhances flexibility and adaptability, allowing the sensors to maintain optimal performance even in dynamic and challenging wound environments.

In summary, the judicious selection and integration of advanced materials, coupled with the implementation of signal amplification and antifouling strategies, contribute to the development of sensors that meet the demands of the in situ wound biomarker analysis. These advancements pave the way for improved accuracy, longevity and reliability in monitoring wound healing processes.

System integration and data processing

The emergence of advanced wound monitoring technologies and the integration of telemedicine into wound care are revolutionizing chronic wound management. The development of wireless smart bandages marks a significant milestone, signalling the beginning of a new era in closed-loop wound monitoring and treatment. These advanced bandages incorporate pivotal components such as data collection systems on wound conditions, advanced data processing capabilities, adjustable therapeutic delivery systems and modules for both wireless communication and energy supply[11,95,139–141]. The incorporation of state-of-the-art data processing techniques, including artificial neural network, instance-based algorithms and decision tree algorithms[142], further enhances the functionality of these technologies. For example, decision tree algorithms can provide clear logical decision-making paths for therapeutic actions based on real-time wound status, enabling decisions like when to intensify antimicrobial therapy. Additionally, the application of artificial intelligence (AI) in image processing stands out for wound classification and assessment, in which traditional assessments largely rely on the subjective experience and visual evaluations of clinicians[143,144]. Machine-learning algorithms, in particular, have shown great promise for processing wound images and signals, identifying wound features, interpreting pathological signals and predicting healing trajectory. The ability to analyse and interpret medical images with high precision introduces a level of objectivity and consistency that can substantially improve the efficiency of wound clinics, surpassing the limitations of manual examinations. Nevertheless, as AI-driven tools for wound assessment gain prevalence in clinical settings, their accuracy must be meticulously validated. Ensuring that these tools provide precise wound evaluations is crucial for supporting clinicians in delivering informed, evidence-based care[145]. This technological advancement promises to transform wound care practices by providing data-driven insights that support more informed clinical decisions.

Despite its immense potential, the development of consistent and reliable AI-driven wound care systems requires the creation of extensive training data sets and their validation against a wide range of diverse and complex clinical scenarios. Moreover, ensuring the privacy and security of patient data presents a formidable challenge owing to the digital nature of data transmission and storage. Equally important is the task of training health-care professionals to adeptly use and interpret the data generated by these advanced systems, which continues to be an area requiring focused effort and resources.

Wearable closed-looped systems present possibilities for telemedicine, enabling the analysis of wound condition and delivery of health-care services remotely[146–148]. The ascent of telemedicine has empowered patients with chronic wounds to receive continuous, quality care without frequent hospital visits. This is especially beneficial for patients in rural areas or those facing mobility issues, as it improves the accessibility to specialized wound care services and provides real-time and monitoring consultations for patients with chronic wounds. These applications gain momentum owing to the convenience they offer to both health-care providers and patients, thereby boosting the therapeutic efficacy and improving patient adherence[149–151].

The integration of wireless smart bandages with telemedicine platforms allows health-care providers to remotely monitor the wound progress and make informed decisions about treatment adjustments, ultimately enhancing the overall efficiency of wound management.

Regulatory and commercialization considerations

The development of new wound healing technologies and biomaterials is a multifaceted journey demanding substantial investments in research and development[152]. Beyond scientific and technical challenges, navigating the regulatory and commercialization landscape is equally crucial[153]. There are several pivotal steps in the translational process and regulatory pathways pertinent to wound management strategies. Clinical and commercial considerations intrinsic to wound healing strategies are also critical.

Regulatory and communication path

In addressing the translational process of wound management strategies, it is crucial to consider both universal and locale-specific clinical practices and regulatory frameworks. Globally, a common thread includes the need for ensuring safety, efficacy and quality in wound care products, whereas locally, strategies must adapt to the varying regulatory criteria. This global-to-local spectrum underscores the diversity in regulatory paths and communication necessary for the successful worldwide application of advanced wound healing strategies. This section focuses on the specifics within the regulatory process, offering insights that are applicable both within and outside the US context.

Wound care dressings and devices are classified according to the risk associated with the wound, ranging from class I to III in the USA, China and Australia, class I, IIa, IIb and III in the European Union and class I to IV in Canada. Class I representing low-risk categories, which only require minimal regulatory standards for approval. For example, in regulated markets such as the USA, Europe and China, wound dressings are typically classified as class I medical devices, with the onus on manufacturers to maintain safety and quality post-approval. However, in emerging markets, classifications can be less clearly defined, leading to a reliance on established approvals from the USA and Europe as benchmarks for quality and safety, thus avoiding additional approval processes[154,155].

The FDA approval process for wound care products is extensive and involves multiple submissions before initiating clinical trials. These processes are designed to evaluate the physical and chemical properties of these wound dressings and therapeutic products. Wound care products undergo classification by the FDA into categories such as drugs, devices, biological products or combination products. Despite the critical importance of advancing wound care, the clinical translation of these products encounters various challenges, including a complex wound healing process in different wound types, outdated tools and standards for wound categorization and evaluation, an overcrowded and inefficient market flooded with similar products, constraints tied to FDA-acceptable outcome for wound closure and a dearth of standard care practices with reproducible data collection. The 510(k)-approval process, although intended to streamline product entry into the market, has inadvertently contributed to a crowded landscape marked by overlapping and redundant wound healing products. Rectifying this situation requires collaborative efforts among key decision-makers and legislators to formulate a comprehensive strategic plan for optimizing and developing a more effective wound care ecosystem.

Medical devices are categorized into class I, II or III based on risk levels, accompanied by specific regulatory controls ensuring safety and effectiveness (Table 1 and Box 1). Class I devices, posing minimal risk, are subject to general controls and exempt from premarket notification 510(k). Examples of class I device include non-resorbable gauzes and sponges for external use, hydrophilic wound dressings, occlusive wound dressings, hydrogel wound dressings and burn dressings. Wound care products that surpass class I risk levels may fall into class II category, necessitating a substantial equivalence review and specific controls, often evaluated through a premarket notification 510(k) submission. Notable examples of class II devices encompass wound dressing with animal-derived material, absorbable synthetic wound dressings, wound therapy bioelectronic devices (NPWT and hyperbaric oxygen therapy) and wound biosensors. Class III devices, carrying higher risks or life-supporting functions, generally involve innovative compositions and clinical applications, requiring a premarket approval (PMA) application. PMA is a rigorous FDA process designed for high-risk medical devices that supports or sustains human life or presents a potential, unreasonable risk of illness or injury. It requires proof of safety and effectiveness, often including results from clinical trials. By contrast, the 510(k) process is for devices that are substantially equivalent to a legally marketed device that is not subject to PMA, allowing a more streamlined process. The Center for Devices and Radiological Health (CDRH) oversees a range of wound care devices across all classes, which vary in classification based on their intended use and technology. Notably, wound dressings combined with drugs, such as antimicrobial-containing wound dressings, fall under the unclassified product code FRO and are generally regulated through the 510(k) pathway, whereas interactive wound and burn dressings promoting wound healing are classified as class III devices[156,157].

The de novo process provides a pathway for the classification of novel devices into class I or II. Recent examples include NPWT devices, extracorporeal shock wave devices for hard-to-heal wounds, bacterial protease activity detectors, pressure ulcer management tools and wound autofluorescence imaging devices. This dynamic classification process accommodates emerging technologies and fosters innovation in the realm of wound care.

Clinical data may be requested in premarket submissions when non-clinical testing is insufficient to establish substantial equivalence. Such information should be provided through Investigational Device Exemption (IDE) studies, literature reviews, real-world evidence (RWE) or other valid scientific evidence. Developers are strongly encouraged to submit pre-submissions (Q-Submissions) for feedback, especially for innovative devices featuring novel materials or indications for use. CDRH supports a collaborative approach in the development of innovative wound care devices, offering programmes such as the breakthrough devices programme and guidance on utilizing real-world evidence for regulatory decision-making. Interested parties are urged to explore these pathways and engage with the FDA to foster innovation in wound care[7].

Table 1 | Translational process and regulatory pathways for advancing wound management strategies

	Class I (low risk)	Class II (intermediate risk)	Class III (high risk)	Unclassified
Categories	Non-resorbable gauze/sponge for external use Hydrophilic wound dressings Occlusive wound dressings Hydrogel wound dressings and burn dressings	Wound dressings with animal-derived material Absorbable synthetic wound dressings Wound therapy bioelectronics (NPWT, ultrasound and HBOT) Wound biosensors	Interactive wound and burn dressings that promote or accelerate wound healing Product code MGR	Antimicrobial-containing wound dressings
Regulatory pathway	Most are exempt from premarket notification 510(k) Should not contain drugs, biologics or animal-derived material	510(k) pathway under the KGN product code Substantial equivalence Special controls	Premarket approval and effectiveness Intended for wound treatment Intended to be a skin substitute Life-supporting or life-sustaining	Product code FRO (dressing, wound and drug) No classification regulation 510(k) pathway
Examples	WOUND FREE; Comfeel Plus; Dynarex Xeroform; Persys Woundstop Care Fibracol Plus; GraftJacket; DermACELL; EpiFix (HCT/Ps); TheraSkin (HCT/Ps)	Talymed; Oasis; Promogran; Algisite; Tegaren; Hyalomatrix; SonicOne Ultrasonic Wound Care System; 3M Prevena Therapy	Integra; Apligraf; Dermagraft	AMNIOFIX; Titan SGS; Omeza Collagen Matrix; Promogran Prisma Matrix

Class I includes low-risk items such as gauze and hydrogel dressings; class II covers intermediate-risk items such as animal-derived materials and biosensors; class III encompasses high-risk devices such as interactive dressings that promote healing. Antimicrobial-containing dressings are noted as unclassified device. HBOT, hyperbaric oxygen therapy; HCT/P, human cells, tissues and cellular and tissue-based product; NPWT, negative pressure wound therapy.

Box 1 | Overview of FDA regulatory approval processes for wound care products

Navigating the regulatory landscape is a critical step in bringing new wound care products to market. Each FDA approval pathway is designed to ensure patient safety and product efficacy, with different requirements based on the novelty and risk level of the device. Here is an overview of the main pathways for market authorization.

510(k) clearance
Targeted at class I and II devices similar to the existing market products, the 510(k) process, taking around 90 days, is a quick pathway to market. It mandates the submission of evidence demonstrating that the new device is as safe and effective as an already legally marketed device. Examples include various wound dressings and over-the-counter products such as Band-Aid and Tegaderm.

Premarket approval
The premarket approval (PMA) is a rigorous scientific and regulatory review to evaluate the safety and effectiveness of class III medical devices, which represent the highest risk category and typically involve more than 180 days to process. PMA devices often bring innovative therapies to market and include examples such as Dermagraft for diabetic foot ulcers and RECELL for burns.

De novo pathway
This process provides a route to classify novel devices of low-to-moderate risk that do not have a legally marketed predicate device. It involves a variable time frame and allows the FDA to grant marketing authorization with special controls to ensure safety and efficacy. The de novo pathway can include more sophisticated care systems, such as the SNaP Wound Care System. It is designed as a portable and lightweight option for negative pressure wound therapy, using mechanical power to create the necessary vacuum for wound healing without the need for batteries.

Each pathway has a critical role in the introduction of safe and effective wound care products. The 510(k) route is ideal for products that can be compared with an existing one, whereas the PMA and de novo pathways cater to novel or higher-risk devices. These regulatory frameworks help ensure that new wound care products are rigorously tested and meet high standards, providing health-care professionals and patients with confidence in the treatments used.

In 2018, the FDA announced plans to modernize the 510(k) programme, emphasizing that new medical devices under this pathway should reflect technological advances or demonstrate compliance with modern safety and performance criteria. The goal was to encourage competition for adopting contemporary features that improve patient care. The FDA aimed to retire outdated predicates (>10 years old) and consider releasing an online list of cleared devices substantially equivalent to predicates older than a decade. The initial steps towards modernization included the release of updated draft guidance in 2019, primarily focusing on premarket performance criteria and testing methodologies for certain devices, excluding tissue engineering products[158,159].

Various complexities in wound healing regulation demand careful attention. These include ensuring the sterility of the wound healing product; addressing combinations of wound healing products, with evolving regulatory flexibility for multiple-agent therapy based on established synergistic interactions and safety profiles from preclinical studies; establishing standards for clinical care or optimal basic wound care within clinical trials and determining product jurisdiction based on the primary mode of action[160].

In conclusion, ongoing reforms at the regulated markets aim to speed up the regulatory process and increase the review consistency. Nevertheless, the most efficient pathway for a sponsor to attain product approval continues to centre on solid foundational, preclinical and clinical science.

Challenges and opportunities beyond clinical translation

Wound healing is a dynamic and intricate process that extends beyond the boundaries of traditional clinical care, presenting several challenges and opportunities. Preclinical investigations have a pivotal role in bridging the gap between innovation and effective wound care therapies, ultimately enhancing the overall quality of wound management practices. Initially, during the concept and feasibility phase, preclinical investigations help in understanding the basic biology related to the intended function of the device, which informs design and development. Before entering clinical trials, researchers must complete rigorous preclinical testing to satisfy regulatory requirements and submit substantial evidence to the FDA, typically in the form of an Investigational Device Exemption. These studies serve as foundational steps in the rigorous evaluation of wound care interventions, focusing on safety, efficacy and feasibility. Detailing the type and scope of preclinical evidence required by the FDA is essential for ensuring compliance and facilitating a smoother approval process. For medical devices, these investigations encompass an array of essential elements, including biocompatibility testing, biomechanical analysis and in vivo evaluations using animal models that simulate human wound healing processes. For drugs, clarifying the extent and specificity of preclinical data required by the FDA, such as toxicity profiles and pharmacokinetics, is essential. As the FDA no longer requires animal tests for the approval of new medicines[161], alternative approaches such as organ-on-chip technology could be used to study the efficacy of proposed wound care products[162]. Innovative preclinical research approaches, such as organ-on-a-chip models, advanced imaging techniques and multi-omics profiling, could enhance the predictive value of preclinical studies and accelerate the development of clinically relevant wound care interventions.

The journey to commercialize wound care products extends well beyond obtaining regulatory approval and clinical validation, encompassing a multifaceted strategy and detailed planning. Market acceptance is contingent upon proving cost–effectiveness, seamless integration with current health-care protocols and congruence with the priorities of payers and providers. Scaling up production necessitates careful planning to confirm that manufacturing capabilities can satisfy market demand without sacrificing product quality. Moreover, the success of commercialization relies heavily on engaging patients effectively and implementing comprehensive education programmes

to enhance awareness, encourage adoption and ensure correct usage of new wound care technologies. Such efforts are pivotal in ensuring that advancements in wound management smoothly transition from clinical validation to becoming integral components of routine health care, thereby enhancing patient outcomes on a widespread level.

Additionally, incorporating companion diagnostic strategies is crucial for guiding therapy initiation and conclusion, as well as for its optimization. Particularly in the post-pandemic world, technologies that can assist in measuring and managing care remotely at home are essential.

With the development of telemedicine, considerations related to data privacy and security are paramount[163,164]. These encompass environmental factors such as ensuring private spaces for telehealth to protect patient confidentiality, technological aspects such as securing data and enhancing digital literacy to prevent unauthorized access and operational challenges such as navigating telehealth reimbursement policies and providing adequate training for health-care providers. Addressing these multifaceted concerns is essential for building trust in remote wound care technologies and promoting their effective use .

Wound healing transcends the confines of traditional clinical care, with preclinical investigations playing a key role not only in meeting regulatory mandates but also in deepening the understanding of wound biology. This foundational knowledge is critical for innovation and the advancement of wound care therapies. Beyond regulatory compliance, the path to commercialization entails addressing market acceptance, scalability of production and active engagement with patients and health-care providers to educate and ensure the effective adoption of new treatments in the wider health-care ecosystem.

Conclusions and perspectives

This Review highlights major advances in the realm of wound healing biomaterials and technologies. These innovations not only show promise for the effective treatment of chronic wounds but also have the potential to revolutionize the landscape of clinical wound management. Our exploration has extended to considerations vital for regulatory approval and commercialization, underscoring the imperative role of translational processes and the incorporation of both preclinical and clinical studies in the developmental phase. This holistic approach is key to bridging the gap between pioneering research and practical clinical applications.

Looking forward, the field of wound management is poised for further exploration and innovation. The ongoing development of new biomaterials, bioengineering approaches and telemedicine technologies presents a compelling opportunity to enhance patient outcomes and alleviate the burden associated with chronic wounds. The frontiers of regenerative medicine and tissue engineering, including stem cell therapy and 3D bioprinting, hold transformative potential for regenerating damaged tissues and organs[165–169]. Advanced manufacturing technologies offer new opportunities for the development of multifunctional personalized wound care devices, which are crucial owing to the intricate and diverse nature of complex wound structures and types[12,170–172]. For instance, 3D bioprinting could be used to create custom-fitted wound care devices, such as dressings and skin grafts, that conform precisely to the unique topography of the wound of a patient. This approach not only improves physical fit and user comfort but also enhances the therapeutic efficacy and monitoring signals by ensuring proper contact and integration with the wound bed. Furthermore, 3D printing allows for the incorporation of various materials and living agents, such as antibacterial agents, growth factors or stem cells, into a single platform. The integration of different functionalities within a personalized device aims to enhance healing outcomes by providing a cohesive solution that addresses multiple aspects of wound management concurrently.

Moreover, the integration of AI and machine learning into wound care emerges as a powerful tool for predicting wound healing trajectories, ushering in a new era of precision and personalized wound management[145,173–176]. As we embrace these innovative approaches, the synergy between the state-of-the-art technologies and conventional wound care practices is poised to redefine the standards of patient care and elevate therapeutic efficacy.

Addressing global disparities in wound care is crucial. In developed regions such as North America and Europe, advanced wound management strategies and personalized therapy are the next frontier. Meanwhile, in developing regions such as sub-Saharan Africa and parts of Asia, where health-care resources are scarce and the prevalence of infectious diseases complicates chronic wound management, there is a dire need for cost-effective and scalable solutions. Such disparities underscore the necessity for innovative, affordable wound care solutions in resource-constrained environments and highlight the potential for international collaboration in research and training. For example, in low-income and middle-income countries, the unique needs for wound care management emphasize the necessity for materials and technologies that are accessible, affordable and user-friendly, capable of addressing the local prevalence of diseases, including those with infectious complications. Essential practical considerations include the provision of training for health-care workers, the adaptability of solutions to local climates and resources and the reinforcement of community-based care. There is a significant focus on research into materials that can be locally produced or sourced to fulfil these requirements effectively. It is imperative for the wound care community to strive for an equitable distribution of advancements, ensuring that effective wound management is accessible across diverse global contexts and bridging the gap between varied economic and geographical landscapes.

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