EDITORIAL

Human Wounds and Its Burden: An Updated Compendium of Estimates

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Submitted for publication January 15, 2019. Accepted in revised form January 15, 2019.

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Significance: A 2018 retrospective analysis of Medicare beneficiaries identified that ~8.2 million people had wounds with or without infections. Medicare cost estimates for acute and chronic wound treatments ranged from $28.1 billion to $96.8 billion. Highest expenses were for surgical wounds followed by diabetic foot ulcers, with a higher trend toward costs associated with outpatient wound care compared with inpatient. Increasing costs of health care, an aging population, recognition of difficult-to-treat infection threats such as biofilms, and the continued threat of diabetes and obesity worldwide make chronic wounds a substantial clinical, social, and economic challenge.

Recent Advances: Chronic wounds are not a problem in an otherwise healthy population. Underlying conditions ranging from malnutrition, to stress, to metabolic syndrome, predispose patients to chronic, nonhealing wounds. From an economic point of view, the annual wound care products market is expected to reach $15–22 billion by 2024. The National Institutes of Health's (NIH) Research Portfolio Online Reporting Tool (RePORT) now lists wounds as a category.

Future Directions: A continued rise in the economic, clinical, and social impact of wounds warrants a more structured approach and proportionate investment in wound care, education, and related research.

Keywords: human wound burden, wound care economics, military wound care, wound care training and education

INTRODUCTION

A 2009 REVIEW OF THE state of human skin wounds and the threat they present to public health and the health care economy provided an overview of the far-reaching impact of chronic wounds. There is a need for allocation of resources to understand the mechanistic basis of cutaneous wound complications.[1] The current article is intended to provide an update on the rising threat that chronic wounds present to global health and economy. A recent retrospective analysis of the Medicare 5% dataset for 2014 analyzed all wound categories, including acute and chronic wounds, and identified that about 8.2 million Medicare beneficiaries had at least one type of wound or related infection.[2] Medicare cost projections for all wounds ranged from $28.1 billion to $96.8 billion, including costs for infection management, among which surgical wounds and diabetic ulcers were the most expensive to treat.[2] Furthermore, outpatient costs ($9.9–$35.8 billion) were higher than inpatient costs ($5.0–$24.3 billion), possibly because of an increase in outpatient wound treatments that are currently provided.[2]

DOI: 10.1089/wound.2019.0946

CHRONIC WOUNDS

Wounds that have not progressed through the normal process of healing and are open for more than a month are classified as chronic wounds.[3] There are varying etiologies of chronic wounds, all of which burden the health care system. Patients suffering from diabetes and obesity are at a high risk of developing chronic wounds. A vast majority of the people who have a prolonged open wound usually also have other major health conditions. The simultaneous presence of a combination of chronic diseases is called a comorbidity. Chronic wounds are often complicated by comorbidities, making it difficult to track chronic wounds as a disease in itself.[3] As such, research funding directly addressing the study of chronic wounds is disproportionately low compared with the overall impact of chronic wounds as a health care problem.[4,5] National Institutes of Health has recently set up the first consortium of its kind, a national Diabetic Foot Consortium (NIDDK; FOA: DK17-014; NOT-DK-18-017), aimed at bringing experts across the United States together to improve the care of diabetic foot ulcers (DFUs).

Chronic wounds are mostly seen in the elderly population.[2,6] In the United States, 3% of the population >65 years of age have open wounds. By 2020, the US government estimates that the elderly population will be over 55 million, suggesting that chronic wounds will continue to be an increasingly persistent problem in this population.[7] Overall, in the United States ~2% of the total population are estimated to be affected by chronic wounds.[8] The impact of chronic wounds is also adverse worldwide. For example, a 2016 report from Wales estimated a 6% prevalence of chronic wounds with a 5.5% cost to the National Health Service (NHS).[9]

In the world's largest wound-dressing markets, United States and Europe, there is a significant demand for wound care products. Globally, the annual cost for wound care was an average of $2.8 billion in 2014. It is projected to rise up to $3.5 billion in 2021.[10] The 2018 market research report predicts that the global wound-closure products market will exceed $15 billion by 2022.[11] The advanced wound care market targeting surgical wounds and chronic ulcers is expected to exceed $22 billion by 2024, driven by technological advancement, rising incidences of chronic wounds, increasing government support, and a rising geriatric population.[12]

PRESSURE ULCERS

Pressure, or pressure in combination with shear and/or friction, promotes the development of localized ulcers called pressure ulcers (PUs). PU care is expensive and costs more than $11 billion annually in the United States per the Agency for Healthcare Research and Quality (AHRQ) statistics.[13] Cost of individual patient care ranges from $20,900 to $151,700 per PU.[13] Apart from hospital costs, additional charges for food, transportation, and maintenance is ~$43,180 per year.[13] Elderly patients; patients with stroke, diabetes, dementia; and those with impaired/limited mobility or sensation are extremely vulnerable to PU. Prolonged sedentary stays in the intensive care unit can also drive PU development in otherwise healthy patients.

The incidence of PU increases with age and is promoted by a lack of skin perfusion, moisture, and nutrition.[14] In the United States around 2.5 million people develop PUs annually.[13] They are usually preventable, but they can be lethal if proper, timely care is not received.[15–19] The global market for PU care products is expected to reach $4.5 billion by 2024.[20] Factors that spur this increase include the aging population and associated mobility and neurological disorders.[20]

DIABETES

The Centers for Disease Control and Prevention (CDC) recently released a study that indicated that more than 100 million adults are living with diabetes or prediabetes in the United States.[21] As of 2015, 30.3 million Americans (9.4% of the US population) live with diabetes; besides, 84.1 million have prediabetes, which if left untreated often leads to type 2 diabetes (T2D) within 5 years.[21] Diabetes prevalence has been found to increase with age. Four percent of adults aged 18–44, 17% of adults aged 45–64 years, and 25% of those aged ≥65 years have diabetes.[21]

Worldwide, there are an estimated 400 million people living with diabetes.[22] In reference to the statistical studies by the World Health Organization (WHO) in 91 countries globally, it was identified that a tiny island country in Micronesia, Nauru, had the highest prevalence rate of 30.9% in 2010.[23] This was projected to rise to 33.4% by the year 2030.[23] United Arab Emirates was next in line with 18.7% prevalence in 2010, and a projected increase to 21.4% in 2030.[23] The age of diabetes onset in developing countries is 45–64.[24] By 2030 it is predicted that developing countries will have more people (>65 years of age) with diabetes (82 million) than developed countries (48 million).[25]

The prevalence of foot ulcers (FUs) is high in the diabetic population and has a neuropathic origin.[26,27] The annual prevalence of FUs is estimated

to be 4–10%, and the risk of development of these ulcers in diabetics is estimated to be anywhere from 15% to 25%.[28] The management of DFUs costs $9–$13 billion in the United States.[26]

By 2026, the T2D market is expected to rise from $28.6 billion to an estimated $64 billion. A compound annual growth of 8.4% is expected in the United States, France, Germany, Italy, Spain, the United Kingdom, and Japan.[29] In the United States, the demand for insulin pumps is expected to rise to a $3.8 billion business by 2022, driven by the increasing number of people with diabetes, as well as technological advances in treatment.[30]

FOOT ULCERS

An open sore on the foot is called a FU. It may be shallow, confined only to the surface of the skin. Deep FUs can involve full thickness of the skin, muscle, tendons, and bones. FUs are common in people with diabetes and individuals with compromised blood circulation.[31] Despite advanced health care and pharmacotherapy techniques that are widely available, the prevalence of FU has not changed in the past two decades.[32] Fourteen percent to 24% suffer from amputation.[33] Neuroischemic ulcers are particularly associated with limb amputations.[27]

Recently, a systematic review and meta-analysis of the global epidemiology of FUs was performed using PubMed, EMBASE, ISI Web of Science, and Cochrane database searches. This was the largest analysis of its kind, including >800,000 subjects from 33 countries. The global DFU prevalence was found to be 6.3%. The lower prevalence of DFU in Europe (5.1%) compared with North America (13.0%) presents a striking difference. Out of 33 countries, Belgium had the highest prevalence with 16.6% and Australia the lowest with 1.5%. Men appeared to be more prone to FUs than women (4.5% vs. 3.5%). Furthermore, FUs were seen more often in patients with T2D compared with type 1 diabetes (6.4% vs. 5.5%).[34,35] In general, patients with FUs were older, had a lower body mass index (BMI), longer diabetes duration, higher hypertension rates, higher incidence of diabetic retinopathy, and a smoking history, compared with those without FUs.

The global DFU market expects a positive 6.6% compound annual growth rate between 2016 and 2024. At this pace, the market's valuation may reach $4.9 billion by the end of 2024. Regionally, the United States dominated the global market in 2016 with an estimated share of 38.1%. It is expected to remain dominant through the forecast period (2024).[36]

VENOUS ULCERS

A vast majority (70%) of lower-extremity ulcers are caused by chronic venous insufficiency.[37] In the United States and Europe, people >65 years of age are vulnerable to venous ulcers.[38] The prevalence of venous ulcers is 1% of the population globally among those aged 18–64.[39] In the United States, 10–35% of the population suffer from some kind of chronic venous issues with 4% (>65 age group) of the cases having active ulcers.[40] In the United States and the United Kingdom, venous leg ulcers cost around $2.5 billion and £300–600 million, respectively.[41] The annual expenditure to treat a venous ulcer is estimated at $10,563.[42] For chronic, nonhealing venous ulcers, the treatment expenditure is estimated to be ~$34,000 or higher.[42] Chronic venous ulcers burden economic productivity by resulting in the loss of 4.6 million work-days per year.[43]

OVERWEIGHT AND OBESITY

According to a recently updated report from the WHO, worldwide obesity has nearly tripled between 1975 and 2016.[44] Excessive accumulation of fat complicates numerous aspects of vital functions within the body, causing illness and posing a risk for an increase in additional health complications. For adults, WHO defines overweight as a BMI ≥25. Obesity is defined as a BMI ≥30.[44] Estimates from 2016 indicated that 39% of adults (1.9 billion; ≥18 years) worldwide were overweight, and 13% (>650 million) were obese.[44] Among these, women were more prone to overweight or obesity than men. The threat of obesity is not a menace only for adults. Globally, 340 million children and adolescents, aged 5–19, were overweight or obese in 2016.[44] In children <5 years, 41 million were either overweight or obese.[44]

Overweight and obese are at a high risk for noncommunicable diseases[44–46] such as:

- Cardiovascular diseases (primarily heart disease and stroke)
- Diabetes and associated chronic wounds
- Musculoskeletal disorders
- Some cancers (including endometrial, breast, ovarian, prostate, liver, etc).

Childhood obesity[47,48] is associated with a predisposition to breathing difficulties, increased tendency toward fractures, hypertension, increased risk of cardiovascular disease, insulin resistance, and psychosocial impacts.[49,50]

In adults, the association between obesity and multiple complications such as impaired or totally

failed cutaneous wound healing, particularly following surgery, has been identified by various groups.[51–60] Being overweight or obese significantly increases the likelihood of infection-related complications compared with those within a healthy weight range.[61] There are many factors that contribute to the chronicity of infection in obese people. Decreased vascularization of the adipose tissue is a major cause for increased infection in obese patients.[53] Such poor perfusion limits the supply of host immune cells that represent key components of host defenses against infection.[53,62–64]

In obese individuals, intentional weight loss was associated with ~15–18% reduction in all-cause mortality.[65,66] Intragastric balloons (IGBs) are the leading treatment options for obesity and associated diseases. The growing acceptance of minimally invasive surgical methods for IGB insertion is expected to fuel the rising use of this methodology. The IGB market value is expected to exceed $270 million by 2024.[67]

PERILS OF CHRONIC WOUNDS

Access and delivery of wound care are both significant problems that challenge patients suffering from chronic wounds. Lack of access to specialized wound care has resulted in amputations and loss of work productivity.[8,68–70] In the United States, chronic ulcers are conservatively estimated to cost the health care system $28 billion each year as a primary diagnosis and up to $31.7 billion as a secondary diagnosis.[71] According to the American Diabetes Association (ADA), over 9–12 million Americans suffer from chronic ulcers.[72] The mortality rate for leg ulcers after the first amputation has dramatically doubled from 20% to 50% in the first 3 years to 70% after 5 years.[72] There is a profound psychological impact on the patients suffering from chronic wounds, such as loneliness, separation from an active social life, and depression. These psychosocial stressors further worsen healing outcomes.[73,74]

ACUTE WOUNDS

Disruptions in the integrity of the skin that heals uneventfully with time are considered acute wounds.[3] Surgical and traumatic wounds, abrasions, or superficial burns are generally considered acute wounds.[3] Every time the integrity of the cutaneous barrier is compromised, a wound is created. Wound infections complicate recovery from surgery and significantly increase the cost of wound care postsurgery. The development of novel and practical concepts to prevent and treat these wound infections are key to effective wound management.

In 2014, acute wounds resulted in 17.2 million hospital visits, including ambulatory/outpatient and inpatient surgical visits.[75] The majority (57.8%) of these visits occurred in hospital-owned outpatient settings, while 42.2% were inpatient.[75] Outpatient visits were primarily (48.6%) covered by private insurers, while Medicare primarily (43.4%) covered inpatient surgical stays.[75]

Hospital discharge data derived from the Healthcare Cost and Utilization Project (HCUP) from burn-related hospital inpatient stays and emergency department visits identify that although there have been significant improvements in treatment options for burn injuries, the frequency and associated costs of these injuries remain high.[76] Almost half million patients were treated for burns in 2011. Costs estimates show that ~$1.5 billion was spent in burn injury care in 2010. An additional $5 billion in costs was associated with lost work-hours. The length of inpatient stay of burn patients was estimated to be twice that of nonburn-related stays.[76]

Surgical site infections (SSI) represent a major concern in overall health care in the United States and worldwide.[77–79] It is the second leading cause of hospital-acquired infections costing $3.5–$10 billion per year.[80,81] Despite all efforts, SSI contributes to mortality in 75% of cases.[82,83]

Emergency wound care for acute wounds has relevance in combat settings and preparedness against natural disasters, terrorist attacks, and other such events that result in acute injuries. Survivors of bombings are primarily impacted at the soft tissue and musculoskeletal system level.[84] Amputations are the unfortunate end result of the most extreme of these injuries and reported to occur in 1–3% of blast victims.[84,85] Acute wound care accompanied by associated infections may highly impact occupational health.

INFECTION

Bacteria rapidly colonize in open skin wounds after burn injury[86–90] or surgical incisions.[51,91–96] Microorganisms colonizing these wounds are typically the patient's normal flora[97–101] or may be transferred via contact with contaminated water, fomites, or the soiled hands of health care workers.[102–106] Gram-positive bacteria such as *Staphylococcus aureus*, *Enterococcus* spp., and Gram-negative organisms such as *Pseudomonas aeruginosa*, *Acinetobacter* spp., fungi like *Candida* spp., *Aspergillus* spp., are all among a list of common

pathogens that can cause acute wound infections, and several of them are resistant to antibiotics.[107]

An important factor in the failure of a sore to heal is the presence of polymicrobial consortia, living cooperatively in highly organized biofilms. The biofilm shields the pathogenic microbes from antimicrobial therapy and the patient's immune response. Biofilm infections have been linked to wound chronicity.[89,90,108–112] Recent studies reveal that biofilm infection may directly hinder wound closure or cause defective wound closure where the wound site appears closed but the repaired skin lacks barrier function.[87,89,90,112] Such observation calls for a revision of the current wound care endpoint. Covering of a wound and a lack of discharge may not be adequate criteria to declare a wound closed. It is important to add that the repaired skin must have physiological functionality. Thus, covering of the wound, a lack of discharge, and restoration of barrier function should be considered as criteria for wound closure in patients. It is suspected that wounds that appear closed, but are deficient in barrier function, lend themselves to wound recurrence. Patient-based studies (NCT 02577120) are currently in progress to test this hypothesis.

MALNUTRITION

The process of wound healing, involving *de novo* tissue generation, is a metabolic and calorie-demanding process. From a microenvironment standpoint, energy needs to be generated to enable cellular repair mechanisms, chemotactic responses (growth factors and cytokine response), cell motility, division, and differentiation.[113,114] At a macroenvironment scale, patients with nonhealing wounds often suffer from nutritional deficiencies.[115] Those with, compared with those without, nutritional deficits are more likely to develop chronic wounds that are slower to heal.[116–118]

STRESS

Another key determinant relating to wound outcomes is psychosocial stress.[52,73,119–122] Stress impairs cellular immunity, compromising wound healing. The discipline of psychoneuroimmunology (PNI) is of direct relevance to wound healing outcomes.[123,124] PNI provides a key insight into how the immune system bi-directionally communicates with the central nervous and endocrine systems and how these communications impact health outcomes.[123,124] Stress-induced immune dysregulation results in impaired wound healing.[123,125,126]

SCAR AND FIBROSIS

Scars and associated functional as well as aesthetic concerns represent a huge burden on health care.[127] Burn wounds usually leave hypertrophic scars after they have healed. In particular, the face is highly susceptible to excessive scarring, causing functional deficits. Some of the critical facial characteristics following thermal injury of the face include ectropion (epithelial-ocular junction), eversion of the lip (epithelial-oral junction), and excessive skin contracture. Deficits such as oral incompetence are common. Such disorders cause social, emotional, and psychological burdens. Patients with such facial disfigurations showed symptoms of depression, anxiety, and hostility, compared with a matched normal control group, for a period of up to 1 year post trauma.[128] Other than the face, scarring is a substantial health care problem today. The global skin scar therapy market is expected to reach around $35 billion by 2023.[129]

PHYSICIAN EDUCATION

Comprehensive education is critical for the development of wound care management as a discipline in mainstream medicine.[130] Formal wound care education in US medical schools is often weak at best. Of 55 schools surveyed throughout the United States, only seven offered a formal wound healing elective.[131] Typically, education and training in wound care for the medical students within the United States do not exceed >9.2 h in the 4-year curriculum.[132] To help address this gap in medical training, the American College of Wound Healing and Tissue Repair was founded to help train physicians specialize in wound care. This institution is currently working toward accreditation by the American Board of Medical Specialties and hopes to achieve this by 2022.[130]

In Europe, wound care education lacks consensus in relation to the minimum education needed to be an expert in wound care.[133] Various diploma and certificate programs are available in France, England, and Wales. The European Wound Management Association (EWMA) is working toward establishing a core standard for acceptable wound management education.[133] In Denmark, however, a 2-year additional educational experience following basic specialty training has been developed for medical doctors.[133]

NURSING EDUCATION, PHYSICAL THERAPY, AND OSTOMY

Traditionally, wound healing has been under the aegis of basic nursing practices,[134] such as wound

covering management, therapeutic nutrition, and mobility and psychosocial support. Nurses play a crucial role in handling and managing acute wounds and chronic wounds such as PUs, bedsores, FUs, and venous ulcers. The Wound Ostomy and Continence Nurses (WOCN) Society is the oldest wound care society that has board-certified over 6,000 nurses worldwide.[134] They are considered the gold standard for certification in wound nursing, and this process requires completion of a rigorous curriculum followed by stringent recertification processes.[134] In 2010, the Organization of Wound Care Nurses (OWCN) was established.[135] It provides the foundation and free-of-cost training for all the licensed nurses who are practicing in different care settings. Wound care and ostomy education programs for nurses are increasingly becoming available in an effort to improve nursing service quality.[136]

Appropriate professional use of multiple wound care disciplines may markedly impact wound care.[137–139] Physical therapy represents one such major discipline. Trained physical therapists may employ numerous treatment regimens, such as wound debridement, modalities, edema management, positioning, orthotic use, and mobility improvement. Occupational therapists may provide edema management, wound debridement, positioning, toileting programs, self-feeding, and wheelchair management as relevant to the need of the patient. Addressing supportive interventions such as physical and occupational therapy and nutrition management are likely to promote the rate of wound healing, thereby lowering the overall costs of wound care. After all, the longer a patient's healing time, the higher the cost to the facility.

Wound, ostomy, and continence nurses, in addition to being educated and trained to provide acute and rehabilitative care, represent an important component of the wound care ecosystem.[140–142] Ostomies, stomas, acute and chronic wounds, and urinary and fecal incontinence often present severe physical challenges to wound patients. These lead to emotional and social issues that may be addressed by properly trained allied medical professionals. Limitations in well-structured education of wound care providers may be viewed as a significant barrier to uniform evidence-based wound care throughout the country.

PATIENT EDUCATION

Literature addressing patient-centered wound care has mostly focused on quality of life (QoL), pain, adherence, and coping. A key concern from the patients' perspective is improved provider recognition of patients' concerns in treatment planning and request for personalized approaches. The evolution to shared wound care decision making is what patients are seeking.[143,144] Engaging patients' awareness and involvement in wound management is key to ensuring successful healing outcomes.[145]

COMBAT WOUND CARE

In the military and related defense services, wounds and trauma are a common problem. In 2017, the National Academies of Science, Engineering, and Medicine reported a new vision for a national trauma care system with the ultimate aim of "zero" preventable deaths after injury to benefit those in combat.[146] This vision is based on studies conducted between 2001 and 2011, which identified that ~75% of combat deaths were caused by explosions and lack of timely and appropriate care before the patient reached a medical treatment facility.[146]

The Department of Defense (DoD) and the US Department of Veterans Affairs (VA) are the two federal government institutions involved in providing health care to the 3.9 million US military members who served in Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF), the 17 million veterans from prior periods, and the 1.3 million active personnel and their families.[147]

The DoD covers active service members, and the VA provides medical support to eligible retirees. The TRICARE for Life program is a wraparound plan meant to supplement Medicare coverage of military retirees and to pay for military hospitals and health care workers.[148] The VA estimates that around 25% of military veterans have diabetes[149,150] (compared with 9% of the civilian adult population). The economic burden of lower limb amputations in diabetic veterans was $206 million.[151]

The Combat Casualty Care Research Program is a collaborative, multidisciplinary partnership that utilizes clinical and translational research to provide state-of-the-art wound care.[152] With an effort to maximize restoration of function and QoL in service members with combat-related extremity trauma, the VA and DoD have increased their research and clinical care efforts with a focus on regenerative medicine.[153]

CLOSING REMARKS

Based on estimates originating from independent sources, it is clear that the magnitude of wounds as

a health care problem is sharply rising. Resources allocated to the education, care, and research of wounds continues to be disproportionately low and deserves strategic attention. A key challenge in all of these three domains—education, care, and research—is the ability to recruit interdisciplinary talent that would work together cohesively as one team.

ACKNOWLEDGMENTS AND FUNDING SOURCES

Work on wound care in this program is supported by the National Institutes of Health awards R01NR015676, R01GM077185, R01GM108014, R01DK114718, U01DK119099, and R01NR013898.

AUTHOR DISCLOSURE AND GHOSTWRITING

No competing financial interests exist. The content of this article was expressly written by the author listed.

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Abbreviations and Acronyms

BMI = body mass index
DFU = diabetic foot ulcer
DoD = Department of Defense
FU = foot ulcer
IGB = intragastric balloon
PNI = psychoneuroimmunology
PU = pressure ulcer
QoL = quality of life
SSI = surgical site infection
T2D = type 2 diabetes
VA = Veterans Affairs
WHO = World Health Organization