

# Nutrition in patients with chronic non-healing ulcers: a paradigm shift in wound care

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**Abstract:** Chronic ulcers continue to pose a significant clinical and economic burden for both patients and wound care practitioners. Despite good standard of care (SOC), many wounds fail to heal. Wound healing requires a complex cascade of physiologic and immunologic processes as well as proper nutrition. An adequate balance of macro- and micronutrients is important to support the cellular activities that are necessary for repairing and remodeling of tissue. Despite being well documented in a number of clinical studies there continues to be a gap in recognizing nutritional deficits as well as appropriate clinical interventions in patients with chronic wounds. Effective management of malnutrition in patients with chronic wounds requires collaboration among multiple clinical disciplines. A holistic nutritional management approach may yield both clinical and economic benefits.

**Keywords:** wound care, chronic wounds, parenteral nutrition, micronutrients, macronutrients, wound healing, nutrition management, malnutrition, nutrition assessment

## Introduction

The growing prevalence of diabetes, obesity, changing lifestyle, and the aging population continues to drive an increase in the incidence of chronic wounds. Over 6 million people have chronic wounds in the USA alone and an excess of \$20 billion is spent annually on treatment.<sup>1,2</sup> While many therapies have become available, management and treatment of chronic ulcers remain a challenge. Approximately a third of diabetic foot ulcer (DFU) patients treated with standard of care (SOC) will benefit from the therapy.<sup>3</sup> For venous leg ulcers (VLUs), healing rates range from 30–60% at 24 weeks.<sup>4</sup>

Wound healing requires a complex cascade of physiologic and immunologic processes as well as proper nutrition. An adequate balance of macro- and micronutrients is important to support the cellular activities that are essential for repairing and remodeling of tissue. Malnutrition can alter collagen synthesis, immune function, and wound tensile strength. The importance of nutrition in wound healing is just beginning to be recognized by wound care practitioners.<sup>5–7</sup>

## Chronic wounds

Unlike acute wounds, chronic wounds do not proceed through an orderly process of regeneration and repair. The healing process can be lengthy and burdensome for patients. Factors such as excessive bacterial burden, inappropriate moisture balance, inadequate circulation, and malnutrition can halt the normal healing process. In addition to proper wound care, management of chronic wounds requires attention

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to basic nutrition; however, nutrition often receives little to no attention. Malnutrition is widespread even in developed countries. Elderly patients, in particular, are at an increased risk of developing nutritional deficiencies. In patients with a chronic wound, there is a complex interaction between diet, nutritional deficiency, infection, and wounds.

Adequate protein is vital for platelet function, fibroblast proliferation, and wound remodeling.<sup>8</sup> Protein deficiency can impair capillary formation, fibroblast proliferation, proteoglycan and collagen synthesis.<sup>9</sup> Moreover, a protein deficiency can delay wound healing by prolonging the inflammatory phase.<sup>8</sup> Furthermore, lower albumin levels in patients are linked to impaired wound healing.<sup>10</sup> Besides providing the necessary energy for the tissue repair and regeneration process, carbohydrates also play a role in cell communication. Lipids, in addition to serving as the most calorie dense macronutrient, are necessary for cell membrane stabilization.

In addition to macronutrients, micronutrients also play a critical role in the wound healing process. Vitamin A is required for the formation of granulation tissue, synthesis of collagen, epithelialization and macrophage functioning.<sup>8,11</sup> Vitamin C also plays a role in collagen synthesis.<sup>11,12</sup> Decrease in vitamin K can lead to a prolonged inflammatory phase.<sup>11</sup> Iron is an important mineral required for oxygen transport and antibody production. Deficiency in iron can lead to tissue hypoxia, decreased wound tensile strength and decreased immune function.<sup>11</sup>

## Nutrition screening and assessment

Factors commonly included in screening assessments include weight history, body mass index (BMI), clinical laboratory assessments and recent food intake. There are several nutritional screening tools available; however, they differ in scope (Table 1). The Prognostic Nutritional Index (PNI) was designed to assess the risk of poor outcome after surgery.<sup>12</sup> PNI is calculated using the serum albumin level and periph-

eral blood total lymphocyte counts. It has become a useful screening tool for various types of cancer, such as gastric cancer, pancreatic cancer, hepatocellular carcinoma, and colorectal cancer.<sup>13–15</sup> Similarly, the Subjective Global Assessment (SGA) was developed for use in surgical patients, but has now become a common screening tool for hospitalized patients.<sup>16</sup> SGA is based on medical history and clinical findings, and it has been used as a reference standard for developing other nutritional screening tools for use in patients with chronic renal disease.<sup>17</sup> The Public Awareness Checklist is another test aimed at increasing nutrition awareness in elderly patients.<sup>18,19</sup> The Mini Nutritional Assessment (MNA<sup>®</sup>) is designed specifically to identify elderly patients who are malnourished or at risk of malnutrition.<sup>20,21</sup> MNA has recently received much attention for the ease of use and feasibility in any clinical care setting. MNA was originally comprised of 18 questions and has now been truncated to 6 questions to streamline the screening process. The questions on short form (MNA-SF) assess medical history, weight, diet, and a physical examination.<sup>22,23</sup> The MNA-SF retains the validity of the original MNA and is recommended by European Society for Clinical Nutrition and Metabolism (ESPEN).<sup>24</sup> Based on recent evidence, the US Wound Registry (USWR) also recommended MNA as the validated nutritional screening tool of choice for wound care.<sup>25,26</sup> Furthermore, the USWR has established a clinical quality measure (CQM) for nutritional screening that employs the MNA.<sup>26</sup> The MNA-SF is used widely in our wound clinics to improve patient outcomes. It has effectively allowed us to assess nutrition risk and offer nutritional intervention to increase protein and calorie intake, which are essential for wound management.

## Nutritional support

Patients with chronic wounds have a higher rate of complications, including infections, which can affect wound healing. It is essential to address deficiencies in a patient's diet to accelerate wound healing. Adequate energy needs to

**Table 1** Selected screening assessments

Screening assessments	Source, year	Assessment parameters
Maastricht Index	Kuzu et al, <sup>34</sup> 2006	BMI, albumin, prealbumin, and total lymphocyte count
Malnutrition Universal Screening Tool (MUST)	Malnutritional Advisory Group, UK, <sup>35</sup> 2003	Includes BMI, weight loss, acute disease
Mini-Nutritional Assessment-Short Form (MNA-SF)	Rubenstein et al, <sup>21</sup> 2001	Includes recent intake, weight loss, mobility, acute disease, physiological stress, BMI
Subjective Global Assessment (SGA)	Detsky et al, <sup>36</sup> 1987	Medical history and physical examination. Includes weight, intake, GI symptoms, functional capacity
Prognostic Nutritional Index (PNI)	Dempsey et al <sup>12</sup>	Calculated based on the serum albumin concentration and peripheral blood lymphocyte count

**Abbreviations:** BMI, body mass index; GI, gastrointestinal.

be provided through oral or parenteral delivery nutrition. The European Pressure Ulcer Advisory Panel (EPUAP) recommended a minimum of 30–35 kcal/kg of body weight for patients with pressure ulcers.<sup>27–29</sup> For patients who are underweight or losing weight, the National Pressure Ulcer Advisory Panel (NPUAP) recommends increasing the caloric intake to 35–40 kcal/kg of body weight.<sup>27–29</sup> The Agency for Healthcare Research and Quality (AHRQ) recommends protein intake between 1.25 and 1.5 g/kg of body weight, and fluid intake of 1 mL/(kcal·day<sup>-1</sup>).<sup>29,30</sup>

Oral nutrition supplementation (ONS) can provide the essential proteins, vitamins, and minerals needed to meet the nutritional requirements. ONS provide arginine and selected micronutrients such as vitamin C and zinc. Evidence from recent studies has shown that formulations rich in protein, vitamin C, and zinc are effective in significantly improving healing.<sup>31–33</sup> The effectiveness of ONS requires a patient to be able to swallow and to comply with ONS prescribed daily dosage. Enteral nutrition requires a tube and thus is contraindicated in patients with chronic wounds. Additionally, enteral nutrition can be limited by intolerance issues including nausea, vomiting, bloating, abdominal pain, and diarrhea.

Patients who are severely malnourished or exhibit malabsorption and have stalled wound healing can also benefit from parenteral nutrition (PN). PN provides patients with the essential nutrients intravenously. The solution contains dextrose, amino acids, lipids, electrolytes, vitamins, and trace elements, such as zinc, iron, and copper. The contents of PN are

determined by age, weight, height, and the medical condition of patients. PN is usually prescribed through a central venous catheter. Because it is delivered intravenously, patient compliance is ensured and gastrointestinal intolerance is avoided. PN should be monitored closely and adjusted as necessary.

## A paradigm shift

The importance of nutrition in wound healing has been well documented in a number of clinical studies; however, there continues to be a gap in practice in the recognition of nutritional deficits as well as appropriate clinical interventions in patients with chronic wounds. Effective management of malnutrition in patients with chronic wounds requires collaboration among multiple clinical disciplines. Wound care continues to be managed in silos; however, the new era of quality care requires a more holistic approach.

To drive a paradigm shift in advanced wound care, we are conducting important research in nutrition and wound healing. The planned study employs an individualized nutritional management process incorporating a Registered Dietitian Nutritionist (RDN) and a Board Certified Nutrition Support Pharmacist (BCNSP) to develop a plan of care for each participant (Figure 1).

This real world evidence study will follow participants with chronic non-healing ulcers supplemented with PN at up to 20 sites across the US. Participant's nutritional status will be assessed using the MNA at baseline. Clinical laboratory tests will include a comprehensive metabolic panel (CMP),

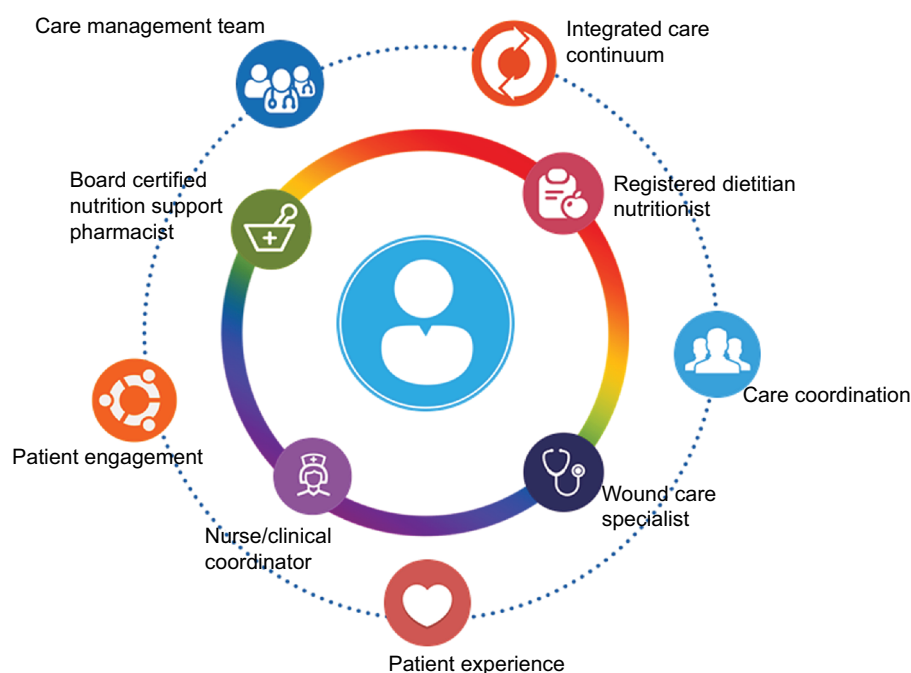


Figure 1 Patient-centered care model.

albumin, pre-albumin, magnesium, and phosphate. In addition, a 3-day food record will be collected along with a Wound Quality of Life (WQOL) questionnaire at baseline and the end of the study. The food diary will be used to complete a calorie/protein count. Pain assessment will be carried out weekly using the Numeric Pain Rating Scale. Wound size, depth, and volume will be assessed at baseline and every week during the length of the study. Participants' nutritional intake will be assessed by Nutritional Healing, LLC (Nashville, TN, USA).

A team of registered dietitians, wound care nurses, and pharmacists will develop a plan of care for each participant using MNA, food diary, wound notes, and lab results. Following an assessment of a RDN, participants will receive parenteral nutrition if they have adequate calorie/protein intake but suspected malabsorption syndrome. Oral nutrition will be encouraged to maintain intestinal integrity. Participants will be followed for 12 weeks to assess the direct effect of the nutritional management. Labs will be drawn weekly at home health visits. New formulations of PN will be developed for participants based on clinical laboratory results. Weekly home health nursing visits will be conducted for the peripherally inserted central catheter (PICC) dressing change.

The effects of these nutritional regimens will be individually evaluated during the study. This clinical model may yield both clinical and economical benefits and further our understanding of the role of nutrition in wound healing. This study may unlock a nutritional intervention that plays a vital role in the healing of chronic non-healing wounds, currently a vexing problem for many patients and wound care practitioners.

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## Disclosure

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