

WOUND CARE



Smoking, Chronic Wound Healing, and Implications for Evidence-Based Practice

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ABSTRACT

Chronic wounds are rising in prevalence and creating significant socioeconomic burdens for patients and healthcare systems worldwide. Therefore, it is now more important than ever that clinicians follow evidence-based guidelines for wound care when developing personalized treatment plans for their patients with chronic wounds. Evidence-based guidelines for treating venous leg ulcers, diabetic foot ulcers, and pressure ulcers, the 3 main categories of chronic wounds, focus primarily on biologic therapies. However, there are also evidence-based guidelines for treating behavioral risks to poor healing, such as smoking, which should be incorporated into treatment plans when appropriate. The purpose of this article was to review the mechanisms through which smoking adversely impacts the wound healing process, and propose strategies for incorporating evidence-based guidelines for treating tobacco dependence into treatment plans for patients with chronic wounds who smoke.

KEY WORDS: chronic wound healing, evidence-based practice, smoking, tobacco dependence treatment.

Introduction

Chronic wounds create extensive economic and social burdens on our global society. It has been estimated that in the United States alone, chronic wounds affect 6.5 million people resulting in annual treatment costs up to \$25 billion.¹⁻⁴ Furthermore, in developed countries, approximately 1% to 2% of the population is expected to experience a chronic wound during their lives.⁵ Chronic wounds are associated with advancing age, obesity, and diabetes mellitus; their incidence and associated costs are expected to increase dramatically over time.⁶ Considering the vast financial, social, and clinical impact of chronic wounds, it is essential that clinicians treating patients with these conditions consider all modifiable factors that may delay wound healing including smoking.

Cigarette smoking negatively impacts wound healing on multiple levels.⁷⁻¹⁰ As a result, chronic wound patients who continue to smoke should be encouraged to quit and provided tools by healthcare providers to assist with that process. Existing evidence suggests that smokers are more successful with abstinence when presented with repeated personalized messages urging them to quit along with assistance in their attempts to quit smoking.¹¹ The purpose of this article was to (1) review the mechanisms through which smoking negatively impacts the wound healing process, (2) present the current evidence-based guidelines for treating tobacco dependence, and (3) propose strategies for incorporating the clinical guidelines into chronic wound care treatment plans of patients who smoke.

Chronic Wounds

A chronic wound is defined as one that fails to progress through the timely, sequential steps of healing that end with wound closure; chronic wounds generally remain open for greater than 3 months.¹² Nearly all chronic wounds can be grouped into 3 major categories: leg ulcers, diabetic ulcers, and pressure ulcers (PUs). Venous leg ulcers comprise the largest single group of leg ulcers treated in wound care clinics.¹³ Current statistics suggest approximately 15% of venous ulcers never heal or reoccur once or more times in up to 71% of affected patients.^{14,15} It has been estimated that venous ulcers incur treatment costs of approximately \$3 billion annually in the United States and cause a loss of approximately 2 million working

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days.^{1,2,16-18} Diabetic foot ulcerations (DFUs) that fail to heal result from a combination of peripheral vascular disease and neuropathy.¹⁹ Approximately 1 in 4 individuals with diabetes mellitus will develop a foot ulcer during their lifetime and 15% of DFUs will lead to amputation.²⁰ In the United States, DFUs account for 25% to 50% of the costs related to diabetic care.²¹ Pressure ulcers also pose significant problems, especially for those aged 65 years or older who suffer from impaired mobility, inadequate nutritional intake, or a critical illness. Total annual costs related to PU care in the United States have been estimated to be as high as \$11 billion and predictions are that expenditures will continue to rise because of the growth in the aging population.²² In addition to the extensive financial costs, PUs are associated with impaired health-related quality of life.²²

Although each of the major chronic wound types can be characterized by unique pathobiological processes, all have shared characteristics, including chronic inflammation, a proteolytic environment secondary to bacteria, underlying ischemia, and recurrent ischemia-reperfusion cycles.²³ Cigarette smoking impairs the function of several cell types such as neutrophils and macrophages important to inflammatory and bactericidal activity²⁴ and also compromises oxygen delivery to tissues. Thus, cigarette smoking has detrimental effects that compound the underlying pathobiology of chronic wounds.^{10,25}

The harmful effects of cigarette smoking on wound healing have been reported in multiple studies. A higher incidence of wound complications associated with smoking include prolonged wound healing times,^{8,9} dehiscence,^{26,27} tissue flap necrosis,²⁸⁻³⁰ anastomotic leakage,³¹ decreased wound tensile strength,³² and infection.^{9,33,34} Conversely, smoking cessation has been associated with a reduction in incisional wound infections^{33,35} and other wound healing complication rates.⁷ In fact, many surgeons are hesitant to perform certain elective or aesthetic surgeries on individuals who reject smoking cessation advice. Although few studies have evaluated the effects of cigarette smoking specifically on chronic wound healing, the evidence of its negative impact on acute wound healing suggests that assessing for tobacco use and treating tobacco dependence in the chronic wound population should be a high priority for clinicians.

■ Smoking and Wound Healing

Wound healing is a complex process that can be divided into at least 3 continuous, but overlapping stages: an inflammatory stage, a proliferative stage leading to tissue restoration, and tissue remodeling stage.^{24,36} Wound healing is regulated by a synergistic interplay among multiple cell types, cytokines, and growth factors at the wound site. Normal tissue oxygen pressures are necessary for the entire reparative process including cell migration to wound sites, bacterial defense, and collagen synthesis.³⁷ The

healing trajectory can be interrupted at any stage by tissue hypoxia.³⁸ Hypoxia has also been found to increase wound infection risk in surgical patients partially due to reduction of bactericidal actions of neutrophils.³⁹⁻⁴¹ Tissue hypoxia is viewed as a fundamental mechanism through which cigarette smoking disrupts acute wound healing.^{42,43} Adverse effects of smoking on tissue oxygen concentrations have been demonstrated after smoking just 1 cigarette regardless of smoking history.^{42,44,45} Furthermore, Jensen and colleagues⁴² reported that “pack-per-day” smokers experience tissue hypoxia during a significant portion of each day.

It has been estimated that cigarette smoke contains more than 4000 toxic compounds. The primary toxins associated with impaired wound healing are nicotine and the gases carbon monoxide and hydrogen cyanide.⁴⁶ The definitive mechanisms through delay healing are not understood, but all have been shown to impair oxygen supply to tissues.^{42,47,48}

Perhaps the most frequently studied tobacco smoke constituent in relation to tissue hypoxia is nicotine. Nicotine is a colorless alkaloid that is rapidly absorbed during smoking; it is hypothesized to act as a major component of reduced blood flow owing to its vasoconstrictive actions.⁴⁹ Some studies suggest that nicotine is harmful to skin and subcutaneous tissue because it stimulates the sympathetic nervous system to release catecholamines, which trigger peripheral vasoconstriction and diminish tissue perfusion rates.⁵⁰⁻⁵² Tissue perfusion rates are also diminished by increased blood viscosity that results when catecholamines stimulate platelet aggregation via the adenylate cyclase system. Increased blood viscosity is also thought to be a causative component of nicotine-induced tissue hypoxia.^{47,53} Nevertheless, evidence concerning the impact of nicotine on tissue perfusion and wound healing remains mixed. Recent studies have challenged the belief that nicotine is the major agent in tobacco smoke causing reduced blood flow, tissue hypoxia, and subsequent wound complications.²⁵ For example, Sorensen and colleagues²⁵ reported a temporary, marginal increase in skin blood flow, a significant decrease in subcutaneous blood flow and no effect on the aerobic metabolism of tissue, when infusing 1.0 mg of nicotine intravenously, an amount similar to a nicotine replacement drug.²⁵ These findings are supported by other studies showing that nicotine-replacement drugs had no adverse effects on acute wound healing^{33,54} unless given in toxic doses,^{55,56} suggesting that nicotine alone is not responsible for the total vasoactive effect of smoking or the association between smoking, local tissue hypoxia, and impaired wound healing.

Carbon monoxide and hydrogen cyanide are also hypothesized to negatively affect wound healing. Carbon monoxide leads to tissue hypoxia because it reduces the oxygen content of blood by binding to hemoglobin. Carbon monoxide has a 200 times greater affinity to bind

hemoglobin than oxygen.^{46,47} As a result of a shift to the left in the oxygen dissociation curve, oxygenated hemoglobin in the bloodstream is reduced resulting in impaired tissue perfusion and cellular hypoxia.^{52,57} Hydrogen cyanide also affects tissue oxygenation by impeding cellular oxygen metabolism via inhibition of the enzyme system necessary for this metabolic process.^{48,58}

Although the exact mechanisms by which nicotine, carbon monoxide, and hydrogen cyanide lead to tissue hypoxia are not entirely understood, the negative impact of smoking on cellular function during the wound healing process has been reported by numerous studies. For example, cigarette smoke has been associated with a reduced proliferation of erythrocytes,⁴⁷ white blood cells,⁴⁷ and fibroblasts.^{47,59,60} Diminished numbers of erythrocytes lead to inadequate oxygen availability, which results in tissue hypoxia. White blood cells (macrophages) are essential for the phagocytosis of tissue debris, bacteria, and apoptotic neutrophils during the inflammatory stage of healing. They also generate a host of cytokines that signal subsequent healing processes such as angiogenesis. Smoking not only reduces white blood cell migration to the wound site, but also diminishes lymphocyte function,^{9,61} cytotoxicity of natural killer cells,^{9,61} macrophage sensing of gram-negative bacteria,⁶² and the bactericidal activity of neutrophils.⁶³ Smoking is also associated with a reduction in fibroblast proliferation during the proliferative stage of wound healing. Fibroblasts produce essential structural proteins such as collagen fibronectin that are needed for granulation tissue formation and epithelialization.^{59,60,64} Collagen is the primary structural protein that affects a healing wound's tensile strength and research has demonstrated that its production is diminished in smokers.⁶⁵

Considered collectively, these data provide compelling evidence that smoking impairs wound healing. However, most of these studies evaluated the effect of smoking on acute wound healing following surgery. Less is known about the influence of cigarette smoke on chronic wounds, although a relationship between smoking and an increased likelihood of PU formation has been observed in at least 1 study of patients with spinal cord injuries.⁶⁶ Figure 1 illustrates a proposed model of how smoking and the toxic compounds contained in cigarette smoke may reduce healing in patients with chronic wound induced by venous dysfunction, prolonged exposure to pressure or shear, or diabetes. Additional studies are needed to elucidate the specific effects of smoking on chronic wound healing.

Several clinical practice guidelines provide evidence-based practice recommendations for clinicians who treat patients with chronic wounds.⁶⁷⁻⁷² However, these guidelines do not provide specific recommendations to assist patients in quitting smoking or techniques for tobacco dependence treatment. Creating an appendix to the guidelines containing this information would provide clinicians with the resources that are needed to help smokers quit and thus potentially improve healing outcomes for these patients.

■ Evidence-Based Guidelines for Treating Tobacco Dependence

Smoking cessation is a dynamic process that typically requires smokers to make several serious attempts before achieving long-term success. Many smokers express the desire to quit smoking each year, but only one-third are actually successful.⁷³ The US Public Health Service *Treating Tobacco Use and Dependence* guideline provides

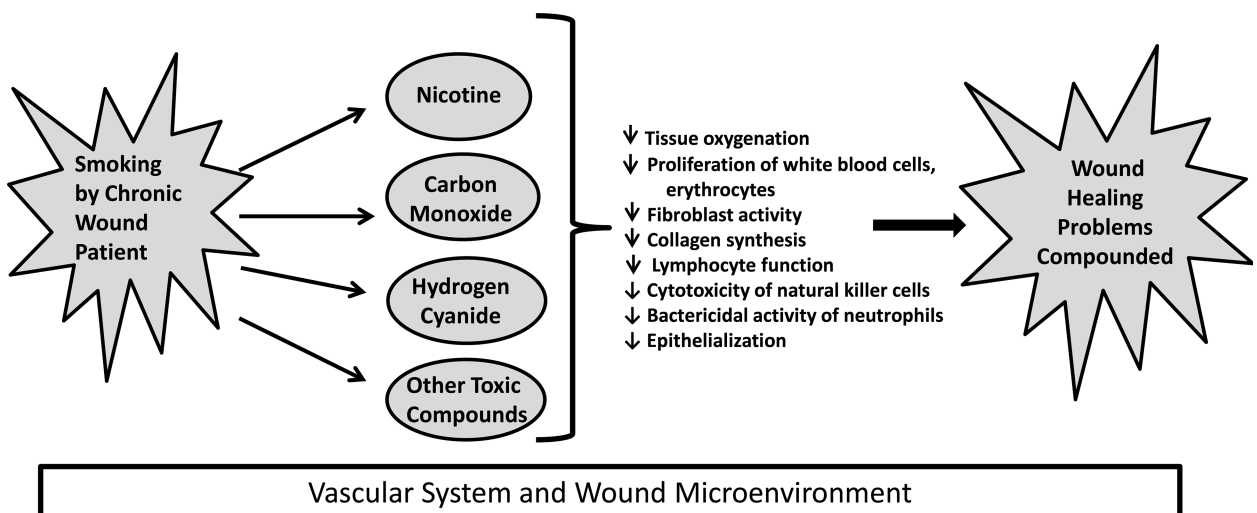


FIGURE 1. Detrimental effects of smoking on healing of chronic wounds. Diagram illustrating how smoking in a patient with a chronic wound leads to inhalation of toxic components that have negative effects on tissue oxygenation and cellular activity in the vascular system and microenvironment of a chronic wound.

evidence-based recommendations for tobacco dependence treatment.¹¹ Several studies have examined the implementation of the US Public Health Service guideline in the ambulatory setting and have found that approximately one-third of physician visits do not include measurement of tobacco use status^{73,74} despite guideline recommendations. When multiple clinicians (ie, physicians, nurses, pharmacists, social workers etc) advise a patient to quit smoking, it increases the patient's motivation to quit and the number of serious attempts to quit (Table 1).¹¹

Guidelines for smoking cessation follow 5 A's: Ask, Advise, Assess, Assist, and Arrange (Table 1).¹¹ Patients should be asked about their tobacco use and it should be documented at every visit. Patient who smoke are advised to quit smoking via a clear, strong personalized message delivered by a clinician. They should also be assessed for willingness to quit smoking. It is critical to assess patients who have recently quit smoking for challenges to remaining abstinent. Patients who are willing to make a quit attempt should be offered assistance with cessation with pharmacotherapy and either provided or referred to counseling or behavioral treatment. Subsequent contacts should be arranged for patients to follow up on the previous "A's" discussions. Providing routine assistance to all patients who are interested in tobacco dependence treatment is the most important step that a clinician can provide.¹¹

■ Smoking Cessation Counseling and Problem-Solving Skills

When counseling patients, teaching practical problem-solving skills and providing support and encouragement are important. Patients should be taught to recognize situations or smoking cues that may increase the risk of smoking or relapse such as being around other smokers, stress, or drinking alcohol. They need assistance in developing coping skills in order to anticipate and avoid temptation and trigger situations and cope with smoking urges. Some examples are learning distraction techniques and changing routines, assistance with accomplishing lifestyle changes that reduce stress and exposure to smoking cues, and learning basic information about smoking and successful quitting. Supportive counseling also may include encouragement for quit attempts, expression of concern and willingness to help, asking about fears and ambivalence regarding quitting, and encouraging patient discussion about the quitting process.¹¹

■ Pharmacotherapy

Successful smoking cessation is a multicomponent strategy. Pharmacotherapy, along with behavioral counseling and problem-solving skills, offers the highest success for smoking cessation.^{11,75-77} The first-line agents discussed in this section have been found to be safe and effective for

smoking cessation (Table 2). Pharmacotherapy includes nicotine replacement therapy (NRT), bupropion, and varenicline. Bupropion was the first nonnicotine medication to show efficacy with smoking cessation and was approved for use in smoking cessation in 1997.⁷⁸ The possible mechanisms of action of bupropion include blockade of neuronal reuptake of dopamine and norepinephrine and blockade of nicotinic acetylcholinergic receptors. It can be used in combination with nicotine replacement medications. Bupropion is contraindicated for patients with seizure disorders and anorexia nervosa or patients taking monoamine oxidase inhibitors.

Varenicline is a nonnicotine medication that has been used for tobacco dependence treatment since 2006. It is a partial agonist of the $\alpha 4\beta 2$ subtype of the nicotinic acetylcholine receptor and therefore should not be used with nicotine replacement products. Varenicline has the highest 6-month abstinence rate compared to placebo of all the available pharmacotherapies. It is well tolerated and should be used with a reduced dose in renal dysfunction patients. Patients with a history of psychiatric illness should be monitored closely.⁷⁵

Nicotine replacement agents are available in several forms: inhalers, patches, gums, nasal sprays, and lozenges. Some are available over the counter and some by prescription only (Table 2). The goal of NRT medications is to at least partially replace the nicotine obtained by cigarettes and to reduce the severity of nicotine withdrawal. The form of nicotine replacement medication offered can be based on patient preference and previous history when attempting to quit smoking. Other factors to consider may include whether the patient has dentures or skin sensitivities, in which cases the clinician may not want to recommend the gum or patch forms of NRT (Table 2).¹¹

■ Smoking Cessation in Patients With Wounds

Patients with wound healing complications typically have recurring visits (daily, weekly, and monthly) in a wound care clinic or home care setting. These regularly recurring visits provide an excellent opportunity for clinicians to deliver evidence-based tobacco dependence treatment interventions to patients who continue to smoke. For wound care patients who continue to smoke or those who are having additional difficulty with successful cessation, the following 5R's (relevance, risks, rewards, roadblocks, and repetition) intervention may be helpful.¹¹ The clinician can advise a patient to quit smoking; however, it is important to allow patients to address each topic in their own words. The clinician can fill in gaps, point out discrepancies, and help refine the patient's responses. The patient must first indicate why quitting smoking is personally relevant, being as specific as possible. Some reasons a wound patient may cite are personal health concerns, cost, and the health effects on children or grandchildren in the home. The patient

TABLE 1.

The 5A's Model for Treating Tobacco Use and Dependence and Suggestions for Implementing in Wound Care Clinics

The 5A's Model for Treating Tobacco Use and Dependence ^a		
5 A's	5A's Definitions	Suggestions for Implementation in a Wound Care Clinic
Ask	Systematically, identify all tobacco users at every visit.	Obtain smoking status from each patient at each visit along with vital signs.
Advise	In a clear, strong, personalized message, urge all tobacco users to quit.	Make connection between decreased wound healing and continued smoking. Use specific examples of how wound healing is affected by smoking such as: <ul style="list-style-type: none"> • Smoking ↓ blood flow and oxygen to wound • Smoking ↑ risk of infection • Smoking slows healing • Smoking ↓ strength of scar tissue
Assess	For current tobacco users, determine willingness to make a quit attempt.	For patients willing to make a quit attempt, continue with 5 A's. For patients not ready to make a quit attempt, refer to the 5 R's: relevance, risk, rewards, roadblocks, and repetition (see <i>Strategies to promote smoking cessation in wound management patients</i>).
Assist	<ul style="list-style-type: none"> • For patients willing to make a quit attempt, help with a quit plan: <ul style="list-style-type: none"> ○ Set a quit date, ideally within 2 wk ○ Tell family, friends, and coworkers about plans to quit ○ Anticipate challenges to the quit attempt, including nicotine withdrawal symptoms ○ Remove tobacco products from the environment ○ Recommend or provide a prescription for first-line pharmacotherapy (eg, varenicline, bupropion, nicotine replacement), See Table 2. ○ Provide a supportive clinical environment (eg, "our clinic staff is supportive in your quit attempt). ○ Provide supplementary materials including information on quit lines (ie, 1-800-QUIT-NOW). ○ Strategies for after the quit date: <ul style="list-style-type: none"> ■ Strive for total abstinence ■ Identify what was helpful and not helpful during quit attempts in the past ■ Anticipate triggers or challenges when quitting The 5 D's are useful when coping: <ul style="list-style-type: none"> ■ DELAY: wait a few minutes; the urge to smoke will pass. ■ DRINK: water, juice, or other soft drink (no caffeine or alcohol). ■ DO something: take a walk, do something with your hands, find some distraction. ■ DEEP BREATHS: take several deep breaths (slowly in, slowly out) and the urge will pass ■ DICUSSS: talk to someone about how you are feeling—family, friends, coworkers. ■ It is more difficult to quit smoking with other smokers in the house. <p>For patients unwilling to quit at this time, provide interventions to increase quit attempts in the future (see <i>Strategies to promote smoking cessation in wound management patients</i>).</p> <p>For recent quitters, provide relapse prevention strategies</p>	<ul style="list-style-type: none"> • Patients willing to make a quit attempt, address each point listed to the left, then follow up at each visit. • Patients unwilling to quit: continue to ask about smoking status and advise to quit at each subsequent visit, offering assistance if the patient shows interest. • Patients who are recent quitters, congratulate on their success, and offer support and/or encouragement at each visit.
Arrange	All patients who received previous A's should receive follow-up.	Follow up with each wound patient at each visit. Serial wound care visits represent a teachable moment for tobacco dependence treatment.

^aAdapted from the US Public Health Service *Treating Tobacco Use and Dependence* Clinical Practice Guideline.¹¹

TABLE 2.

First-Line Pharmacotherapy (Most Effective When Used in Combination With Behavioral Counseling)^a

Pharmacotherapy	Dosage	Duration	Available	Warnings/Side Effects
Bupropion SR (Zyban, Wellbutrin)	150 mg once daily (days 1-3); 150 mg twice daily	Start 1-3 wk before quit date; duration 2-6 mo	Prescription only; Generic available (may be combined with nicotine replacement therapy)	Do not use with history of seizure or eating disorders, current monoamine oxidase inhibitor. Insomnia, dry mouth
Varenicline (Chantix)	0.5 mg once daily (days 1-3); 0.5 mg twice daily (days 4-7); 1 mg twice daily	Start 1 wk before quit date duration 3-6 mo	Prescription only	Use with caution: significant renal impairment or on dialysis, serious psychiatric history. Nausea, insomnia, abnormal/ vivid dreams
Nicotine nasal spray (Nicotrol NS)	1 dose = 1 squirt per nostril; 1-2 doses per hour; 8-40 doses per day	duration 3-6 mo; taper at end	Prescription only	Do not use with asthma. Nasal irritation
Nicotine inhaler (Nicotrol inhaler)	6-16 cartridges per day Inhale 80 times per cartridge	duration 6 mo; taper at end	Prescription only	Local irritation of mouth and throat; may improve after use
Nicotine patch (Generic, Nicoderm CQ, Nicotrol)	One patch per day; available strengths: 21 mg, 14 mg, 7 mg If ≥ 10 cigarettes per day: 21 mg If ≤ 10 cigarettes per day: may start with 14 mg	duration 6 mo; may use longer	Over the counter; Generic available	Do not use if have severe eczema or psoriasis. Insomnia, local skin reaction
Nicotine Gum (Nicorette)	1 piece q 1-2 hours; 6-15 pieces per day; available strengths: 2 mg, 4 mg If ≤ 24 cigarettes: 2 mg If ≥ 25 cigarettes: 4 mg	duration 6 mo; may use longer	Over the counter; Generic available	Do not eat 15 min before or during use. Mouth soreness, stomachache
Nicotine lozenge (Commit)	Weeks 1-6: 2-4 mg q 1-2 h Weeks 7-9: 2-4 mg q 2-4 h Weeks 10-12: 1-2 mg q 4-8 h available strengths: 2 mg, 4 mg	duration 3-6 mo	Over the counter; Generic available	Do not eat 15 min before or during use. Hiccups, cough, heartburn

^aAdapted from the US Public Health Service *Treating Tobacco Use and Dependence* Clinical Practice Guideline.¹¹

should next identify potential risks associated with continuing to smoke such as decreased blood flow and oxygen to wound, increased risk of infection, slower healing, and decreased strength of scar tissue. It is important for the patient to identify potential rewards of smoking cessation such as faster healing of wound, increased mobility or activity following wound healing, alleviation of comorbid health conditions such as coronary heart disease and peripheral vascular disease, improved pulmonary symptoms, cough and dyspnea, and improved smell and taste that may lead to improved nutritional intake and thus faster wound healing.

Finally, the patient should identify barriers or roadblocks to quitting and the clinician should provide counseling or interventions that address these barriers such as problem-solving counseling, or medications discussed in the general recommendations section. Typical roadblocks to successfully quitting smoking may include withdrawal symptoms, fear of failure, weight gain, lack of support,

depression, fear of losing the enjoyment of tobacco, being around other tobacco users, and limited knowledge of effective tobacco dependence treatment. Roadblocks specific to patients with chronic wounds frequently include immobility that prohibits working or regular daily activities. Lack of daily activities due to immobility may lead to boredom or anxiety, which may decrease the likelihood of success in quitting. We recommend repeating the 5 R's every time the patient sees the clinician.

Conclusion

Chronic wounds are a significant health problem. Wound healing may be impaired by multiple factors, including smoking. Because cigarette smoking is a modifiable factor, WOC nurses and other wound care clinicians should incorporate personalized, evidence-based smoking cessation strategies in their care plans in order to improve healing outcomes in this population.

KEY POINTS

- ✓ Although the exact mechanisms by which smoking compromises wound healing are not entirely understood, the negative impact of smoking has been reported by numerous studies.
- ✓ Wound care guidelines could be expanded to include the treatment of *behavioral* risks to poor healing, such as smoking.
- ✓ WOC nurses and other wound care clinicians should provide the resources to aid patients with chronic wounds to quit smoking.

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