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# The Power of Vitamin C: A Scoping Review of Pressure Injury Wound Healing With Vitamin C Supplementation

## Abstract

### Background

Pressure injuries are a significant health concern in Canada, with the occurrence as high as 26% across all health care settings. Researchers have studied the effectiveness of vitamin C in the healing of pressure injuries. The purpose of this scoping review is to synthesize the existing literature on the role of vitamin C in pressure injury wound healing and identify gaps within the current literature landscape.

### Methods

A scoping review of the literature was conducted using the framework developed by Arksey and O'Malley, along with the PRISMA-ScR guidelines. PubMed, Medline, CINAHL, and EMBASE databases were searched for human studies published in English that investigated the effectiveness of vitamin C in reducing wound size and/or accelerating the rate of pressure injury healing. The authors extracted data using a predefined form to summarize information on study type, patient descriptions, study design, interventions, and outcomes.

### Results

Nine articles met the review criteria. Six were randomized control trials, and the remaining 3 were observational studies. Seven studies acknowledged the benefit of vitamin C in pressure injury wound healing. One study reported no observed difference in healing within the control and treatment groups, and 1 study did not support the idea of increased vitamin C for wound healing.

### Conclusion

The current evidence suggests a possible correlation between vitamin C supplementation and pressure injury wound healing. Research with randomized control trial study designs that have large sample sizes is necessary to investigate the exclusive role of vitamin C and its impact on pressure injury wound healing.

**Key Words:** Pressure ulcer, pressure injury, bedsore, decubitus ulcer, decubitus injury, ascorbic acid, vitamin C, ascorbate, wound healing

# La puissance de la vitamine C : une revue de portée sur la cicatrisation des plaies de lésions de pression avec supplémentation en vitamine C

## Résumé

### Contexte

Les lésions de pression représentent un problème de santé majeur au Canada, avec une incidence pouvant atteindre 26 % dans l'ensemble des milieux de soins de santé. Des chercheurs ont étudié l'efficacité de la vitamine C dans la cicatrisation des lésions de pression. L'objectif de cette revue de portée est de synthétiser la littérature existante sur le rôle de la vitamine C dans la cicatrisation des plaies de

lésions de pression et d'identifier les lacunes présentes dans la documentation actuelle.

**Méthodes**

Une revue de portée de la littérature a été réalisée en utilisant le cadre élaboré par Arksey et O'Malley, ainsi que les lignes directrices PRISMA-ScR. Les bases de données PubMed, Medline, CINAHL et EMBASE ont été consultées pour identifier des études sur des sujets humains publiées en anglais qui examinaient l'efficacité de la vitamine C dans la réduction de la taille des plaies et/ou l'accélération du taux de cicatrisation des lésions de pression. Les auteurs ont extrait les données à l'aide d'un formulaire prédéfini afin de résumer l'information sur le type d'étude, la description des patients, la méthodologie, les interventions et les résultats.

**Résultats**

Neuf articles répondaient aux critères de la revue. Six étaient des essais randomisés contrôlés et les trois autres étaient des études observationnelles. Sept études ont reconnu l'effet bénéfique de la vitamine C sur la cicatrisation des plaies de lésions de pression. Une étude n'a observé aucune différence de cicatrisation entre les groupes témoin et expérimental, et une autre n'a pas appuyé l'hypothèse d'un apport accru en vitamine C pour favoriser la cicatrisation.

**Conclusion**

Les données actuelles suggèrent une corrélation possible entre la supplémentation en vitamine C et la cicatrisation des plaies de lésions de pression. Des recherches menées sous forme d'essais randomisés contrôlés avec de grands échantillons sont nécessaires afin d'examiner le rôle exclusif de la vitamine C et son impact sur la cicatrisation des lésions de pression.

**Mots-clés :** ulcère de pression, lésion de pression, plaie de lit, escarre, lésion de décubitus, acide ascorbique, vitamine C, ascorbate, cicatrisation des plaies

**Conflicts of Interest:**
The authors declare that there are no conflicts of interest regarding the publication of this paper.

**Availability of Data and Materials:**
The data supporting the findings are available upon request from the author for correspondence.

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## INTRODUCTION

Pressure injuries (PIs) are a significant health concern in Canada. The National Pressure Injury Advisory Panel (NPIAP) defines PIs as "localized damage to the skin and underlying soft tissue usually over a bony prominence or related to a medical or other device."[1] These injuries may appear as intact skin or open areas that can extend down to underlying structures, such as muscle or bone. Pressure injuries can stem from prolonged pressure and/or pressure combined with shear forces, causing increased discomfort.[1] The microclimate, nutrition, perfusion, patient comorbidities, and skin tissue condition may influence soft tissue tolerance to pressure and shear.[1] The NPIAP staging system is used to characterize PIs, detailing the extent of tissue loss and the physical appearance of the injury caused by pressure, friction, and/or shear (Figure 1).[1]

Graves et al.[2] examined data in 2014 from 38 studies conducted in 11 countries that investigated the frequency and occurrence rates of chronic wounds. Pressure injuries were found to be the most common type of chronic wound, with their prevalence ranging from 1.1% to 26.7% in hospitals, 6% to 29% in community care settings, and 7.6% to 53.2% in long-term care (LTC) facilities.[2] Within the Canadian health care system, the occurrence of PIs is notable at 26% across all settings.[3] In addition to the impact of PIs on patients' quality of life, there is also the financial burden to health care systems. In Ontario, it was estimated in 2013 that hospital-acquired PIs can cost in the area of $44,000 for Stage 2, while Stage 4 PIs could cost up to $90,000.[4] Despite attempts to enhance prevention through regulations, the rates of PIs in Canada have not substantially decreased compared to other countries, with ongoing concern regarding their management and prevention.[5]

Adequate nutrition is a fundamental part of skin health. Several essential nutrients in the human body may play a crucial role in the wound healing process. Among these, vitamin C is known to be a principal participant.[6] The daily Recommended Dietary Allowance (RDA) for vitamin C is 75 mg for women and 90 mg for men aged 19 and above.[7] Generally, a well-balanced diet will meet the body's daily requirements for vitamin C.[8] However, diets that do not provide at least 10 mg of vitamin C per day will lead to a deficiency and manifest symptoms, such as fatigue, capillary fragility, and impaired wound healing.[7] Vitamin C deficiency, also known as scurvy, remains a concern in Canada. Dadgar et al.[9] conducted a study examining hospital records in Hamilton, Ontario, over 9 years. They discovered that 52 patients exhibited plasma ascorbic acid (AA) levels below the recommended levels, indicating a scurvy diagnosis.[9] The Health Measures Survey collected biomarkers for vitamin C status in 2012 and 2013, which identified that slightly less than 3% of Canadians had a vitamin C deficiency.[6]

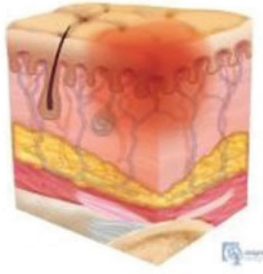
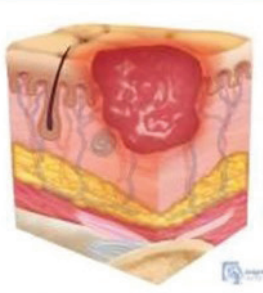
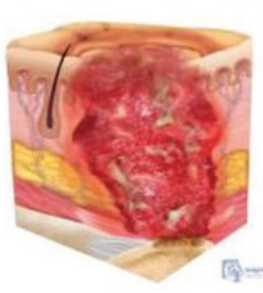
Vitamin C plays a role in all phases of the wound healing process.[6] A study of vitamin C deficient animals with wounds found inadequate collagen and scar formation as well as deviations in fibroblast formation.[10,11] Other more recent studies have added to our understanding of the role this micronutrient plays in the human body.[12,13] However, the scientific community has yet to reach a consensus on the exact amount of vitamin C required for PI wound healing beyond levels that prevent deficiency.[12,13] Implementing evidence-based PI man-

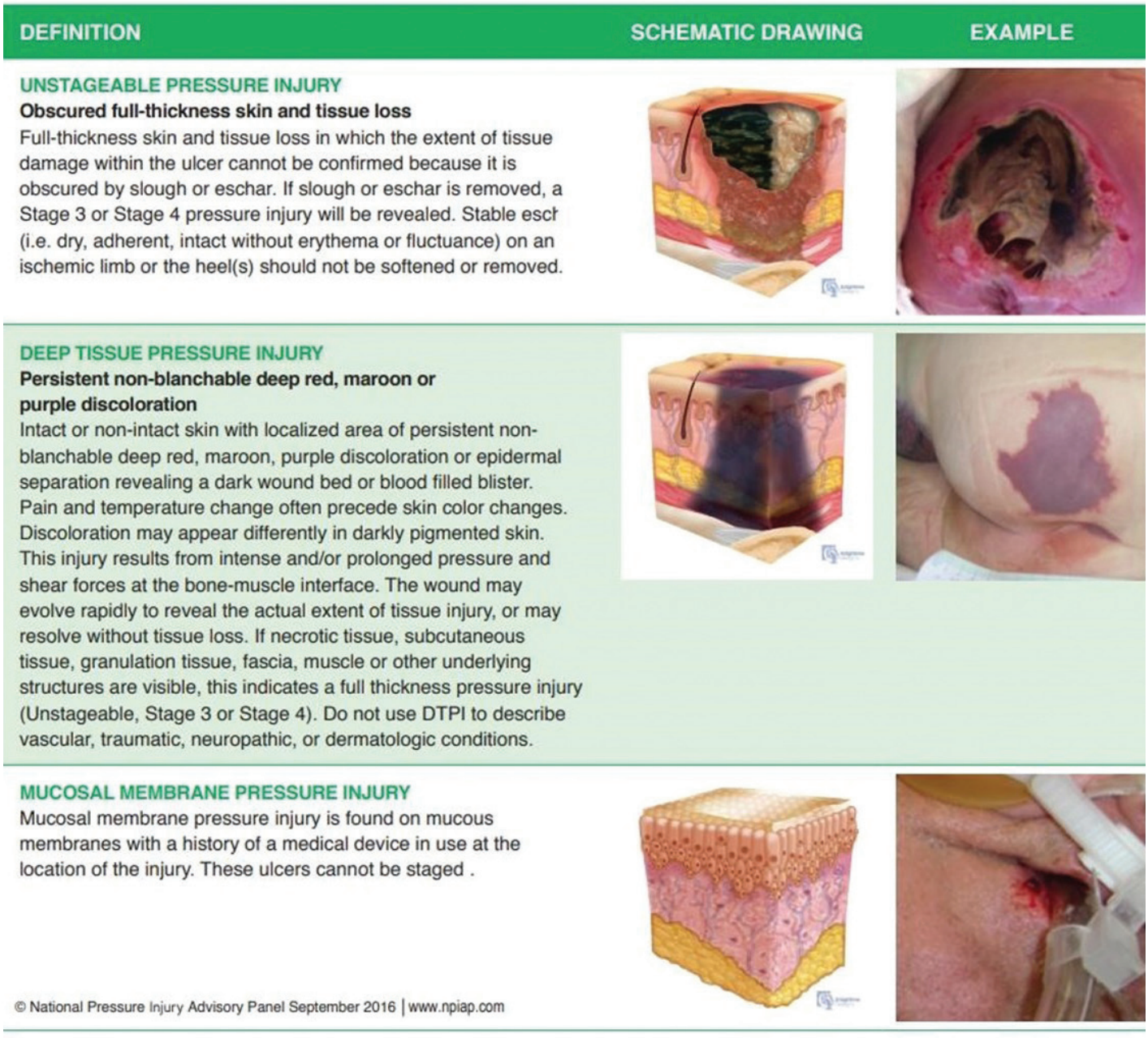
Figure 1: National Pressure Injury Advisory Panel (NPIAP) Pressure Injury and Stages[1]

# PRESSURE INJURY AND STAGES

A pressure injury is localized damage to the skin and underlying soft tissue usually over a bony prominence or related to a medical or other device. The injury can present as intact skin or an open ulcer and may be painful. The injury occurs as a result of intense pressure, prolonged pressure or pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, co-morbidities and condition of the soft tissue.

NPIAP
NATIONAL PRESSURE INJURY ADVISORY PANEL

| DEFINITION | SCHEMATIC DRAWING | EXAMPLE |
|---|---|---|
| **STAGE 1 PRESSURE INJURY**<br>**Non-blanchable erythema of intact skin**<br>Intact skin with a localized area of non-blanchable erythema, which may appear differently in darkly pigmented skin. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Color changes do not include purple or maroon discoloration; these may indicate deep tissue pressure injury. |  |  |
| **STAGE 2 PRESSURE INJURY**<br>**Partial-thickness skin loss with exposed dermis**<br>Partial-thickness loss of skin with exposed dermis. The wound bed is viable, pink or red, moist, and may also present as an intact or ruptured serum-filled blister. Adipose (fat) is not visible and deeper tissues are not visible. Granulation tissue, slough and eschar are not present. These injuries commonly result from adverse microclimate and shear in the skin over the pelvis and shear in the heel. This stage should not be used to describe moisture associated skin damage (MASD) including incontinence associated dermatitis (IAD), intertriginous dermatitis (ITD), medical adhesive related skin injury (MARSI), or traumatic wounds (skin tears, burns, abrasions). |  |  |
| **STAGE 3 PRESSURE INJURY**<br>**Full-thickness skin loss**<br>Full-thickness loss of skin, in which adipose (fat) is visible in the ulcer and granulation tissue and epibole (rolled wound edges) are often present. Slough and/or eschar may be visible. The depth of tissue damage varies by anatomical location; areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage or bone are not exposed. If slough or eschar obscures the extent of tissue loss this is an Unstageable Pressure Injury. |  |  |
| **STAGE 4 PRESSURE INJURY**<br>**Full-thickness loss of skin and tissue**<br>Full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage or bone in the ulcer. Slough and/or eschar may be visible. Epibole (rolled edges), undermining and/or tunneling often occur. Depth varies by anatomical location. If slough or eschar obscures the extent of tissue loss this is an Unstageable Pressure Injury. |  |  |




From: National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Quick Reference Guide. Emily Haesler (Ed.). Cambridge Media: Osborne Park, Western Australia; 2014. Used with permission of the National Pressure Ulcer Advisory Panel June 2024.

agement is crucial. The purpose of this scoping review is to summarize the available literature on the effectiveness of vitamin C for supporting PI healing as well as identify any gaps within the current literature.

## METHODS

### Protocol and Registration

This scoping review employs the approach outlined by Arksey and O'Malley to comprehensively map, review, and synthesize existing evidence across domains.[14] Evidence will be reported in accordance with the Preferred Reporting Items for Systematic Review and MetaAnalysis extension for Scoping Reviews (PRISMA-ScR) checklist.[15] Unlike systematic reviews, which meticulously assess individual studies, scoping reviews map, review, and synthesize existing evidence across various domains without delving into the fine-grained critique of each study. This makes scoping reviews particularly useful for identifying knowledge gaps and providing an overview of the available literature.

Pressure injury is the term that aligns with the most up-to-date NPIAP terminology. Before this term and staging systems were updated, terms such as bedsores or pressure ulcers (PUs) and staging with Roman numerals were used. This scoping review retains the terminology authors used in their

**Table 1:** *The Electronic Databases, Search Strategies, and Corresponding Number of Articles*

| ELECTRONIC DATABASES | SEARCH STRATEGIES | EXTENT OF SEARCH | NUMBER OF ARTICLES |
|---|---|---|---|
| PubMed<br>https://pubmed.ncbi.nlm.nih.gov<br>(Accessed on 1 March 2024) | (pressure ulcer) OR (pressure injury) OR (pressure sore) OR (bedsore) OR (decubitus ulcer) OR (decubitus injury) AND (ascorbic acid) OR (vitamin c) OR (ascorbate) AND (wound healing) | In all fields | 45 |
| Medline<br>https://www.ncbi.nlm.nih.gov<br>(Accessed on 1 March 2024) | (wound healing or wound).tw. or Wound Healing/ AND Ascorbic Acid/ or Ascorbic Acid.tw. or vitamin C.tw. or Ascorbate.tw. AND Pressure Ulcer/ or pressure injury.tw. or pressure ulcer.tw. or bedsore*.tw. or bed sore*.tw. or decubitus ulcer.tw. or decubitus injury.tw. | In all fields | 37 |
| CINAHL<br>https://search.ebscohost.com<br>(Accessed on 1 March 2024) | (MH "Pressure Ulcer") OR "Pressure Ulcer or pressure injury or pressure ulcer or bedsore* or bed sore* or decubitus ulcer or decubitus injury" AND (MH "Ascorbic Acid") OR "Ascorbic Acid or Ascorbic Acid or vitamin C or Ascorbate" AND (MH "Wound Healing") OR "wound healing" | In all fields | 34 |
| EMBASE<br>https://ovidsp-dc2-ovid-com.proxy1.lib.uwo.ca/ovid-new-b/ovidweb.cgi<br>(Accessed on 1 March 2024) | (wound healing or wound).tw. or Wound Healing/ AND Ascorbic Acid/ or Ascorbic Acid.tw. or vitamin C.tw. or Ascorbate.tw. AND Pressure Ulcer/ or pressure injury.tw. or pressure ulcer.tw. or bedsore*.tw. or bed sore*.tw. or decubitus ulcer.tw. or decubitus injury.tw. | In all fields | 68 |

studies.[16] This scoping review also retains author references to ascorbate or AA, which are other terms for vitamin C.[12]

### Inclusion and Exclusion Criteria

This comprehensive review explored published original studies, randomized controlled trials (RCTs), case series, case-control studies, and individual case studies. Only studies published in English that assessed the effects of vitamin C on wound healing were considered. Study inclusion was not limited by publication dates, with consideration given to any study published before March 1, 2024. Inclusion criteria included individuals aged 18 or older with any stage of PI or PU, deep tissue injury, unstageable PI or PU, and/or medical device-related PI that had either oral or enteral AA supplementation.

Exclusion criteria included topical or intravenous vitamin C, non-human studies, non-PI-related wounds, and age less than 18. We excluded non-published or grey literature, commentaries, editorials, and opinion papers as these were not relevant because they were not grounded in scientific principles. Systematic reviews and meta-analyses were also excluded to avoid potential duplication of evidence.

### Information Sources and Search

One author used the PubMed, Medline, CINAHL, and EMBASE databases to conduct the search on March 1, 2024, with the assistance of a science librarian, utilizing all identified key words (Table 1). The search terms utilized were pressure ulcer, pressure injury, bedsore, decubitus ulcer, decubitus injury, ascorbic acid, vitamin C, ascorbate, and wound healing.

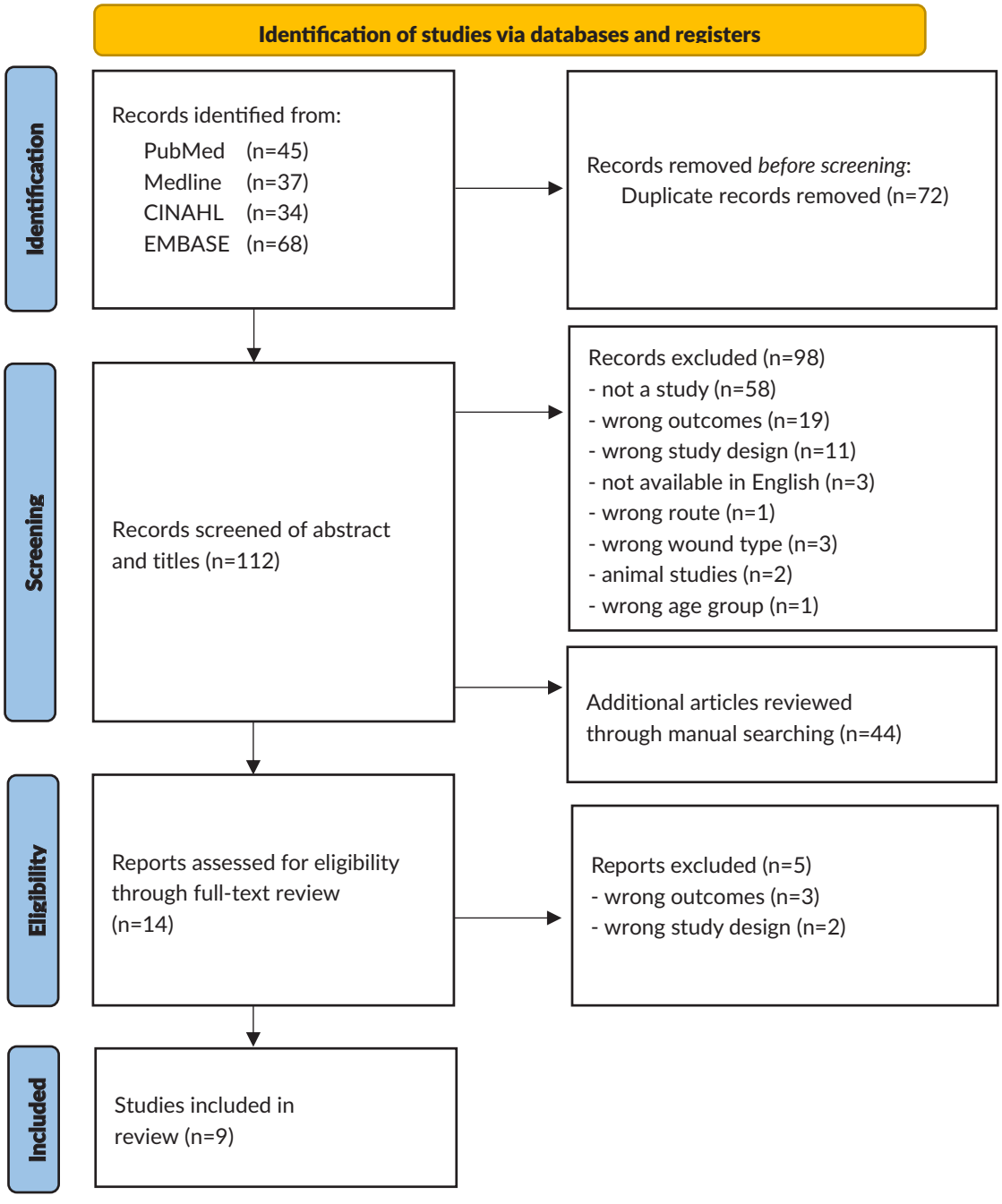
### Selection of Sources of Evidence and Data Charting Process

Two independent reviewers evaluated the titles and abstracts of these results to determine whether each article warranted a more in-depth review. The reviewers followed instructions to include articles even when there was insufficient information to establish their relevance definitively. A third author was available if any conflicts arose. Eighteen articles were identified through manual reference list searches and examined to determine if any additional studies met the search criteria. The authors reviewed 14 full articles. All authors discussed results and reached a consensus, with 9 studies meeting the full inclusion criteria (Figure 2).

### Data Items and Synthesis of the Results

This scoping review focuses on articles related to vitamin C in the context of the healing of PIs. The authors first collated the relevant information from the selected articles in an Excel spreadsheet for data collection and then synthesized the data into a more comprehensive table in the results. This original spreadsheet documented author names, study title, date, location, intervention(s), comparators, duration, population, aim, methodology, outcome measures, essential results, and any exclusions.

**Figure 2:** *PRISMA-ScR Study Selection*[5]




From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

## RESULTS

### Selection, Characteristics of Sources of Evidence, and Summary Results

The database search initially yielded 184 publications, but after eliminating duplicate articles and examining titles and abstracts, 14 full-text studies were reviewed, with 9 articles deemed suitable for inclusion.[17-25] All studies investigated the healing of PIs, with 5 studies being RCTs and 4 being observational studies. The studies and their characteristics, including study design, year of publication, type(s) of interventions, study population, and key findings, are summarized in Tables 2 and 3.

Publication dates for the 9 selected studies ranged from 1972 to 2010. These studies looked at vitamin C supplementation on its own, in an oral nutrition supplement (ONS), or as a specific enteral formula and provided patients in the treatment group up to 1000 mg of vitamin C daily.[17-25] Seven of these studies reported an accelerated PI healing rate or significant reduction in PI size.[18-24]

One of the first human studies examining PI wound healing with vitamin C was conducted in 1972 by Burr et al.,[17] who administered 1000 mg of AA daily for 3 days to 7 paraplegic patients who had PIs. The authors analyzed biopsies of these patients' wounds and found that AA stimulated the production of collagen, which is an essential element in accelerating wound healing.[17] This study[17] was one of the first to establish the possible relationship between vitamin C and PI wound healing in humans.

A study by Heyman et al.[18] investigated the impact of a high-protein ONS enriched with arginine, vitamin C, vitamin E, and zinc on healing PUs in 245 nursing home residents over 9 weeks, alongside standard care. Results showed a significant reduction in ulcer size (53%), improved wound healing, and decreased exudation, highlighting the effectiveness of the enriched ONS in supporting recovery($P<0.0001$).[18]

An RCT conducted by Cereda et al.[19] examined whether a disease-specific nutritional approach is more effective than a standard dietary approach for healing PUs. The study included 28 elderly patients with Stage II, III, and IV PUs who were examined in the treatment group over 12 weeks.[19] Patients received either a standard oral diet or a standard enteral formula, with the treatment group receiving added protein, arginine, zinc, and vitamin C.[19] The treatment group had accelerated PU healing ($P<0.05$),[19] with the authors noting that disease-specific nutritional support is both viable and safe to utilize and should be prioritized over the standard approach to enhance the rate of wound healing.[19]

Additionally, a prospective double-blind controlled trial conducted by Taylor et al.[20] studied 20 surgical patients, with those in the treatment group receiving 500 mg of AA twice a day and the control group receiving a placebo. The PIs were assessed using serial photography and wound tracings after 1 month, with the results being statistically significant, indicating that patients in the treatment group had an 84% reduction in PIs compared to 42.7% in the control group ($P<0.05$).[20]

In an RCT Desneves et al.[21] conducted, 16 inpatients with Stage 2, 3, or 4 PUs received a daily standard hospital diet, a standard diet plus 2 high-protein/energy supplements, or a standard diet plus 2 high-protein/energy supplements containing an additional 9 g of arginine, 500 mg of vitamin C, and 30 mg of zinc. Only the group receiving supplementary arginine, vitamin C, and zinc showed a clinically significant improvement in healing, despite no significant changes in biochemical markers, dietary intake, or weight in any of the other groups ($P<0.01$).[21]

In contrast, an RCT by Ter Riet et al[22] published in 1995 reached a different conclusion. Eighty-eight patients with Stage II to Stage IV PUs were randomly selected from 11 nursing homes and 1 hospital in the Netherlands. In the treatment group, 43 patients received a 500 mg AA supplement twice daily, while 45 received 10 mg of vitamin C twice daily in the control group.[22] Surprisingly, the data did not demonstrate a strong correlation between vitamin C and improved healing of PUs (90% CI 0.44 to-1.39).[22] The authors did, however, highlight that vitamin C deficiency can lead to delayed wound healing.[22]

A protein-rich oral nutritional supplement enriched with arginine, vitamin C, and zinc on Stage III and IV PUs was administered to 39 patients over 3 weeks in an open intervention study by Frias Soriano et al.[23] Their results showed a significant (29%) reduction in median wound area ($P<0.001$) and improvements in wound condition, including decreased exudate and necrotic tissue ($P<0.07$).[23]

Another RCT by van Anholt et al[24] administered at multiple facilities demonstrated that over 8 weeks 22 non-malnourished patients receiving ONS appeared to have a significant reduction in the size and severity of Stage III to IV pressure ulcers compared to the control group.[24] These researchers found that patients who showed improved wound healing outcomes had a significantly higher blood vitamin C level than the control group.[24] They concluded that vitamin C is crucial in accelerating wound healing ($p \leq 0.016$), potentially decreasing the frequency of dressing changes and related medical expenses.[24]

A randomized, prospective, controlled, non-blinded study by Theilla et al.[25] analyzed the impact of an enteral feeding formula enriched with eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA), and vitamins A, C, and E on PU healing in critically ill, mechanically ventilated patients with acute lung injury compared to a non-enriched formula given to those in the control group.[25] The authors observed no significant differences in the healing of existing PUs between the treatment and control groups.[25] However, the treatment group demonstrated a significantly lower incidence of new PU development compared to the control group ($p=0.05$).[25]

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1 SAT-BSER-05-869347 VAC Peel and Place BSER.

2 In a simulated use test with 12 nurse and surgeon users. Average time of 01:48. SAT-MTF-05-995965 Marketing study for Solventum V.A.C. Peel and Place dressing.

* Compared to 3M traditional NPWT foam dressing.

3 Source: Allen D, Robinson T, Schmidt M, Kieswetter K. Preclinical assessment of novel longer-duration wear negative pressure wound therapy dressing in a porcine model. Wound Rep Reg. 2023;31:349-359. Information contained within conducted animal studies has not been evaluated by the U.S. Food & Drug Administration.

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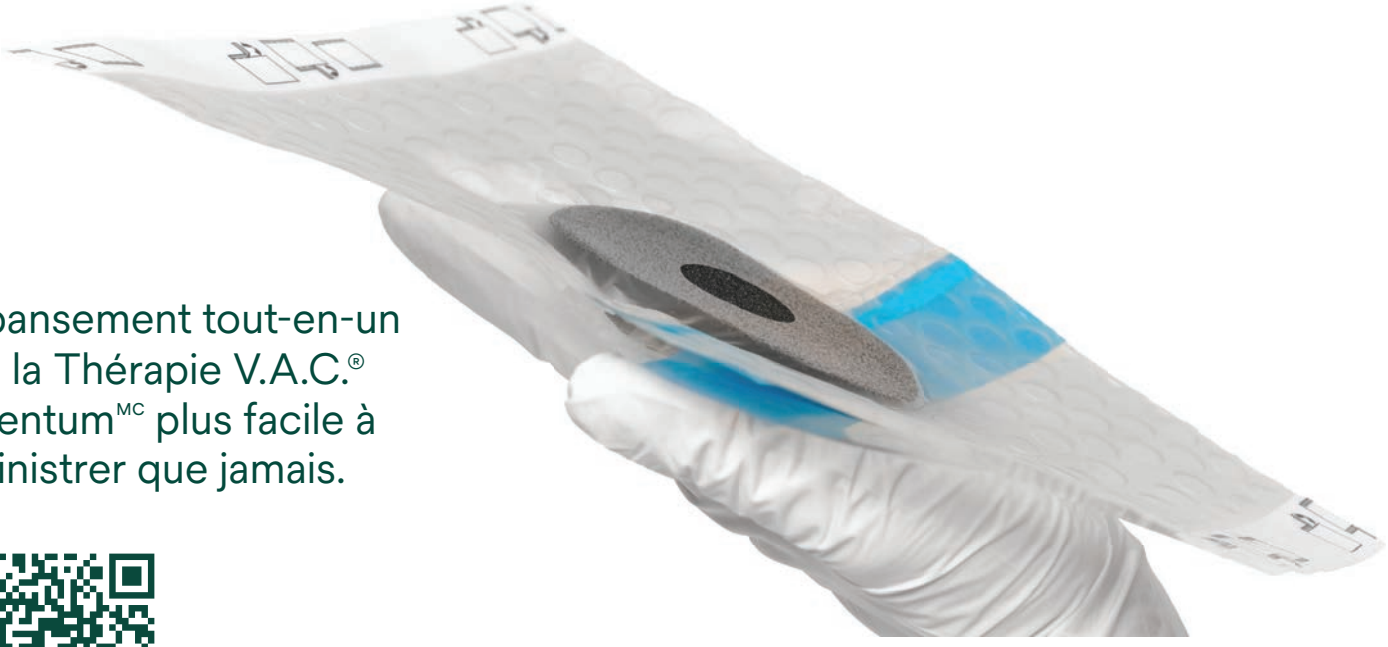

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1 SAT-BSER-05-869347, rapport de l'évaluation sur la sécurité biologique portant sur le V.A.C. Kit de pansement Peel and Place.

2 Lors d'un essai d'utilisation simulé comportant 12 utilisateurs infirmiers et chirurgiens. Temps moyen de 1 min 48 s. SAT-MTF-05-995965, évaluation de marketing portant sur le Solventum V.A.C. Pansement Peel and Place.

* Par rapport à un Pansement en mousse pour thérapie par pression négative 3M[MC] traditionnel.

3 Source : ALLEN, D., T. ROBINSON, M. SCHMIDT et K. KIESWETTER. « Preclinical assessment of novel longer-duration wear negative pressure wound therapy dressing in a porcine model », *Wound Rep. Reg.*, vol. 31 (2023), p. 349-359. L'information contenue dans les études menées chez les animaux n'a pas été évaluée par la Food and Drug Administration des États-Unis.

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**Table 2.:** *Characteristics and Result Summaries of the Studies Included in the Scoping Review*

| AUTHOR (YEAR) | COUNTRY | STUDY TYPE; DESIGN | AIM/PURPOSE | STUDY POPULATION | RESULTS |
|---|---|---|---|---|---|
| Burr et al.[17] (1972) | England | Prospective; Case Control Study | Determining the relationship between vitamin C and wound healing by analyzing leucocyte ascorbic acid (LAA) concentration in different populations | Group One:<br>91 paraplegic patients<br>(52 male, 39 female)<br>Group Two:<br>41 hospital staff<br>(20 male, 21 female)<br>Subgroup 1: 33 patients with pressure sores (20 male, 13 female)<br>Subgroup 2: Smoking versus non-smoking<br>Subgroup 3: 72 males, 60 females<br>Subgroup 4: 10 experimental group<br>(5 = 500 mg AA BID x 3; 2 = 2 x 250 mg AA BID x 3; 3 = lactose capsules BID) | LAA concentrations were lower in the paraplegic patients than the control group.<br>LAA concentrations were lower in patients with pressure sores than patients without.<br>LAA concentrations for males were lower than for females.<br>LAA lower for smokers than for non-smokers.<br>LAA concentrations of male patients with pressure sores who smoked were significantly lower than the corresponding control subjects ($P<0.05$), and the same was true of the non-smoking female patients.<br>Female non-smokers had significantly higher LAA concentrations than male non-smokers ($P < 0.05$).<br>Biopsy samples from the second biopsy stained for collagen more intensely than those from the first. |
| Heyman et al.[18] (2008) | Belgium and Luxembourg | Prospective; Open Study | Effects of an oral nutrition supplement (ONS) plus standard care on the healing of European Pressure Ulcer Advisory Panel (EPUAP) grade II–IV pressure ulcers | Intervention Group:<br>Patients with EPUAP grade II–IV PU (n= 245; 157 males, 59 females; mean age of 82.2) received 3 servings of ONS (Cubitan) daily for 9 weeks, along with standard pressure ulcer care<br>Control Group: N/A | A high protein ONS enriched with arginine, vitamin C, vitamin E, zinc significantly decreased the mean PU area over 9-week period.<br>At 3 weeks, the average PU area had significantly reduced from $1580 \pm 3743 mm^2$ to $1103 \pm 2999 mm^2$ ($p<0.0001$).<br>At 9 weeks, the average PU area was $743 \pm 1809 mm^2$, which is a significant reduction of 53% when compared with baseline ($p<0.0001$).<br>Complete wound closure occurred after 3 and 9 weeks in 16 (7%) and 49 (20%) of the PU.<br>Amount of exudate decreased with ONS ($P < 0.0001$). |
| Cereda et al.[19] (2009) | Italy | RCT;<br>Single- Blind | If disease-specific nutritional approach is more beneficial than a standard dietary approach to healing in elderly subjects with Stage II, III, and IV pressure ulcers | Intervention Group: (n=13; 4 male, 9 female; mean age 82.1) received disease-specific nutrition treatment consisting of the standard hospital diet (at least 30 kcal/ kg per day) plus 400-mL oral supplement or specific enteral formula enriched with protein (20% of the total calories), arginine, zinc, and vitamin C<br>Control Group: (n=15; 6 male, 9 female; mean age of 81.4) received standard hospital diet (at least 30 kcal/ kg per day) | The PUSH score revealed a significant difference at Week 12 ($P<0.05$) and the reduction in ulcer surface area significantly higher in the treated patients within 8 weeks.<br>Those in the intervention group who received a standard hospital diet plus supplement with at least 500 kcal, 34 g protein, 6 g arginine, 500 mg vitamin C, and 18 mg zinc (400 ml) had a higher rate of healing. |
| Taylor et al.[20] (1974) | Great Britain | Prospective; RCT; Double-Blind | Effectiveness of large doses of AA on the healing of pressure sores on surgical patients | Surgical patients (n=20; 8 male, 12 female; average age of 74.5)<br>Intervention: (n=10) received 1 500 mg AA white tablet twice daily<br>Control: (n=10) received 1 white tablet twice daily | Sixty percent of those in the intervention group completely healed compared to only 30% of those in the control group.<br>Administration of vitamin C significantly improved the healing rate of pressure sores ($P<0.005$). |

| AUTHOR (YEAR) | COUNTRY | STUDY TYPE; DESIGN | AIM/PURPOSE | STUDY POPULATION | RESULTS |
|---|---|---|---|---|---|
| Desneves et al.[21] (2005) | Australia | RCT; Single-Blind | If a standard diet plus 2 high protein supplements containing additional 9 g arginine, 500 mg vitamin C, and 30 mg zinc will improve the rate of PU healing | Total cases: N=16 patients with Stage II–IV PUs according to the Australian Wound Management Association Clinical Practice Guidelines<br>Intervention Group 1: (n=6; 4 male, 2 female) received a standard hospital diet<br>Intervention Group 2: (n= 5; 3 males, 2 females; mean age 83.2) received a standard diet plus 2 high-protein/energy supplement<br>Intervention Group 3: (n=5; 3 males; 2 females) a standard diet plus 2 high-protein/energy supplements containing additional arginine (9 g), vitamin C (500 mg), and zinc (30 mg) | Baseline PUSH scores were similar between groups (8.7 +/- 0.5).<br>Patients receiving additional arginine, vitamin C, and zinc demonstrated a clinically significant improvement in pressure ulcer healing (9.4 +/- 1.2 vs. 2.6 +/- 0.6; baseline and week 3, respectively; p<0.01). |
| Ter Riet et al.[22] (1995) | Netherlands | RCT; Double-Blind | Effectiveness of 500 mg AA in the treatment of PUs | Total cases: (n= 88) patients with Stage II–IV PUs<br>Intervention Group: (n=43) received 500 mg AA BID<br>Control Group: (n=45) received 10 mg ascorbic acid twice daily | There was no difference noted in those receiving AA verses those in the control group (HR 0.78, 90% CI 0.44 to -1.39).<br>Supplementation of vitamin C does not accelerate PU healing. |
| Frias Soriano et al.[23] (2004) | Spain | Prospective; Open Cohort Study | Effectiveness of an oral supplement that is rich in protein, arginine, vitamin C, and zinc in the healing of PUs | Total cases: (n=39) patients with Grade III or IV PUs | A significant increase in granulation tissue after 1 week was noted with a significant decrease in incidences of infection (p=0.008; p=0.008) and a decrease in incidence of necrotic tissue (p=0.07).<br>After 3 weeks, the median PU area reduced from 23.6 $cm^2$ to 19.2 $cm^2$ ($P < 0.001$).<br>Nutritional supplements that are rich in protein, arginine, vitamin C, and zinc resulted in a significant reduction in wound area and improved wound condition. |
| van Anholt et al.[24] (2010) | Czech Republic, Belgium, The Netherlands, and Curacao | RCT; Double-Blind | To determine if the addition of a high-protein, arginine- and micronutrient-enriched ONS will improve healing of PU in non-malnourished patients | Total cases: (n=43) with pressure ulcers grade 3 or 4 using EPUAP<br>Intervention Group: (n=22) received a high-energy supplement enriched with arginine, antioxidants, and other micronutrient oral supplements<br>Control Group: (n=21) received non-caloric, flavoured placebo (similar in taste and appearance) | There was accelerated PU healing in the intervention group compared with the control in 8 weeks ($p \leq 0.016$). |
| Theilla et al.[25] (2007) | Israel | RCT; Non-Blinded | To compare a high-fat and low-carbohydrate enteral formula which was enriched in lipids vitamins A, C, and E with a high-fat and low-carbohydrate enteral formula in PU development and healing affects in patients suffering from acute lung injury | Total cases: (n=95) patients suffering from acute lung injury.<br>Intervention Group: (n=46; 7 PU) received a high-fat, low-carbohydrate enteral formula enriched.<br>Control Group: (n=49; 14 PU) received a high-fat, low-carbohydrate enteral formula. | No difference was observed in the healing of existing pressure ulcers in the study as opposed to the control group.<br>There was a significantly lower rate of occurrence of new PUs observed in the study group compared to the control group (p<0.05).<br>There were 8 new PUs in the intervention group compared to 10 in the control group (RR 0.85, 95% CI 0.37 to 1.97; p=0.71). |

**Table 3:** *Summary of Included Studies*

| AUTHOR (YEAR) | TREATMENT GROUP | CONTROL GROUP | ROUTE OF ADMINISTRATION | MEASUREMENT OF HEALING |
|---|---|---|---|---|
| Burr et al.[17] (1972) | 1. 500 mg of AA BID for 3 days (n=5)<br>2. 250 mg x 2 AA BID for 3 days (n=2) | Placebo capsule BID for 3 days (n=3) | Oral | 1. Biopsy<br>2. Histological photograph |
| Heyman et al.[18] (2008) | Three servings a day of ONS taken in addition to their normal diet or enteral feed for 9 weeks<br>Per 200 ml ONS serving provides 250 kcal/20 g protein, 3 g arginine, 250 mg vitamin C, 38 mg vitamin E, and 9 mg zinc, plus other micronutrients | No control | Oral | 1. Measurement (L x W) with a ruler<br>2. Subjective assessment (exudate, necrotic tissue, and signs of infection) |
| Cereda et al.[19] (2009) | Disease-specific nutrition treatment consisting of the standard diet plus a 400-mL oral supplement or specific enteral formula enriched with protein, arginine, zinc, and vitamin C (n=13) | Standard nutrition (hospital diet or standard enteral formula) (n=15) | Oral or Enteral | 1. PUSH Tool<br>2. Area measurement ($mm^2$ and %) |
| Taylor et al.[20] (1974) | 500 mg AA BID for 4 weeks (n=10) | Placebo BID for 4 weeks (n=10) | Oral | 1. Subjectively by staff<br>2. PI tracing independently<br>3. Weekly photographs |
| Desneves et al.[21] (2005) | 1. Standard hospital diet plus 2 tetrapaks of a defined arginine-containing supplement, supplying additional 2100 kJ (500 kcal), 21 g protein, 0 g fat, 500 mg vitamin C, 30 mg zinc, and 9 g of arginine (n=6) for 3 weeks<br>2. Standard hospital diet plus 2 tetrapaks of a high-protein, high-energy supplement providing an additional 2100 kJ (500 kcal), 18 g protein, 0 g fat, 72 mg vitamin C, and 7.5 mg zinc (n=5) for 3 weeks | Standard hospital diet (n=5) for 3 weeks | Oral | 1. PUSH Tool |
| Ter Riet et al.[22] (1995) | 500 mg AA twice daily (n=43) for 12 weeks in addition to standardized treatment | 10 mg AA twice daily (n=45) for 12 weeks in addition to standardized treatment | Oral | 1. Weekly photographs |
| Frias Soriano et al.[23] (2004) | ONS (250 calories, 20 g protein, 250 mg vitamin C, 37.6 mg vitamin E, and 9 mg zinc) daily for 3 weeks (n=39) | No control | Oral | 1. Subjective assessment by staff<br>2. Surface area measurement |
| van Anholt et al.[24] (2010) | High-energy supplement enriched with arginine, antioxidants, and other micronutrient oral supplements (n=22) for 8 weeks | Non-caloric, flavoured placebo (n=21) for 8 weeks | Oral | 1. Measurement (L x W) with a ruler<br>2. Surface area measurement |
| Theilla et al.[25] (2007) | High-fat, low-carbohydrate, enteral formula enriched in lipids (eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA)), and vitamins A, C, and E (n=46) | High-fat, low-carbohydrate, enteral formula (n=49) | Enteral | 1. Subjective assessment using NPUAP Staging by researchers |

## DISCUSSION

This scoping review has some limitations. Despite the extensive literature search conducted with several large databases, the number of studies looking at vitamin C and PI healing specifically was limited, so the inclusion criteria were broader than desired. In addition, variability among the populations studied, such as differences in the culture, nationality, and gender of the patients, makes it difficult to determine whether these variances might account for the differences in results between studies.

Furthermore, the amount of vitamin C was not always consistent across the studies examined, and some studies offered treatment groups other nutrients, protein, or calories in addition to vitamin C. For example, 1 study included 250 mg of vitamin C in the ONS formula, which provided 250 calories, 20 g of protein (3.0 g of arginine), 37.6 mg of vitamin E, and 9.0 mg of zinc, all of which were administered for 3 weeks.[23] Another study that investigated the use of ONS had a formula containing 575 mg of vitamin C, 46 g of protein (6.9g of arginine), 87 mg of vitamin E, and 21 mg of zinc for 9 weeks.[18]

The measurement of PI healing also varied across studies, with some utilizing validated tools, such as the Pressure Ulcer Scale for Healing (PUSH Tool), and others relying on subjective assessment, either physically or with serial photography.

The majority of studies that examined the effect of vitamin C on its own, in an enteral formula, or an ONS observed positive results on PI healing.[17-21,23,24] However, many of the patients in the treatment groups also received macronutrients in varying quantities as well as other micronutrients, which makes it challenging to decipher if vitamin C alone impacted the healing ability of PIs.[17–21,23,24]

The methodological diversity of the included studies poses both strengths and challenges. Most studies had small sample sizes, heterogeneity in PI severity and patient populations, and variability in intervention durations, which limit the generalizability of findings.[17-25] Vitamin C levels were not consistently monitored, leaving gaps in understanding the mechanistic pathways underlying the observed effects.[17-25]

In the study by Heyman et al.,[18] the authors reported a significant reduction in the mean PU area with ONS; however, this study lacked a control group or exclusion criteria, which leaves room for variability and likely impacted the study's results.[18]

Desneves et al.[21] came to a similar conclusion in their investigation of supplementation with ONS and/or enhanced nutrients (arginine, vitamin C, and zinc) in addition to a standard hospital diet. While the sample size was much smaller, this RCT was more robust in its methods.[21] The authors used a validated wound assessment tool (PUSH tool), utilized appropriate blinding, and had a control group and almost perfect compliance with ONS consumption.[21]

Theilla et al.[25] observed no difference in healing rates in their treatment group that received an enriched enteral feed compared to those in a standard enteral feeding group. However, the treatment group experienced fewer new PU developments, suggesting a potential preventive benefit rather than a therapeutic effect.[25] This study was non-blinded, had a small sample size with short follow-up, and may have been impacted by inter-rater variability.

The only study that did not support the idea of vitamin C supplementation for improving the healing rate of PIs did recognize the human body's need for adequate vitamin C levels and noted that scurvy can lead to delayed wound healing.[22] In this study, patient comorbidities and immobility could have been confounding factors, impacting the validity of the results.

Of the 9 studies that met the inclusion criteria for this scoping review, only 3 examined the impact of vitamin C alone on PI healing.[17,20,22] Of these, only 2 were RCTs, and both used the same dosage of vitamin C in their treatment groups.[20,22] However, all 3 studies had small sample sizes with confounding factors, such as comorbidities and baseline nutritional status, which makes generalizability of the findings difficult.[17,20,22]

Studies investigating ONS enriched with arginine, zinc, and vitamin C reported substantial reductions in wound size, improved wound conditions, and higher healing rates.[18,19,21,24] This also decreases the reliability on the effectiveness of vitamin C alone, as other nutrients, along with increased calories and protein, were provided to treatment groups in these studies.[18,19,21,24] It is well known that insufficient intake or an imbalance of energy, protein, and other nutrients can cause malnutrition, which can make people more susceptible to skin breakdown and prevent healing.[26,27] This fact, along with the findings of the ONS studies, supports the notion that enhanced nutritional interventions may be more effective than standard diets in addressing the unique metabolic demands of patients with PIs.

It is evident from this scoping review that, in addition to regular preventive therapy for patients at risk of PIs, nutritional treatment with enhanced vitamin C and other nutrients appears to have a positive effect on PI healing. It cannot be proven that vitamin C alone is successful in enhancing PI healing without more research, which should aim to refine our understanding of the specific effects of vitamin C dosage to support the optimization of intervention strategies to maximize therapeutic potential.

## CONCLUSION

Pressure injuries have a substantial impact on a patient's quality of life and pose a financial burden to the Canadian health care system. Vitamin C is a micronutrient that is crucial for wound healing, and scurvy remains a concern in Canada. Any advancements in wound management knowledge that

lead to more effective treatments would be beneficial for health care providers and individuals. This scoping review investigated current research on vitamin C and PI wound healing to summarize the existing literature and identify gaps. The current evidence suggests a possible association between vitamin C supplementation and PI wound healing. There is insufficient evidence to draw conclusions about the actual effect of vitamin C on PI healing, so the authors cannot make any recommendations based on the current literature. Some limitations of this review include variability in the populations studied, inconsistent vitamin C dosages, and varying measurement methods for PI healing, all of which may impact the interpretation of the results. Research with RCT study designs conducted in the Canadian population that have large sample sizes is necessary to investigate the exclusive role of vitamin C and its impact on PI wound healing. •

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