

ORIGINAL ARTICLE

Evidence-based review of the effects of nutritional supplementation for pressure ulcer prevention

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Abstract

The objective of this evidence-based review was to explore whether the evidence supports the use of nutritional supplements in pressure ulcer (PU) prevention strategies. Several electronic databases, including Ovid MEDLINE (1946 to May week 32 019), Ovid EMBASE (1947 to May 28, 2019), EBSCO CINAHL (until June 13, 2019), Scopus (until July 9, 2019), and the Web of Science (until June 13, 2019) were searched. No limitation was placed on the year of publication. Studies considered for inclusion were those with adult populations, and only English language texts with available full text were reviewed. AMSTAR (a measurement tool to assess systematic reviews) was used to evaluate the quality of the studies included in the systematic review. The Oxford Centre for Evidence-Based Medicine (OCEBM) 2011 Levels of Evidence was used to assess the level of evidence. Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) was used to assess guideline article, and Appraisal tool for Cross-Sectional Studies (AXIS) was also used for cross-sectional studies. The search identified 1761 studies. After the application of inclusion and exclusion criteria, 24 studies were retained of various designs, including 10 systematic reviews, five clinical reviews, three randomised controlled trials, two observational studies, one quasi-experimental study, one cross-sectional study, one cohort study, and one Clinical Guideline. Two were rated as high-quality reviews, 14 were rated as moderate-quality reviews, five were rated as low-quality reviews, and three were rated as critically low-quality reviews. The majority of the reviewed studies were of low-to-moderate quality because of biases in the study design and incomplete data reporting, which did not fulfil the reporting criteria of the appraisal tools. However, the majority of the studies showed a reduction in PU incidence after nutritional supplement though not significant. Whether the use of pharmacological appraisal tools to assess non-pharmacological studies is appropriate is unclear. Regardless of the low-to-moderate quality of the studies in this review, nutritional supplements appear to play a role in PU prevention.

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KEYWORDS

evidence-based review, nutrition supplement, pressure injury, pressure ulcer, prevention

Key Messages

- Malnutrition is a major public health concern which is associated with significant morbidity and mortality
- Nutritional deficits, amongst other factors, are associated with pressure ulcer development therefore optimising a patients nutritional status is important
- Nutritional supplements are often used as an adjunctive treatment to aid pressure ulcer healing and there is good evidence to support their use in this way
- The evidence seems to suggest that the incidence of pressure ulcers is reduced with the use of nutritional supplements however the studies are of short duration with small sample sizes making it difficult to draw firm conclusions
- The role of nutritional supplements to improve wound healing is well recognised however the evidence for supplementation to prevent pressure ulcers is limited based on the current evidence

1 | INTRODUCTION

Pressure ulcers (PUs) are localised injuries of the skin and underlying tissue, typically adjacent to bony prominences that result from sustained mechanical loading, including pressure and shear loading [National Pressure Injury Advisory Panel (NPIAP), European Pressure Ulcer Advisory Panel (EPUAP), and Pan Pacific Pressure Injury Alliance (PPPIA) 2019]. PUs are common problems that significantly contribute to patients' morbidity, mortality, and health-related quality of life.¹ According to the NPIAP, EPUAP, and PPPIA (2019), the prevalence of PUs in health care ranges from 0% to 72.5%, with large variations observed between different countries and clinical settings. The prevalence and incidence rates are generally higher among specific populations who are at increased risk of developing PUs, such as those receiving palliative care, those with spinal cord injuries, neonates, and infants (NPIAP, EPUAP and PPPIA 2019). PU prevention is generally viewed as preferable to PU treatment because PU treatment may require additional management plans, such as surgical debridement and longer hospital stays, utilising increased hospital resources^{2,3} and increasing the financial burden associated with health care costs. In the United Kingdom (UK), PU treatment costs up to 4% of the annual health care budget, or £750 million annually, with expenses estimated at £30 000 per individual PU (NPUAP, EPUAP, and PPPIA 2019). In addition, PU development can be due caused by various risk factors other than pressure and shear stress, such as nutritional deficits, immobility, moisture, and perception.

Malnutrition can be defined as a subacute or chronic nutrition state, in which the combination of varying

degrees of under- or overnutrition and inflammatory activity results in changes to body composition and impaired function.⁴ Because malnutrition can occur both during hospital stays and out-patient treatment, it is recognised as a major public health concern, associated with a significant economic burden and increases in morbidity, mortality, hospital readmissions, and lengths of hospital stays.⁵ Nutritional factors are often neglected when caring for patients with or at an increased risk of developing PUs.⁶ Additionally few of the current published clinical guidelines fully address the importance of adequate nutritional supplementation in both prevention and treatment. Even when guidelines do mention the topic, nutrition tends to be mentioned in general terms, stating that an adequate nutrient supply is important for at-risk patients.

A Cochrane Review performed by Langer and Fink⁷ stated the difficulty of reaching a conclusion regarding the ability of nutritional supplementation to reduce the risk of PU development, despite the existence of multiple studies comparing the various dosages of energy and protein combined with nutrients provided by standard hospital diets. Although some studies have reported that nutritional supplements did not reduce the incidence of PU development,^{8,9} other studies^{7,10-15} have suggested that nutritional deficiencies increased the incidence of PU development among high-risk patients. Therefore, the existing evidence regarding the role of nutritional supplements in the prevention of PUs remains unclear. A wider evidence-based review (EBR) exploring the role of nutritional supplements in PU prevention is necessary to better understand the links between nutrition and PU development. This EBR examined the relationship

between nutrition, nutritional supplements, and PU development.

2 | METHODS

This review focused on the value of nutritional supplements as a component of a PU prevention strategy. Nutritional supplements included the addition of proteins, amino acids, antioxidants, and zinc in addition to a regular diet. Table 1 shows the PICO parameters used to identify appropriate publications for inclusion in this review.

Several electronic databases [(Ovid MEDLINE (1946 to May week 32 019), Ovid EMBASE (1947 to 28th May 2019), EBSCO CINAHL (until 13th June 2019), Scopus (until 9th July 2019), and the Web of Science (until 13th June 2019)) were searched. Boolean operators were used to construct the search strategy.¹⁶ All initial results were hand-searched by title and abstract to determine whether they were likely to meet the review inclusion and exclusion criteria; a full-text article was obtained for those that passed the initial review. This review was limited to publications in English given a lack of locally available translators. The review was undertaken as part of the requirements of an academic course, and no second reviewer was available to verify the selection of papers or the extraction of data.

The search terms used were “pressure ulcer”; “pressure injury”; “pressure sore”; “decubitus”; “decubitus ulcer”; “decubitus sore”; “bedsore”; “nutrition”; “enteral nutrition”; “parenteral nutrition”; “diet”; “diet therapy”; “tube fed”; “tube feed”; “tube feeding”; “prevention”; “randomised controlled trial”; “single-blind”; “double-blind”; “triple-blind”; “placebo”; “quantitative study”; “clinical trial”; “controlled clinical trial”; and “case study”.

2.1 | Appraisal tools

The Critical Appraisal Skills Program (CASP) was used to appraise the publications retrieved through the search strategy. The Consolidated Standards of Reporting Trials (CONSORT) was used to assess the quality of randomised controlled trials (RCTs).¹⁷ The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to assess systematic reviews (SR).¹⁸ During the searches performed on Web of Science and Scopus, grey literature were included in the search strategies. Therefore, no additional search strategy was used to identify grey literature from any other website. After the inclusion and exclusion criteria were applied, the full texts of potentially qualifying publications were retrieved.

TABLE 1 Patient/problem, intervention, comparison, outcome (PICO) parameters

| | |
|---------------------|--|
| Patient/ problem | Adults patients who are at high risk of developing pressure ulcers, including older individuals without terminal illness or malignancy |
| Intervention | Nutritional supplements, including protein, energy, antioxidant, amino acid, and zinc supplements |
| Comparison | Patients who are at risk of developing pressure ulcers without the use of specific nutrient supplementation |
| Outcome | Incidence of pressure ulcers in high-risk patients |

To rate the studies included in this review, a measurement tool to assess systematic reviews (AMSTAR) was used to evaluate the quality of the studies cited. The Appraisal of Guidelines for Research and Evaluation Instrument (AGREE II) tool was used to appraise clinical practice guidelines. Included studies were evaluated for level of evidence using the Oxford Centre of Evidence-Based Medicine Levels of Evidence (OCEBM) CASP.¹⁹ Cross-sectional studies were assessed using the Appraisal tool for Cross-Sectional Studies (AXIS). The CASP checklist was used to appraise all remaining studies, including observational studies, quasi-experimental studies, and cohort studies.

3 | RESULTS

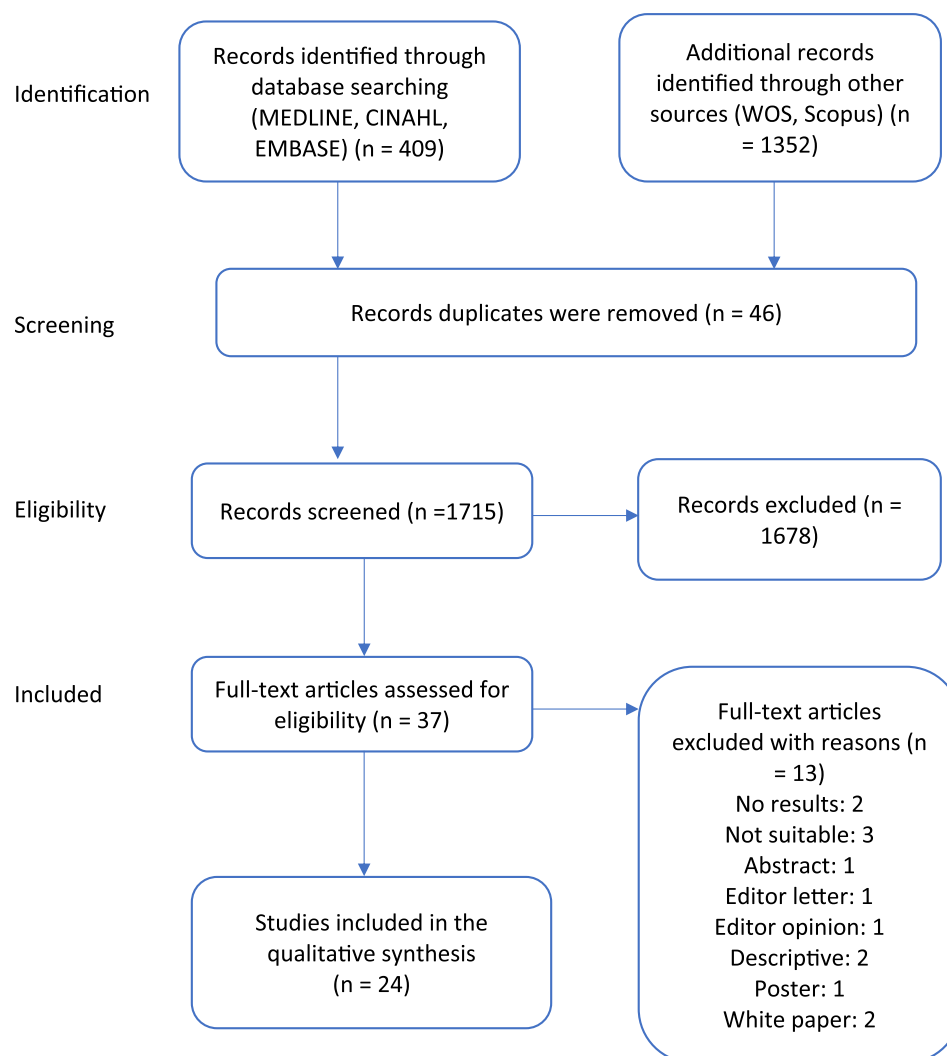
The search results of the PRISMA flow chart are shown in Figure 1.

A total of 1761 search results were identified from the raw data. After screening for duplication, the assessment of inclusion and exclusion criteria, and verifying the availability of full-text articles, 37 articles were reviewed for full-text assessment. The full-text assessment resulted in the exclusion of 13. The remaining 24 articles were included in the final review. The PRISMA flowchart is presented in Figure 1. Summaries of all included articles are presented in Tables 2 and 3.

3.1 | Review and evidence level for systematic reviews (SRs)

Among the 24 included articles, 15 articles were review articles, 3 were RCTs, 2 were observational studies, 1 was a cohort study, 1 was a quasi-experimental study, 1 was a cross-sectional study, and 1 was a clinical guideline.

FIGURE 1 PRISMA flow chart



Of the 15 review articles, the majority were rated as moderate-quality reviews ($n=9$) because of common issues identified by the appraisal tools, including no meta-analysis; no heterogeneity calculation; no report of the sources of funding for the included studies; and the inclusion and exclusion criteria were only partially elaborated. However, the reviews by Langer and Fink⁷ and by Stratton et al²⁶ were rated as high-quality reviews by AMSTAR, with a CEBM rating of Level 1 evidence. These two SRs followed the recommended methodology for SR articles. Three SRs were rated as critically low-quality by AMSTAR, with CEBM ratings of Level 2 evidence.^{12,32} These three SRs featured similar biases to the previous studies described. Additional biases included a lack of a PICO framework to identify the parameters that the authors aimed to explore; no description of the search engines used to identify studies; no external reviewers to review study selection or minimise biases during the review process; and no assessment of the risks of biases of the included studies. However, the importance of nutritional

supplementation cannot be denied, therefore nutritional intervention be considered for high risk patients who are at risk of developing PUs.

3.2 | Quality of the retrieved studies

Three RCTs were included in the EBR.^{8,9,34} All of the included RCTs were also reviewed by the other SR authors.^{7,21–27,29,30} The meta-analysis of these three RCTs was previously performed by two SR articles^{7,26}; therefore, no meta-analysis was performed in this EBR. These three RCTs were rated as moderate-quality by AMSTAR, with a CEBM rating of Level 2 evidence. All three RCTs shared similar selection biases in their methodology, and no mention was made of a registration number of their studies.^{8,9}

Two of the included studies were observational studies.^{35,36} Both of these studies were rated as low-quality by CASP, with a CEBM rating of Level 3 evidence. Both of these studies were characterised by selection biases. No explanation was provided for the selection of the

TABLE 2 Data included in this review

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|--|--|---|--|--|
| <i>Systematic review and meta-analysis</i> | | | | |
| 20 | Critical-care patients | To identify factors that are independently associated with an increased risk of developing PU and evaluate the risk factors associated with study quality | Quality appraisal for all included articles, which were primarily observational studies | 158 articles out of 1753 abstracts identified, of which 18 fulfilled the eligibility criteria. These included 13 prospective cohort studies and 5 retrospective record reviews. Authors concluded that nutrition was recognised as a factor in PU development, theoretically; however, the results failed to demonstrate a connection between nutrition status and PU development among critical-care patients |
| 21 | Critically ill patients | To identify the effectiveness of single strategies designed to reduce the incidence and prevalence of hospital-acquired PU development in ICUs compared with no strategy, other strategies, or usual practice | Primary outcomes: <ul style="list-style-type: none"> • The incidence of PUs in the ICU • The prevalence of PUs in the ICU or “point prevalence” Secondary outcomes: <ul style="list-style-type: none"> • Severity of PU • Time to PU occurrence from ICU admission • Number of PUs per patients • Adverse effects caused by or associated with using the prevention strategy | 675 papers identified from the search strategies, only 35 were found to fully meet the inclusion criteria. After appraisal by two independent reviewers, 24 papers were found to be of sufficient quality for inclusion. 6566 participants, all ICU patients, and all studies were conducted worldwide. Diet intervention significantly associated with a reduction in hospital PU incidence ($P = .05$) |
| 22 | Older individuals | To identify all published systematic reviews concerning nonpharmacologic interventions used to prevent PUs | To gather evidence regarding non-pharmacological interventions to prevent PUs | 110 systematic reviews were identified out of 675 abstracts. The authors found five RCTs that met their inclusion criteria (related to this EBR). The authors noticed that nutrition intervention during acute hospital admission might slightly reduce the incidence of PUs at 2 to 4 weeks in patients who are at risk of developing PUs. However, this evidence seems too limited, with a risk ratio (RR) of 0.85 and a 95% confidence interval (95% CI) of 0.74–0.98 |
| 7 | People of any age and sex with or without existing | Clearly described nutritional supplementation (enteral | Primary outcomes: | After merging the results and removing duplicates, with |

(Continues)

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|------------------------|--|--|---|--|
| | PU, in any care setting, irrespective of primary diagnosis | or parenteral nutrition) or special diets. Comparison between supplementary nutrition plus standard diet versus standard diet alone and between different types of supplementary nutrition were eligible | <ul style="list-style-type: none"> • The proportion of participants developing new PUs • Time to complete healing • Secondary outcomes: • Acceptability of supplements • Side effects • Costs • Rate of complete healing • The rate in change of ulcer size • Health-related quality of life | <p>potentially relevant trials, full-text copies were retrieved for 23 RCTs included in the review. However, only nine trials were included in this EBR. In these nine trials, one trial was excluded for pooled analysis because no data were presented, and no response was received for the request from the Cochrane group. Thus, in eight trials, only one trial showed significant beneficial effects of nutrient supplements to prevent PU development. The median sample size was 88 participants, with a range of 12 to 4023 patients</p> |
| 23 | Adults of any age group in any care setting | To review those SRs, which assessed parenteral and enteral nutritional supplementation in PU prevention | Compared nutritional intervention with control or standard of care | Two systematic reviews were included, assessing parenteral and enteral nutritional supplements. The authors commented that most of the RCTs in the reviews had a poor methodology, such as lack of information regarding randomisation, lack of blinding of outcome assessment, high withdrawal rates, and lack of intention-to-treat analyses |
| 24 | Adults of any age group in any care setting | To review those SRs, which assessed parenteral and enteral nutritional supplementation in PU prevention | Compared nutritional intervention with control or standard of care | Two systematic reviews were included, which assessed parenteral and enteral nutritional supplements. The authors noticed Reddy et al ²⁵ did not report outcome data for the included RCTs or perform a meta-analysis. Langer and Fink (2007) identified four RCTs comparing a combination of nutritional supplements consisting of energy and protein in different dosages. Only one study showed significant effects in reducing PUs, whereas the other three studies did not show significant effects |

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|--|---|---|--|---|
| 25 | Adults of any age group in any care setting | To systematically review the evidence examining interventions to prevent PUs | To assess the effectiveness of non-pharmacological treatments, such as those used to prevent PUs, creating unique methodological challenges | Five RCTs targeted impaired nutrition. A total of 13 845 patients in the selected studies enrolled. Only one RCT showed a significant reduction in PU development by giving adequate nutritional supplements |
| 26 | All adult populations with nutritional status of either well-nourished or malnourished and regardless of whether patients had PUs were at risk of developing them | All studies using oral nutritional supplements or enteral feeding tubes (all routes and methods), including those simultaneously using or compared with dietary counselling or parenteral nutrition or simultaneous standard diet, in either hospitals or community settings | PU incidence; PU healing; quality of life; complications; mortality; dietary intake; nutritional status | A total of 916 studies were identified by the search strategy, but only 15 complied with the inclusion criteria and were included in the systematic review. Of these, five RCTs were included in the meta-analysis. The other 21 studies were rejected from the systematic review and meta-analysis because of not being an original study; using an ineligible nutritional intervention; using ineligible subjects; or because it was not possible to source the document or an English translation of it. A total of 3209 participants in the 15 studies identified. Four RCTs of oral nutritional supplements and one RCT of enteral tube feeding were included in their meta-analysis. Significant reductions in PU development among those studies with adequate nutrients supplements (especially high-protein feeds) |
| <i>Clinical review/literature review</i> | | | | |
| 27 | Older individuals | To develop explicit and transparent clinical and practical recommendations, to prevent and treat PUs using non-pharmacological interventions in older patients on the basis of the current best evidence. This study was performed as part of the Optimal evidence-based Non-drug Therapies in Older People (ONTOP) project | The ONTOP group will discuss and evaluate the net health benefits of the anticipated balance of benefits and harms across all clinically critical outcomes | Included five RCTs and pooled four trials because one RCT reported incomplete data; noted a small significant benefit for nutrition intervention (RR: 0.85; 95% CI: 0.74–0.98) and low heterogeneity ($I^2 = 0\%$) |

(Continues)

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|------------------------|--|--|---|--|
| 28 | Did not specifically mention which age group of patients that authors refer to | To review the evidence-based intervention for the prevention and treatment of PUs. No specific search engines mentioned | No specific explanation given | Cited two studies with 672 critically ill inpatients over the age of 65, which compared a standard diet with two oral nutritional supplements per day to standard diet alone; their studies showed a decreased incidence of PUs at 15 days |
| 29 | Adult patients in any age group in any health care setting | To review the comparative clinical utility of PU risk assessment instruments and the benefits and harms of preventive interventions | The search results were able to provide evidence of effects of using risk assessment instruments to inform the use of preventive intervention; to evaluate the benefits and harms of various preventive interventions | Six trials were evaluated for nutritional interventions to prevent Pus, but only five were rated as one had poor quality because of the inadequate description of randomisation and allocation concealment methods and assessors were not blinded. Thus, the authors found little evidence in supporting the effectiveness of enteral or oral nutritional supplementation for preventing PUs |
| 30 | Adult patients in any age group; must be involved in the study of oral nutritional supplement enriched with arginine | The search focused specifically on studies performed with the specific oral nutritional supplement (Cubitan, Nutricia Advanced Medical Nutrition, The Netherlands) | To examine the effect of a specific nutritional intervention on PU healing, clinical studies performed with a specific oral nutritional supplement enriched with arginine, vitamin C, and zinc for the healing of PUs were reviewed | The authors retrieved six clinical studies, with a total of 851 participants, and found two studies also included in this EBR. Hommel et al ³¹ showed fewer patients with a hospital-acquired PU when an oral nutritional supplement was given twice a day postoperatively compared with the control group. ⁹ showed the incidence of PUs in the placebo group was 59%, which was slightly higher than that in the supplement group (55%); however, not significant |
| 32 | Adult patients in any age group, but the authors did not specifically mention the criteria | No specific intervention explained in the authors' review article | To review the current literature to assess the strength of evidence surrounding the role of nutrition therapy in the prevention and treatment of PUs | The authors only included one systematic review article to discuss the issues raised. They believed that with adequate nutritional support, patients' nutritional status would be improved and less likely to develop PUs |

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|-------------------------------------|--|--|---|---|
| 33 | Adult patients in any age group who were at-risk of developing PU; however, the authors did not specifically mention the criteria | No specific intervention explained in author review article | To investigate the role of nutrition in the prevention of PUs and focus on the effects of mixed nutritional support on PU development in at-risk groups and on nutritional status as a predictor of PU development, with specific reference to albumin | Five RCTs were included only one RCT was showed a significant reduction in PU incidence after nutritional supplement intervention. The remaining four RCTs did not appear to be significant for PU reduction. However, all five RCTs showed PU reductions in the findings |
| 12 | Patients older than 65 years | Focused on older patients' nutritional status and the connection between nutritional status and the development of PUs | To describe the importance of nutrition in reducing the risk of PUs and to focus on nursing interventions in older patients | Eight studies were included, with three studies of high quality and five were of medium quality |
| <i>Randomised controlled trials</i> | | | | |
| 34 | Adult patients who were suffering from an acute lung injury, defined by a $\text{PaO}_2/\text{FiO}_2$ ratio below 250, were included in the prospective, randomised, non-blinded study | This study was a prospective, randomised, but not blinded study | To compare the incidence and the healing of PUs in a sample of critically ill, mechanically ventilated patients suffering from acute lung injury between those receiving a diet enriched in lipids (eicosapentaenoic acid), gamma-linolenic acid, vitamins A, C, and E with those receiving a comparable diet of macronutrients | No significant difference was found. The number of PUs increased from 14 to 23 (day 4) and 24 (day 7) in the control group as opposed to an increase of 7 to 12 (day 4) and 15 (day 7) in the study group. Significantly less PU occurrence was observed among the patients receiving the study formulas compared with the control group (15 versus 24, $P < .05$) |
| 9 | All patients with hip fractures at three centres in the Netherlands | A randomised, double-blind, placebo-controlled study | To investigate the effects of a high-protein supplement, enriched with arginine, zinc, and antioxidants, on the development of PU in patients with hip fractures, in a double-blind, placebo-controlled design | 103 patients complied with selection criteria and were included in the study. 57% of the patients in the total study population developed PU, and 23% of the patients developed a PU of stage II. In the placebo group, the incidence of PU was 59%, which was slightly higher than in the supplement group (55%) but not significant (difference: 0.037; 95% CI: -0.16 to 0.23) |
| 8 | Patients with hip fracture, a pressure-score risk score of 8 points or more, and informed consent was obtained | Randomised clinical trial | To investigate the effects of tube feeding on protein and energy intake, nutritional status, and the development and severity of pressure sores, with either supplementary tube | At 1 week, 20 of 54 patients (37%) in the tube feeding group and 30 of 62 patients (48%) in the control group had clinically relevant pressure sores ($P = .26$, Fisher's test). At 2 weeks, |

(Continues)

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|-----------------------------------|---|--|--|---|
| | | | feeding or no supplementary tube feeding, in addition to the hospital diet, in patients with a fracture of the hip and a concomitant high risk for the development of pressure sores | 25 of 48 patients (52%) of the tube feeding group and 30 of 53 patients (57%) in the control group had clinically relevant pressure sores ($P = .69$, Fisher's test). Although the maximum pressure sore grading at 1 and 2 weeks appeared to be lower in the tube feeding group, no significant difference was found ($P = .35$ and $P = .12$ respectively, Mann–Whitney U test) |
| <i>Observational/cohort study</i> | | | | |
| 35 | Patients older than 18 years in home care residing in the area covered by Districts III and IV of the Municipality of São José do Rio Preto | Descriptive study | To verify the nutritional profiles of patients bedridden with PU; the presence of malnutrition, weight loss, BMI and nutritional intake were compared with the risk of PU; malnourished patients or those who presented weight loss greater than 5% in the last month or greater than 10% in the last 6 months, or with BMI below normal, or insufficient nutritional intake, were more predisposed to the potential risk of developing PU | 91.6% of participants were bedridden, and all of them were diagnosed with diseases requiring medications. All patients had developed PUs at various stages of. Most importantly, they noticed the requirement of the caloric-protein intake was not far below the nutritional needs of the subjects. Some patients were unable to have a good intake of foods because of medications that made them unable to take a proper meal |
| 36 | Adults patients older than 18 years, cognitively intact, at risk of PU development because of restricted movement; and hospital length of stay of no less than 3 days | A multisite, observational study with randomisation data collection in 4 medical wards at 2 public metropolitan hospitals in Queensland, Australia | To describe the nutritional intake of hospitalised patients at risk for PUs, and determine predictors of inadequate energy and protein intake | They found out that renal ward patients were four times more likely to eat less in relation to energy and protein compared with all other wards. Patients who did not consume any oral nutrition support were five times more likely not to meet energy requirements, and more than 15 times more likely not to meet protein requirements. No significant difference in energy and protein consumption was observed among the other wards |
| 37 | Advanced dementia patients with a percutaneous | A propensity-matched cohort study of nursing home residents with advanced | To determine if percutaneous endoscopic gastrostomy tubes prevent or help heal | The results showed the PEG feeding tube insertion doubles the risk of new PU |

TABLE 2 (Continued)

| Study Reference Number | Type of participants | Types of intervention | Types of outcomes | Primary outcomes and secondary outcomes |
|---------------------------------|--|--|---|--|
| | endoscopic gastrostomy tube | cognitive impairment and recent need for assistance in eating was conducted by matching each nursing home residents who had a feeding tube inserted during hospitalisation | PUs in nursing home residents with advanced cognitive impairment | |
| <i>Quasi-experimental study</i> | | | | |
| 38 | Patients with hip fractures admitted to the orthopaedic ward at a Swedish university hospital | Quasi-experimental, pre- and post-test comparison group design without random group assignment | To investigate if any differences exist between patients receiving nutritional intervention preoperatively and over 5 days postoperatively and patients who did not, in terms of postoperative complications, rehabilitation, length of stay, and food and liquid intake | Five days postoperatively, significantly fewer patients in the intervention group had PUs (18.0%) compared with those in the control group (36.0%). When patients with PUs at admission were excluded, the incidence was calculated to be 28.0% in the control group and 18.0% in the intervention group |
| <i>Cross-sectional study</i> | | | | |
| 39 | Adult patients at intensive care surgical, medical, and interdisciplinary specialities in hospitals all over Germany | Cross-sectional study (point prevalence) | To assess the allocation of preventive measures for patients at risk for PUs and the evidence of applied preventive measures in intensive care settings regarding EPUAP and AHCPR guidelines | The study showed 83% of all patients were at risk for PUs based on the total score of the Braden scale cut-off point of ≤ 20 . The total prevalence of PUs was 27.2%. 68.6% of patients were found to have nutritional supplement for preventive measures of PUs |
| <i>Guidelines</i> | | | | |
| 40 | Adult patients in any setting; however, the authors did not clearly describe criteria | A comprehensive, evidence- and consensus-based guideline was developed to address the prevention of PUs | This guideline was presented in generic terms; the details of specific tests, therapies, and procedures are the discretion of an interdisciplinary team of health care professionals who establish, implement, and evaluate policies and procedures directed at the prevention of PUs | The authors found the management of nutrition shall be provided to prevent the formation of PUs which received evidence level of I, II and III. However, the impact of nutrition in the prevention of PUs remains controversial, as commented by the authors |

12 patients examined in the study by Poletti et al,³⁵ whereas Robert et al³⁶ only recruited patients without metabolic effects on nutritional status.

Teno et al³⁷ reported a cohort study, which was rated as moderate-quality by CASP, and rated by CEBM as

Level 3 evidence. No baseline nutritional status was obtained for the patients recruited in the study, and the risk of selection bias was identified because the study only assessed advanced dementia patients, a disease that might affect nutrient intake.

TABLE 3 Summary of the included studies, their review quality, and their level of evidence

| Study Reference Number | Appraisal summary | CEBM | Quality |
|------------------------|--|---------|-------------------------|
| 20 | No meta-analysis was performed No heterogeneity evaluation performed No grey literature search identified The inclusion and exclusion criteria were partially explained | Level 2 | Moderate (AMSTAR) |
| 35 | No explanation for the selection of 12 patients in the study Standard of care was not mentioned No explanation of any confounding factors was taken into consideration No confidence intervals were calculated | Level 3 | Low (CASP) |
| 21 | No meta-analysis was performed Conflict of interest was not mentioned The inclusion and exclusion criteria were partially explained | Level 2 | Moderate (AMSTAR) |
| 22 | No meta-analysis was performed Did not report the source of funding for the included studies The inclusion and exclusion criteria were partially explained Heterogeneity of the study was not assessed | Level 1 | Moderate (AMSTAR) |
| 27 | PICO was not described No meta-analysis was performed Did not report the source of funding for the included studies The inclusion and exclusion criteria were not described in detail | Level 1 | Moderate (AMSTAR) |
| Evans et al (2015) | PICO was not described No explicit statement to explain why the review was established prior to the conduct of the review No explanation of their selection of study designs for inclusions in the review No search engines described No other reviewers to review the selected studies No detail list of inclusion and exclusion of studies described No report of sources of funding for the included studies No meta-analysis was performed No risk of bias accounted for individual studies No quantitative synthesis was performed | Level 2 | Critically Low (AMSTAR) |
| 7 | Cochrane Database Systematic Review Followed the Cochrane Collaboration tool for assessing those RCTs The reporting structure followed the appraisal tools assessment and provided all the information stated in the appraisal tools. | Level 1 | High (AMSTAR) |
| 36 | No nutritional status for patients Only recruited patients without metabolic effects on nutritional status and authors limited protein intakes to 0.8–1.0 g/kg Observation of the studies only performed for 24 hours The implications of malnourishment in renal patients developing PUs was not shown in the data. The authors only commented that patients who are at risk of PU development have insufficient oral intake, especially in renal ward patients | Level 3 | Low (CASP) |
| 29 | No obvious usage of PICO being addressed in the review Inclusion and exclusion criteria were briefly explained in the review No meta-analysis was performed No heterogeneity was calculated No report of funding sources for included studies | Level 1 | Moderate (AMSTAR) |

TABLE 3 (Continued)

| Study Reference Number | Appraisal summary | CEBM | Quality |
|------------------------|---|----------------|-------------------------|
| 37 | Propensity-match cohort study No baseline nutritional status of patients being recruited in the study Selection bias because of assessment of advanced dementia patients only | Level 3 | Moderate (CASP) |
| 23 | No excluded lists explained or elaborated in the review The included lists were partially explained No source of funding described for included studies No meta-analysis was performed No heterogeneity was calculated for included studies | Level 1 | Moderate (AMSTAR) |
| 30 | No details of the excluded lists were explained No source of funding reported for included studies No meta-analysis was performed Risk of bias was not assessed | Level 2 | Low (AMSTAR) |
| 32 | No use of PICO No details were given for the inclusion and exclusion criteria in their review No explanation of any specific types of studies included in the review, such as RCTs, clinical trials, or non-randomised clinical trials No search engines or strategy mentioned in the review No external reviewers independently assess those included studies No review of the source of funding for included studies No meta-analysis was performed No heterogeneity was calculated No risk of bias was assessed Conflict of interest not mentioned by authors | Level 2 | Critically Low (AMSTAR) |
| 39 | Cross-sectional study assessing health care workers in compliance in using EPUAP and AHCPR guidelines to manage ICU patients at risk of PU development No baseline prevalence data of PUs in Germany was reported in the study results Reliability in reporting the data results, as not all intensive care specialities and unconscious patients were recruited in this study | Not Applicable | Low (AXIS) |
| 38 | Quasi-experimental study to evaluate whether nutritional intervention can reduce post-hip fracture operative complications and improve rehabilitation Reliability of the results data for analysis, as initially recruited 100 patients; however, 58 patients excluded from the study. Only 15 patients included in the intervention group and 27 patients in the control group No confidence interval was calculated for the postoperative PU complications; however, only the predictors of PU have confidence intervals No baseline nutritional status assessed | Level 3 | Moderate (CASP) |
| 24 | No excluded lists explained or elaborated in the review The included lists were partially explained No source of funding included for studies No meta-analysis was performed No heterogeneity was calculated for those included studies | Level 1 | Moderate (AMSTAR) |
| 40 | Objective not clearly explained as the guideline is meant for adults, older individuals, paediatric age groups, or special population, such as critically ill patients Included and excluded papers not clearly explained | Not Applicable | Low (AGREE) |

(Continues)

TABLE 3 (Continued)

| Study Reference Number | Appraisal summary | CEBM | Quality |
|------------------------|--|---------|-------------------------|
| | Recommendation in guideline usage not elaborated No external reviewers to review the guidelines to avoid any biases No cost information or economic evaluation mentioned Conflict of interest for authors was not mentioned | | |
| 34 | Randomised, prospective, controlled study Not double-blind study Selection bias as the control group at baseline included 14 patients with PUs and 7 patients in the intervention group to begin the study | Level 2 | Moderate (CONSORT) |
| 33 | No PICO used No external reviewers to come up with an agreement for the included studies No list of excluded studies was explained No meta-analysis was calculated, although only RCTs were included No report on the source of funding for the included studies No explanation on the heterogeneity of the observed results No conflict of interest mentioned by the author | Level 2 | Moderate (AMSTAR) |
| 12 | No listing of excluded studies and no reasons given for those excluded studies The included studies were not described in details No risk of bias technique was used for included RCTs No source of funding report for included studies No meta-analysis was performed No risk of bias explained for the included studies No heterogeneity was assessed No conflict of interest reported by the authors | Level 2 | Critically Low (AMSTAR) |
| 25 | No report of the source of funding for included studies No meta-analysis performed on those RCTs | Level 1 | Moderate (AMSTAR) |
| 26 | Systematic review and meta-analysis of this article were performed perfectly. As authors explained in details their objective, search engines and criteria of inclusion and exclusion were explained well. There was detail listed for those excluded studies and explanation were given. Meta-analysis was performed, and risk of bias of the studies was explained. | Level 1 | High (AMSTAR) |
| 9 | Randomised, double-blind assessment on the effect of nutritional supplementation on the prevention of PUs in hip-fracture patients. No methods of randomisation explained No baseline nutritional status was measured No registration number mentioned in the study No mentioned if the full protocol of the study able to be located No excluded subjects in the study | Level 2 | Moderate (CONSORT) |
| 8 | Randomised clinical trial of pressure sores and tube feeding in patients with a fractured hip Randomisation method was not explained Not double-blind study No subgroup analysis Registration number of the study and full protocol located were not mentioned in the study | Level 2 | Moderate (CONSORT) |

Shahin et al³⁹ reported a cross-sectional study, which was rated as low-quality by AXIS because of a lack of

baseline data regarding the PU prevalence rate prior to the study and a lack of explanation for missing data. This

study was also characterised by selection bias in the reliability of the reported results because not all intensive care specialities and unconscious patients were included in this study.

The study by Gunnarsson et al³⁸ was rated as moderate-quality by CASP, with a CEBM rating of Level 3 evidence because of the number of patients excluded from the study ($n=58$ from a total of 100) and a lack of confidence intervals calculated for the complications associated with postoperative PUs. In addition, no assessment was performed for baseline nutritional status.

The study by Stechmiller et al⁴⁰ was rated as low-quality by AGREE II because of incomplete data reporting, such as objectives of the guideline being poorly explained and no clear explanation of which population group the guideline is suitable for. In addition, justification for the inclusion and exclusion of recommendations was not discussed in detail. Furthermore no external review by independent reviewers was undertaken which is a risk for bias.

4 | DISCUSSION

Overall this review of the evidence has determined that the existing studies were of mixed quality. The majority of the included studies were rated as moderate-quality ($n = 14$), two studies were rated as high quality, three were rated as critically low quality, and five were rated as low quality. When reviewing the findings of the included studies, most studies did not show significant effects of nutrient supplements on the incidence of PU development. This outcome could be because of small numbers of sample sizes recruited in each study, short study durations, difficulty blinding the assessors and patients, selection biases, or allocation concealment biases, all of which could affect the analysis of the results. In relation to high-risk patients there was little to no evidence to support the use of nutritional supplements for the prevention of PUs. Based on the assessment of study quality using the various appraisal tools, the evidence regarding the use of nutritional supplements for PU prevention is poor.

The available appraisal tools do not assess the evidence associated with a particular topic. Instead, these studies primarily review the study design to determine whether the authors have made a good attempt to reduce bias in their studies. For example, authors must state a clear objective for their studies. Authors must also reveal whether they have performed a thorough search to identify relevant articles for inclusion in their studies and state their applied inclusion and exclusion criteria to allow the determination of whether the criteria applied were appropriate for the stated objective. When

appraising different types of studies, the authors should attempt to report all necessary data to avoid any biased reporting to ensure a high-quality study.

Overall, in the present EBR, the common issues encountered with the included SR studies were the lack of a stated PICO study design, a lack of detailed explanation for articles exclusion, a lack of meta-analysis, failure to assess heterogeneity, no detail explanation of risks of bias, and no sources of funding reported. Thus, the majority of the review studies were rated as low-to-moderate quality. Among the included RCTs, all were found to feature selection biases, allocation biases, and concealment biases. Therefore, all three RCTs were rated as moderate quality. This blinding of assessors and patients was difficult to perform in the RCTs that were assessed, and the appraisal tools used to assess the quality of these studies reduce the quality rating for those studies in which no blinding was performed. The remaining studies and guideline were a mixture of low-to-moderate quality studies. This type of quality appraisal is especially appropriate for the review of pharmacological studies, rather than non-pharmacological studies, such as whether a nutritional intervention can contribute to the prevention of PU development. Therefore, the current appraisal tools may not be appropriate for assessing these types of studies, in which blinding is difficult to accomplish.

The low quality of the studies does not necessarily indicate that the quality of the data regarding the use of nutritional supplements to prevent PUs is equivalent to low evidence or no evidence; these assessment tools are not designed to assessing the quality of the data regarding the effects of nutritional supplements on PU prevalence. Patients require adequate nutrients, especially malnourished patients who are at a high risk of developing PUs. The exact understanding of each micronutrient and macronutrient component and their effects on PU prevention and the mechanisms associated with prevention are not well understood.⁴¹

Understanding the interactions between wound healing and nutrition is challenging because the human body and wound healing are complex entities involving multifaceted processes; thus, the nutritional requirements for wound healing can vary across patients and wound types. Therefore, determining specific nutrient guidelines for specific wound types in varying patient groups can be challenging. Therefore, the value of including nutritional supplements to support PUs prevention remains an open question. The evidence identified through this EBR focused upon a limited range of nutrients (protein, amino acid, and antioxidants), and the individual studies were often methodologically weak. Well-designed, randomised controlled studies are necessary to identify whether

supplementation confers benefits in terms of reduced PU incidence above any reductions associated with the implementation of high-quality standards of care prevention.

4.1 | Implications for the review for practice and research

Nutritional supplementation remains mandatory for those patients whose nutritional status is rated as malnourished and below, regardless of their risk for developing PUs. For those patients who are at risk of developing PUs, nutritional supplementation should be included in the patients' management plans. Healthcare stake holders, government policy makers, clinicians and guideline committees need to take into account the strength of existing evidence when making decisions about how to implement nutritional supplementation strategies for PU prevention and management, especially for high risk patients. Despite the low-to-moderate quality of the studies included in the review, nutritional intervention should be included in the patient's management plan, as neglecting their nutritional requirements would be unethical.

Although the majority of the included articles included some forms of bias, the statements in the appraisal tools used to assess the studies are based on a specific type of reporting expected by the tools. Therefore, to perform a robust study, an appropriate study design should address each statement addressed in the appraisal tools. However, the use of pharmacological tools to assess non-pharmacological studies may require further consideration and discussion. In addition, the nutrient amounts calculated in the studies require individual determinations, based on the patient's nutritional status and requirements, which prevents the implementation of some steps required by these assessment tools to reduce bias.

4.2 | Limitations of the review

The limitations of this EBR included the inability to include non-English studies because of lack of translation resources. In addition, the authors of the studies were not contacted to determine whether any additional information could be obtained. Assessing the quality of these studies was difficult, as AMSTAR was established in 2007 and was revised in 2017 because of the identification of discrimination in their questionnaire. Therefore, the use of AMSTAR to assess the quality of review studies may identify biases, particularly among studies that were performed using the older guidelines before 2017, which includes most of the studies included in this EBR. These

older studies may be rated lower using the newer AMSTAR questionnaire than using the original AMSTAR questionnaire. Another limitation was that because of different search terms used in this study compared with other authors, some studies included in other studies were not included in this study. Therefore, the search result yields could be different.

5 | CONCLUSION

The majority of the included studies were determined to be of moderate or low-quality for the assessment of nutritional supplementation to prevent PU development, as most of the studies were found to have some flaws in their methodology, especially the short duration of the studies and the small sample sizes. However, the use of pharmacological appraisal tools to assess the quality and level of evidence in non-pharmacological studies may be an inappropriate use of these appraisal tools. Although the quality of most of the included studies was rated as moderate and low, nutritional supplementation should still be viewed as mandatory, and as the failure to provide adequate nutrients to malnourished patients and those patients who are at risk of developing PUs would be unethical. Future studies should consider the use of appropriate sample sizes and appropriate follow-up durations to ensure that the studies have high power for the analysis of the results.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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