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Please refer to the original source for the final version of this work: <u>https://doi.org/10.1016/j.jtv.2020.05.004</u> Prevention and treatment of pressure injuries: A meta-synthesis of Cochrane Reviews

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Abstract

Background

There are many high-quality systematic reviews to inform practice around pressure injury (PI) prevention and treatment. However, they are often unable to provide recommendations for practice and research due to low quality trials.

Objectives

To evaluate current systematic review evidence on the prevention and treatment of PI.

Methods

This meta-synthesis was guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Only Cochrane Reviews were included. Evidence from reviews was independently screened and assessed for risk of bias and certainty using Grading of Recommendations, Assessment, Development and Evaluations by two authors, with a third resolving discrepancies. Methodological quality of included reviews was assessed using the second version of A Measurement Tool to Assess Systematic Reviews, and a narrative synthesis undertaken.

Results

Twenty-five Cochrane Reviews were included; eight for PI prevention and 19 for PI treatment. Prevention reviews included 102 studies (27,933 participants). Treatment reviews included 154 studies (over 16,936 participants). Three prevention reviews and nine treatment reviews reported risk of bias, judging the included trials as having low or very low certainty evidence. Two reviews reported moderate certainty evidence. Methodological quality of the systematic reviews was rated as high for eight reviews (7/19 for treatment and 1/6 for prevention). Recommendations for prevention included repositioning, nutrition and support surfaces. Recommendations for treatment focused on nutrition and repositioning.

Conclusions

This meta-synthesis confirms the low-certainty of PI prevention and treatment trials, resulting in few recommendations to inform clinical practice. Generation of high-quality evidence on PI prevention and treatment is imperative.

Highlights

• •

Pressure injuries continue to impact patient outcomes at great cost.

• •

Meta-reviews enable critical appraisal of the scope and certainty of evidence.

• •

Certainty of evidence low in systematic reviews of pressure injury studies.

• •

High-quality research on pressure injury prevention and treatment is needed.

1

Introduction

From the earliest recognition of the importance of essential health-care practices [1], clinicians - principally nurses - have focused on promoting skin health and preventing 'bedsores' or pressure injuries (PI). Also referred to as pressure ulcers, these potentially preventable injuries are caused by damage to the skin and underlying tissue from pressure, shear or a combination of both [2]. Prevention, early diagnosis and treatment of PI is a global priority, formalised via international and national safety and quality health service standards [2, 3]. However, hospital-acquired PIs (HAPIs) are relatively common adverse events, with prevalence rates ranging from 6.4% to 17.6% [45678]. This is of particular concern given that there has been a reported increase in PI in the US, despite other adverse events having decreased [4]. While there are differences in defining, assessing and detecting HAPIs [4, 5, 910111213], there is clear evidence that these injuries result in poor patient outcomes including psychological distress and pain [14, 15], extended hospital length of stay [12, 13], and significantly escalated healthcare costs [12, 13]. Across countries, the high cost of PI is well documented [6, 12, 16].

While PI prevention and treatment occur within a multi-disciplinary setting, it is often the registered nurse (RN) who makes decisions about what strategies to use for PI prevention and treatment and/or makes recommendations to other healthcare professionals about appropriate interventions [17]. Ideally, these strategies and or recommendations are based on high-quality/certainty reviews of evidence. (Terminology for assessing evidence moved from "quality" to 'certainty" in 2017. The term "certainty" will be used from this point). Considered the gold standard of evidence within the hierarchy of study designs for research into effectiveness [18], Cochrane Reviews provide a valuable reference point for evidence to answer research questions via a priori eligibility criteria and explicitly stated methodologies [19]. They not only summarise research evidence but also critically appraise the certainty/quality of that evidence [19]. Cochrane and other high quality reviews can be used to inform clinical practice guidelines for effective PI prevention and treatment, which will likely require a range of implementation strategies – such as education and awareness campaigns - to actually change practice [20]. Yet, the extent to which Cochrane reviews provide useful information to assist nurses' decision-making and provide guidance for researchers remains unknown. Therefore, a closer examination of the practice and research implications from Cochrane Reviews that examine PI prevention and treatment is needed.

Meta-reviews are often used as a starting point to inform the development of practice and research recommendations and clinical practice guidelines and act as justification for further research [21]. While a meta-review of wounds (including PI) was published several years ago [22], a more detailed and critical up-to-date review is needed. The aim of this meta-synthesis of PI prevention and PI treatment Cochrane Reviews was to: critically synthesise and appraise recommendations for nursing practice and research as reported in Cochrane Reviews' of strategies for PI prevention and treatment in hospitalised patients.

Methods

A meta-synthesis of Cochrane systematic reviews was undertaken.

2.1

Protocol and registration

The review was registered on the International Prospective Register of Systematic Reviews (CRD42018117938), available

at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=117938 .

2.2

Eligibility criteria

The SPICE framework was used to determine our inclusion and exclusion criteria based on: setting (S), population (P), intervention (I), comparison (C), and evaluation (E), in addition to characteristics such as year of publication and language [23].

Setting was any care setting, including hospital, home, residential aged care or long-term care facility. Population included Cochrane Reviews with a focus on any patient group or individuals who received PI prevention and/or treatment. The decision to focus on Cochrane Reviews was made because they follow a rigorous process, as documented in their handbook [19], with specific sections on the implications for practice and research. Cochrane Reviews were included if they examined interventions for PI prevention or treatment, which could be implemented by RNs or where RNs recommended their implementation to other health professionals. As such, interventions included but were not restricted to, dressings, education, debridement and use of topical agents. Interventions nurses could recommend or request use of, such as topical antibiotics and antiseptics were also included. There were no restrictions on *comparators* used. Rather, comparators were as defined by the authors of the Cochrane Review. Evaluation was based on specific recommendations as described in the "implications for practice" and "implications for research" sections of each Cochrane Review and in the abstract. Practice recommendations were assessed if they: 1) made a definitive recommendation to undertake a practice or not to undertake a practice and/or; 2) reported certainty of evidence for that recommendation. Research recommendations were also assessed when presented. As review outcomes were not the primary point of our evaluation, there were no restrictions for inclusion and exclusion based on outcome.

2.3

Information sources and search strategy

A search of the Cochrane Wounds group (<u>https://www.cochranelibrary.com/search</u>) was conducted on January 23rd [,] 2020. The titles and abstracts of all Cochrane Reviews on the Wounds group website were screened. The Cochrane Library was also searched for reviews using the term 'pressure injury' or 'pressure ulcer' in titles, abstract or keywords. There were no restrictions on publication year or location.

2.4

Study selection

Reviews identified in the search process were exported to an Endnote library for screening. Three authors (WC, CW, EH) independently screened reviews to assess whether reviews met inclusion and

exclusion criteria. Initial screening was conducted on titles and abstracts. Articles that required further examination then proceeded to full-text screening and discrepancies were resolved via discussion among the review team. A PRISMA flow chart of Cochrane Reviews included in this meta-synthesis was developed to illustrate the flow of articles through this review [21].

2.5

Data collection process

A standardised data extraction form was developed by the authors to collect review data, which they piloted on two randomly selected reviews prior to the commencement of data extraction. A data dictionary detailing the data to be extracted was also developed and used to ensure consistency in data extraction. The data extraction tool included the following information (where available): source (author, year, reference, number of pages in full review and until reference list), sample (number of studies and participants identified), interventions (interventions, comparators), outcomes, certainty of the body of evidence, findings, implications for practice, and implications for research. Following training in using the tool (comprising written instructions, template of a data extraction form, an exemplar of an extracted review and training reviews for data extraction for assessment and feedback), data extraction was conducted on each study independently by pairs of two authors (RW, LM, ZM, AE, CW, BG, EH) and adjudicated by a third (WC) if required [24]. Meta-reviewers did not undertake data extraction on Cochrane Reviews they had authored.

2.6

Outcomes

We planned to report on the following outcomes related to the prevention and treatment of PI:

• 1.

Reported certainty of the body of evidence;

• 2.

Number and content of PI prevention and treatment strategies.

2.7

Risk of bias and quality appraisal

Cochrane Reviews are methodologically robust and follow a strict process for each step in the review. Authors of the Cochrane review are required to assess the risk of bias of individual studies. They also assess the certainty of the body of evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach [25]. The GRADE approach is a transparent and structured system for rating the certainty of evidence for each outcome across included studies, resulting in the assessment of one of four grades: 1) high (further research is very unlikely to change confidence in the estimate of effect); 2) moderate (further research is likely to have an important impact on confidence in the estimate of effect), 3) low (further research is very likely to have an important impact on confidence in the estimate of effect), and; 4) very low (there is uncertainty about the estimate) [25]. As published Cochrane protocols and reviews undergo a series of expert peer appraisals, the risk of bias or certainty of evidence was not reassessed. Rather, tabular summaries of the certainty of evidence using GRADE were extracted. We did, however, assess the methodological quality of the Cochrane Reviews using the second version of A Measurement Tool to Assess Systematic Reviews (AMSTAR 2) (2017). This critical appraisal tool comprising 16 items, provided a broad assessment of quality including the identification of methodological weaknesses using the identification of critical and non-critical domains [26]. Items were assessed using a scale of: yes; partial yes; no, and; no meta-analysis conducted. The overall quality of each Cochrane review was considered in relation to seven critical domains (items 2,4,7,9,11, 13, 15), or non-critical methodological weakness (items 1,3,5,6,8,10, 12, 14,16). Specifically, AMSTAR 2 authors propose that reviews must meet seven critical domains (item 2: registration of the protocol prior to the commencement, item 4: adequacy of the literature review, item 7: justification for the exclusion of studies, item 9: risk of bias of included studies and when interpreting results, item 11: appropriateness of a meta-analysis, item 13: the impact of risk of bias in individual studies and item 15: impact of publication bias); as failure to meet these critical domains and or if numerous non-critical methodological weaknesses were present, it would affect a review's validity and conclusions. As suggested by the AMSTAR 2 authors, we used these domains to provide an overall rating (i.e., a score) of confidence in the results of the review, using the ratings of High, Moderate, Low and Critically Low confidence [26].

In addition to rating the AMSTAR 2 critical domains for the overall confidence in the results of the review, a summary score (percentage) of included Cochrane reviews which met each item in the AMSTAR 2 was created. One author (EH) critically appraised the methodological quality of each Cochrane review using the AMSTAR 2 [26]. A second author (CW) independently assessed a sample (20%) of reviews and achieved a good agreement (at least 80% as recognised by AMSTAR 2 [26]). Discrepancies were resolved through discussion or adjudicated by a third reviewer when needed (WC) [24].

2.8

Synthesis of results

A narrative synthesis of the recommendations for practice and research sections of the Cochrane reviews was undertaken, guided by the following questions:

•

How many recommendations are made (no/yes) based on the "abstract", "recommendations for practice" and "recommendations for research" sections of the reviews?

•

What are the recommendations? (These were categorised as those that recommended a practice and those that recommended not undertaking a practice.)

• •

What is the quality/certainty of the body of evidence for each recommendation?

3

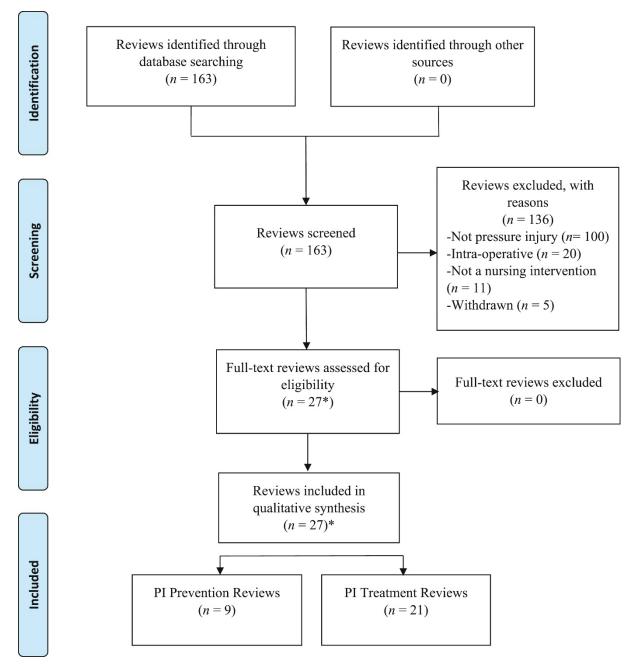
Results

3.1

Study selection

The PRISMA flow chart of Cochrane reviews (Fig. 1) shows the number of studies identified, screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage [21]. There were 27 reviews included in the qualitative syntheses; nine for PI prevention [272829303132333435], and 21 for PI treatment

[28 , 31 , 34 , 363738394041424344454647484950515253]. Three reviews [28 , 31 , 34], examined both PI prevention and treatment. Three reviews [39 , 43 , 50], explored multiple wounds types, though only data relating to PI treatment were extracted.



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Fig. 1

PRISMA Flow Chart [21]. *Three reviews assessed both PI Prevention and PI Treatment.

3.2

Study characteristics

Table 1 provides a summary of the PI prevention Cochrane Reviews. Nine reviews published between 2013 and 2019 were included [282930 , 323334 , 47], with a total of 106 studies (94 RCTs, 4 c-RCT, 3 Quasi-RCT, 4 trials and 1 economic) containing over 30,540 patients/participants (range = 499 to 17,460). One study did not report specific participant numbers but rather referred to staff from seven hospitals and 105 nursing homes [32]. Only five reviews reported GRADE assessments and certainty of evidence as *Very low* to *Low* [27 , 30 , 32 , 34 , 35]. Two reviews did not have any eligible studies to assess [33 , 47], and the remaining three reviews did not assess GRADE noting the "lack of clear or reliable evidence" and/or risk of bias for individual studies [282930].

Table 1

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
Gillespie (2014)	4 (3 RCT and 1 economic); 502	Adults without an existing PI	Repositioning frequencies and positioning schedules	Alternate schedules or standard practice: Repositioning frequencies (2, 3, 4, & 6 hourly turning); Positions: (90° lateral, 30° lateral, tilt)	 New PI of any stage of grade Cost Cost Incremental cost per event avoided Pain Quality of life Patient satisfaction
^a Joyce (2018)	4 (1 controlled before-and- after study, 1 RCT, 1 c-RCT and 1 quasi- experimental cluster trial); 499	Participants of any age, in any care setting, who were at risk of developing a PI, or who had an	Organisational interventions: provider- orientated, patient- orientated, structural and regulatory	Usual service delivery for PI prevention	 PI incidence rate Adverse events •

Characteristics of included PI prevention Cochrane Reviews (n = 9).

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
		existing PI (any stage)			Incidence proportion risk Healthy related Quali life Patient satisfaction Staff satisfaction
^a Langer (2014)	23 (RCTs); 6963	Participants of any age and sex with or without existing PIs, in any care setting, irrespective of primary diagnosis	Clearly described nutritional supplementation (enteral or parenteral nutrition) or special diets.	Supplementary nutrition plus standard diet versus standard diet alone and between different types of supplementary nutrition (e.g. enteral vs parenteral)	Incidence of new ulce Acceptability of supplements Side effects Costs Rate of complete hea Rate in change of size ulcer Quality of life
McInnes (2015)	59 (54 RCT, 2 Quasi RCT and 3 trials); 17,460	Participants receiving health care who were at risk of	Various types of support surfaces	Various types of support surfaces	• • Incidence of new ulce • •

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
		developing Pls, in any setting			Cost Patient comfort Durability/longevity of the devices Acceptability of the devices for healthcare staff Quality of life
Moore (2019)	2 (1 c-RCT and 1 RCT); 1487	Participants without PIs, of any age, in any healthcare setting	Structured, systematic pressure ulcer risk assessment tools	Other structured PI risk assessment tools; No structured pressure injury risk assessment; Unaided clinical judgement	Incidence of new ulce Severity of new PI •• Time to ulcer development •• PI prevalence
Moore (2018)	18 (1 c-RCT and 17 RCT); 3629	Participants of any age, without a PI, but considered to be at risk of developing a PI, in any care setting	Dressings Topical agents Dressings with topical agents	Different dressing, topical agent or combing topical agent and dressing or no intervention or standard care	 Pressure ulcer incider Adverse events Stage of any new Pls •

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Time to ulcer development Costs of interventions Quality of life Pain at dressing chan Patient acceptability/satisfac Hospital LOS
^a Moore (2015)	O studies; O	Participants of any age, in any setting who were at risk of developing a PI, or who had an existing PI were intended	Wound care team	Individual healthcare professional	 Complete healing and rate Absolute or percentage change in PI area or volume Proportion of PIs head Time to complete woo healing Pain All-cause mortality

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					• •
					Quality of life
Porter- Armstrong (2018)	5 (1 c-RCT and 4 RCT); Staff from 7 hospitals and 105 nursing homes	All healthcare staff involved in frontline PI prevention, delivering regular care to any patient group deemed 'at risk' of PI	Educational intervention for healthcare professionals on pressure ulcer prevention	No intervention/usual practices, education delivered in a different format, different components of education	Change in health professionals' knowle Incidence of new PIs Change in health professionals' clinical behaviour PI severity Quality of life
Zhang (2015)	0 studies; 0	Participants in any care setting, of any age or sex, without a PI were intended	Massage therapy	Placebo, Standard care or other interventions	Incidence of new PIs Severity of the new P Costs of intervention Pain Quality of life

First Author (year)	# studies in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					• • Adverse events associated with mass

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Note: ^a Joyce et al. (2018), ^a Langer and Fink (2014) and Moore and Webster (2015) measured both pressure injury prevention and treatment; PI = Pressure injury/ulcer; RCT = randomised controlled trial; c-RT = cluster randomised trial; LOS = length of stay; N/A = not applicable as no studies found; *Outcomes in italics do not have an associated Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment.

<u>Table 2</u> provides a summary of the PI treatment Cochrane Reviews. Twenty-one reviews published between 2006 and 2020 included 178 studies

[28, 31, 34, 363738394041424344454647484950515253], and 18,348 participants (range = 40 to 6963). Eleven reviews reported the GRADE assessments of the certainty of evidence for each outcome across included studies, judging them to be mostly *low* or *very low* quality [34, 38, 40414243, 45, 49, 515253]. Only three reviews reported *moderate* quality/certainty evidence [49, 52, 53]. Of those seven reviews that did not use GRADE, authors described the studies as having "lack of evidence", "poor quality evidence", "no clear evidence", "insufficient evidence", "no good evidence" and/or "increased risk of bias". Three reviews did not have eligible studies to assess [31, 47, 48].

Table 2

Characteristics of included PI Treatment Cochrane Reviews (n = 21).

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
Arora (2020)	20 (RCT); 913	Patients of any age and gender, in any care setting described as having at least one PI	Electrical stimulation (ES)	Sham/no ES (plus standard care)	 Proportion of ulcers healed Time to complete hea Adverse events

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					 PI surface area PI Severity PI Severity Rate of PI healing Depression Quality of life Consumer's perception treatment effectivenes
Akbari Sari (2006)	3 (RCT); 146	Patients of any age, and in any care setting described as having a PI	Therapeutic ultrasound Combination of ultrasound & ultraviolet light with laser	Sham ultrasound or standard treatment	 Healing rate of change ulcer area Time to complete heal Proportion of ulcers healed Costs Quality of life Pain and acceptability

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
Aziz (2015)	2 (RCT); 60	Participants of any age and in any care setting described as having a PI	Electromagnetic therapy (EMT)	Sham EMT or other (standard) treatment	 Proportion of ulcers healed Rate of change in ulce area Time to complete heal Costs Quality of life Pain Treatment acceptability
Chen (2014)	7 (RCT); 403	Participants of any age with pressure ulcers of any stage in any care setting	Phototherapy in combination with usual pressure ulcer management	Sham phototherapy (in addition to standard treatment), another type of phototherapy (in addition to standard treatment) or standard or conventional treatment alone	 • •<

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Quality of life
Dat (2012)	PI: 1 (RCT); 41 Review: 7 (RCT); 347	Participants of any age and disease state with acute or chronic wounds	Aloe vera, aloe- derived products and combination of aloe vera and other dressings	Placebo, standard wound care or other wound healing interventions (e.g. Saline gauze dressing)	Proportion of complet healed wounds Time to complete heal Change in wound size Cosmetic appearance wound healing Incidence of adverse events Incidence of infection

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
Dumville (2015)	6 (RCT); 336	Adults with a diagnosis of PI (stage II or above) managed in any care setting	Alginate dressings	Different types of alginate dressings compared with each other; alginate dressings compared with other dressing types; and alginate dressings compared with other interventions (possibly non- dressing treatments, e.g. topical treatments)	 Wound infection Adverse events Adverse events Change in wound size Complete wound healt Time to complete wou healing Proportion of ulcers healed at follow-up Quality of life Resource use Other Wound recurrence
Dumville, Stubbs (2015)	11 (RCT); 523	Adults with a diagnosis of PI (stage II or above) managed in any care setting	Hydrogel dressings	Different types of hydrogel dressings compared with each other; hydrogel dressings compared with other dressing types; and hydrogel	 Proportion of PIs heal at follow-up • • Wound infection

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
				dressings compared with other interventions (possibly non- dressing treatments e.g. topical treatments)	Adverse events Adverse events Complete wound heal Time to complete wou healing Change and rate in wound size Quality of life Resource use Cost Wound recurrence
Dumville, Webster (2015)	4 (RCT); 149	Adults with a diagnosis of PI (stage II or above) managed in any care setting	Negative pressure wound therapy (NPWT), both commercial and non-commercial treatments	Dressings, topical treatments, moist wound healing	 • •<

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Complete wound heal Time to complete wou healing Quality of life Wound infection Pain Resource use Cost Wound recurrence
^a Joyce (2018)	4 (1 controlled before-and- after study, 1 RCT, 1 c-RCT and 1 quasi- experimental cluster trial); 499	Participants of any age, in any care setting, who were at risk of developing a PI, or who had an existing PI (any stage)	Organisational interventions: provider- orientated, patient-orientated, structural and regulatory	Usual care for PI treatment Usual follow up care	 PI healing Proportion of complet healed wounds Time to complete hea Adverse events •

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Health-related quality life Patient satisfaction Staff satisfaction
Jull (2015)	PI: 1 (RCT); 40 Review: 26 (25 RCT and 1 Quasi-RCT); 3011	Participants of any age with an acute or chronic wound	Honey	Dressings or other topical agents (e.g. saline soaks)	 Time to complete wou healing Proportion of complet healed wounds Incidence of adverse advents Hospital LOS Change in wound size Incidence of infection Quality of life
^a Langer (2014)	23 (RCT); 6963	Participants of any age and sex with or without	Clearly described nutritional supplementation	Supplementary nutrition plus standard diet versus	• • Time to complete heal

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
		existing PIs, in any care setting, irrespective of primary diagnosis	(enteral or parenteral nutrition) or special diets	standard diet alone and between different types of supplementary nutrition (e.g. enteral versus parenteral)	Acceptability of supplements Side effects Costs Rate of complete heal Rate in change of size ulcer Quality of life
McInnes (2018)	19 (RCT); 3241	Participants with existing PIs (of any grade) in any setting	Various pressure- relieving support surfaces	The interventions compared with themselves, and when the interventions were compared with usual or standard care	 Time to complete hea Number of ulcers heal Rate of change in the area/volume of the ulcer(s) Healing of existing PI Participant comfort •

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Costs Durability of the devic Reliability of the devic Acceptability of the devices
McGinnis (2014)	1 (RCT); 141	Participants with existing heel PIs of any grade and in any care setting	Pressure-relieving, devices including mattresses and specific heel devices	Other pressure- relieving devices	Proportion of heel ulce healed Time to complete heal Costs Patient comfort Ease of use Quality of life Adverse events
Moore (2013)	3 (RCT); 169	Participants of any age, in any health care setting, with existing PIs	Wound cleansing	Cleansing compared with no cleansing; One cleansing solution compared with another; One	• • PI healing • •

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
				cleansing technique compared with another (e.g. irrigation, swabbing, soaking, immersion).	PI status tool
Moore (2015)	0 studies; 0	Participants of any age, in any healthcare setting, with existing PIs were intended	Repositioning	Repositioning compared with no repositioning, frequencies of repositioning and different positions for repositioning (e.g. 90-degree lateral rotation, 30-degree tilt)	 Healing rates of pressinulcers Time to complete heal Absolute or percentag change in PI area or volume over time Proportion of PIs heale Procedural pain Quality of life

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					• • Ease of repositioning • • Adverse events
Moore (2016)	0 studies; 0	Participants of any age, in any setting who are wheelchair users and have an existing PI were intended	Bed rest	No bed rest	 • •<
^a Moore, (2015)	0 studies; 0	Participants of any age, in any setting who had a PI or were at risk of developing a PI were intended	Wound care team	Individual healthcare professional	 PI incidence Resource use Hospital LOS Patient satisfaction

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					• • Morbidity
Norman (2016)	12 (RCT); 576	Adults diagnosed with a PI of category 2 or above (i.e. worse) managed in any care setting	Topical agents	Other dressings and ointments without antimicrobial properties and alternative antimicrobials	 Wound healing Adverse events Adverse events Change in wound size Pain Changes in bacterial resistance Infection resolution MRSA eradication Quality of life Resource use Costs
Vermeulen (2007)	PI: 2 (RCT); 718 Review: 3 (RCT); 847	Adults aged 18 years and over, with contaminated and infected open	Topical silver in foam and alginate dressings	Best local practice (i.e. a range of dressings) for 4	• • Healing rate • •

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
		wounds of any aetiology, and in any care setting		weeks; Alginate for 4 weeks	Days of wound infection Adverse effects Use of systemic antibiotics Pain Patient satisfaction Quality of life Costs
Walker (2017)	8 (RCT); 483	Participants of any age with a diagnosis of PI Category/Stage II or above in any care setting	Foam dressings as a treatment for patients with a PI	Various other dressings	Incidence of healed pressure ulcers Time to complete hea Adverse events Cost effectiveness

First Author (year)	# studies included in review (study type); # patients	Population	Intervention	Comparator	Outcome*
					Reduction in ulcer size Quality of life PI recurrence Pain Patient satisfaction/acceptabi
Westby (2017)	51 (RCT); 2947	Participants with a diagnosis of PI, Stage 2 and above, managed in any care setting	Dressings, topical agents	Various other dressings and topical agents (e.g. saline gauze)	 • • • • • • • • Time to complete head

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Note: ^a Joyce et al. (2018), ^a Langer and Fink (2014) and Moore and Webster (2015) measured both pressure injury prevention and treatment; PI = Pressure injury/ulcer; RCT = randomised controlled trial; c-RT = cluster randomised trial; LOS = length of stay; N/A = not applicable as no studies; *Outcomes in italics did not have an associated Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment.

3.3

Quality of Cochrane Reviews

<u>Table 3</u> presents the methodological quality assessment of the reviews using the AMSTAR 2 tool. In total, 12 reviews [30, 31, 333435, 38, 404142, 45, 47, 53], were rated as *high confidence*, 11 reviews [27, 32, 37, 39, 43, 44, 4849505152], were rated as *moderate confidence* and three reviews [28, 29, 46], were rated as *low confidence*. A single review, published over 10 years ago was rated as *critically low* [36]. For reviews that did not include any identified studies (n = 4) [31, 33, 47, 48], or were not able to conduct a meta-analysis (n = 17) [3031323334, 37, 39404142, 44454647484950], some AMSTAR 2 items could not be assessed and

were not included in the summary score. Only 23 reviews were assessed on items 8–10 and 13–14, and only 10 reviews were examined for items 11–12 and 15.

Table 3

Methodological quality assessment of the included reviews using the AMSTAR 2 tool (n = 27).

	Review	1. Question and inclusion	2. Protocol	3. Study design justification	4. Comprehensive search	5. Study selection		7. Excluded studies justification	Included	9. Ri of bi (R
	PI Preventio	on								
1	Gillespie et al. (2014)	Y	Y	N	Y	Y	Y	Y	Y	Y
2	*Joyce et al. (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y
3	*Langer & Fink (2014)	Y	Υ	N	Y	Y	Y	Y	Y	Y
4	McInnes et al. (2015)	Y	Y	N	Y	Y	Y	Y	Y	Y
5	Moore & Patton (2019)	Y	Υ	N	Y	Y	Y	Y	Y	Y
6	Moore & Webster (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y
7	*Moore et al. (2015)	Y	Y	Y	Y	Y	Y	Y	NSI	N
8	Porter- Armstrong et al. (2018)	Y	Y	N	РҮ	Y	Y	Y	Y	Y
9	Zhang et al. (2015)	Y	Y	N	Y	Y	Y	Y	NSI	N

	Review	1. Question and inclusion	2. Protocol	3. Study design justification	4. Comprehensive search	5. Study selection		7. Excluded studies justification	Included	9. Ri of bi (R
	Percentage of PI prevention Cochrane reviews meeting each criterion	100	100	33	89	100	100	100	100	10
	PI Treatment									
1	Arora et al. (2020)	Y	Y	Ν	Y	Y	Y	Y	Y	Y
2	Akbari Sari et al. (2006)	Y	РҮ	N	Y	Y	Y	N	РҮ	Y
3	Aziz & Bell-Syer (2015)	Y	РҮ	Ν	Y	Y	Y	Y	Y	Y
4	Chen et al. (2014)	Y	Y	Ν	Y	Y	Y	Y	Y	Y
5	Dat et al. (2012)	Y	Y	Ν	РҮ	Y	Υ	Y	Y	Y
6	Dumville, Keogh et al. (2015)	Y	Υ	Y	Y	Y	Y	Y	Y	Y
7	Dumville, Stubbs et al. (2015)	Y	Υ	Y	Y	Y	Y	Y	Y	Y
8	Dumville, Webster et al. (2015)	Y	Y	Y	Y	Y	Y	Y	Y	Y

	Review	1. Question and inclusion	2. Protocol	3. Study design justification	4. Comprehensive search	5. Study selection	6. Data extraction	7. Excluded studies justification	8. Included studies details	9. Ri of bi (R
9	*Joyce et al. (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y
10	Jull et al. (2015)	Y	Y	Y	РҮ	Y	Y	Y	Y	Y
11	*Langer & Fink (2014)	Y	Y	Ν	Y	Y	Y	Y	Y	Y
12	McGinnis & Stubbs (2014)	Y	Y	N	Y	Y	Y	Y	Y	Y
13	McInnes et al. (2018)	Y	Y	N	Y	Y	Y	Y	Y	Y
14	Moore & Cowman (2013)	Y	РҮ	Ν	Y	Y	Y	Y	РҮ	Y
15	Moore & Cowman (2015)	Y	Y	Ν	Y	Y	Y	Y	NSI	N:
16	*Moore et al. (2015)	Y	Y	Y	Y	Y	Y	Y	NSI	N
17	Moore et al. (2016)	Y	Y	Ν	Y	Y	Y	Y	NSI	N
18	Norman et al. (2016)	Y	Y	N	РҮ	Y	Y	Y	Y	Y
19	Vermeulen et al. (2007)	Y	РҮ	N	Y	Y	Y	Y	РҮ	Y

	Review	1. Question and inclusion	2. Protocol	3. Study design justification	4. Comprehensive search	5. Study selection		7. Excluded studies justification	Included	9. R o bi (F
20	Walker (2017)	Υ	Y	Ν	РҮ	Y	Y	Y	Y	Y
21	Westby et al. (2017)	Y	Y	Ν	РҮ	Y	Y	Y	Y	Y
	Percentage of PI treatment Cochrane reviews meeting each criterion	100	81	29	76	100	100	95	83	1(
	Percentage of the total Cochrane reviews meeting each criterion	100	85	26	78	100	100	96	86	1(

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Note: Y = yes, PY = partial yes, N = no, NSI = no studies identified, NMC = no meta-analysis conducted. Bolded items are included in AMSTAR 2 critical domains. Rating AMSTAR 2 guidance: *High* = review has 'no or one non-critical weakness'; *Moderate* = review has 'more than one non-critical weakness'; *Low* = review has 'one critical flaw with or without non-critical weaknesses'; *Critically low* = review has 'more than one critical flaw with or without non-critical weaknesses.

*These reviews examined both PI prevention and treatment.

The most prominent weakness assessed was the lack of study design justification (Item 3). While all reviews provided a clear statement that only RCTs were included, only seven reviews provided an explanation for this criterion [31, 34, 35, 40414243]. Other identified weaknesses included insufficient reporting about: funding sources (Item 10), where only 65% reviews (15 of 23 reviews that could be assessed) reported this information

[28, 30, 34, 35, 38, 40414243, 45, 4950515253] and; statistical methods used (Item 12), where 60% of reviews (six of ten reviews that could be assessed) adequately addressed this item [27, 28, 35, 38, 52, 53]. We were unable to assess the publication bias (Item 15) for most of the

reviews due to the absence of a quantitative synthesis, where for seven of ten reviews that could be assessed (70%) were found to adequately address this impact [27, 35, 38, 43, 515253]. The final identified weakness in the reviews were authors reporting a conflict of interests and funding (Item 16), with five reviews (19%) failing to address how these potential conflicts of interest were managed [32, 46, 48, 49, 52].

The Cochrane reviews also had common areas that were clear strengths with 96% including a list of excluded studies with justification (Item 7), 86% describing the studies in sufficient detail (Item 8), and 85% having an *a priori* design (Item 2). All reviews addressed items: 1 (including components of PICO – Patient, population or problem, Intervention, Comparison or control, Outcome); 5 and 6 (performing study selection and data extraction in duplicate); 9 (satisfactory technique for assessing risk of bias); 11 (appropriate pooling for meta-analysis); 13 (accounting for risk of bias in individual studies in the interpretation and discussion of results) and, finally; item 14 (having a satisfactory explanation and or discussion of heterogeneity in the results).

4

Recommendations for practice

Table 4 provides a summary of the practice recommendations based on the certainty of evidence in reviews. There were four PI prevention recommendations, which came from three of the eight PI prevention Cochrane Reviews [272829]. These recommendations focused on interventions regarding repositioning, nutrition and support surfaces. The certainty of evidence to support these recommendations was not provided for two reviews [28, 29], and was very low quality for the remaining review [27]. However, these reviews were published prior to the GRADE requirement. Overall, two of these reviews were assessed as being of *high* quality [27, 29] using AMSTAR 2 and one as being of *moderate* quality [28]. There were two specific PI treatment recommendations, which came from two of the 19 PI treatment Cochrane Reviews [28, 47]. These recommendations focused on interventions around nutrition and repositioning. The certainty of evidence to support these recommendations was not provided for both reviews. Overall, one review was rated as *high* quality [47], and the other as *low* quality [28] using AMSTAR 2.

Table 4

Pressure injury (PI) practice recommendations.

Authors	Intervention	Finding	Evidence Quality	Summary of Recommendation	Other Considerations				
Pressure Ir	Pressure Injury Prevention								
Gillespie et al., 2014	Repositioning	No significant differences in PI based on repositioning frequency or angle	Very low- quality evidence	Repositioning (" optimal frequency with which this should occur must consider the other negative effects of turning")	Consider potential negative effects on patient (e.g. sleep disruption, pain) and s (e.g. musculoskeletal injuries)				

Authors	Intervention	Finding	Evidence Quality	Summary of Recommendation	Other Considerations
^a Langer et al., 2014	Nutrition	No significant differences in PI based on nutritional interventions	Concluded evidence of variable quality	Nutrition assessment for malnourished or those at risk of malnourishment	Provide nutrition interventions if neede
McInnes et al., 2015	Support surfaces	Foam alternatives to standard foam mattresses reduce PI incidence	Concluded evidence of variable quality	Use high-specification foam mattresses for those at high risk	In a UK context, alternating-pressure mattresses may be mo cost-effective compare to alternating-pressure overlays
McInnes et al., 2015	Support surfaces	Pressure-relieving overlays on the operating table reduce post- operative PI incidence	Concluded evidence of variable quality	Consider pressure relief for high risk patients in the operating theatre	

Pressure Injury Treatment

^a Langer et al. <i>,</i> 2014	Nutrition	No significant differences based on nutritional interventions	Concluded evidence of variable quality	Nutrition assessment for malnourished or those at risk of malnourishment	Provide nutrition interventions if neede
Moore & Cowman 2015	Repositioning	No studies found	Concluded evidence of variable quality	Regular repositioning	No ^b RCT evidence but good biological plausibility

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a Same Cochrane Review including the same recommendation for prevention and treatment.

b RCT = Randomised Controlled Trial.

While many of the review authors commented on the lack of quality research that prevented making specific recommendations, they identified other practice considerations that might also assist nurses in their decision-making process. For example, four reviews [404142 , 52] related to the use of dressings for the treatment of PI, suggested considerations such as wound and dressing characteristics, patient comfort, and cost as factors that may influence practice. However, these were more generic than specific recommendations.

Of the 25 reviews included in this systematic meta-synthesis (including two that focused on both prevention and treatment interventions [28, 31]), four reviews reported finding no studies,

preventing any recommendations of interventions (including bed rest [48], wound care teams (for both prevention and treatment of PI) [31], health professional education [32], and massage [33]).

5

Recommendations for PI prevention and treatment research

Recommendations for future research for both prevention and treatment reviews were categorised into the following: further rigorous research (RCTs and c-RCTs); research based on health and public policy priorities; and high-quality methodological approaches. Our analysis determined that investigative areas of 8/9 PI prevention reviews and 14/21 PI treatment reviews required further RCT research with: objective outcomes using standardised validated tools; explicit inclusion and exclusion criteria; powered sampling; allocation concealment; blinded outcomes; intention to treat analysis; baseline comparability; follow up and completion according to the CONSORT guidelines. Future research should focus on: effects and frequency of repositioning; nutritional assessment; effectiveness of support surfaces; investigation of the patient experience and satisfaction; product acceptability; adverse events; quality of life; pressure ulcer staging; durability of devices; pain and time to heal (for PI treatment) and; related cost/economic analyses.

6

Discussion

Recommendations to inform practice and research were extracted and analysed from 27 PI prevention and treatment reviews. Only four [28, 29, 36, 46] of 27 reviews (15%) received low quality ratings, and these were generally older reviews, published between 2006 and 2015. Cochrane Review methodology is evolving regularly and thus it is not surprising that older reviews were generally less likely to be rated high. Three PI prevention reviews [272829], and two of PI treatment reviews [28, 47], were able to make specific (rather than general) recommendations for practice. While recommendations acknowledged available resources [17], and the need for clinical judgement, they were unable to provide specific clinical guidance to inform direct-care nurses due to the generalised uncertainty of evidence [54]. While Cochrane's mission is to promote evidenceinformed health decision-making via high-quality systematic reviews based on the state and quality of existing evidence [55], there is ample research evidence showing that simply creating, synthesising and disseminating new knowledge, does not change practice [20, 56]. Implementation science has evolved over the past few decades to provide numerous frameworks and theories to close this evidence-practice gap. As such, while reviews may make recommendations for practice, without active strategies to promote the uptake of new practices or stopping ineffective practices, some benefits of high-quality research and reviews may not be realised.

Authors of a survey to assess awareness of evidence published in Cochrane Reviews reported low knowledge among nurses [57], indicating a disconnect between review recommendations and consistency of practice [17]. However, this lack of engagement may also extend to Clinical Practice Guidelines, with evidence suggesting nurses prefer to consult with colleagues or rely on their intuition or beliefs [58596061], rather than evidence-based recommendations to inform clinical decision-making. Additional barriers such as: a lack of basic research education [62]; time constraints in busy clinical settings [63, 64]; and limited support from senior nurses with knowledge and experience in research [65], also contribute to nurses' negative attitude to pressure injury prevention [66, 67], resulting in low-value care [58, 68]. The updated international Clinical Practice Guidelines advocate tailored approaches to pressure injury prevention and treatment based on patient preference, available resources and best evidence [2]. Notwithstanding guidelines, many

Cochrane Review authors note the validity of individual studies analysed are at high risk of bias and therefore, of low quality. Importantly, this does not invalidate the relationship between the use of widely accepted practices to prevent and treat PI in health settings. Rather it signals the need for high quality research and ultimately greater emphasis on multi-faceted and tailored implementation strategies, that focus on methods to improve adoption, sustainment, and scale-up of interventions that bridge the gaps in clinicians' decision-making and practice [20, 596061].

Inconsistencies in trial methodologies contributed to the heterogeneity of reported outcomes [57] in included Cochrane Reviews. Assessment of the methodological quality of included reviews using AMSTAR 2 [26] revealed significant weaknesses related to lack of study design justification, insufficient reporting of funding sources and statistical methods. While some may think the AMSTAR penalises reviews that include meta-analyses; this is only the case if the meta-analysis has flaws, which should assist readers who have limited knowledge of meta-analysis methodology. Despite this, the overall quality of included Cochrane Reviews was rated as moderate to high-quality. Just as it takes time for the uptake of evidence in practice, so too it has taken time for methodological advances to be adopted by researchers. Therefore, it was not surprising that older reviews did not always use GRADE. Cochrane now promotes the move towards using GRADE criteria as per their reviewer's handbook [25]. A long-term, collective and focused effort by researchers to ensure the methodological quality of future research, and reviewers' commitment to assessing the quality and consistency of studies is therefore crucial in addressing these inconsistencies.

There is movement in this space with the Cochrane Collaboration and the Core Outcome Measures in Effectiveness Trials (COMET) initiative to promote the application of an agreed standardised set of outcomes [69]. From this, an international, multidisciplinary team of experts have come together with the aim of developing and implementing core outcome sets in dermatology to ensure trial evidence is comparable and useful for clinical decision-making [70]. Known as the Cochrane Skin Group Core Outcome Set Initiative (CSG-COUSIN), it includes the Outcomes for Pressure Ulcer Trials (OUTPUTs) group. The group recently published a protocol outlining their plan to develop core outcome sets for PI prevention so that results from PI clinical trials can be reviewed and used by researchers and clinicians [6162636465 , 71], and inform researchers in planning future trials.

Ideally, a focussed strategy to map the state of evidence is needed to identify the gaps, generate and implement high-quality evidence, and identify and de-implement low-value care [58, 68]. This strategy includes adequately powered head-to-head trials to define which PI prevention and treatment strategies are most clinically and cost-effective in an era of increasingly constrained budgets [72]. Finally, the impact on patients who may be subjected to the discomfort and inconvenience of different PI strategies, and time-constrained nurses should be evaluated using appropriate self-report measures.

6.1

Limitations

Following a process previously undertaken by Ubbink and colleagues [22], this meta-synthesis only included Cochrane Reviews of trials. The inclusion of non-Cochrane reviews –i.e., reviews with both randomised and non-randomised methodologies - may have provided additional evidence on the beneficial effects of various treatments [26, 73, 74]. However, arguably the inclusion of non-randomised trials may have led to an over-estimation of treatment effects and contributed to a waste of limited research funding [54]. While Cochrane Reviews generally have a robust patient focus and are increasingly undertaking qualitative syntheses that address the patient experience

[55], they favour replicable quantitative research designs as RCTs, c-RCTS or where appropriate, quasi-RCTs, to map and analyse the cause and effect of evidence.

7

Conclusion

While this meta-analysis provides good, albeit somewhat generic advice for researchers, evidencebased clinical guidance on the prevention and treatment of PI based solely on systematic reviews is limited because of the lack of powered trials. Despite 20 years of Cochrane Reviews, the number of adequately powered, robust and independently funded trials remain a persistent problem due to the lack of clear and reliable evidence. As such, an evidence vacuum contributes to wound care recommendations and guidelines based on clinical opinion that perpetuates low-value care. There is an urgent need for well-designed trials in PI prevention and treatment to overcome clinical uncertainty for nurses and ensure quality outcomes for health consumers. Given the cost of wounds to the health care system, this should be a government funding priority.

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Declaration of competing interest

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