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Prevention and Management of Pressure Ulcers.

This document is a compilation of 2 reports related to the prevention and treatment of pressure ulcers, which were published individually in July 2009. Each report retains its original pagination, table of contents, and reference list. The compilation contains the following titles:

1. Pressure Ulcer Prevention: an evidence-based Analysis
2. Management of Chronic Pressure Ulcers: and evidence-based analysis

July 2009

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

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Pressure Ulcer Prevention

An Evidence-Based Analysis

April 2009

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

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About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practising medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

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Executive Summary

In April 2008, the Medical Advisory Secretariat began an evidence-based review of the literature concerning pressure ulcers.

Please visit the Medical Advisory Secretariat Web site, http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html to review these titles that are currently available within the Pressure Ulcers series.

1. *Pressure ulcer prevention: an evidence based analysis*
2. *The cost-effectiveness of prevention strategies for pressure ulcers in long-term care homes in Ontario: projections of the Ontario Pressure Ulcer Model (field evaluation)*
3. *Management of chronic pressure ulcers: an evidence-based analysis (anticipated pubicstion date - mid-2009)*

Purpose

A pressure ulcer, also known as a pressure sore, decubitus ulcer, or bedsore, is defined as a localized injury to the skin/and or underlying tissue occurring most often over a bony prominence and caused by pressure, shear, or friction, alone or in combination. (1) Those at risk for developing pressure ulcers include the elderly and critically ill as well as persons with neurological impairments and those who suffer conditions associated with immobility. Pressure ulcers are graded or staged with a 4-point classification system denoting severity. Stage I represents the beginnings of a pressure ulcer and stage IV, the severest grade, consists of full thickness tissue loss with exposed bone, tendon, and or muscle. (1)

In a 2004 survey of Canadian health care settings, Woodbury and Houghton (2) estimated that the prevalence of pressure ulcers at a stage 1 or greater in Ontario ranged between 13.1% and 53% with nonacute health care settings having the highest prevalence rate (Table 1).

Executive Summary Table 1: Prevalence of Pressure Ulcers*

Setting	Canadian Prevalence, % (95% CI)	Ontario Prevalence, Range % (n)
Acute care	25 (23.8–26.3)	23.9–29.7 (3418)
Nonacute care†	30 (29.3–31.4)	30.0–53.3 (1165)
Community care	15 (13.4–16.8)	13.2 (91)
Mixed health care‡	22 (20.9–23.4)	13.1–25.7 (3100)
All health care settings	26 (25.2–26.8)	13.1–53.3 (7774)

*CI indicates confidence interval.

†Nonacute care included sub-acute care, chronic care, complex continuing care, long-term care, and nursing home care.
‡Mixed health care includes a mixture of acute, nonacute, and/or community care health care delivery settings.

Pressure ulcers have a considerable economic impact on health care systems. In Australia, the cost of treating a single stage IV ulcer has been estimated to be greater than $61,000 (AUD) (approximately $54,000 CDN), (3) while in the United Kingdom the total cost of pressure ulcers has been estimated at £1.4–£2.1 billion annually or 4% of the National Health Service expenditure. (4)

Because of the high physical and economic burden of pressure ulcers, this review was undertaken to determine which interventions are effective at preventing the development of pressure ulcers in an at-risk population.

Review Strategy

The main objective of this systematic review is to determine the effectiveness of pressure ulcer preventive interventions including Risk Assessment, Distribution Devices, Nutritional Supplementation, Repositioning, and Incontinence Management.

A comprehensive literature search was completed for each of the above 5 preventive interventions. The electronic databases searched included MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature. As well, the bibliographic references of selected studies were searched. All studies meeting explicit inclusion and exclusion criteria for each systematic review section were retained and the quality of the body of evidence was determined using the Grading of Recommendation Assessment, Development, and Evaluation (GRADE) system. (5) Where appropriate, a meta-analysis was undertaken to determine the overall estimate of effect of the preventive intervention under review.

Summary of Findings

Risk Assessment

There is very low quality evidence to support the hypothesis that allocating the type of pressure-relieving equipment according to the person's level of pressure ulcer risk statistically decreases the incidence of pressure ulcer development. Similarly, there is very low quality evidence to support the hypothesis that incorporating a risk assessment into nursing practice increases the number of preventative measures used per person and that these interventions are initiated earlier in the care continuum.

Pressure Redistribution Devices

There is moderate quality evidence that the use of an alternative foam mattress produces a relative risk reduction (RRR) of 69% in the incidence of pressure ulcers compared with a standard hospital mattress. The evidence does not support the superiority of one particular type of alternative foam mattress.

There is very low quality evidence that the use of an alternating pressure mattress is associated with an RRR of 71% in the incidence of grade 1 or 2 pressure ulcers. Similarly, there is low quality evidence that the use of an alternating pressure mattress is associated with an RRR of 68% in the incidence of deteriorating skin changes.

There is moderate quality evidence that there is a statistically nonsignificant difference in the incidence of grade 2 pressure ulcers between persons using an alternating pressure mattress and those using an alternating pressure overlay.

There is moderate quality evidence that the use of an Australian sheepskin produces an RRR of 58% in the incidence of pressure ulcers grade 1 or greater. There is also evidence that sheepskins are uncomfortable to use. The Pressure Ulcer Advisory Panel noted that, in general, sheepskins are not a useful preventive intervention because they bunch up in a patient's bed and may contribute to wound infection if not properly cleaned, and this reduces their acceptability as a preventive intervention.

There is very low quality evidence that the use of a Micropulse System alternating pressure mattress used intra operatively and postoperatively produces an RRR of 79% in the incidence of pressure ulcers compared with a gel-pad used intraoperatively and a standard hospital mattress used postoperatively (standard care). It is unclear if this effect is due to the use of the alternating pressure mattress intraoperatively or postoperatively or if indeed it must be used in both patient care areas.

There is low quality evidence that the use of a vesico-elastic polymer pad (gel pad) on the operating table for surgeries of at least 90 minutes' duration produces a statistically significant RRR of 47% in the incidence of pressure ulcers grade 1 or greater compared with a standard operating table foam mattress.

There is low quality evidence that the use of an air suspension bed in the intensive care unit (ICU) for stays of at least 3 days produces a statistically significant RRR of 76% in the incidence of pressure ulcers compared with a standard ICU bed.

There is very low quality evidence that the use of an alternating pressure mattress does not statistically reduce the incidence of pressure ulcers compared with an alternative foam mattress.

Nutritional Supplementation

There is very low quality evidence supporting an RRR of 15% in the incidence of pressure ulcers when nutritional supplementation is added to a standard hospital diet.

Repositioning

There is low quality evidence supporting the superiority of a 4-hourly turning schedule with a vesico-elastic polyurethane foam mattress compared with a 2-hourly or 3-hourly turning schedule and a standard foam mattress to reduce the incidence of grade 1 or 2 pressure ulcers.

Incontinence Management

There is very low quality evidence supporting the benefit of a structured skin care protocol to reduce the incidence of grade 1 or 2 pressure ulcers in persons with urinary and/or fecal incontinence.

There is low quality evidence supporting the benefit of a pH-balanced cleanser compared with soap and water to reduce the incidence of grade 1 or 2 pressure ulcers in persons with urinary and fecal incontinence.

Conclusions

There is moderate quality evidence that an alternative foam mattress is effective in preventing the development of pressure ulcers compared with a standard hospital foam mattress.

However, overall there remains a paucity of moderate or higher quality evidence in the literature to support many of the preventive interventions. Until better quality evidence is available, pressure ulcer preventive care must be guided by expert opinion for those interventions where low or very low quality evidence supports the effectiveness of such interventions.

Abbreviations

CI	Confidence interval
GRADE	Grading of Recommendation Assessment, Development, and Evaluation
ICU	Intensive care unit
MAS	Medical Advisory Secretariat
NPUAP	National Pressure Ulcer Advisory Panel
RAS	Risk assessment scale
RCT	Randomized controlled trial
RNAO	Registered Nurses Association of Ontario
RR	Relative risk
RRR	Relative risk reduction

Systematic Review

Overall Objective

The main objective of this systematic review is to determine the effectiveness of pressure ulcer preventive interventions. The following preventive interventions are reviewed in this report:

1. Risk Assessment
2. Distribution Devices
3. Nutritional Supplements
4. Repositioning
5. Incontinence Management

Methods

A comprehensive literature search was completed for each of the above 5 preventive interventions. The electronic databases searched included MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, the Cochrane Library, and the Cumulative Index to Nursing and Allied Health Literature. In addition, the bibliographic references of selected studies were searched. All search strategies are presented in full in Appendices 1 through 5. After a review of the title and abstracts, relevant studies were obtained and the full report evaluated. All studies meeting explicit inclusion and exclusion criteria for each preventive intervention systematic review section were retained and the quality of the body of evidence, defined as 1 or more relevant studies, was determined using GRADE. (5) Where appropriate, a meta-analysis was undertaken to determine the overall estimate of effect of the preventive intervention under review.

Assessment of Quality of Evidence

The quality of the body of evidence was examined according to the GRADE Working Group criteria. (5) Quality refers to criteria such as the adequacy of allocation concealment, blinding, and losses to follow-up and completion of an intention to treat analysis. Consistency refers to the similarity of effect estimates across studies. If there is important unexplained inconsistency in the results, confidence in the estimate of effect for that outcome decreases. Differences in the direction of effect, the size of the effect, and the significance of the differences guide the decision about whether important inconsistency exists. Directness refers to the extent to which the interventions, population, and outcome measures are similar to those of interest.

The GRADE Working Group used the following definitions in grading the quality of the evidence:

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Results of Evidence-Based Analyses

The following results of the evidence-based analysis for each preventive intervention will be reported:

- results of literature search
- characteristics of included studies
- quality assessment of individual studies
- results including meta-analysis (where applicable)
- GRADE evidence profile
- summary of results

Risk Assessment Scales

Research Question

The literature was searched to determine the effect of using a pressure ulcer risk assessment tool on the incidence of pressure ulcers. The search strategy is presented in Appendix 1.

Methods

Inclusion Criteria

- systematic reviews (with/without meta-analysis), randomized controlled trials (RCTs), and nonrandomized controlled clinical trials
- studies involving a population at risk for developing pressure ulcers
- studies evaluating the use of any risk assessment scale (RAS) for pressure ulcer development compared with not using an RAS or with clinical judgment
- studies reporting the incidence of new pressure ulcer measured as the number (proportion) of persons developing a new pressure ulcer
- studies reporting the stage of pressure ulcer or in which the stage can be inferred from the description of the ulcer

Exclusion Criteria

- studies determining the validity and reliability properties of an RAS
- studies reporting only the number of pressure ulcers (number of wounds) as an outcome measure

Primary Outcome Measure

The primary outcome measure was the incidence of pressure ulcers measured as the number (proportion) of persons developing a new pressure ulcer.

Results of Literature Search

Two systematic reviews (6;7) and 3 non-RCT studies (8-10) were obtained from the literature search strategy (Table 1). The objective of both systematic reviews was to determine the effectiveness of using a pressure ulcer RAS to reduce the incidence of pressure sores. McGough (6) searched the literature up to June 1997, and Pancorbo-Hidalgo et al. (7) searched up to 2003. McGough (6) limited the literature search to RCT designs and reported that there were no RCTs found that determined the effectiveness of RASs on the incidence of pressure ulcers. Pancorbo-Hidalgo et al. (7) did not limit their search to a specific study design and found 3 non-RCTs. The Medical Advisory Secretariat completed an updated literature search from 2003 to February 2008 and did not find additional studies to add to the body of evidence reported by Pancorbo-Hidalgo et al. (7) What follows is a report and evaluation of the 3 non-RCT studies described in the systematic review by Pancorbo-Hidalgo et al. (7)

Table 1: Quality of Evidence of Included Studies – Risk Assessment*

Study Design	Level of Evidence†	Number of Eligible Studies	MAS Update to Systematic Review
Systematic reviews of RCT	1	2	0
or			
Large RCT	1		
Large RCT unpublished but reported to an international scientific meeting	1(g)		0
Small RCT	2		0
Small RCT unpublished but reported to an international scientific meeting	2(g)		0
Non-RCT with contemporaneous controls	3a	3	0
Non-RCT with historical controls	3b		0
Non-RCT presented at international conference	3(g)		0
Surveillance (database or register)	4a		0
Case series (multisite)	4b		0
Case series (single site)	4c		0
Retrospective review, modeling	4d		0
Case series presented at international conference	4(g)		0

*MAS indicates Medical Advisory Secretariat; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meeting. (11)

Characteristics of Included Studies

Table 2 reports the characteristics of the studies included in this systematic review. Gunningberg et al. (9) used a prospective controlled study design (contemporaneous controls), whereas the studies completed by both Hodge et al. (10) and Bale (8) used a before-and-after study design. The mean ages in this body of evidence ranged from 60 to 80 years. All studies used different RASs as well as different pressure ulcer classification systems to measure the study outcome. The characteristics of the RASs used are reported in Table 3.

Table 2: Characteristics of Included Studies – Risk Assessment*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Gunningberg et al.,1999 Prospective controlled design Consecutive admissions	124	Persons with hip fractures Mean age: 82 y	n = 58 Daily risk assessment score (RAS) completed on all participants. All patients with a Modified Norton Scale of < 21 (considered high risk for developing a pressure ulcer) were identified with a risk alarm sticker stating "Pressure ulcer prevention; active nursing care"	n = 66 Participants in this group received ordinary pressure prevention (e.g., cushions, turning) and no RAS was competed	Discharge and 2 weeks post operatively	Number of persons with new pressure ulcers Surrey Pressure Ulcer Classification system
Bale, 1995 Before-and-afterstudy design Consecutive admissions	223	Palliative care/ hospice setting Mean age: 67 y (*SD ±12)	n = 104 (phase 2) Participants in this group received a pressure support system allocated according to the Adapted Norton RAS where persons with a score of: i) ≤ 10 received a hollow core fiber overlay ii) 11–15 received an alternating air mattress overlay iii) ≥ 16 received an alternating pressure mattress This group also received ordinary pressure prevention (cushions, regular repositioning)	n = 161 (phase 1) Participants in this group received a hollow core fiber overlay or at the request of the patient continued using the same overlay/mattress used before admission. If they were considered by the nurse to be at high risk, a more sophisticated alternating pressure mattress replacement was allocated. Allocation was based on the opinion of the attending nurse and not on the results of an RAS. This group also received ordinary pressure prevention (cushions, regular repositioning).	Risk assessment was done every 48 hours for each group until participant died or was discharged Mean follow-up: 12 days	Number of persons with new pressure ulcers Torrence Pressure Ulcer Classification system

(continued)

Table 2: Characteristics of Included Studies – Risk Assessment (continued)*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Hodge et al., 1990 Before-and-after study design Consecutive enrollment	181	Neuro-surgery, general medicine, orthopedic, and oncology units Median age range: 60–69 y	n = 89 (phase 2) Norton Risk Assessment Scale used Staff received 3 weeks of training and education on the use of the Norton Scale before using it	n = 92 (phase 1) Standard care No RAS used	10 days	Number of preventive interventions per patient Number of persons with worsening skin condition Shea Classification System

*SD indicates standard deviation

Table 3: Characteristics of the Risk Assessment Scales

Study	Risk Assessment Scale	Scale Variables
Gunningberg et al., 1999	Modified Norton	Mental condition Physical activity Mobility Food intake Fluid intake Incontinence General physical condition
Bale, 1995	Adapted Norton	General physical condition Mobility Nutritional status Pain continence Special risk factors
Hodge et al., 1990	Norton	Physical condition Mental condition Activity Mobility Incontinence

Quality Assessment of Included Studies

The quality assessment for each of the 3 studies included in this review is reported in Table 4. Gunningberg et al. (9) used a prospective controlled study design with consecutive sampling and an alternate allocation scheme to assign participants to either the treatment or control interventions. Important study limitations included that the outcome measure of new pressure ulcers was not assessed independently of the treatment exposure status and that there was greater loss to follow-up in the control group compared with the treatment group at both discharge (41% vs. 8%, respectively) and 2 weeks postoperatively (53% vs. 26%, respectively). This latter limitation could possibly account for the lack of a statistically significant difference in the incidence of pressure ulcers between treatment groups.

Bale (8) used a before-and-after study design with consecutive enrollment and therefore the participants allocated to phase 1 (control) were different than those allocated to phase 2 (treatment). Major methodological limitations included the use of an adaptive version of the Norton RAS that had not been

validated, and, like Gunningberg et al., (9) an outcome measure that was not assessed independently of the treatment exposure status. Interestingly, however, the patients in phase 2 (treatment) had higher risk assessment scores, indicating an increased risk for developing a pressure ulcer, than participants in phase 1 (control). It is likely this would have biased the results in favor of fewer pressure ulcers in the control group; however, instead there were statistically significantly more new pressure ulcers in the control group compared with the treatment group (22.4% vs. 2.5%).

Hodge et al. (10) also used a before-and-after study design with consecutive enrollment. Therefore, there were different participants allocated between phase 1 (control) and phase 2 (treatment). Hodge et al. did not report the incidence of pressure ulcers as a primary outcome but instead the purpose of the study was to investigate the effect on nursing practice and patients' skin condition of using an RAS compared with not using an RAS. This was a well-conducted study with few if any methodological limitations biasing the study results. Unlike Gunningberg et al. (9) and Bale, (8) Hodge et al. (10) did assess the outcome measure independently of the treatment exposure status. In phase 1 the nurses caring for the study participants were unaware of the purpose of the study. In phase 2, the Norton RAS was done independently from the collection of the outcome measure (number of treatment interventions per patient). Finally, a standardized checklist of nursing interventions was used for data collection.

Table 4: Individual Study Quality Assessment – Risk Assessment*

Study	Inclusion/ Exclusion Criteria Stated	Consecutive Sampling Used	Are Baseline Characteristics in Groups Similar?	Is Treatment Valid and Reliable?	Is a Reliable and Valid Outcome Measure Used?	Is Outcome Measure Done Independently of Exposure Status?	Is Duration of Follow-Up Adequate?	Loss to Follow-Up, %
Gunningberg et al., 1999	✓	✓ Floor 1 was allocated to treatment and floor 2 to control. Each floor was sent every fourth patient with a hip fracture as a study participant.	✓ There were no significant differences in age or gender between groups.	✓ Modified Norton RAS	✓	x	✓	x Total study population: 26% loss to follow-up at discharge 40% loss to follow-up at 2 weeks postop By group: loss to follow-up at 2 weeks 53% in control group and 26% in treatment group Loss to follow-up at discharge 8% in treatment group and 41% in control group

Table 4: Individual Study Quality Assessment – Risk Assessment (continued)*

Study	Inclusion/ Exclusion Criteria Stated	Consecutive Sampling Used	Are Baseline Characteristics in Groups Similar?	Is Treatment Valid and Reliable?	Is a Reliable and Valid Outcome Measure Used?	Is Outcome Measure Done Independently of Exposure Status?	Is Duration of Follow-Up Adequate?	Loss to Follow-Up, %
Bale, 1995	✓	✓	✓ Demographic details of the patients did not differ between the 2 phases. Both groups were well matched for age, total days studied, and reason for terminating the study. There was a higher percentage of men included in phase 2 than in phase 1. Women were noted to have a 2-fold chance of developing pressure sores. Patients in phase 2 had higher risk assessment scores (increased risk of pressure ulcers) than in phase 1. This should have biased results in favor of less pressure ulcers in the control group.	x The RAS had not been formally evaluated in its modified form.	✓	x	✓	0

Table 4: Individual Study Quality Assessment – Risk Assessment (continued)*

Study	Inclusion/ Exclusion Criteria Stated	Consecutive Sampling Used	Are Baseline Characteristics in Groups Similar?	Is Treatment Valid and Reliable?	Is a Reliable and Valid Outcome Measure Used?	Is Outcome Measure Done Independently of Exposure Status?	Is Duration of Follow-Up Adequate?	Loss to Follow-Up, %
Hodge et al., 1990	✓	✓	✓ Demographic data were similar between groups. The experimental group had higher Norton Scale scores (13.53) than did the control group (12.18), indicating that the experimental group had better initial skin condition.	✓	✓	✓ Outcome measure independent of treatment exposure. A standardized checklist of nursing interventions was used as a reference for recording outcome measure of occurrence of interventions. In phase 1 the nature of the research was not known to the nursing careers. Norton ratings were done independent of data collection of the outcome measure in phase 2.	✓	0

*RAS indicates risk assessment scale.

Results

The main findings from each of these 3 studies are reported in Table 5. The individual study results were not amenable to meta-analysis because of the different study designs and outcome measures used between studies. Gunningberg et al. (9) did not find a significant difference between the treatment and control groups in the incidence of pressure ulcers. The high rate of attrition from the control group in the Gunningberg et al. (9) study may have contributed to the negative results of that study.

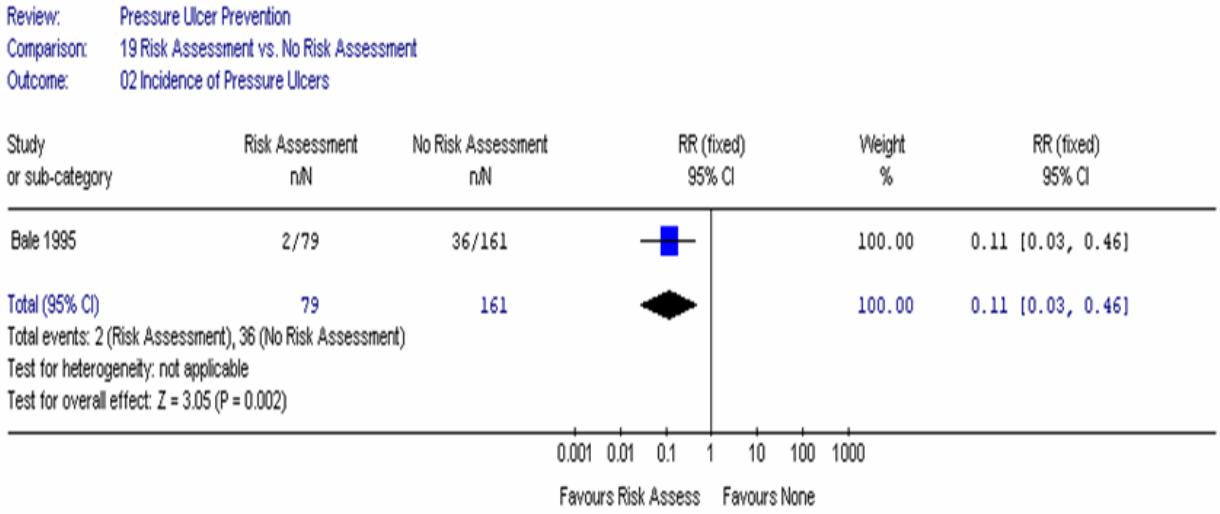
Bale (8) reported that using an RAS significantly reduced the incidence of pressure ulcers compared with not using one (22.4% vs. 2.5%, control vs. treatment, $P < .0001$). The significant result from Bale (8) may be due to the tailoring of the type of pressure-relieving preventive intervention to the person's risk level. Figure 1 presents the results reported by Bale.

Hodge et al. (10) reported that there was on average a significantly higher number of preventative interventions used per person ($P < .0001$) when an RAS was incorporated into nursing practice compared with not doing so. Furthermore, preventive interventions were used earlier in the hospital stay for persons receiving an RAS compared with the group that did not have an RAS completed ($P < .002$). However, there was no difference reported in the incidence of pressure ulcers between treatment groups.

Table 5: Study Results – Risk Assessment

Study	Treatment	Control	Conclusions
Gunningberg et al., 1999	Incidence of pressure ulcers: At discharge 20/51 (39.2%) At 2 weeks postop. 15/43 (34.9%)	Incidence of pressure ulcers: At discharge 17/48 (35.4%) At 2 weeks postop 16/41 (39%)	Incidence of pressure ulcers at discharge is not significantly different between groups. The intervention does not reduce the risk of developing pressure ulcers
Bale, 1995	Incidence of pressure ulcers: 2/79 (2.5%)	Incidence of pressure ulcers: 36/161 (22.4%)	The intervention significantly reduces the incidence of pressure ulcers ($P < .0001$) (RR, 0.11; 95% CI, 0.03–0.46).
Hodge et al.,1990	Average of 18.96 prevention interventions/patient	Average of 10.75 prevention interventions/patient	There was a significant difference in preventative interventions/patient between groups ($P < .001$). Interventions were used earlier for treatment group vs. control group (on day 1, 61% vs. 50%, $P < .002$). No significant difference in the incidence of pressure ulcers between treatment and control groups Less deterioration in elbow skin condition in treatment vs. control ($P < .05$)

CI indicates confidence interval; RR, relative risk.



CI indicates confidence interval; RR, relative risk.

Figure 1: Risk Assessment Versus No Risk Assessment

Grade of Evidence

The overall quality of evidence using the GRADE assessment method is reported by outcome measure in Tables 6 and 7. Because of the serious limitations in attrition rate in the study by Gunningberg et al., (9) only the Bale (8) study was considered as the body of evidence for the outcome of incidence of pressure ulcers. The quality of evidence is very low, indicating an estimate of effect that is uncertain. The study by Hodge et al. (10) formed the body of evidence for the outcome "number of preventive interventions used per person." The quality of evidence is also very low for this outcome, indicating that the estimate of effect is very uncertain.

Table 6: GRADE Evidence Profile – Risk Assessment Versus No Risk Assessment Outcome: Incidence of Pressure Ulcers*

Study	Design	Quality†	Consistency	Directness	Other Modifying Factors‡	No. of Patients			
						RAS	No RAS	RR (95% CI)	Quality/ Importance
Bale, 1995	Observa-tional	Some serious limitations	N/A	No uncertainty about directness		161	104	0.11 (0.03–0.46)	**Very Low**/ Critical
	LOW	**VERY LOW**	**VERY LOW**	**VERY LOW**	**VERY LOW**				

*CI indicates confidence interval; N/A, not applicable; RAS, risk assessment scale; RR, relative risk.
†Version of Norton Scale used in study was not validated, †outcome measure not obtained independently of treatment exposure (−1).
‡Possible confounding should bias in favor of control but it did not (+1).
Sparse data (−1).

Table 7: GRADE Evidence Profile – Risk Assessment Versus No Risk Assessment Outcome: Number of Preventive Interventions Used*

Study	Design	Quality	Consistency	Direct-ness†	Other Modifying Factors†	No. of Patients			
						RAS	No RAS	Mean No. of Interventions per Patient	Quality/ Importance
Hodge et al., 1990	Observ-ational	None	N/A	No uncertainty about directness		92	89	10.75 (control) vs. 18.96 (treatment)	**Very Low**/ Important
	LOW	**LOW**	**LOW**	**LOW**	**VERY LOW**				

*N/A indicates not applicable; RAS, risk assessment scale.
†Sparse data.

Summary of Results

There is very low quality evidence to support the hypothesis that allocating the type of pressure-relieving equipment according to the person's level of pressure ulcer risk statistically decreases the incidence of pressure ulcers. Similarly, there is very low quality evidence to support the hypothesis that incorporating an RAS into nursing practice increases the number of preventative measures used per person and that these interventions are initiated earlier in the care continuum. However, completing a risk assessment did not affect the incidence of pressure ulcers.

Pressure Redistribution Devices

Research Question

The literature was searched to determine the effect of using various pressure redistribution devices including mattresses, overlays, and sheepskins on the incidence of pressure ulcers in a population at risk for developing pressure ulcers. The search strategy is presented in Appendix 2.

Methods

Inclusion Criteria

- systematic reviews (with/without meta-analysis) or RCTs
- studies involving a population at risk for developing pressure ulcers
- studies evaluating the use of static or dynamic mattresses and/or mattress overlays compared with standard foam and/or other static of dynamic distribution devices
- studies evaluating the use of sheepskins compared with a standard foam mattress or other static or dynamic distribution devices
- studies reporting the incidence of pressure ulcers measured as the number (proportion) of persons developing a new pressure ulcer
- studies reporting the stage of pressure ulcer or in which the stage can be inferred from the description of the ulcer

Types of Devices

For the purpose of this review, dynamic pressure redistribution devices (also called high tech) were defined as alternating devices where cells in the mattress surface alternately inflate and deflate. Static devices (also called low tech) were defined as conforming surfaces that distribute the body weight over a large area.

Studies evaluating any of the following distribution devices were included in this review:

High-Tech Surfaces (Dynamic Surfaces)

- alternating pressure
- low air loss beds
- air fluidized beds
- turning beds/frames (profiling beds)

Low-Tech Surfaces (Static Surfaces)

- alternative foam (e.g., convoluted/cubed, high density foam)
- gel-filled
- fiber-filled
- water-filled
- air-filled
- bead-filled
- silicore-filled

- sheepskins

Exclusion Criteria

- studies in which the type of redistribution support surface could not be determined

Primary Outcome Measure

The primary outcome measure was the incidence of pressure ulcers measured as the number (proportion) of participants developing a new pressure ulcer.

Results of Literature Search

One systematic review (12) and 1 systematic review with meta-analysis (13) were each obtained from the literature search strategy (Table 8). The objective of both systematic reviews was to determine the effectiveness of pressure redistribution surfaces on the incidence of pressure ulcers. Cullum et al. (13) searched the medical literature up to and including January 2004, limiting the search to RCTs comparing the effectiveness of beds, mattresses, and cushions on the incidence of pressure ulcers. A total of 41 RCTs were retrieved from the literature. Reddy et al. (12) searched the medical literature up to and including June 2006, also limiting the search to RCTs with clinically relevant outcome measures. An additional 5 RCTs to those retrieved by Cullum et al. (13) were obtained. Cullum et al. (13) completed a meta-analysis of the evidence whereas Reddy et al. (12) did not. Table 9 reports the results of the meta-analyses completed by Cullum et al. (13)

We completed an updated literature search to that completed by Reddy et al. (12) and Cullum et al., (13) up to and including October 2007. Five new RCTs (2 large (14;15) and 3 small (16-18)) were obtained. We report in this review 3 statistically significant meta-analyses from the Cullum et al. (13) review as well as 3 updated meta-analyses to those completed by Cullum et al. (13)(Table 9. In addition to these 6, we report 3 new comparisons not reported by Cullum et al. (13) (Table 10). In total, the 9 comparisons reported in this review include:

Acute Care Setting

Comparison 1: Alternative Foam Versus Standard Foam
Comparison 2: Alternative Foam Versus Alternative Foam
Comparison 3: Alternating Pressure Mattress or Overlay Versus Standard Foam Mattress
Comparison 4: Alternating Pressure Mattress Versus Alternating Pressure Overlay
Comparison 5: Australian Sheepskin Versus Standard Treatment
Comparison 6: Alternating Pressure Mattress (Micropulse System) Versus Standard Care

Peri-Operative and Operative Setting

Comparison 7: Dry Vesico-Elastic Polymer Pad Versus Standard Operating Table Foam Mattress
Comparison 8: Air Suspension Bed Versus Standard Intensive Care Unit (ICU) Bed

Intensive Care Unit Setting

Comparison 9: Alternating Pressure Mattress Versus Alternative Foam

Table 8: Quality of Evidence of Included Studies – Pressure Redistribution Devices*

Study Design	Level of Evidence	Number of Eligible Studies	MAS Update to Systematic Review
Systematic reviews of RCT or	1	2 systematic reviews	
Large RCT,			2
Large RCT unpublished but reported to an international scientific meeting	1(g)†		0
Small RCT	2		3
Small RCT unpublished but reported to an international scientific meeting	2(g)		0
Non-RCT with contemporaneous controls	3a		0
Non-RCT with historical controls	3b		
Non-RCT presented at international conference	3(g)		
Surveillance (database or register)	4a		
Case series (multisite)	4b		
Case series (single site)	4c		
Retrospective review, modeling	4d		
Case series presented at international conference	4(g)		

*MAS indicates Medical Advisory Secretariat; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meeting. (11)

Table 9: Results of Meta-Analyses Completed by Cullum et al.*

Comparison	No. of Studies	No. of Participants	Outcome	Results RR (95% CI)	MAS Update to Analysis
Constant low pressure supports vs. standard foam mattresses	7	1,166	Incidence of pressure ulcers	Studies too heterogenous Meta-analysis not done	No
Alternative foam mattress vs. standard foam mattress	5	2,016	Incidence of pressure ulcers	0.40 (0.21–0.74)	Yes 1 new study Berthe et al., 2007
Comparisons between alternative foam supports	3	629	Incidence of pressure ulcers	Meta-analysis not done	Yes 1 new study Gray and Smith, 2000
Comparisons between CLP supports	6	592	Incidence of pressure ulcers	Meta-analysis not done	No
AP vs. standard foam mattress	1	327	Incidence of pressure ulcers	0.32 (0.14–0.74)	Yes 1 new study Sanada et al., 2003

(continued)

Table 9: Results of Meta-Analyses Completed by Cullum et al. (continued)*

Comparison	No. of Studies	No. of Participants	Outcome	Results RR (95% CI)	MAS Update to Analysis
AP vs. constant low pressure	8	1,019	Incidence of pressure ulcers	0.82 (0.57–1.19)	No
i) AP devices vs. silicore or foam overlay	4	331	Incidence of pressure ulcers	0.91 (0.71–1.17)	No
ii) AP devices vs. water or static air mattress	3	458	Incidence of pressure ulcers	1.26 (0.60–2.61)	No
AP and CLP in ICU/post-ICU (factorial design)	6	936	Incidence of pressure ulcers	Not statistically significant	No
Comparison between AP devices					
i) Airwave. vs. large cell ripple	1	62	Incidence of pressure ulcers (all comparisons)	0.42 (0.17–1.04)	No
ii) Airwave vs. Pegasus Carewave	1	75		Not estimable	No
iii) Trinova vs. control	1	44		0.20 (0.01–3.94)	No
Air suspension bed vs. standard bed	1	98	Incidence of pressure ulcers	0.24 (0.11–0.53)	No
Air-fluidized therapy vs. dry flotation	1	12	Rate of wound breakdown	1.00 (0.20–4.95)	No
Kinetic treatment table vs. standard	1	2	Incidence of pressure ulcers	Meta-analysis not done	No
Operating table gel overlay vs. no overlay	1	416	Incidence of pressure ulcers	0.53 (0.33–0.85)	No
AP mattress (Micropulse System) / overlay vs. standard care intraoperatively and postoperatively	2	368	Incidence of pressure ulcers	0.21 (0.06–0.70)	No
Seat cushions	3	441	Incidence of pressure ulcers	Meta-analysis not done	Not done

*AP indicates alternating pressure; CI, confidence interval; CLP, constant low pressure; ICU, intensive care unit; MAS, Medical Advisory Secretariat; RR, relative risk.
Source: Cullum et al. (13)

Table 10: New Meta-Analyses Not Found in Cullum et al.

Comparison	No. of Studies	No. of Participants	Results RR (95% CI)
Alternating pressure mattress vs. alternating pressure overlay	1	1,972	0.96 (0.74–1.24)
Sheepskin vs. standard treatment	2	738	0.42 (0.22–0.81)
Alternate pressure vs. alternate foam	2	151	0.89 (0.54–1.47)

Comparison 1: Alternative Foam Mattress Versus Standard Foam Mattress

Characteristics of Included Studies

Six studies compared alternative foam mattresses with standard foam mattresses. (14;19-23) The study characteristics are reported in Table 11. All studies included patients admitted to an acute care setting. A variety of alternative foam mattresses were used in the treatment group. Standard mattresses in the control group were described by all included studies other than Berthe et al. (14) The author was contacted for this information but a response was not received. The follow-up study period in these 6 studies ranged from 10 days to 7 months. Four studies used an explicit pressure ulcer grading system (Table 12): 2 used different versions of the Torrence scale, the third used a modification of the Shea Scale, and the fourth used a grading system developed at the Dutch consensus meeting from 1985. Variations in the scales included grade 1 ranging from persistent erythema to blanching erythema and grade 2 from blister formation and nonblanching erythema. Collier (19) reported on the outcome of deterioration in skin condition, and Gray and Campbell (20) reported the incidence of pressure ulcers but did not report using an explicit grading system.

Of note, the study by Russell et al. (22) used a vesico-elastic and polyurethane (CONFOR-Med Mattress) foam mattress in the treatment group and 5 different types of mattresses as the control. Among the 5 different types of mattress, Russell included the transfoam mattress, which both Collier (19) and Santy et al. (23) used as the treatment (alternative foam) group. As well, the Softfoam appears to be a high-density foam mattress and thus more like an alternative foam mattress than a standard foam mattress.

Table 11: Study Characteristics – Alternative Foam Versus Standard Foam*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Collier, 1996	99	General medical ward patients	7 types of new foam mattresses: Clinifloat Omnifoam Softform STMS Therarest Transfoam Vapourlux	Standard 130 mm mattress (NHS Contract)	6 months	Deterioration in skin condition No pressure ulcer grading system reported
Gray and Campbell, 1994	170	Ortho, trauma, vascular, and medical oncology patients Waterlow score ≥ 15 No existing pressure ulcers	Softform	Standard 130 mm mattress	10 days	Incidence of pressure ulcers No pressure ulcer grading system reported
Hofman et al., 1994	36	Patients with femoral neck # Pressure ulcer risk score ≥ 8	Comfortex DeCube mattress	Standard polyproleen SG 40 mattress	2 weeks	Incidence of pressure ulcers ≥ grade 2 (blister formation) Grading system according to the Dutch consensus meeting for the prevention of pressure ulcers 1985
Russell et al., 2003	1168	Acute care, ortho, and rehab patients ≥ 65 y Waterlow score 15–20	CONFOR-Med mattress (Vesico-elastic and polyurethane foam)	Standard hospital mattress (5 types): Transfoam Softfoam Linknuse KingsFund with Spenco or Propad overlay	8–17 days (median days in study)	Incidence of Torrance grade 2 (nonblanching erythema) or worse Torrance Grading system
Santy et al., 1994	552	Hip # patients > 55 years No pressure ulcer stage ≥ 3	4 types of foam mattresses: CliniFloat Transfoam Therarest Vaperm	Standard 150 mm mattress (NHS contract mattress)	2 weeks	Skin deterioration or stage 3 pressure ulcer Adapted Torrance grading system
Berthe et al., 2007	1,729	Patients admitted to medical or surgical departments in acute care hospital	Kliniplot mattress	Standard hospital mattress (not described)	7 months	Development of pressure ulcer grade 1 or greater on the modified Shea scale

NHS indicates National Health Service.

Table 12: Pressure Ulcer Classification Systems – Studies of Alternative Foam Versus Standard Foam

Scale	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Dutch consensus meeting for the prevention of pressure ulcers 1985	Normal skin	Persistent erythema	Blister formation	Superficial (sub)cutaneous necrosis	Deep subcutaneous necrosis	N/A
Torrance	N/A	Blanching erythema	Non blanching erythema	N/A	N/A	N/A
Modified Torrance	Normal skin	Blanching hyperemia	Non blanching hyperemia	Ulceration through sub-cutaneous tissue	Lesion extends into subcutaneous fat	N/A
Modified Shea	Normal skin	Persistent erythema of the skin (> 24 h)	Blister formation	Dry pressure sore	Subcutaneous necrosis	Granulating wound

N/A indicates not applicable.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 13. Only 2 studies, Russell et al. (22) and Gray and Campbell, (20) explicitly describe allocation concealment methods. Santy et al. (23) was contacted and confirmed that allocation concealment was maintained by using sealed opaque envelopes. Similarly, other than Collier, (19) appropriate blinding of the patient or outcome assessor was not completed in any study.

Table 13: Individual Study Quality Assessment – Alternative Foam Versus Standard Foam*

Study	RCT†	Concealment‡	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Collier, 1996	x	x	x	Unclear	9%	x
Gray and Campbell, 1994	✓	✓	x	x	0%	✓
Hofman et al., 1994	✓	Unclear	✓	x	22%	x
Santy et al., 1994	✓	✓	✓	x	26%	✓
Russell, 2003	✓	✓	✓	x	23%	✓
Berthe et al., 2007	✓	x	✓	x	0%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.
†The study methods must establish that the randomization scheme used allowed each participant an equal chance of getting any of the study interventions. Therefore, the study was accepted as an RCT if the report stated either that the treatments were “randomly allocated” or that a random number table was used.
‡Concealment was adequate if the authors stated that opaque envelopes were used or there was evidence of a third party involvement for treatment allocation.

Results

The analysis completed by Cullum et al. (13;24) included the study by Russell et al. (22) (Figure 2); however, this analysis may be criticized as the control group in the study by Russell et al. (25) included an alternative foam mattress and is therefore dissimilar to the control groups of the other studies in the meta-analysis. Given this, the resultant relative risk (RR) estimate may represent an underestimate of the effect of an alternative foam mattress. It also may account for the large statistical heterogeneity in the analysis (I^2 = 77.3%). We completed a meta-analysis but removed the study by Russell et al. (22) (Figure 3). The resultant RR (random effects model) was 0.31 (95% confidence interval [CI], 0.21–0.46) with a corresponding I^2 value of 0%. Because the type or description of standard mattresses was not reported by Berthe et al., (14) we did not include this study in our meta-analysis. The author of the study was contacted for this information but did not reply.

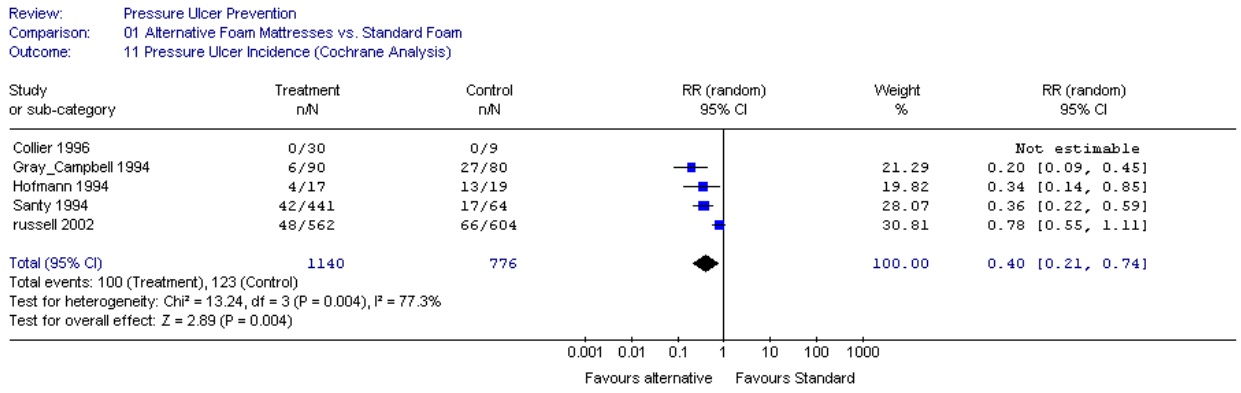
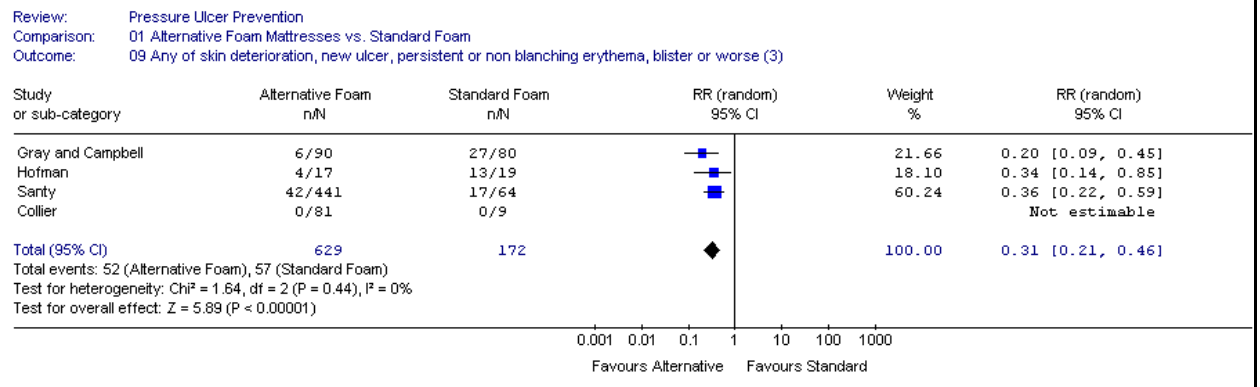


Figure 2: Alternative Foam Versus Standard Foam – Cullum et al. Meta-Analysis

Source: Cullum et al. (13;24)



CI indicates confidence interval; RR, relative risk.

Figure 3: Medical Advisory Secretariat Meta-Analysis – Alternative Foam Versus Standard Foam

Grade of Evidence

Table 14 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of alternative foam mattresses compared with standard foam hospital mattresses. The quality of the body of evidence is moderate.

Table 14: GRADE Evidence Profile – Alternative Foam Versus Standard Foam* Mattress Outcome: Any of Skin Deterioration, Mew Ulcer, Persistent or Nonblanching Erythema, Blister or Worse

Studies	Design	Quality†	Consistency	Directness	Other Modifying Factors‡	No. of Patients			
						AF	SF	RR (95% CI)	Quality/ Importance
Collier, 1996	RCT	Some serious limitations	No important inconsistency	No uncertainty about directness		629	172	.31 (0.21–0.46)	**MOD/** Critical
Gray and Campbell, 1994	RCT								
Hoffman et al., 1994	RCT								
Santy et al., 1994	RCT								
	HIGH	**LOW**	**LOW**	**LOW**	**MOD**				

*AF indicates alternative foam; MOD, moderate; RCT, randomized controlled trial; RR, relative risk; SF, standard foam.
†Unclear concealment methods (Hoffman); unblinded outcome assessment (all studies); moderate loss to follow-up (Santy) (−1).
‡Strong association (RR < 0.5) (+1).

Summary of Results

There is high quality evidence that the use of an alternative foam mattress produces an RRR of 69% in the incidence of pressure ulcers.

Comparison 2: Alternative Foam Mattress Versus Alternative Foam Mattress

Characteristics of Included Studies

Cullum et al. (13) reported 3 studies comparing different types of alternative foam mattresses including that completed by Santy et al., (23) Kemp et al., (26) and Vyhlidal et al. (27) However, the study by Santy et al. (23) was incorporated into the analysis of alternative foam mattresses compared with standard mattresses, so it is unclear why it was included in this comparison of alternative foam mattress versus alternative foam mattress. Therefore, we removed this study from the analysis. Our literature search found 1 additional study completed by Gray and Smith (16) comparing different types of alternative foam mattresses. This study was added to the body of evidence for this comparison. The study characteristics are reported in Table 15. All studies included patients admitted to an acute care setting. A variety of alternative foam mattresses were used in the treatment and control groups. All studies used an explicit pressure ulcer grading system (Table 16).

Table 15: Characteristics of Included Studies – Alternative Foam Versus Alternative Foam*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Kemp et al., 1993	84	General medicine, acute geriatric medicine and long-term care 65 years or older Braden score of < 6 Free of pressure ulcers on admission	Foam 1: Convoluted foam overlay (3–4 inches thick); these were the standard overlays used in the hospital	Foam 2: Solid foam overlay (4 inches solid sculptured overlay)	1 month	Incidence of pressure ulcers grade 1 or greater NPUAP 1989 scale used
Vyhlidal et al., 1997	40	Musculoskeletal, cardiovascular, neurological	Foam 1: Maxifloat solid foam mattress with heel insert, 1.5 inches thick	Foam 2: Iris 3000 (4-inch dimpled foam overlay)	10–21 days	Incidence of pressure ulcers stage I or greater Bergstrom Skin Assessment used
Gray and Smith, 2000	33	Admitted for bed rest or surgery	Foam 1: Transfoam wave mattress	Foam 2: Transfoam mattress	10 days	Incidence of pressure ulcers (all grades) Torrance Scale used

*NPUAP indicates National Pressure Ulcer Advisory Panel.

Table 16: Pressure Ulcer Classification System – Alternative Foam Versus Alternative Foam*

Scales	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
NPUAP Scale 1989	N/A	Nonblanchable erythema of intact skin	Break in skin (blister or abrasion)	Break in skin exposing subcutaneous tissue	Break in skin exposing muscle or bone	N/A
Bergstrom Skin Assessment	No redness or breakdowns	Erythema only, redness does not disappear for 24 hours after pressure is relieved	Break in skin such as blisters or abrasions	Break in skin exposing subcutaneous tissue	Break in skin extending through tissue and subcutaneous layers, exposing muscle or bone Dark necrotic tissue	N/A
Torrance Scale 1983	N/A	Area of blanching hyperemia	Nonblanching hyperemia	Ulceration progresses through the dermis to subcutaneous tissue	Ulceration extends into the subcutaneous fat, muscle becomes inflamed	Infective necrosis affects the deeper fascia and muscle

*N/A indicates not applicable; NPUAP, National Pressure Ulcer Advisory Panel.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 17. Of the 3 studies comprising the body of evidence, only 1, that by Gray and Smith, (16) reported adequate methods for both treatment allocation concealment and blinding the outcome assessments. None of the studies determined a sample size a priori. Loss to follow-up was negligible in all studies.

Table 17: Quality Assessment of Included Studies*

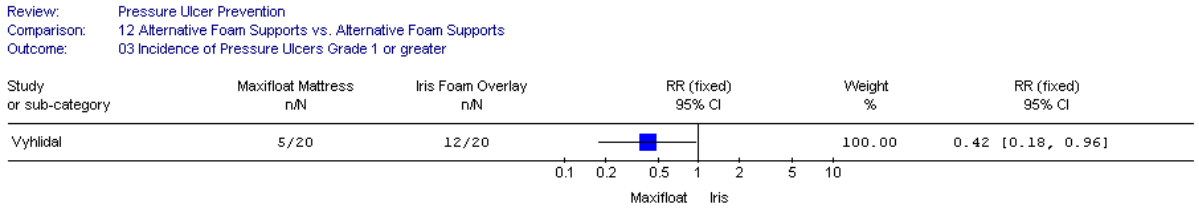
Study	RCT†	Concealment‡	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Kemp et al., 1993	✓	x	x	unclear	0%	✓
Vyhlidal et al., 1997	✓	x	x	unclear	0%	✓
Gray and Smith, 2000	✓	✓	x	✓	0%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.
†Accepted as an RCT if report stated study was "randomly allocated" or used a random number table. The study methods must establish that the randomization scheme used allowed each participant an equal chance of getting any of the study interventions.
‡Concealment was adequate if the authors stated that opaque envelopes were used or there was evidence of a third party involvement for treatment allocation.

Results

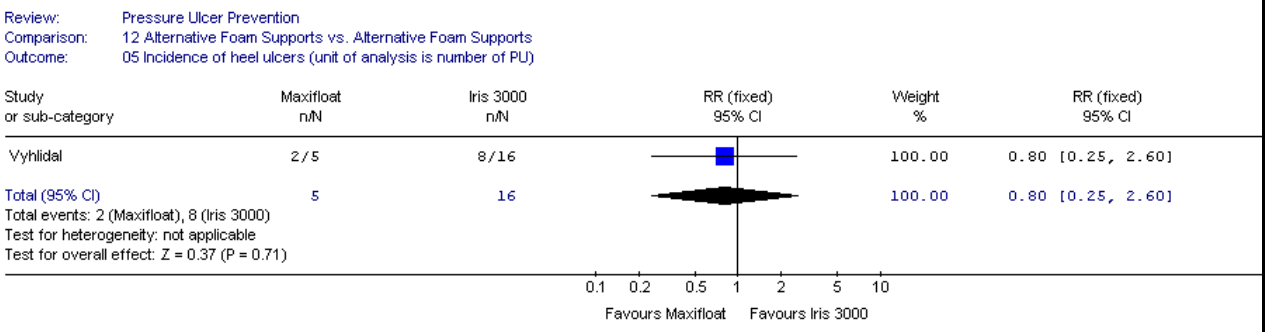
A meta-analysis for this comparison was not completed because of the variety of mattress types included in the individual studies. Figure 4 reports the results of the study completed by Vyhlidal et al. (27) Results indicate that the Maxifloat mattress statistically significantly decreases the incidence of grade 1 pressure ulcers compared with the Iris Foam Mattress. However, the Maxifloat group was significantly heavier than the Iris Foam group (body mass index 35 vs. 29, respectively) which may have lowered the risk for developing a pressure ulcer in the Maxifloat group. As well, the Maxifloat group also used heel guards. Because of this, we analyzed the study results to determine if there were fewer heel ulcers in the Maxifloat group accounting for an overall lower incidence of pressure ulcers between the Maxifloat and the Iris mattresses. Results indicated that there was no statistically significant difference in heel ulcers between groups (RR [fixed], 0.80; 95% CI, 0.25–2.60) (Figure 5). Therefore, the small sample size as well as the aforementioned issues regarding baseline characteristics of the groups may have biased the results of the study in favor of the Maxifloat mattress and thus the results of this study should be interpreted with caution.

The results of the studies by Kemp et al. (26) and Gray and Smith (16) are reported in Figures 6 and 7, respectively. Both studies report a statistically nonsignificant result.



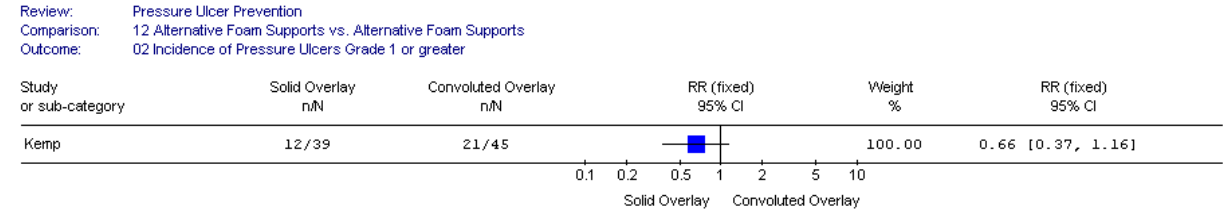
CI indicates confidence interval; RR, relative risk.

Figure 4: Alternative Foam Mattress Versus Alternative Foam Mattress – Vyhlidal et al. – Incidence of Pressure Ulcers



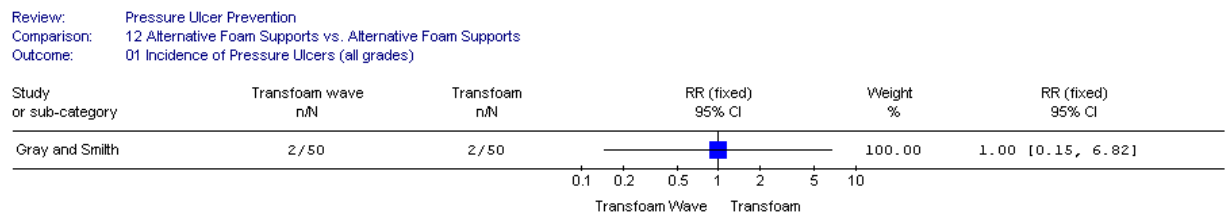
CI indicates confidence interval; PU, pressure ulcers; RR, relative risk.

Figure 5: Alternative Foam Mattress Versus Alternative Foam Mattress – Vyhlidal et al. – Incidence of Heel Ulcers



CI indicates confidence interval; RR, relative risk.

Figure 6: Alternative Foam Mattress Versus Alternative Mattress – Kemp et al.



CI indicates confidence interval; RR, relative risk.

Figure 7: Alternative Foam Mattress Versus Alternative Mattress – Gray and Smith

Grade of Evidence

Table 18 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of alternative foam mattresses (Foam 1) compared with alternative foam mattresses (Foam 2). The quality of the body of evidence is very low for the outcome of incidence of pressure ulcers grade 1 or greater.

Table 18: GRADE Evidence Profile – Alternative Foam Alternative Foam Versus Alternative Foam* Outcome: Incidence of Pressure Ulcers Grade 1 or Greater

Studies	Design	Quality†	Consistency‡	Direct-ness§	Other Modifying Factors‖	No. of Patients		RR, (95% CI)	Quality/ Importance
						Foam 1	Foam 2		
Vyhlidal et al., 1997	RCT	Some serious limitations	Important inconsistency	Some uncertainty about directness	Yes	5 39	16 45	0.42 (0.18–0.96)	**Very Low/** Critical
Kemp et al., 1993	RCT					50	50	0.66 (0.37–1.16)	
Gray and Smith, 2000	RCT **HIGH**	**MOD**	**LOW**	**VERY LOW**	**VERY LOW**			1.00 (0.15–6.82)	

*CI indicates confidence interval; MOD, moderate; RCT, randomized controlled trial; RR, relative risk.
†Kemp, Vyhlidal: no concealment and unclear if outcome assessor was blinded (−1).
‡Differences in size of effect between studies (−1).
§Different types of mattresses compared. Uncertain how to generalize comparisons (−1).
‖One small trial for each foam mattress type comparison (−1).

Summary of Results

The evidence does not support the superiority of any one type of alternative foam mattress. The quality of this evidence is very low.

Comparison 3: Alternating Pressure Mattress or Overlay Versus Standard Foam Mattress

Characteristics of Included Studies

In the systematic review by Cullum et al., (13) only the study by Andersen et al. (28) was reported comparing an alternating pressure mattress with a standard foam mattress. We found 1 additional RCT to add to this body of evidence, that completed by Sanada et al. (18) Therefore, 2 studies comprise the body of evidence comparing an alternating pressure mattress or overlay with a standard foam mattress. The study characteristics are reported in Table 19. All studies included patients admitted to an acute care setting. The follow-up study period was 10 days in the Andersen et al. (28) study. Sanada et al. (18) reported that follow-up was continued until a pressure ulcer developed. Both studies used an explicit but different pressure ulcer grading system (Tables 20 and 21).

Table 19: Characteristics of Included Studies – Alternating Pressure or Overlay Versus Standard Foam*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Andersen et al., 1982	482	Patients with acute conditions selected from emergency admissions	1. Alternating pressure air mattress. Alternating in 5-minute intervals N = 166 2. Water-filled mattress N = 155	Standard mattress (no details given) N = 166	10 days	Changes in skin integrity recorded as nondecubitus or decubitus
Sanada et al., 2003	123	Persons who have had a stroke, general surgery patients, and terminally ill patients who require head elevation (45 degrees)	1. Single-layer (1-cell) air cell overlay 2. Double-layer (2-cell) air cell overlay Cell pressure alternating in 5-minute intervals	Standard mattress (Paracare® made of polyester)	Until pressure ulcer developed	Incidence of stage I and stage II pressure ulcers using NPUAP classification

* NPUAP indicates National Pressure Ulcer Advisory Panel.

Table 20a: Pressure Ulcer Classification System Used by Andersen et al., 1982 – Alternating Pressure or Overlay Versus Standard Foam

Scale/Study	Nondecubitus	Decubitus
Changes in skin integrity / Andersen et al., 1982	Normal skin, redness, and infiltration, extravasations	Bullae, black necrosis, skin defect

Source: Andersen et al., 1982 (28)

Table 20b: Pressure Ulcer Classification System Used by Sanada et al., 2003 – Alternating Pressure or Overlay Versus Standard Foam*

Scale/Study	Grade 1	Grade 2	Grade 3	Grade 4
NPUAP Scale, 1989 / Sanada et al., 2003	N/A	Nonblanchable erythema of intact skin.	Break in skin (blister or abrasion)	Break in skin exposing subcutaneous tissue

*N/A indicates not applicable; NPUAP, National Pressure Ulcer Advisory Panel.
Source: Sanada et al., 2003 (18)

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 21. Of the 2 studies comprising the body of evidence, only 1, that by Sanada et al., (18) reported adequate allocation concealment methods and also completed a sample size calculation a priori. Neither study used a blinded assessment method for the outcome measure. Loss to follow-up ranged from 20% to 24%.

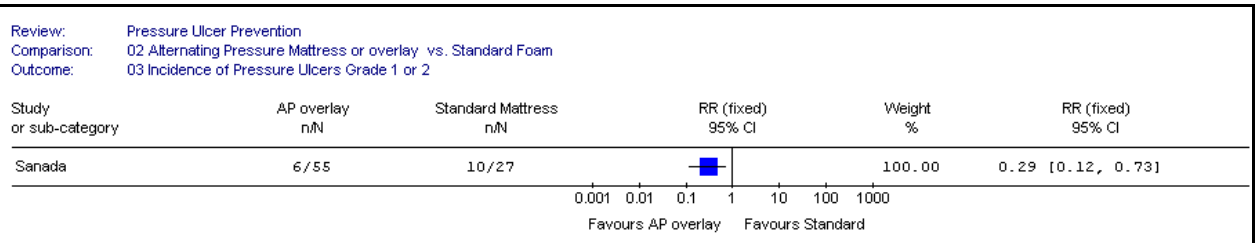
Table 21: Quality Assessment of Included Studies – Alternating Pressure or Overlay Versus Standard Foam*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Andersen et al., 1982	Unclear	x	✓	x	20%	x
Sanada et al., 2003	✓	✓	x	x	24%	x

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

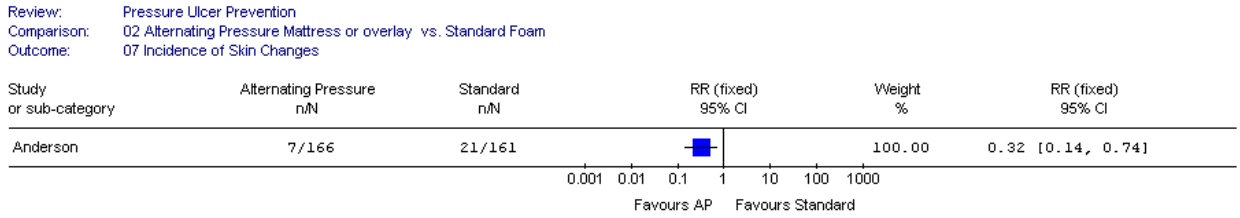
Results

A meta-analysis was not completed because of the different outcome measures used between studies (incidence of stage 1 and 2 pressure ulcers vs. changes in skin integrity). The results of each study are reported in Figures 8 and 9, respectively. Both studies report similar RR (fixed) estimates and 95% CIs.



AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 8: Alternating Pressure or Overlay Versus Standard Foam – Sanada et al.



AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 9: Alternating Pressure or Overlay Versus Standard Foam – Anderson et al.

Grade of Evidence

Tables 22 and 23 report the GRADE evidence profile for the body of evidence evaluating the effectiveness of an alternating pressure mattress or overlay versus a standard foam mattress. Table 22 reports that the quality of evidence is very low for the outcome of the incidence of grade 1 or 2 pressure ulcers, and Table 23 reports low quality of evidence for the outcome of changes in skin integrity.

Table 22: GRADE Evidence Profile – Alternating Pressure Overlay Versus Standard Foam Mattress
Outcome: Incidence of Grade 1 or 2 Pressure Ulcer*

Studies	Design	Quality†	Consistency‡	Directness¶	Other Modifying Factors#	No. of Patients			
						APO	SFM	RR (95% CI)	Quality/ Importance
Sanada et al., 2003	RCT	Some very serious limitations	N/A	Some uncertainty about directness	Sparse data	55	27	0.29 (0.12–0.73)	**Very Low**/ Critical
	HIGH	**LOW**	**LOW**	**VERY LOW**	**VERY LOW**				

*APO indicates alternating pressure overlay; CI, confidence interval; N/A, not applicable; RR, relative risk; SFM, standard foam mattress.
†Follow-up period unclear, unblinded outcome assessment and 24% dropout rate. (Sanada) (−2).
‡Not applicable (1 study).
¶Results obtained from a Japanese study population (−1).
#No difference between 1-cell mattress and either control or 2-cell mattress. However, the 2-cell group is significantly different from the control. Sanada et al. combined the results of the 1-cell mattress group and the 2-cell mattress group and compared this combined group with the control group. Since 1 cell is no different from control, combining 1-cell data with the 2-cell data (which is different from control) should bias the alternating pressure group in favor of control diluting the effect of the AP mattress. But the effect was not diluted and therefore GRADE is increased by 1 because all plausible confounders would have reduced the effect but didn't (+1).
#Sparse data (−1).

Table 23: GRADE Evidence Profile – Alternating Pressure Mattresses Versus Standard Foam Mattress
Outcome: Changes in Skin Integrity*

Studies	Design	Quality†	Consistency	Directness	Other Modifying Factors	No. of Patients			
						AP	SFM	RR (95% CI)	Quality/ Importance
Andersen et al., 1982	RCT	Some very serious limitations	Not applicable	No uncertainty about directness	None	166	161	0.32 (0.14–0.74)	**Low**/ Important
	HIGH	**LOW**	**LOW**	**LOW**	**LOW**				

*AP indicates alternating pressure; CI, confidence interval; RCT, randomized controlled trial; RR, relative risk; SFM, standard foam mattress.
†Unclear if this is a true RCT, inadequate concealment, unblinded outcome assessments (−2).

Summary of Results

There is very low quality evidence that the use of an alternating pressure overlay is associated with an RRR of 71% in the incidence of grade 1 or 2 pressure ulcers compared with a standard foam mattress.

There is low quality evidence that the use of an alternating pressure mattress is associated with an RRR of 68% in the incidence of skin changes compared with a standard foam mattress.

Comparison 4: Alternating Pressure Mattress Versus Alternating Pressure Overlay

Characteristics of Included Studies

One study compared the use of an alternating pressure mattress with an alternating pressure overlay. (29) The study characteristics are reported in Table 24. This comparison is not reported in the review by Cullum et al. (13) The study by Nixon et al. (29) included patients admitted to an acute care setting. The median follow-up time period was 9 days. An explicit pressure ulcer classification system was used to measure the outcome (Table 25).

Table 24: Characteristics of Included Study – Alternating Pressure Mattress Versus Alternating Pressure Overlay

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Nixon et al., 2006 N = 1972	1,972	Acute or elective vascular, orthopedic, medical, or care of elderly admissions Existing pressure ulcer of grade 2 or less	Alternating pressure mattress	Alternating pressure overlay	30 days and 60 days Median was 9 days	New pressure ulcer of grade 2 or worse Skin classification system

Table 25: Skin Classification System – Study of Alternating Pressure Mattress Versus Alternating Pressure Overlay

Scale/Study	Grade 0	Grade 1a	Grade 1b	Grade 2	Grade 3	Grade 4	Grade 5
Skin classification system	No skin changes	Redness to skin (blanching)	Redness to skin (nonblanching)	Partial thickness wound involving epidermis or dermis only	Full thickness wound involving sub-cutaneous tissue	Full thickness wound through sub-cutaneous tissue to muscle or bone	Black eschar

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 26. The study by Nixon et al. (29) was well conducted. Methodological limitations include only an unblinded outcome assessment.

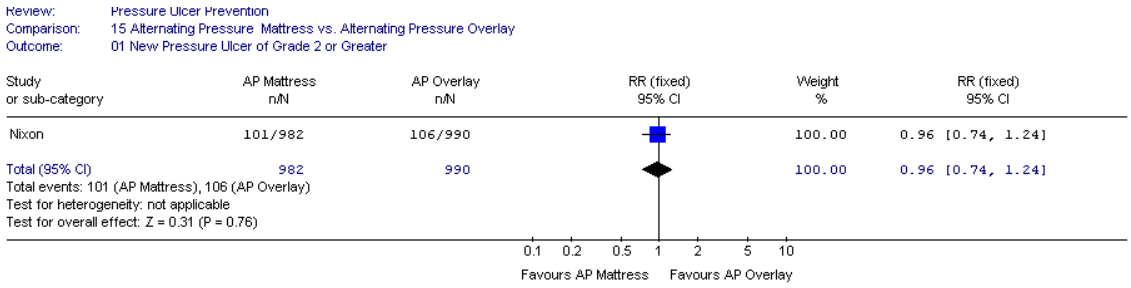
Table 26: Quality Assessment of Included Study – Alternating Pressure Mattress Versus Alternating Pressure Overlay

Study	RCT	Concealment	Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Nixon et al., 2006	✓	✓	✓	x	6%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

The results of the study completed by Nixon et al. (29) are reported in Figure 10. There was no statistically significant difference between alternating pressure mattress and an alternating pressure overlay in the incidence of pressure ulcers grade 2 or greater.



AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 10: Alternating Pressure Mattress Versus Alternating Pressure Overlay

Grade of Evidence

Table 27 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of an alternating pressure mattress compared with an alternating pressure overlay. The quality of evidence is moderate for the outcome of incidence of grade 2 or greater pressure ulcers.

Table 27: GRADE Evidence Profile – Alternating Pressure Mattresses Versus Alternating Pressure Overlay
Outcome: Incidence of Pressure Ulcers Grade 2 or Greater*

Studies	Design	Quality†	Consistency	Directness	Other Modifying Factors	No. of Patients			
						APM	APO	RR (95% CI)	Quality/ Importance
Nixon et al., 2006	RCT	Some serious limitations	Not applicable (1 study)	No uncertainty about directness	None	982	990	0.96 (0.74–1.24)	**MOD/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**MOD**				

*APM indicates alternating pressure mattress; APO, alternating pressure overlay; CI, confidence interval; MOD, moderate; RCT, randomized controlled trial; RR, relative risk.
†Unblinded assessment (−1).

Summary of Results

There is moderate quality evidence that there is a statistically nonsignificant difference in the incidence of grade 2 or greater pressure ulcers between persons using an alternating pressure mattress and using an alternating pressure overlay.

Comparison 5: Australian Sheepskin Versus Standard Treatment

Characteristics of Included Studies

Two studies compared the use of an Australian sheepskin overlay and sheepskin heel and elbow protectors with the use of a standard hospital mattress and other constant low pressure devices as needed. (17;30) The study characteristics are reported in Table 28. All studies included patients admitted to an acute care setting, and treatment and control interventions were exactly the same in both studies. In the study by McGowan et al., (30) patients were followed until discharge from hospital; however, the authors did not report the average length of hospital stay for the study population. Jolley et al. (17) reported the follow-up period to be 7 days. Both studies used the same pressure ulcer classification system (Table 29).

Table 28: Characteristics of Included Studies – Australian Sheepskin Versus Standard Treatment*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
McGowan et al., 2000	297	Emergency and elective patients admitted to orthopedic wards	Australian sheepskin overlay, sheepskin heel and elbow protectors as needed	Standard hospital mattress, CLP device as needed	Study endpoint was discharge from hospital or transfer to a rehab ward Mean time (days) to study endpoint was not reported	Incidence of pressure ulcers stage I or greater Used the US Agency for Health Care Policy and Research Scale
Jolley et al., 2004	441	Patients at low to moderate risk of developing a pressure ulcer on the Braden Pressure Ulcer Risk Assessment scale	Australian sheepskin overlay, sheepskin heel and elbow protectors as needed	Standard hospital mattress, CLP device as needed	7 days	Incidence of pressure ulcers stage I or greater Used the US Agency for Health Care Policy and Research Scale

*CLP indicates constant low pressure; US, United States.

Table 29: Pressure Ulcer Classification System – Studies of Australian Sheepskin Versus Standard Treatment

Scale/Study	Grade 1	Grade 2	Grade 3	Grade 4
US Agency for Health Care Policy and Research Scale McGowan et al., 2000	Nonblanching erythema or erythema not resolving within 30 minutes of pressure relief. Epidermis remains intact. Reversible with intervention	Partial thickness loss of skin layers involving epidermis and possibly penetrating into but not through dermis. May present as blistering with erythema and/or induration; wound base moist and pink; painful; free of necrotic tissue	Full thickness tissue loss extending through dermis to involve subcutaneous tissue. Presents as shallow crater unless covered by eschar. May include necrotic tissue, undermining, sinus tract formation, exudate, and/or infection. Wound base is usually not painful.	Deep tissue destruction extending through subcutaneous tissue to fascia and may involve muscle layers, joint, and/or bone. Presents as a deep crater. May include necrotic tissue, undermining, sinus tract formation, exudate, and/or infection. Wound base is usually not painful.
US Agency for Health Care Policy and Research Scale Jolley et al., 2004	Nonblanchable erythema or intact skin	Partial thickness skin loss involving epidermis, dermis, or both	Full thickness skin loss involving damage or necrosis of subcutaneous tissue that may extend down to but not through underlying fascia	Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone, or supporting structures

*US indicates United States.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 30. Both studies are methodologically sound except for using an unblinded outcome assessment process.

Table 30: Quality Assessment of Included Studies – Australian Sheepskin Versus Standard Treatment*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
McGowan et al., 2000	✓	✓	✓	x	6%	x
Jolley et al., 2004	✓	✓	✓	x	18%	✓

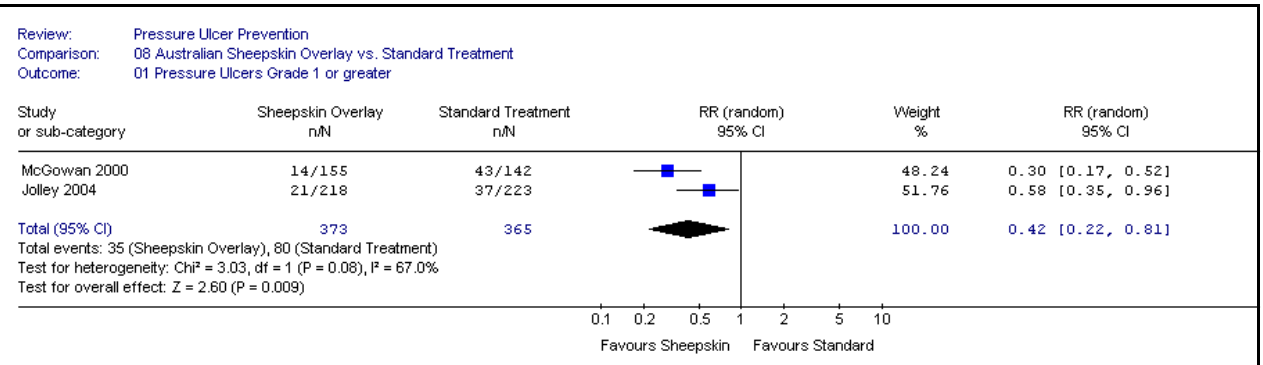
*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

Figure 11 reports the result of the meta-analysis for this body of evidence. There is a statistically significant reduction in the RR of pressure ulcers grade 1 or greater in persons using an Australian sheepskin compared with persons using standard treatment. This corresponds to an RRR of 58%. The I^2 value is 67%, indicating moderate statistical heterogeneity in the analysis.

Complications with sheepskins were also reported in both studies. Jolley et al. (17) reported that 10 patients using sheepskins complained that the sheepskin was uncomfortable and too hot. Sensitivity to the wool surface was also reported. Participants in the McGowan et al. (30) study reported that the sheepskins were hot and curled up in the bed. Six participants withdrew before completion of the study because the sheepskin caused an irritation and was too hot or uncomfortable.

To contextualize the evidence, the secretariat convened a Pressure Ulcer Advisory Panel comprised of clinical experts in pressure ulcer management. This advisory panel noted that in general sheepskins are not an acceptable preventive intervention because they bunch up in the patient's bed and may contribute to wound infection if not properly cleaned.



CI indicates confidence interval; RR, relative risk.

Figure 11: Australian Sheepskin Overlay Versus Standard Treatment

Grade of Evidence

Table 31 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of the Australian sheepskin compared with standard care. The quality of evidence is moderate for the outcome of incidence of pressure ulcers grade 1 or greater.

Table 31: GRADE Evidence Profile – Australian Sheepskin Versus Standard Treatment Outcome: Incidence of Pressure Ulcers Grade 1 or Greater*

Studies	Design	Quality†	Consistency	Directness	Other Modifying Factors‡	No. of Patients			
						AS	SC	RR (95% CI)	Quality/ Importance
Jolley et al., 2004 McGowan et al., 2000	RCT	Some very serious limitations	No important inconsistency	No uncertainty about directness	Strong association	373	365	0.42 (0.22–0.81)	**Moderate**/ Critical
	HIGH	LOW	LOW	LOW	MOD				

*AS indicates Australian sheepskin; CI, confidence interval; MOD, moderate; RCT, randomized controlled trial; RR, relative risk; SC, standard care.
†Studies not blinded, McGowan et al. did not complete an intention-to-treat analysis (−2)
‡Strong association (< 0.5)

Summary of Results

There is moderate quality evidence that the use of an Australian sheepskin produces an RRR of 58% in the incidence of pressure ulcers grade 1 or greater. There is also evidence that sheepskins are uncomfortable to use. The Pressure Ulcer Advisory Panel noted that in general sheepskins are not a useful preventive intervention because they bunch up in a patient's bed and may contribute to wound infection if not properly cleaned, and this reduces their acceptability as a preventive intervention.

Comparison 6: Alternating Pressure Mattress (Micropulse System) Versus Standard Care

Characteristics of Included Studies

Two studies compared the Micropulse System alternating pressure mattress with standard care. (31;32) The study characteristics are reported in Table 32. Both studies included patients having surgery for 2 or more hours. The follow-up study period was 7 days for both studies. Both studies used the National Pressure Ulcer Advisory Panel (NPUAP) pressure ulcer classification system (Table 33).

Table 32: Characteristics of Included Studies – Alternating Pressure Mattress (Micropulse System) Versus Standard Care*

Study	Population	Treatment	Control	Follow-Up	Outcome
Aronovitch et al., 1999	Elective surgery for 3 hours' duration	Micropulse System AP intraoperatively and postoperatively	Gel pad in OR and pressure Guard II hospital replacement mattress postop.	7 days	Incidence of pressure ulcers grade 1 or greater NPUAP (1989) Scale and the wound ostomy, and continence nurses Society staging system used
Russell and Lichtenstein, 2000	Cardiothoracic surgery for at least 4 hours	AP Micropulse System intraoperatively and postoperatively	Gel pad intraop. and standard mattress postop.	7 days	Development of pressure ulcers grade 1 or greater NPUAP scoring system used

*AP indicates alternating pressure mattress; NPUAP, National Pressure Ulcer Advisory Panel; OR, operating room.

Table 33: Pressure Ulcer Classification System – Alternating Pressure Mattress (Micropulse System) Versus Standard Care*

Scale / Study	Grade 1	Grade 2	Grade 3	Grade 4
NPUAP, 1989	Nonblanchable erythema of intact skin	Partial thickness skin loss involving epidermis and/or dermis. The ulcer is superficial and presents as an abrasion blister or shallow crater.	Full thickness skin loss involving damage or necrosis of subcutaneous tissue which may extend down to but not through underlying fascia. The ulcer presents as a deep crater with or without undermining of adjacent tissue.	Full thickness skin loss with extensive destruction, tissue necrosis or damage to muscle, bone, or supporting structures

*NPUAP indicates National Pressure Ulcer Advisory Panel.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 34. The study by Aronovitch et al. (31) did not satisfy any of the quality assessment criteria. Similarly, other than using an adequate allocation concealment process and proper randomization methodology, Russell and Lichtenstein (32) also did not satisfy many of the quality assessment criteria.

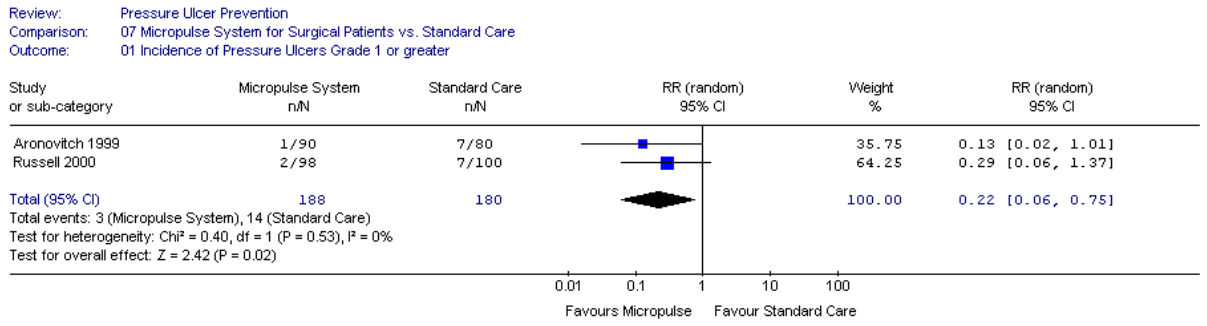
Table 34: Quality Assessment of Included Studies – Alternating Pressure Mattress (Micropulse System) Versus Standard Care*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Aronovitch et al., 1999	x Randomization by week	x	x	x Not reported	x	x
Russell and Lichtenstein, 2000	✓	✓ Opaque envelopes	x	x	x Not reported	✓

* ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

Figure 12 reports the results of the meta-analysis of the Aronovitch et al. and Russell and Lichtenstein studies. (31;32) There is a statistically significant reduction in the incidence of pressure ulcers (RR, 0.21; 95% CI, 0.06–0.70), suggesting an RRR in pressure ulcers of 79%. A limitation of the study design in both studies is that the Micropulse System alternating pressure mattress was used both intraoperatively and postoperatively. Because of this, it is unknown if the effect of this system is due to its use intraoperatively or postoperatively, or indeed if it needs to be used in both phases.



CI indicates confidence interval; RR, relative risk.

Figure 12: Alternating Pressure Mattress (Micropulse System) Versus Standard Care

Grade of Evidence

Table 35 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of the alternating pressure Micropulse System (AP) compared with a gel-pad intraoperatively and a standard mattress postoperatively (Standard care, SC) . The quality of evidence is very low for the outcome of incidence of pressure ulcers grade 1 or greater pressure.

Table 35: GRADE Evidence Profile – Alternating Pressure Mattress Intraoperatively and Postoperatively Versus a Gel Pad Intraoperatively and a Standard Mattress Postoperatively Outcome: Incidence of Pressure Ulcers Grade 1 or Greater*

Studies	Design	Quality†	Consistency	Directness‡	Other Modifying Factors§	No. of Patients			
						AP	SM	RR (95% CI)	Quality/ Importance
Aronovitch et al., 1999 Russell and Lichtenstein, 2000	RCT **HIGH**	Some very serious limitations **LOW**	No important inconsistency **LOW**	Some uncertainty about directness **VERY LOW**	**VERY LOW**	188	180	0.21 (0.06–0.70)	**Very Low/** Critical

*AP indicates alternating pressure; CI, confidence interval; RCT, randomized controlled trial; RR, relative risk; SM, standard mattress.
†Aronovitch used randomization by week, had inadequate allocation concealment, did not report using a blind outcome assessment procedure, did not report losses to follow-up, and did not complete an intention-to-treat analysis (−2). Russell did not report using a blind outcome assessment procedure and did not report losses to follow-up.
‡Unclear if standard treatment of gel pad intraoperatively can be generalized to the Ontario context (−1).
Standard postoperative mattress not described by Aronovitch.
§Strong evidence of association but sparse data (+1/-1).

Summary of Results

There is very low quality evidence that the use of an alternating pressure Micropulse System used intraoperatively and postoperatively produces an RRR of 79% in the incidence of pressure ulcers compared with a gel-pad intraoperatively and a standard mattress postoperatively (standard care). It is unclear if the effect is due to the use of the alternating pressure mattress intra operatively or postoperatively, or if indeed it must be used in both patient care areas.

Comparison 7: Dry Vesico-Elastic Polymer Pad Versus Standard Operating Table Foam Mattress

Characteristics of Included Studies

One study compared an operating table vesico-elastic polymer pad (gel pad) with a standard operating room table foam mattress. (32;33) The study characteristics are reported in Table 36. The follow-up study period was 1 postoperative day. The Torrance pressure ulcer classification grading system was used to measure the outcome (Table 37). Of note, in this classification system a grade 1 pressure ulcer includes blanching erythema.

Table 36: Characteristics of Included Studies – Dry Vesico-Elastic Polymer Pad Versus Standard Operating Table Foam Mattress

Study	Population	Treatment	Control	Follow Up	Outcome
Nixon et al., 1998	Vascular, general, or gynecological surgery Pressure ulcer of stage 2a or greater	Dry vesico-elastic polymer pad in operating room	Standard operating room table 3-inch foam mattress covered in a thick impervious material	Day 1 postop	Pressure ulcers stage 1 or greater

Table 37: Pressure Ulcer Classification System – Study of Dry Vesico-Elastic Polymer Pad Versus Standard Operating Table Foam Mattress

Scale/ Study	Grade 0	Grade 1	Grade 2a	Grade 2b	Grade 3	Grade 4	Grade 5
Torrance Scale / Nixon et al., 1998	No skin discoloration	Redness to the skin Blanching occurs	Redness to the skin Nonblanch-ing area	Superficial damage to epidermis	Ulceration progressed through the dermis	Ulceration extended into subcutaneous fat	Necrosis penetrating the deep fascia and extending to muscle

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 38. The study by Nixon et al. (33) satisfied all 6 quality assessment criteria.

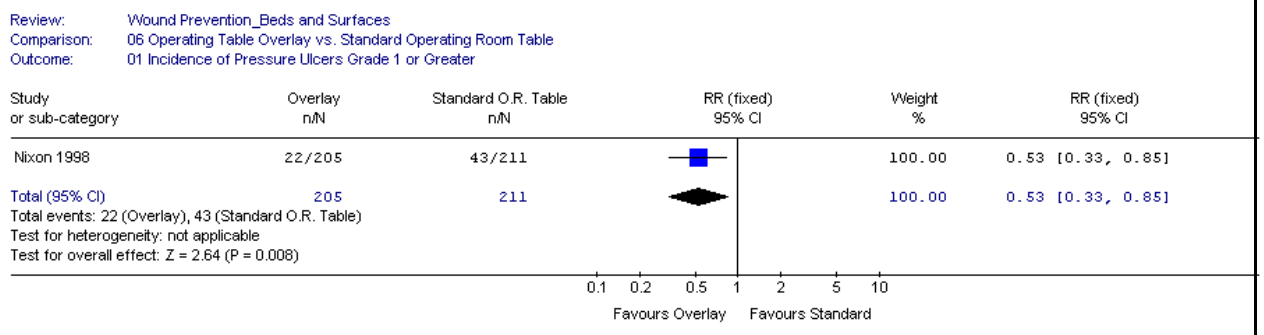
Table 38: Quality Assessment of Included Studies*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Nixon et al., 1998	✓	✓	✓	✓	8%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

The results of the study by Nixon et al. (33) are reported in Figure 13. There is a statistically significant reduction in the incidence of pressure ulcers grade 1 or greater in person using an operating table gel pad (RR, 0.53; 95% CI, 0.33–0.85) corresponding to an RRR of 47%. Of note, 20% of participants had a surgical time less than 90 minutes including 23% of persons in the treatment group compared with 18% in the control group. There was also a trend for the control group to have a longer duration of surgery and to spend more time in a hypotensive state intraoperatively. These variables may have increased the risk for developing pressure ulcers in the control group compared with the treatment group.



CI indicates confidence interval; O.R., operating room; RR, relative risk.

Figure 13: Operating Table Overlay Versus Standard Operating Room Table

Grade of Evidence

Table 39 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of a vesico-elastic polymer pad compared with a standard operating 3-inch foam mattress (standard care). The quality of evidence is low for the outcome of incidence of grade 1 or greater pressure ulcers.

Table 39: GRADE Evidence Profile – Dry Vesico-Elastic Polymer Pad Versus Standard 3-Inch Foam Mattress on Operating Table
Outcome: Incidence of Pressure Ulcers Grade 1 or Greater*

Studies	Design	Quality	Consistency	Directness†	Other Modifying Factors‡	No. of Patients			
						PP	SF	RR (95% CI)	Quality/ Importance
Nixon et al., 1998	RCT	No serious limitations	N/A	Some uncertainty about directness	Sparse data	205	211	0.53 (0.33–0.85)	**LOW/** Critical
	HIGH	**HIGH**	**HIGH**	**MOD**	**LOW**				

*CI indicates confidence interval; MOD, moderate; PP, polymer pad; RCT, randomized controlled trial; RR, relative risk; SF, standard foam.
†Grade 1 included blanching erythema. International consensus for grade 1 is nonblanching erythema (−1). The duration of follow up is 1 day. The study was not downgraded for this; however, some clinical experts believe this is not a sufficient length of follow-up to measure the outcome of grade 1 or greater pressure ulcers.
‡Only 1 study (−1).

Summary of Results

There is low quality evidence that the use of a vesico-elastic polymer pad (gel pad) on the operating table for surgeries of at least 90 minutes' duration produces a statistically significant RRR of 47% in the incidence of pressure ulcers grade 1 or greater compared with a standard operating table foam mattress.

Comparison 8: Air Suspension Bed Versus Standard Intensive Care Unit Bed

Characteristics of Included Studies

One study compared an air suspension bed with a standard intensive care unit (ICU) bed. (34) The study characteristics are reported in Table 40. The follow-up study period was 17 days on average. The Shea pressure ulcer classification grading system (35) was used to measure the outcome measure (Table 41).

Table 40: Characteristics of Included Studies – Air Suspension Bed Versus Standard Intensive Care Unit Bed*

Study	Population	Treatment	Control	Follow-Up	Outcome
Inman et al., 1993	ICU admissions > 3 days	Air suspension bed	Standard ICU bed	17 days (mean)	Incidence of pressure ulcers Shea classification system used

*ICU indicates intensive care unit.

Table 41: Table Pressure Ulcer Classification System – Study of Air Suspension Bed Versus Standard Intensive Care UnitBed

Scale/ Study	Grade 1	Grade 2	Grade 3	Grade 4	Closed
Shea 1975 / Inman et al., 1993	Indurated area of swelling, heat, and erythema with a superficial breakdown limited to the epidermis	Involves all soft tissue presenting with a full thickness skin ulcer extending to the underlying subcutaneous fat	A necrotic, foul smelling, infected ulcer limited by the deep fascia but extensively involving the fat with undermining of the skin. There is muscle, periosteum and joint involvement.	Pressure ulcer penetrates the deep fascia causing extensive soft tissue spread with osteomyelitis and septic, dislocated joints	Closed pressure sore conceals a deep lesion

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 42. The study by Inman et al. (34) satisfied 4 of the 6 quality assessment criteria; allocation concealment methods were not reported and the outcome assessments were not done in a blinded fashion.

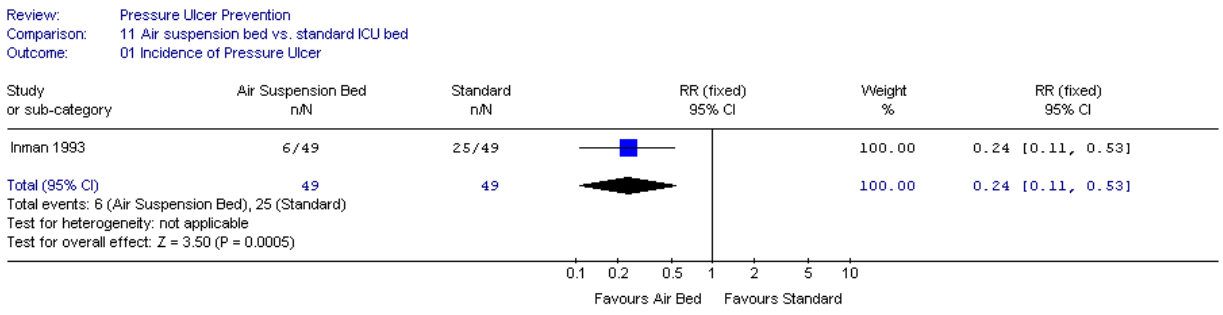
Table 42: Quality Assessment of Included Studies – Air Suspension Bed Versus Standard Intensive Care Unit Bed

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Inman et al., 1993	✓	Unknown	✓	x	2%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

The results of the study by Inman et al. (34) are reported in Figure 14. There is a statistically significant reduction in the incidence of pressure ulcers in person using an air suspension bed in the ICU (RR, 0.24; 95% CI, 0.11–0.53) corresponding to an RRR in the incidence of pressure ulcers of 76%.



CI indicates confidence interval; ICU, intensive care unit; RR, relative risk.

Figure 14: Air Suspension Bed Versus Standard Intensive Care Unit Bed

Grade of Evidence

Table 43 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of an air suspension bed in the ICU versus a standard ICU mattress. The quality of evidence is low for the outcome of incidence of pressure ulcers.

Table 43: GRADE Evidence Profile – Air Suspension Bed Versus Standard Intensive Care Unit Bed
Outcome: Incidence of Pressure Ulcers*

Studies	Design	Quality†	Consistency‡	Directness	Other Modifying Factors§	No. of Patients			
						Air	SM	RR (95% CI)	Quality/ Importance
Inman et al., 1993	RCT	Some serious limitations	N/A	No uncertainty about directness	Sparse data	49	49	0.24 (0.11–0.53)	**Low/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**LOW**				

*Air indicates air suspension bed; CI, confidence interval; MOD, moderate; RCT, randomized controlled trial; RR, relative risk; SM, standard ICU mattress.
†Unclear allocation concealment, outcome assessor not blinded to treatments.
‡Not applicable because there is 1 study.
§One study.

Summary of Results

There is low quality evidence that the use of an air suspension bed in the ICU for ICU stays of at least 3 days produces a statistically significant RRR of 76% in the incidence of pressure ulcers compared with a standard ICU bed.

Comparison 9: Alternating Pressure Mattress Versus Alternative Foam

Characteristics of Included Studies

Two studies compared alternating pressure mattresses with an alternate foam mattress. The study characteristics are reported in Table 44. The follow-up study period was 8 days in the study conducted by Whitney et al.; (36) however, the duration of follow-up was not clearly reported in the study by Stapleton. (37) A different pressure ulcer classification grading system was used to measure the study outcome in each study (Tables 45 and 46).

Table 44: Characteristics of Included Studies – Alternating Pressure Mattress Versus Alternative Foam*

Study	N	Population	Treatment	Control	Follow-Up	Outcome
Whitney et al., 1984	51	Medical-surgical units Patients in bed for 20 hours daily, ages 19–91 years with a mean of 63 years of age 60% of patients were confused, lethargic, and stuporous, and 40% were mentally alert 61% of patients were bedfast.	Alternating pressure consisting of 132 3-inch diameter air cells with 2.5 inch lift and micro air vents for air circulation. The air cells inflated and deflated every 3 minutes. Patient received routine nursing care including turning every 2 hours.	4-inch polyurethane convoluted foam mattress (eggcrate foam mattress)	8 days	Incidence skin breakdown Skin assessment tool
Stapleton, 1986	100	Female elderly patients with fractured neck of femur without existing pressure ulcers Age 65 or greater Scored 14 or less on the Norton scale No pre-existing pressure ulcers. Average age: 81 years	Large Cell Ripple (AP)	Polyether foam pad (CLP) Spenco Pad (CLP)	Unclear	Pressure ulcers of grade 2 or greater Categories from the Border study Category A: superficial/blister Category B-break in skin (no crater) Category C: a break in skin (with crater) Category D: blackened tissue

*AP indicates alternating pressure; CLP, constant low pressure.

Table 45: Pressure Ulcer Classification System Used by Whitney et al., 1984

Scale/Study	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Skin assessment tool Whitney et al., 1984	No redness or skin breakdown	Skin redness, fades in 15 minutes or less	Inflammation of the skin, fading time exceeds 15 minutes, less than 1 hour	Inflammation of the skin fading time exceeds 1 hour	Skin break with redness of surrounding skin: redness fades longer than 1 hour

Source: Whitney et al., 1984 (36)

Table 46: Pressure Ulcer Classification System Used by Stapleton, 1986

Scale/Study	Category A	Category B	Category C	Category D
Pressure ulcer grading Stapleton, 1986	Superficial/blister	A break in skin (no crater)	A break in skin (with crater)	Blackened tissue

Source: Stapleton, 1986 (37)

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 47. The methods of randomization were unclearly reported by Whitney et al. Stapleton allocated patients to the first 2 groups by lottery, and thereafter patients were allocated systematically in rotation. Overall, the quality of both studies was poor.

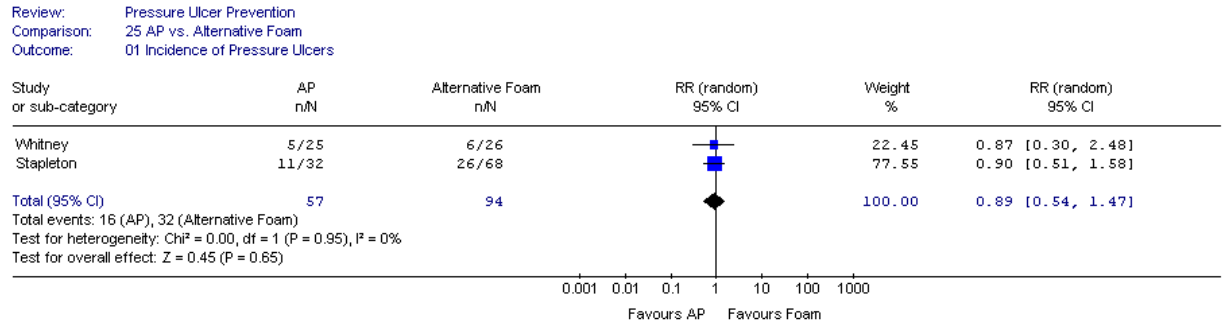
Table 47: Quality Assessment of Included Studies – Alternating Pressure Mattress Versus Alternative Foam*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Whitney et al., 1984	x Methods of randomization unclear	x	x	x Not blinded	None	✓
Stapleton, 1986	x	x	x	x	2%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

The results of the studies by Whitney et al. (36) and Stapleton (37) were pooled and the overall estimate of clinical effect is reported in Figure 15. There is a statistically nonsignificant reduction in the incidence of pressure ulcers in person using an alternating pressure mattress compared with an alternative foam mattress (RR, 0.89; 95% CI, 0.54–1.47).



AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 15: Alternating Pressure Mattress Versus Alternative Foam

Grade of Evidence

Table 48 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of an alternating pressure mattress compared with an alternative foam mattress. The quality of evidence is very low for the outcome of incidence of pressure ulcers.

Table 48: GRADE Evidence Profile – Alternating Pressure Mattress Versus Alternative Foam Outcome: Incidence of Pressure Ulcers*

Studies	Design	Quality†	Consistency	Directness‡	Other Modifying Factors§	No. of Patients			
						AP	AF	RR (95% CI)	Quality/ Importance
Whitney et al., 1984	RCT	Some serious limitations	No important inconsistency	Some uncertainty about directness	Sparse data	57	94	0.89 (0.54–1.47)	**Very Low/** Critical
Stapleton, 1986	**HIGH**	**LOW**	**LOW**	**VERY LOW**	**VERY LOW**				

*AF indicates alternative foam mattress; AP, allternating pressure; CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Unclear allocation concealment, outcome assessor not blinded to treatments, methods of randomization inadequate in Stapleton (37) and unclear in Whitney et al. (36) (−2).
‡Studies were published 20 years ago; it is unknown if the quality and type of alternating pressure mattress is generalizable to that available today (−1).
§Pooled sample size is still small (−1).

Summary of Results

The use of an alternating pressure mattress does not statistically reduce the incidence of pressure ulcers compared with an alternative foam mattress. The quality of evidence supporting this conclusion is very low.

Nutritional Supplementation

Research Question

The literature was searched to determine the effect of using various nutritional supplementation regimens on the incidence of pressure ulcers in a population at risk for developing pressure ulcers. The search strategy is presented in Appendix 3.

Methods

Inclusion Criteria

- systematic reviews (with/without meta-analysis) or RCTs
- studies involving a population at risk for developing pressure ulcers
- studies evaluating the use of nutritional supplementation plus the standard hospital diet compared with the standard hospital diet only
- studies reporting the number (proportion) of persons developing a new pressure ulcer
- studies reporting the stage of pressure ulcer or in which the stage can be inferred from the description of the ulcer (nonblanchable erythema, blisters)

Exclusion Criteria

- studies that looked at discrete dosages of nutritional supplementation (e.g., different dosages of vitamin C or magnesium)

Primary Outcome

The primary outcome was the incidence of pressure ulcers measured as the number (proportion) of participants developing a new pressure ulcer.

Results of Literature Search

Two systematic reviews were obtained from the literature search strategy. (38;39) Langer et al. (38) searched the electronic databases up to 2003 and retrieved 4 relevant RCTs. Stratton et al. (39) searched up to 2004 and retrieved 1 additional relevant RCT. Our search strategy did not retrieve any relevant RCTs in addition to those reported by Stratton et al. and Langer et al. (38;39) (Table 49). Therefore, in total there are 5 relevant RCTs comparing the effectiveness of nutritional supplementation in addition to the standard hospital diet compared with the standard hospital diet alone.

Table 49: Quality of Evidence of Included Studies – Nutritional Supplementation*

Study Design	Level of Evidence	Number of Eligible Studies	MAS Update to Systematic Review
Systematic reviews of RCT	1	2	0
or			
Large RCT		2	
Large RCT unpublished but reported to an international scientific meeting	1(g)†		0
Small RCT	2	3	0
Small RCT unpublished but reported to an international scientific meeting	2(g)		0
Non-RCT with contemporaneous controls	3a		0
Non-RCT with historical controls	3b		n/a
Non-RCT presented at international conference	3(g)		n/a
Surveillance (database or register)	4a		n/a
Case series (multisite)	4b		n/a
Case series (single site)	4c		n/a
Retrospective review, modeling	4d		n/a
Case series presented at international conference	4(g)		n/a

* MAS indicates Medical Advisory Secretariat; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meeting. (11)

Characteristics of Included Studies

Five studies compared the effect of nutritional supplementation on the incidence of pressure ulcers with that of a standard hospital diet. (40-44) The study characteristics are reported in Table 50. Three of the 5 studies included persons with hip fractures. (41;43;44) Nutritional supplementation ranged from 1070 to 6300 kJ/day (254 to 1,500 c/day). The total energy intake in the standard hospital diet of the control groups was reported in only 2 studies. (40;42) The follow-up study period ranged from 2 weeks to 6 months. In the study by Hartgrink et al., (43) the nutritional supplementation was delivered via nasogastric tube. All studies used a different pressure ulcer classification system for the outcome measure (Table 51).

Table 50: Characteristics of Included Studies – Nutritional Supplementation

Study Year	N	Population	Treatment	Control	Follow-Up	Outcome
Delmi et al., 1990	59	Persons with femoral neck fractures after accidental fall > 60 years, mean age of 82	Standard Hospital diet with daily oral nutrition supplement (250 mL; 1060 kJ (254 c); 20.4 g protein; 29.5 g carbo_hydrates; 5.8 lipid; 525 mg calcium; 750 IU vitamin A; 25 IU vitamin D3, vitamin E, B1, B2, B6, B12, C, nicotinamide, folate, calcium panto-thenate, biotin, minerals) 1070 kJ/day (254 c/day)	Standard hospital diet	Up to 6 months post discharge	At 6 months Incidence of bedsores No classification system given
Hartgrink et al., 1998	140	Persons with hip fracture, pressure sore risk score of 8 points or greater and an increased pressure sore risk	Standard hospital diet and additional naso-gastric tube feeding with 1000 mL Nutrison Steriflo energy plus (6300 kJ/L [1,500 c/L] 60 g/L protein) administered with a feeding pump between 9 pm and 5 am 6300 kJ/day (1,500 c/day)	Standard hospital diet alone	2 weeks	Pressure ulcers grade 2 or greater Dutch consensus meeting for the prevention of pressure sores, 1992 pressure ulcer classifi-cation system
Bourdel-Marchasson, 2000	672	65 years of age, and older who were critically ill, immobile, and did not have a pressure ulcer	Standard diet (7500 kJ/day [1800 c/day]) and 2 oral supplements per day (each with 200 ml; 840 kJ (200 c); 30% protein; 20% fat; 50% carbohydrate; minerals and vitamins such as 1.8 mg zinc and 15 mg vitamin C) Persons also received standard pressure ulcer prevention program care (changing positions, special mattresses, cleaning care) 1700 kJ/day (400 c/day)	Standard diet (7500 kJ/day [1800 c/day]) Persons also received standard pressure ulcer prevention program care (changing positions, special mattresses, cleaning care)	15 days or until discharge	Incidence of pressure ulcers Agency for Health Care and Policy Research Pressure Ulcer Classification System
Houwing et al., 2003	103	Persons with a hip fracture	Standard hospital diet and 1 supplement daily (400 mL; 2100 kJ (500 c); 40 g protein; 6g/L arginine; 20 mg zinc; 500 mg vitamin C; 200 mg vitamin E; 4 mg cartenoids) 2100 kJ/day (500 c/day)	Standard hospital diet and noncaloric water-based placebo	Up to 28 days or at discharge	Incidence of pressure ulcer (highest stage was recorded) European Pressure Ulcer Advisory Panel 1998 pressure ulcer classification system

Table 50: Characteristics of Included Studies – Nutritional Supplementation (continued)

Study Year	N	Population	Treatment	Control	Follow-Up	Outcome
Ek et al., 1991	501	Persons newly admitted to long-term medical ward, remaining for at least 3 weeks	200 mL of liquid supplement given twice daily (4 g protein, 4 g fat, 11.8 h carbohydrates, 419 kJ and minerals and vitamins/100 mL) 1700 kJ/day (400 c/day)	Standard hospital diet (9200kJ/day [2,200 c/day])	26 weeks after admission to hospital	Incidence of pressure ulcers Nonspecific pressure ulcer classification system used Persistent discoloration (dark red, reddish-blue color) or epithelial damage or damage to the full thickness of the skin with or without cavity

Table 51: Table Pressure Ulcer Classification System – Studies of Nutritional Supplementation*

Study	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Delmi et al., 1990	N/A	N/A	N/A	N/A	N/A
Hartgrink et al., 1998	Normal skin	Persistent erythema of the skin	Blister formation	Superficial subcutaneous necrosis	Deep subcutaneous necrosis
Bourdel-Marchasson, 2000	N/A	Erythematous skin	Superficial layer of broken or blistered skin	Involves subcutaneous tissue	Ulcer extends into the muscle or bone
Houwing et al., 2003		Nonblanchable erythema of intact skin Discoloration of the skin, warmth, edema, induration, or hardness may also be used as indicators particularly on individuals with darker skin	Partial thickness skin loss involving epidermis, dermis, or both The ulcer is superficial and presents clinically as an abrasion or blister	Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia	Extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss

*N/A indicates not applicable.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 52. All studies were RCTs. The study by Bourdel-Marchasson (40) used a cluster randomization design. None of the studies reported adequate allocation concealment methods or a blinded outcome assessment process. Two studies, Hartgrink et al. (43) and Houwing et al., (45) completed a sample size calculation a priori. The losses to follow-up were greater than 30% in all studies except that completed by Houwing et al. (45)and Ek et al. (42) An intention-to-treat analysis was completed by Bourdel-Marchasson (40) only.

Of note, in the study by Bourdel-Marchasson (40) the study groups were not comparable at baseline with respect to pressure ulcer risk scores. Persons in the nutritional intervention group had lower pressure ulcer risk scores, were less dependent, and had lower serum albumin levels. A multivariate analysis found that patients receiving the intervention were significantly less likely to develop a pressure ulcer compared with controls.

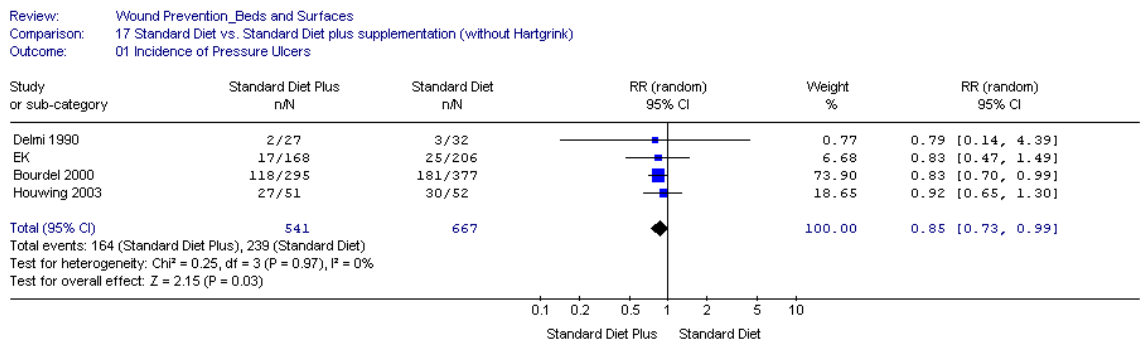
Table 52: Quality Assessment of Included Studies – Nutritional Supplementation*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Delmi et al., 1990	✓	x	x	x	60% at 6 months	Patients who died were not included in the analysis; 6 in the supple-mentation group and 4 in the controls
Hartgrink et al., 1998	✓	x	✓	x	Dropout rate in treatment group was 54% after 1 week because persons were intolerant of the naso-gastric tube feeding At 2 weeks the dropout rate was 33%	x
Bourdel-Marchasson, 2000	✓ (cluster randomization)	x	x	x	30%	✓
Houwing et al., 2003	✓	x	✓	x	3%	x 3 persons not included in analysis
Ek et al., 1991	✓	x	x	Unclear	1%	Missing information on 6 patients

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

Figure 16 reports the results of the meta-analysis of the studies comparing nutritional supplementation and a standard diet to a standard hospital diet alone. There is an overall statistically significant RRR of 15% in the incidence of pressure ulcers in favour of nutritional supplementation to a standard hospital diet. The effect estimate from the study by Hartgrink et al. (43) was not included in the meta-analysis as it was thought that the intervention of 6300 kJ/day (1,500 c/day) supplementation via nasogastric tube was clinically dissimilar to the interventions used in the other 4 studies.



CI indicates confidence interval; RR, relative risk.

Figure 16: Standard Diet Versus Standard Diet Plus Supplementation

Grade of Evidence

Table 53 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of nutritional supplementation plus a standard hospital diet compared with a standard hospital diet alone. The quality of evidence is very low for the outcome of incidence of pressure ulcers.

Table 53: GRADE Evidence Profile – Standard Hospital Diet Versus Standard Hospital Diet Plus Supplementation
Outcome: Incidence of Pressure Ulcers*

Studies	Design	Quality†	Consistency	Directness‡	Other Modifying Factors	No. of Patients			
						SD+	SD	RR (95% CI)	Quality/ Importance
Delmi et al., 1990 Hartgrink et al., 1998 Bourdel-Marchasson, 2000 Houwing et al., 2003	RCT	Some very serious limitations	No important inconsistency	Some uncertainty about directness	None	541	667	0.85 (0.73–0.99)	**Very Low/** Critical
	HIGH	**LOW**	**LOW**	**VERY LOW**	**VERY LOW**				

*CI indicates confidence interval; RCT, randomized controlled trial; RR, relative risk; SD, standard diet; SD+, standard diet plus nutritional supplementation.
†Inadequate allocation concealment, outcome assessor not blinded to treatments allocation, large losses to follow-up (−2).
‡Wide range in follow-up times and energy intake rate of nutritional supplementation, standard hospital diet not described (−1).

Summary of Results

There is very low quality evidence supporting an RRR of 15% in the incidence of pressure ulcers when nutritional supplementation is added to a standard hospital diet.

Repositioning

Research Question

The literature was searched to determine the effect of using different turning schedule frequencies on the incidence of pressure ulcers in a population at risk for developing pressure ulcers. The search strategy is presented in Appendix 4.

Methods

Inclusion Criteria

- systematic reviews (with/without meta-analysis), or RCTs
- studies involving a population at risk for developing pressure ulcers
- studies evaluating the use of various frequencies of turning compared with a standard 2-hour regimen for positioning frequency or other turning schedule frequencies
- studies reporting the number (proportion) of persons developing a new pressure ulcer
- studies reporting the stage of pressure ulcer or in which the stage can be inferred from the description of the ulcer

Exclusion Criteria

- studies evaluating the frequency of position changes with other preventive interventions (other than pressure redistribution surfaces) such that the effect of frequency cannot be determined

Primary Outcome Measure

The primary outcome measure was the incidence of pressure ulcers measured as the number (proportion) of participants developing a new pressure ulcer.

Results of Literature Search

One systematic review and 2 large RCTs were obtained from the literature search (Table 54). (46-48) The study by Vanderwee et al. (48) compared different turning frequencies and positioning, and the study by Defloor et al. (47) compared only different turning schedule frequencies. One Cochrane protocol was also found whose purpose was to conduct a systematic review of research evidence to determine the optimal turning schedule frequency. (49)

The systematic review by Buss et al. (46) determined the most effective time interval for repositioning persons at risk for pressure sore development. The investigators searched Medline, the Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature from the inception of these computerized databases up to the year 2000. Their literature search yielded 5 research reports, 1 of which was the study by Defloor et al. (47) The other 4 studies have not been included in our review for the following reasons: 2 evaluated small shifts in body position, 1 was a non-English thesis, and 1 was a non-RCT.

Table 54: Quality of Evidence of Included Studies – Repositioning*

Study Design	Level of Evidence	Number of Eligible Studies	MAS Update to Systematic Review
Systematic reviews of RCT or Large RCT	1	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g)†		2
Small RCT	2		0
Small RCT unpublished but reported to an international scientific meeting	2(g)		0
Non-RCT with contemporaneous controls	3a		N/A
Non-RCT with historical controls	3b		
Non-RCT presented at international conference	3(g)		
Surveillance (database or register)	4a		
Case series (multisite)	4b		
Case series (single site)	4c		
Retrospective review, modeling	4d		
Case series presented at international conference	4(g)		

* MAS indicates Medical Advisory Secretariat; N/A, not applicable; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meeting. (11)

Characteristics of Included Studies

Table 55 reports the characteristics of the included studies (47;48) The mean age in both studies was 85 years. The follow-up period ranged from 15 days on average in the Vanderwee et al. (48) study to 4 weeks in the study completed by Defloor et al. (47) While both studies used a different pressure classification system for the outcome measure, the classification systems were comparable (Table 56).

Table 55: Characteristics of Included Studies – Repositioning*

Study	Population	Treatment	Control	Follow-Up	Outcome
Vanderwee et al., 2007 N = 235 RCT	Belgian geriatric nursing home residents Median age: 84 (IQR 83–89)	Repositioned with unequal time intervals according to the following sequence: semi-Fowler 30º, right-side lateral position 30º, semi-Fowler 30º, left-side lateral position 30º. Persons lay for 4 hours in a semi-Fowler 30º position and 2 hours in a lateral position 30º. The semi-Fowler was a 30º elevation of the head end and the foot end of the bed. In the lateral position, the patient was rotated 30º with their back supported with an ordinary pillow. The group was lying on a visco-elastic foam overlay mattress (7 cm) The heels were elevated and a standardized sitting protocol was used Persons were asked to stand every 2 hours on their own or with help	Patients were repositioned according to the same turning scheme as used in the treatment group, but with equal time intervals of 4 hours in the lateral 30 and 4 hours in the semi-Fowler 30 position. The group was lying on a visco-elastic foam overlay mattress (7 cm) The heels were elevated and a standardized sitting protocol was used. Persons were asked to stand every 2 hours on their own or with help.	15 days on average	Grade 2–4 lesions European Pressure Ulcer Advisory Panel classification system 1999
Defloor et al., 2005 RCT N = 262 2 hours: n = 63 3 hours: n = 58 4 hours: n = 66 6 hours: n = 63	Geriatric nursing home patients in Belgium Mean age: 85 years (SD 8 years)	Turning every 4 hours Turning every 6 hours A visco-elastic polyurethane foam mattress was used	Turning every 2 hours Turning every 3 hours A standard hospital mattress was used	4 weeks	Grade 2 or greater pressure ulcers AHCPR classification system

*AHCPR indicates Agency for Health Care Policy and Research; IQR, interquartile range; RCT, randomized controlled trial; SD, standard deviation.

Table 56: Table Pressure Ulcer Classification System – Studies of Repositioning*

Study	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
European Pressure Ulcer Advisory Panel classification system 1999	N/A	Nonblanchable erythema	Abrasion or blister	Superficial ulcer	Deep ulcer
AHCPR classification system	N/A	Nonblanchable erythema	Blistering	Superficial ulcer	Deep ulcer

*AHCPR indicates Agency for Health Care Policy and Research; N/A, not applicable.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 57. All studies used a RCT design. The study by Vanderwee et al. (48) did not report using adequate allocation concealment methodology. Neither study used a blinded outcome assessment process.

Table 57: Quality Assessment of Included Studies – Repositioning

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Defloor et al., 2005	✓	✓	✓	x	4.5%	✓
Vanderwee et al., 2007	✓	x	✓	x	0%	✓

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

We could not pool the individual study results of the Defloor et al. (47) and the Vanderwee et al. (48) studies because the treatment and control groups received different interventions. Therefore, we will report on the individual study results.

Vanderwee et al. (48) reported no statistically significant difference in the incidence of pressure ulcers grade 2 or greater in the treatment group compared with the control group (RR, 0.66; 95% CI, 0.37–1.20). Both groups used an alternate foam mattress and were turned every 2 or 4 hours. The similarity in treatment protocols between groups may have contributed to the negative effects.

Defloor et al. (47) used multivariate logistic regression analyses using a standard-care group as a reference, and reported a statistically significant reduction in pressure ulcer lesions of grade 2 or greater in the 4-hourly turning protocol group which was using a pressure redistribution mattress (odds ratio, 0.12; 95% CI, 0.03–0.48).

We completed a subgroup analyses of the Defloor et al. (47) data and report the results in Table 58 and Figures 17 through 22. Results indicate that turning every 4 hours on a pressure redistribution mattress is associated with a 34% RRR in the incidence of grade 1 pressure ulcers compared with turning every 3 hours on a standard foam mattress (Figure 17). We found no difference between the incidence of grade 1 pressure ulcers using a 2-hourly turning schedule and a standard foam mattress compared with a 3-hour turning schedule and a standard foam mattress (RR, 0.90; 95% CI, 0.69–1.16). Therefore, we combined the incidence of grade 1 pressure ulcers for these 2 groups (2 h and 3 h and standard foam mattress) and compared the incidence of grade 1 pressure ulcers with that occurring in the 4-hourly

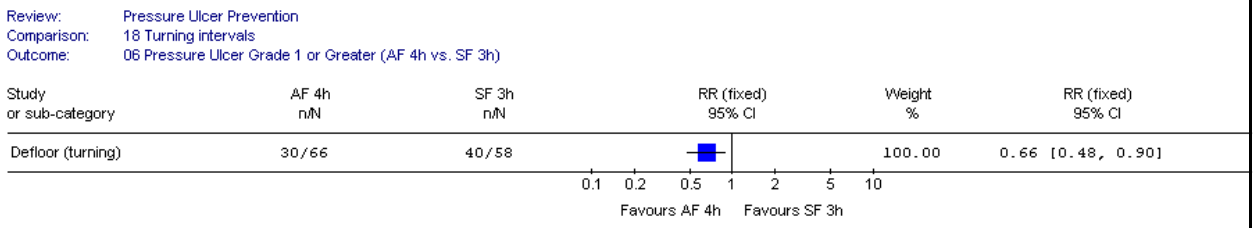
turning schedule group using a pressure redistribution mattress. Results indicate a statistically significant reduction in grade 1 pressure ulcers favoring a 4-hourly turning schedule with a pressure redistribution mattress (RR, 0.70; 95% CI, 0.5– 0.93) (Figure 18).

Similarly, we found a statistically significant reduction in pressure ulcers of grade 2 or greater using a 4-hourly turning schedule with a pressure redistribution mattress compared with either a 2-hourly (RRR of 79%) or 3-hourly (RRR of 87%) turning schedule with a standard foam mattress (Figure 19 and Figure 20). Likewise, a 4-hourly turning schedule with a pressure reducing mattress appears statistically superior to using a 6-hourly turning schedule with a pressure redistribution mattress (Figure 21). Again because there was no difference noted between the 2-hourly turning and 3-hourly turning schedules with a standard foam mattress we combined these 2 groups and compared the incidence of grade 2 or greater pressure ulcers with a 4-hourly turning schedule and a pressure redistribution mattress. Results indicate that a 4-hourly turning schedule was associated with a statistically significant RRR of 84% in grade 2 pressure ulcers compared with the combined incidence rate (RR, 0.16; 95% CI, 0.04–0.66) (Figure 22).

Table 58: Subgroup Analyses – Repositioning*

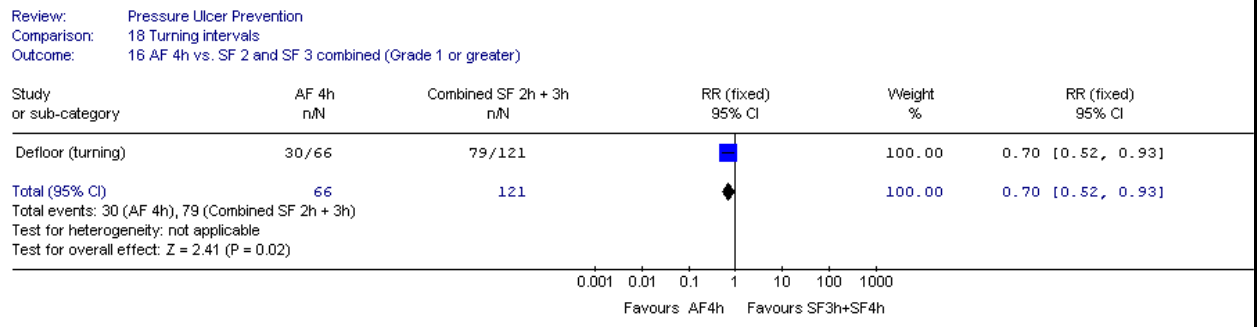
Comparison	RR (95% CI)† Grade 1	RR (95% CI) Grade 2
AF 4h vs. SF 2h	0.73 (0.53–1.02)	**0.21 (0.05–0.94)**
AF 4h vs. SF 3h	**0.66 (0.48–0.98)**	**0.13 (0.03–0.53)**
AF 4h vs. AF 6h	0.73 (0.53–1.02)	**0.19 (0.04–0.84)**
AF 4h vs. SF 2h + SF 3h	**0.70 (0.52–0.93)**	**0.16 (0.04–0.66)**
SF 2h vs. SF 3h	0.90 (0.69–1.16)	0.59 (0.28–1.26)
AF 6h vs. SF2h	1.00 (0.76–1.32)	1.11 (0.48–2.55)
AF 6h vs. SF 3h	0.90 (0.69–1.16)	0.66 (0.32–1.36)

*AF indicates alternative foam mattress (pressure redistribution mattress); CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.
†Fixed effects.



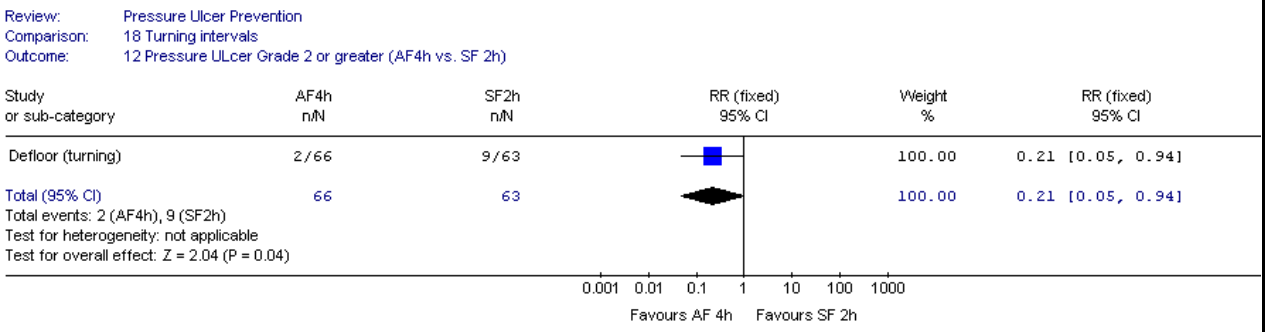
AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 17: Alternate Foam Mattress and Turning 4-hourly Versus Alternate Foam Mattress Turning 3-hourly



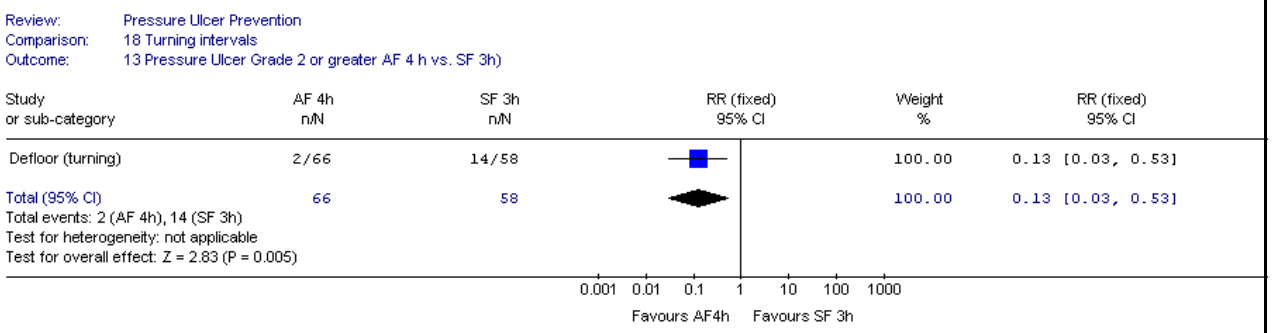
AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 18: Alternate Foam Mattress and Turning 4-hourly Versus Standard Foam Mattress Turning 2-hourly and 3-hourly



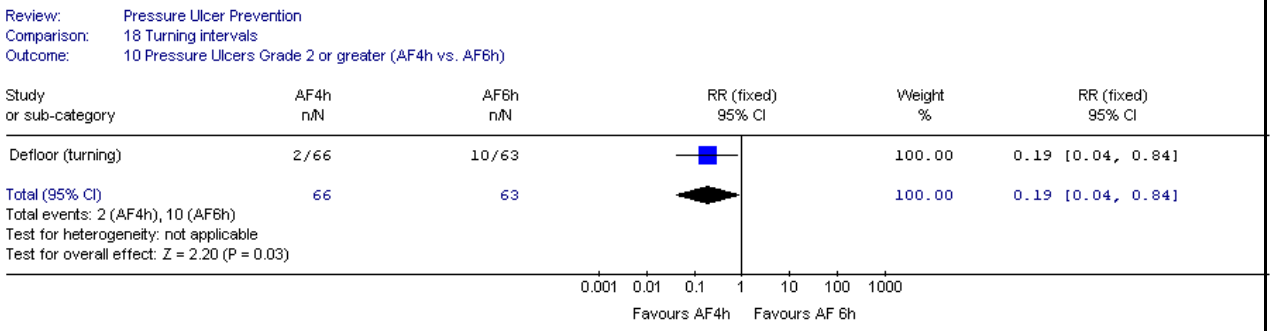
AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 19: Alternate Foam Mattress and Turning 4-hourly Versus Standard Foam Mattress and Turning 2-hourly



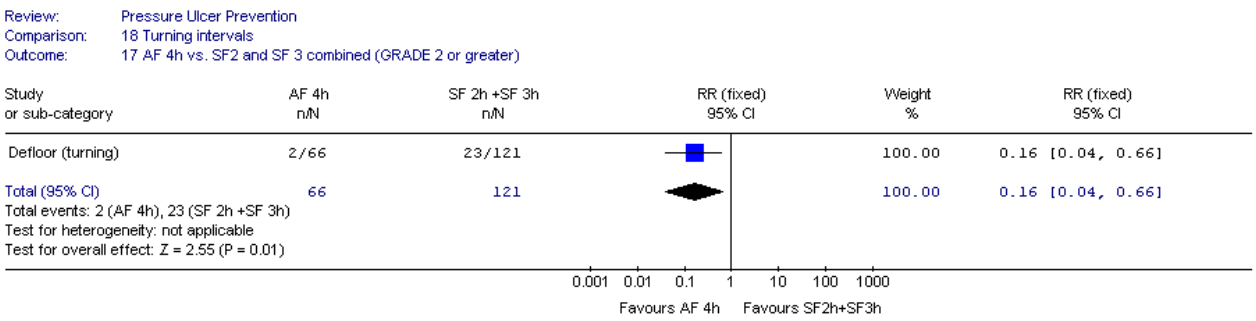
AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 20: Alternate Foam Mattress and Turning 4-hourly Versus Standard Foam Mattress and Turning 3-hourly



AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 21: Alternate Foam Mattress and Turning 4-hourly Versus Alternate Foam Mattress and Turning 6-hourly



AF indicates alternative foam mattress; CI, confidence interval; h, hours; RR, relative risk; SF, standard foam mattress.

Figure 22: Alternate Foam Mattress and Turning 4-hourly Versus Standard Foam Mattress and Turning 2-hourly and 3-hourly

Grade of Evidence

Tables 59 through 61 report the GRADE evidence profile for the body of evidence evaluating the effectiveness of a 4-hourly turning schedule with a pressure reducing mattress compared with a standard foam mattress and a 2-hourly and 3-hourly turning schedule to prevent grade 1 or greater or grade 2 or greater pressure ulcers. The quality of evidence is low.

Table 59: GRADE Evidence Profile – Turning Every 4 Hours Plus Pressure Redistribution Mattress Versus Turning Every 2 or 3 Hours on a Standard Foam Mattress *

Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	No. of Patients		RR (95% CI)	Quality/ Importance
						4h +AP	2h + 3h +SFM		
Defloor et al., 2005	RCT	Some serious limitations†	N/A‡	No uncertainty about directness	Sparse data§	66	121	0.70 (0.52–0.93)	**LOW/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**LOW**				

*AP indicates alternating pressure; SFM, standard foam mattress; RR, relative risk; CI, confidence interval; RCT, randomized controlled trial; N/A, not applicable.
†Lacks blinded outcome assessment (−1)
‡Only 1 study
§Subgroup analyses (−1)

Table 60: GRADE Evidence Profile – Turning Every 4 Hours Plus Pressure Redistribution Mattress Versus Turning Every 2 Hours on a Standard Foam Mattress*

Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	No. of Patients			
						4h +AP	2h +SFM	Relative (RR, 95% CI)	Quality/ Importance
Defloor et al., 2005	RCT	Some serious limitations†	N/A‡	No uncertainty about directness	Sparse data§	66	63	0.21 (0.05–0.94)	**LOW/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**LOW**				

*AP indicates alternating pressure; SFM, standard foam mattress; RR, relative risk; CI, confidence interval; RCT, randomized controlled trial; N/A, not applicable.
†Lacks blinded outcome assessment (−1)
‡One study
§Subgroup analyses (−1)

Table 61: GRADE Evidence Profile – Turning Every 4 Hours Plus Pressure-Reducing Mattress Versus Turning Every 2 or 3 Hours on a Standard Foam Mattress

Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	No. of Patients			
						4h +AP	2h + 3h +SFM	RR (95% CI)	Quality/ Importance
Defloor et al., 2005	RCT	Some very serious limitations†	N/A‡	No uncertainty about directness	Sparse data§	66	121	0.16 (0.04–0.66)	**LOW/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**LOW**				

*AP indicates alternating pressure; SFM, standard foam mattress; RR, relative risk; CI, confidence interval; RCT, randomized controlled trial; N/A, not applicable.
†Lacks blinded outcome assessment (−1)
‡One study
§Subgroup analyses (−1)

Summary of Results

There is low quality evidence supporting the superiority of a 4-hourly turning schedule with a pressure redistribution mattress compared with a 2-hourly or 3-hourly turning schedule and a standard foam mattress to reduce the incidence of grade 1 or 2 pressure ulcers.

Incontinence Management

Research Question

- The literature was searched to determine:The effectiveness of using a structured skin care protocol compared with no structured skin care protocol in persons who have urinary and fecal incontinence
- The effectiveness of using a pH-balanced cleanser compared with soap and water to reduce the incidence of pressure ulcers in persons who have urinary and fecal incontinence.

The search strategy is presented in Appendix 5.

Methods

Inclusion Criteria

- systematic reviews (with/without meta-analysis), RCTs, and non-RCT study designs
- studies involving a population with urinary and fecal incontinence
- studies evaluating the use of a structured skin care protocol defined as having explicit components and a defined regimen of care
- studies comparing a pH-balanced cleanser with soap and water
- studies reporting the number (proportion) of persons developing a new pressure ulcer
- studies reporting the stage of pressure ulcer or in which the stage can be inferred from the description of the ulcer

Exclusion Criteria

- studies reporting only the incidence of dermatitis as an outcome measure

Primary Outcome Measure

The primary outcome measure was the incidence of pressure ulcers measured as the number (proportion) of participants developing a new pressure ulcer.

Results of Literature Search

Skin Care Protocol

Two reports describing the same observational research study were obtained from the literature search (Table 62). The objective of the study was to assess the effectiveness of a skin care protocol on the incidence of pressure ulcers in a geriatric population. The evaluation used a before-and-after research design.

pH-Balanced Cleanser Versus Soap and Water

One small RCT was obtained from the literature that determined the effectiveness of a pH-balanced cleanser for skin care compared with soap and water in persons with urinary and fecal incontinence (Table 62).

Table 62: Quality of Evidence of Included Studies – Incontinence Management*

Study Design	Level of Evidence	Number of Eligible Studies	Medical Advisory Secretariat Update to Systematic Review
Systematic reviews of RCT or Large RCT	1	0	0
Large RCT unpublished but reported to an international scientific meeting	1(g)†		0
Small RCT	2		1
Small RCT unpublished but reported to an international scientific meeting	2(g)		0
Non-RCT with contemporaneous controls	3a		2 (same study)
Non-RCT with historical controls	3b		
Non-RCT presented at international conference	3(g)		
Surveillance (database or register)	4a		
Case series (multisite)	4b		
Case series (single site)	4c		
Retrospective review, modeling	4d		
Case series presented at international conference	4(g)		

RCT indicates randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) An additional designation "g" was added for preliminary reports of studies that have been presented at international scientific meeting. (11)

Comparison 1: Skin Protocols Versus Standard Care

Characteristics of Included Studies

Table 63 reports the characteristics of the included studies comparing the effectiveness of a skin care protocol with that of standard care. Both studies report on the same protocol. The mean age was 81 years. The duration of each study phase was 3 months. While both reports (50;51) described the same study, Hunter et al. (50) reported using the Agency for Health Care Policy and Research pressure ulcer classification system and Thompson et al. (51) using the NPUAP system (Table 64). We were unsuccessful at contacting the authors to reconcile this discrepancy.

Table 63: Characteristics of Included Studies – Skin Protocols Versus Standard Care

Study	Population	Treatment	Control	Follow-Up	Outcome
Hunter et al., 2003 Thompson et al., 2005 N = 136 Observational (before-and-after study design)	Residents in 2 long-term care facility in the US with at least 1-week stay with urinary and fecal incontinence. Incontinence was defined as 2 or more episodes of bladder or bowel incontinence in 1 week. Mean Age: Pre: 83 y Post: 80 y The majority of persons in the before phase of the study also participated in the after phase.	Body wash and skin protectant to routine care **Components** Educational session for nursing staff on how to assess stage I and stage II pressure ulcers, the physiology of ageing skin, the introduction of a nonirritating, pH-balanced, no-rinse cleanser/deodorizer body wash and a skin protectant (a fine grain emulsion consisting of 50% lanolin with beeswax and petrolatum additives) into skin care protocols Skin care protocols included skin assessment techniques, prevention and treatment for dry skin, identification of stage I and stage II pressure ulcers and skin protection and early intervention for incontinence. **Regimen** Cleanse skin with the body wash (Lantiseptic All Body Wash, Summit Industries, Inc, Marietta, GA) after each incontinent episode and to apply the skin protectant (Lantiseptic Skin Protectant, Summit Industries, Marietta, GA) to the skin. Skin protectant was to be applied at least every 8 hours and after every cleansing when incontinent. Check each incontinent resident's skin every 2 hours. Compliance Monitoring surveillance: directors and assistant directors of nursing monitored and reinforced protocol compliance	Completed 3 months before the treatment period. Documentation of skin assessment and pressure ulcer development, treatment, healing time and incontinence. Standard care at each agency included a skin care protocols based on the AHCPR guidelines. Agency skin care protocol included daily skin condition reports, weekly skin assessments, and dietary risk management. Briefs for incontinence were left open for air circulation; periwash and barrier cream were not used unless the resident was at moderate risk for skin breakdown.	3 months for each phase of the study	Incidence of stage 1 and 2 pressure ulcers Agency for Health Care Policy and Research, 1992 classification system And NPUAP definitions

* NPUAP indicates National Pressure Ulcer Advisory Panel.

Table 64: Table Pressure Ulcer Classification System – Studies of Skin Protocols Versus Standard Care*

Study	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
*Hunter et al., 2003 †Thompson et al., 2005	N/A	*Nonblanchable erythema of intake skin †Defined area of persistent redness in light skin. Persistent red, blue or purple in dark skin.	*Partial thickness skin loss involving epidemis and/or dermis. †Partial-thickness skin loss involving the loss of epidermis, dermis, or both. The ulcer is superficial and presents clinically as an abrasion, blister, or shallow crater.	N/A for study	N/A for study

*N/A indicates not applicable.

Quality Assessment of Included Studies

The information in both the Thompson et al. (51) report and the Hunter et al. (50) report was used to complete the quality assessment of the study (Table 65). Of the 8 criteria used to assess the quality, 3 were not satisfied. The study used a convenience sample instead of consecutive enrollment. However, with the exception of 2 residents that declined participation, the study sample included all residents in both facilities that met the inclusion and exclusion criteria. It is unclear if the participants in both the pre phase and the post phase were comparable in terms of age and urinary and fecal incontinence status. However, it is reported that 77% of the study sample participated in both the pre- and post-study phases. Finally, the caregivers were the data collectors, and because of this the outcome measure was not assessed independently of the exposure status.

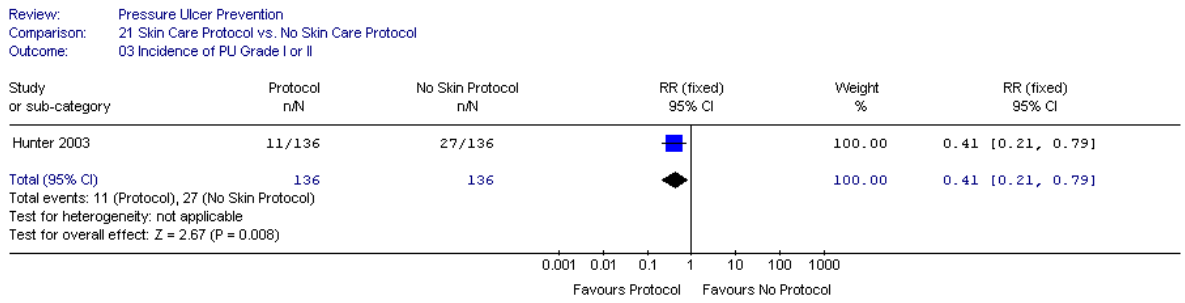
Of note, the investigators state that the only change in the care was the addition of the specific body wash and the skin protector. However, the treatment group (postphase group) also received structured education sessions, and specific components of the skin care protocol were stipulated as well as a skin care regimen (checking patient every 2 hours and apply skin protector at least every 8 hours). Indeed, the authors acknowledge that the education provided to the nursing staff may have influenced the study outcome by either enhancing the knowledge base of the caregivers and/or increasing the caregivers' vigilance for skin assessment. The authors further state that it is difficult to determine whether the decrease in the incidence of pressure ulcers was due to the study treatment (skin care protocol) or an increased staff vigilance for pressure ulcer assessment.

Table 65: Quality Assessment of Included Studies – Skin Protocols Versus Standard Care

Study	Inclusion/ Exclusion Criteria Stated	Consecutive Sampling Used	Are Baseline Characteristics In Groups Are Similar	Is Treatment Valid and Reliable	Is a Reliable and Valid Outcome Measure Used	Is Outcome Measure Done Independently of Exposure Status	Is Duration of Follow-Up Adequate	Loss to Follow-Up (%)
Hunter et al., 2003	✓	X Convenience sample. All residents other than 2 in the facility participated.	Unclear 105 (77%) of the residents in the before phase participated in the after phase. Characteristics of the study sample by phase were not reported.	✓	✓	X Caregivers were the data collectors.	✓ 3-month duration for each phase	✓ 13 persons died and 17 were discharged. The full study sample (n = 136) was used to calculate incidence of pressure ulcers.

Results

There was a significant difference in the total number of persons with stage 1 or 2 new pressure ulcers between phase 1 and phase 2 (19.8% vs. 8.1%, *P* = .000) and therefore a statistically significant RRR of developing a pressure ulcer in persons treated with the skin care protocol compared with the control group (RR, 0.41; 95% CI, 0.21–0.70) (Figure 23). We chose to express the estimate of effect as a RR. However, given that the baseline risk is less than 30%, the odds ratio may be the preferred estimate of effect. (52) The odds ratio is 0.36 (fixed effects model, 95% CI, 0.17–0.75).



CI indicates confidence interval; PU, pressure ulcers; RR, relative risk.

Figure 23: Skin Care Protocol Versus No Skin Care Protocol

Grade of Evidence

Table 66 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of a structured skin care protocol compared with standard care in persons with urinary and fecal incontinence. The quality of evidence is very low for the outcome incidence of pressure ulcers grade 1 or 2.

Table 66: GRADE Evidence Profile – Structured Skin Care Protocol Versus Standard Care Outcome: Incidence of Pressure Ulcers Grade 1 or 2*

Studies	Design	Quality	Consistency	Directness	Other Modifying Factors	No. of Patients		RR(95% CI)	
						Pre	Post	Incidence of pressure ulcers grade 1 or 2	Quality/ Importance
Hunter et al., 2003	Observa-tional	Some serious limitations†	N/A‡	No uncertainty about directness	Sparse data§	136	136	0.41 (0.21–0.79)	**Very Low/** Critical
	LOW	**VERY LOW**	**VERY LOW**	**VERY LOW**	**VERY LOW**				

*RR indicates relative risk; CI, confidence interval; N/A, not applicable.
†Lacks blinded outcome assessment (−1)
‡Only 1 study
§One study n = 136

Summary of Results

There is very low quality evidence supporting the benefit of a structured skin care protocol to reduce the incidence of grade 1 or 2 pressure ulcers.

Comparison 2: pH-Balanced Cleanser Versus Soap and Water

Characteristics of Included Studies

Table 67 reports the characteristics of 1 study (53) comparing the effectiveness of a pH-balanced cleanser with that of soap and water. The treatment group was slightly older than the control group on average. The median number of incontinent episodes per 24 hours was comparable in both groups (4 in the control group and 5 in the treatment group). The treatment group had a longer median length of stay in the nursing home or hospital (1.72 years) compared with the control group (0.38 years). The study used the Stirling pressure sore classification system, which graded pressure sores as either grade 0 (healthy), grade 1 (erythema), or grade 2 (broken skin) (Table 68).

Table 67: Characteristics of Included Studies – ph-Balanced Cleanser Versus Soap and Water*

Study	Population	Treatment	Control	Follow-Up	Outcome
Cooper and Gray, 2001 RCT N = 93	Long-term care residents for elderly or dependent patients in the United Kingdom Any persons with incontinence including i) urinary ii) fecal iii) urofecal, iv) catheterized but fecally incontinent catheterized but bypassing urine and/or fecally incontinent. Mean age: Treatment: 85 y Control: 79 y	Clinisan pH-balanced foam cleanser. pH of 5.5 combined with an emollient, water-repellent deodorant and a water-repellent barrier.	Soap and water Standard hospital soap with pH of 9.5–10.5.	14 days	Incidence of pressure ulcers Stirling Pressure Sore Severity Scale

*RCT indicates randomized controlled trial.

Table 68: Pressure Ulcer Classification System – Study of pH-Balanced Cleanser Versus Soap and Water*

Study	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Cooper and Gray, 2001	Health skin, normal appearance, intact skin with no alteration in the colour	Erythema Discoloration of intact skin, abnormal redness	Broken skin Partial thickness skin loss or damage involving epidermis or dermis	N/A	N/A

*N/A indicates not applicable.

Quality Assessment of Included Studies

The individual study quality assessment is presented in Table 69. The study by Cooper and Gray (53) used an RCT design. Initially, the first 11 subjects were randomized using unmarked envelopes which contained the treatment allocation (soap and water or Clinisan). However, because patients changed hospital rooms frequently, it was difficult to keep treatment assignment organized. Therefore, the investigators switched to a cluster randomization scheme and randomized a unit (ward) to either treatment or control. It is unknown if allocation concealment was maintained for the cluster randomization. The authors do not report completing a sample size calculation. Photographs were taken of the skin (pressure ulcer) and all slides were assessed in a blinded fashion. Loss to follow-up was minimal. An ITT analysis was not completed, but rates of pressure ulcer incidence were calculated on the per-protocol sample.

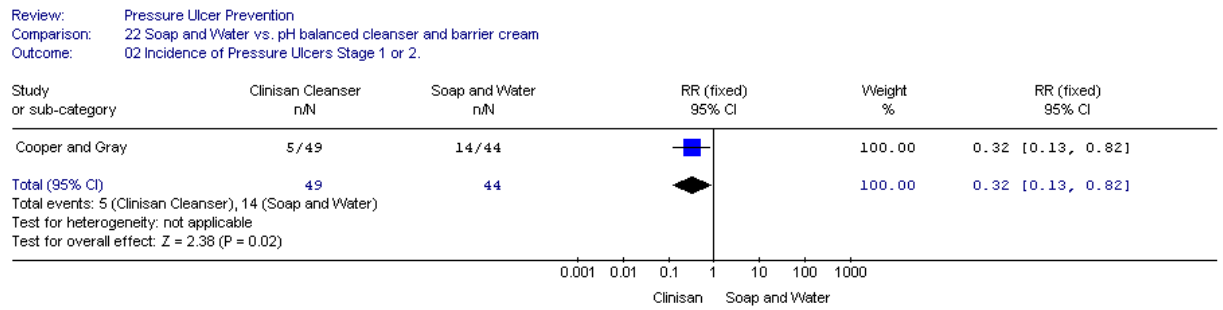
Table 69: Quality Assessment of Included Studies – pH-Balanced Cleanser Versus Soap and Water*

Study	RCT	Concealment	Sample Size Calculation	Blinded Assessment	Loss to Follow-Up	ITT Analysis
Cooper and Gray, 2001	✓	unknown	x	✓	7%	x

*ITT indicates intention-to-treat; RCT, randomized controlled trial.

Results

The incidence of pressure ulcer development grade 1 or 2 was 5/41 (12%) in the treatment group and 14/46 (30%) in the control group (per-protocol analysis). Figure 24 reports an ITT analysis. There is a statistically significant decrease in the incidence of pressure ulcers stage 1 or 2 in the group that received treatment with the pH-balanced cleanser compared with those using soap and water (RR, 0.32 [95% CI, 0.13–0.82]). We chose to present the estimate of effect as an RR because the baseline risk in the control group (soap and water) is 31%. (52)



CI indicates confidence interval; RR, relative risk.

Figure 24: Soap and Water Versus pH-Balanced Cleanser and Barrier Cream

Grade of Evidence

Table 70 reports the GRADE evidence profile for the body of evidence evaluating the effectiveness of a pH-balanced skin cleanser compared with soap and water in persons with urinary and fecal incontinence. The quality of evidence is low for the outcome incidence of pressure ulcers grade 1 or 2.

Table 70: GRADE Evidence Profile – pH-Balanced Skin Cleanser Versus Soap and Water Outcome: Incidence of Pressure Ulcers Grade 1 or 2*

Studies	Design	Quality	Consist-ency	Direct-ness	Other Modifying Factors	No. of Patients			
						pH-Balanced cleanser	Soap and Water	RR (95% CI)	Quality/ Importance
Cooper and Gray, 2001	RCT	Some serious limitations†	N/A‡	No uncertainty about directness	Sparse data§	49	44	0.32 (0.13–0.82)	**Low/** Critical
	HIGH	**MOD**	**MOD**	**MOD**	**LOW**				

*RR indicates relative risk; CI, confidence interval; N/A, not applicable; RCT, randomized controlled trial.
†Concealment status unknown, changed from individual randomization to cluster randomization. Sample size not completed for cluster randomization methods. (−1)
‡ Only 1 study.
§One study n = 93 (−1).

Summary of Results

There is low quality evidence supporting the benefit of a pH-balanced cleanser compared with soap and water to reduce the incidence of grade 1 or 2 pressure ulcers in persons with urinary and fecal incontinence.

Summary of Results

Table 71 consolidates the effect estimates for the comparisons presented in this review. Moderate quality evidence is available to support the use of an alternative foam mattress to reduce the incidence of pressure ulcers compared with a standard foam mattress for patients in acute care.

Moderate quality evidence also exists for 2 other comparisons including:

- alternating pressure mattress versus alternating pressure overlay
- Australian sheepskin versus standard treatment

There is a statistically nonsignificant difference in the incidence of pressure ulcers in persons using an alternating pressure mattress compared with an alternating pressure overlay.

There is a statistically significant difference in the incidence of pressure ulcers in persons using an Australian sheepskin compared with standard care. However, clinical experts indicate this intervention is not feasible given that the sheepskins move about in the bed and may contribute to wound infection.

Table 71: Summary of Systematic Review Results*

Comparison	Evidence	Model	Results RR (95% CI)	Quality of Evidence
Risk assessment scale vs. none or clinical judgment	Bale, 1995	FE	0.11 (0.03–0.46)	Very Low
Alternative foam mattress vs. standard mattress	Gray and Campbell, 1994 Hofman et al., 1994 Santy et al., 1994 Collier, 1996	RE	0.31 (0.21–0.46)	Moderate
Alternative foam mattress vs. alternative foam mattress	Kemp et al., 1993 Vyhlidal et al., 1997 Gray and Smith, 2000	FE FE FE	0.66 (0.37–1.16) 0.42 (0.18–0.96) 1.00 (0.15–6.82)	Very Low
Alternating pressure mattress or overlay vs. standard foam mattress	Andersen et al., 1982 Sanada et al., 2003	FE FE	0.32 (0.14–0.74) 0.29 (0.12–0.73)	Very Low
Alternating pressure mattress vs. alternating pressure overlay	Nixon et al., 2006	FE	0.96 (0.74–1.24)	Moderate
Sheepskin vs. standard treatment	McGowan et al., 2000 Jolley et al., 2004	RE	0.42 (0.22–0.81)	Moderate
Alternating pressure mattress (Micropulse System) vs. standard care in perioperative setting	Aronovitch et al., 1999 Russell and Lichtenstein, 2000	RE	0.21 (0.06–0.70)	Very Low
Vesico-elastic polymer (gel pad) on operating table vs. standard operating table foam mattress	Nixon et al., 1998	FE	0.53 (0.33–0.85)	Low
Air suspension bed vs. standard ICU bed	Inman et al., 1993	FE	0.24 (0.11–0.53)	Low
Alternating pressure mattress vs. alternate foam mattress	Whitney et al., 1984 Stapleton, 1986	RE	0.89 (0.54–1.47)	Very Low
Nutritional supplementation pulse standard diet hospital diet vs. standard hospital diet alone	Delmi et al., 1990 Ek et al., 1991 Bourdel-Marchasson, 2000 Houwing et al., 2003	RE	0.85 (0.73–0.99)	Very Low
Repositioning every 4 hours on an alternative foam mattress vs. every 2 hours on a standard foam mattress	Defloor et al., 2005	FE	0.21 (0.05–0.94)	Low

Structured skin care protocol vs. standard care	Hunter et al., 2003	FE	0.41 (0.21–0.79)	Very Low
pH-balanced cleanser vs. soap and water.	Cooper and Gray, 2001	FE	0.32 (0.13–0.82)	Low

*FE indicates fixed-effects; RE , random-effects; RR, relative risk; CI, confidence interval.

In 2005, the Registered Nurses Association of Ontario (RNAO) systematically reviewed similar preventive interventions for pressure ulcers. (50;54) Table 72 reports the levels of evidence for the interventions assessed in this review at the time of the RNAO review. Our systematic review has improved the level of evidence for risk assessment (from level 5 to level 3a) and skin care (use of a pH-balanced skin cleanser, level 5 to level 2); however, the quality of the evidence is still very low and low, respectively. Overall there remains a paucity of moderate or higher quality evidence in the literature to support many of the preventive interventions. Until better quality of evidence is available, pressure ulcer prevention must be guided by expert opinion for those interventions where low or very low quality evidence supports the effectiveness of such interventions.

Table 72: Registered Nurses Association of Ontario Guidelines 2005

Intervention	Recommendation	Level of Evidence RNAO Guidelines 2005†	Level of Evidence 2008†	Quality of Evidence 2008
Risk assessment	Complete risk assessment	5	3a	Very Low
surfaces	Use high density (alternative) foam mattress	1	1 (SR)	Moderate
	Consider pressure redistribution surfaces intraoperateively for high risk persons.	1	1 (Large RCT)	Low
Turning and positioning	Turn at least every 2 hours on standard foam.	5	5	
	Turn 4-hourly on pressure redistribution mattress.	N/A	2	Low
Skin care	Use protective barriers and pH-balanced skin cleanser.	5	2	Low
	Skin care protocol	N/A	3a	Very Low
Nutrition	Supplement critically ill older clients	1 (large RCT)	1 (SR)	Very Low
Education	Structured, organized and comprehensive educational programs	5	Not Reviewed	N/A
Delivery of care	Interdisciplinary approach	5	Not Reviewed	N/A

RCT indicates randomized controlled trial; SR, systematic review; N/A, not applicable.
†Levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (11) See Table 1 in this report for more detail.
Level 1 = SR or large RCT
Level 2 = Small RCT
Level 3a = Controlled clinical trial.
Level 5 = Expert Opinion

Appendices

Appendix 1: Search Strategy for Risk Assessment

Search date: February 26, 2008
Databases searched: MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, INHTA/CRD

Database: Ovid MEDLINE(R) <1950 to February Week 2 2008>
Search Strategy:

1	exp Pressure Ulcer/ (7358)
2	(((pressure or bed or decubitus) adj2 (sore$ or ulcer$)) or bedsore$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (8686)
3	1 or 2 (8686)
4	exp Risk Assessment/ (87361)
5	exp "Severity of Illness Index"/ (90294)
6	exp "Reproducibility of Results"/ (150807)
7	exp Risk Management/ (104932)
8	exp "Predictive Value of Tests"/ (80491)
9	exp Nursing Assessment/ or exp "Weights and Measures"/ or exp Validation Studies/ (211803)
10	((Norton or Waterlow or Braden or Care Dependency) adj4 (Scale$ or instrument$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (218)
11	(risk adj4 (assess$ or calculat$ or score$ or predict$ or scale$ or instrument$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (125336)
12	or/4-11 (599506)
13	3 and 12 (1627)
14	limit 13 to (english language and humans and yr="1997 - 2008") (1056)
15	limit 14 to (controlled clinical trial or meta analysis or randomized controlled trial) (77)
16	exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (34655)
17	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (67764)
18	exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (522495)
19	exp Double-Blind Method/ (94618)
20	exp Control Groups/ (822)
21	exp Placebos/ (26618)
22	RCT.mp. (2558)
23	or/15-22 (624606)
24	14 and 23 (196)

Database: EMBASE <1980 to 2008 Week 08>
Search Strategy:

1	exp DECUBITUS/ (3867)

2 ((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3146)
3 bedsore$.mp. (154)
4 or/1-3 (4758)
5 exp Validation Process/ or exp Risk Assessment/ or exp Scoring System/ (289704)
6 exp Reproducibility/ (32728)
7 exp Risk Management/ (9906)
8 exp "Prediction and Forecasting"/ (278725)
9 exp Nursing Assessment/ (40)
10 exp "NAMED INVENTORIES, QUESTIONNAIRES AND RATING SCALES"/ (33227)
11 exp Validation Study/ (4404)
12 ((Norton or Waterlow or Braden or Care Dependency) adj4 (Scale$ or instrument$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (70)
13 (risk adj4 (assess$ or calculat$ or score$ or predict$ or scale$ or instrument$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (188794)
14 exp rating scale/ (49508)
15 or/5-14 (643661)
16 4 and 15 (633)
17 limit 16 to (human and english language and yr="1997 - 2008") (421)
18 Randomized Controlled Trial/ (154703)
19 exp Randomization/ (25108)
20 exp RANDOM SAMPLE/ (981)
21 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (279621)
22 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56340)
23 Double Blind Procedure/ (68338)
24 exp Triple Blind Procedure/ (8)
25 exp Control Group/ (1437)
26 exp PLACEBO/ (110247)
27 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (400713)
28 or/18-27 (609634)
29 17 and 28 (100)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to February Week 3 2008>
Search Strategy:

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1 exp Pressure Ulcer/ (5067)
2 (((pressure or bed or decubitus) adj2 (sore$ or ulcer$)) or bedsore$).mp. [mp=title, subject heading word, abstract, instrumentation] (5741)
3 1 or 2 (5741)
4 exp Risk Assessment/ (11570)
5 exp "Severity of Illness Indices"/ (7071)
6 exp "Reproducibility of Results"/ (4649)
7 exp Risk Management/ (5441)

8 exp "Predictive Value of Tests"/ (6607)
9 exp Nursing Assessment/ (10283)
10 exp Scales/ or exp Clinical Assessment Tools/ or exp Braden Scale for Predicting Pressure Sore Risk/ (66516)
11 exp Instrument Validation/ (9215)
12 exp Validation Studies/ (8444)
13 exp Wound Assessment/ (1587)
14 ((Norton or Waterlow or Braden or Care Dependency) adj4 (Scale$ or instrument$)).mp. [mp=title, subject heading word, abstract, instrumentation] (558)
15 (risk adj4 (assess$ or calculat$ or score$ or predict$ or scale$ or instrument$)).mp. [mp=title, subject heading word, abstract, instrumentation] (23282)
16 or/4-15 (110645)
17 3 and 16 (1860)
18 limit 17 to (english and yr="1997 - 2008") (1341)
19 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (65135)
20 RCT.mp. (810)
21 exp Meta Analysis/ (6067)
22 exp "Systematic Review"/ (3491)
23 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (21587)
24 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (12702)
25 exp PLACEBOS/ (4008)
26 or/19-25 (85090)
27 18 and 26 (148)

Appendix 2: Search Strategy for Pressure Redistribution Devices

Search date: October 24, 2007
Databases searched: Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase, Cochrane Library, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to October Week 3 2007>
Search Strategy:

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1 exp Beds/ (1214)
2 (bed or beds or bedding).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (31944)
3 (mattress$ or cushion$ or foam$ or transfoam$ or overlay$ or pad or pads or gel).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (123324)
4 (pressure adj1 (relie$ or reduc$ or device$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (2660)
5 (positioning or reposition$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (15147)
6 (elevation adj1 device$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1)
7 ((low adj pressure) and (support$ or device$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (842)
8 (constant adj1 pressure).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (671)
9 (alternat$ adj1 pressure).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (75)
10 ((air or water) adj1 suspension).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (67)
11 (static adj1 air).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (25)
12 (therarest or clinifloat or vaperm or maxifloat or hammock$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (100)
13 (foot adj1 waffle).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (3)
14 (silicore or pegasus).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (48)
15 (cairwave adj1 therapy).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (4)
16 (turning adj1 table$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1)
17 (kinetic adj1 (table$ or therap$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (42)
18 (air adj bag).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (156)
19 or/1-18 (172565)
20 exp Pressure Ulcer/ (3354)

21 ((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (4099)
22 20 or 21 (4099)
23 19 and 22 (1118)
24 limit 23 to (humans and english language and yr="2004 - 2007") (293)
25 limit 24 to (controlled clinical trial or meta analysis or randomized controlled trial) (35)
26 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (55568)
27 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (329544)
28 exp Double-Blind Method/ (48416)
29 exp Control Groups/ (498)
30 exp Placebos/ (8441)
31 RCT.mp. (2048)
32 or/25-31 (371081)
33 24 and 32 (61)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to October Week 3 2007>
Search Strategy:

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1 exp "bedding and linens"/ or exp "beds and mattresses"/ (2148)
2 (bed or beds or bedding).mp. [mp=title, subject heading word, abstract, instrumentation] (8804)
3 (mattress$ or cushion$ or foam$ or transfoam$ or overlay$ or pad or pads or gel).mp. [mp=title, subject heading word, abstract, instrumentation] (5222)
4 (mattress$ or cushion$ or foam$ or transfoam$ or overlay$ or pad or pads or gel).mp. [mp=title, subject heading word, abstract, instrumentation] (5222)
5 exp Patient Positioning/ (3989)
6 (positioning or reposition$).mp. [mp=title, subject heading word, abstract, instrumentation] (4577)
7 ((low adj pressure) and (support$ or device$)).mp. [mp=title, subject heading word, abstract, instrumentation] (57)
8 (constant adj1 pressure).mp. [mp=title, subject heading word, abstract, instrumentation] (45)
9 (alternat$ adj1 pressure).mp. [mp=title, subject heading word, abstract, instrumentation] (153)
10 ((air or water) adj1 suspension).mp. [mp=title, subject heading word, abstract, instrumentation] (8)
11 (therarest or clinifloat or vaperm or maxifloat or hammock$).mp. [mp=title, subject heading word, abstract, instrumentation] (15)
12 (foot adj1 waffle).mp. [mp=title, subject heading word, abstract, instrumentation] (3)
13 (silicore or pegasus).mp. [mp=title, subject heading word, abstract, instrumentation] (17)
14 (cairwave adj1 therapy).mp. [mp=title, subject heading word, abstract, instrumentation] (2)
15 (turning adj1 table$).mp. [mp=title, subject heading word, abstract, instrumentation] (2)
16 (kinetic adj1 (table$ or therap$)).mp. [mp=title, subject heading word, abstract, instrumentation] (77)
17 (air adj bag).mp. [mp=title, subject heading word, abstract, instrumentation] (54)
18 (elevation adj1 device$).mp. [mp=title, subject heading word, abstract, instrumentation] (1)
19 (static adj1 air).mp. [mp=title, subject heading word, abstract, instrumentation] (8)
20 or/1-19 (17521)
21 exp Pressure Ulcer/ (4966)

22 ((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (5583)
23 21 or 22 (5583)
24 20 and 23 (1430)
25 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (61139)
26 RCT.mp. (741)
27 exp Meta Analysis/ (5741)
28 exp "Systematic Review"/ (3348)
29 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (20170)
30 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (11627)
31 exp PLACEBOS/ (3830)
32 or/25-31 (79660)
33 24 and 32 (164)
34 limit 33 to (english and yr="2004 - 2007") (51)

Database: EMBASE <1980 to 2007 Week 42>
Search Strategy:

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1 exp Bed/ (2465)
2 (bed or beds or bedding).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (50844)
3 (mattress$ or cushion$ or foam$ or transfoam$ or overlay$ or pad or pads or gel).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (205228)
4 (pressure adj1 (relie$ or reduc$ or device$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (5470)
5 (positioning or reposition$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (24928)
6 exp Patient Positioning/ (6783)
7 (elevation adj1 device$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1)
8 ((low adj pressure) and (support$ or device$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (443)
9 (constant adj1 pressure).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1508)
10 (alternat$ adj1 pressure).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (71)
11 ((air or water) adj1 suspension).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (530)
12 (static adj1 air).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (71)
13 (therarest or clinifloat or vaperm or maxifloat or hammock$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (155)
14 (foot adj1 waffle).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (0)
15 (silicore or pegasus).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (42)

16 (cairwave adj1 therapy).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (0)
17 (turning adj1 table$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1)
18 (kinetic adj1 (table$ or therap$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (64)
19 (air adj1 bag).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (174)
20 or/1-19 (286534)
21 exp Decubitus/ (3736)
22 ((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3053)
23 21 or 22 (4571)
24 20 and 23 (968)
25 limit 24 to (human and english language and yr="2004 - 2007") (182)
26 Randomized Controlled Trial/ (150225)
27 exp Randomization/ (24211)
28 exp RANDOM SAMPLE/ (823)
29 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).ti,mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (77407)
30 Double Blind Procedure/ (66927)
31 exp Triple Blind Procedure/ (8)
32 exp Control Group/ (1062)
33 exp PLACEBO/ (105480)
34 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (389019)
35 or/26-34 (514868)
36 25 and 35 (35)

Textwords searched in INAHTA/CRD: (bed or bedding or cushion or pillow or pressure relief or pressure relieving or pressure reduction or mattress or positioning or repositioning or therarest or clinifloat or vaperm or maxifloat or hammock or silicore or pegasus or cairwave) and (pressure sore or pressure ulcer or decubitus or bedsore)

Appendix 3: Search Strategy for Nutritional Supplementation

Search date: October 26, 2007
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, Embase, Cochrane Library, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to October Week 3 2007>
Search Strategy:

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1 exp Pressure Ulcer/ (3354)
2 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (4369)
3 bedsore$.mp. (93)
4 or/1-3 (4411)
5 exp Nutrition Therapy/ (21903)
6 exp Diet/ (54480)
7 exp Food/ (293634)
8 (nutri$ or diet$ or food$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (293881)
9 (enteral or parenteral or protein$ or vitamin$ or mineral$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1339881)
10 exp "amino acids, peptides, and proteins"/ (1912805)
11 exp Dietary Supplements/ or exp Antioxidants/ (137725)
12 growth substances/ or exp vitamins/ (76725)
13 exp "enzymes and coenzymes"/ (819718)
14 exp Enzyme Inhibitors/ (341584)
15 exp Minerals/ (31108)
16 exp Lipids/ (271328)
17 exp Antilipemic Agents/ (28150)
18 or/5-17 (2657807)
19 4 and 18 (760)
20 limit 19 to (humans and english language and yr="2003 - 2007") (271)
21 limit 20 to (controlled clinical trial or meta analysis or randomized controlled trial) (29)
22 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (55568)
23 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (329544)
24 exp Double-Blind Method/ (48416)
25 exp Control Groups/ (498)
26 exp Placebos/ (8441)
27 RCT.mp. (2048)
28 or/21-27 (371080)
29 20 and 28 (49)

Database: EMBASE <1980 to 2007 Week 43>

Search Strategy:

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1 exp Decubitus/ (3741)
2 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3659)
3 bedsore$.mp. (146)
4 or/1-3 (5151)
5 exp nutrition/ or exp diet therapy/ (798997)
6 exp DIET/ (65465)
7 exp FOOD/ (209307)
8 (nutri$ or diet$ or food$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (496473)
9 (enteral or parenteral or protein$ or vitamin$ or mineral$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1894831)
10 exp Amino Acid/ (508877)
11 exp "Peptides and Proteins"/ (3414934)
12 exp Diet Supplementation/ (26443)
13 exp Antioxidant/ (39357)
14 exp Growth Promotor/ (865)
15 exp Vitamin/ (211037)
16 exp Enzyme/ (1265606)
17 exp coenzyme/ (947)
18 exp Enzyme Inhibitor/ (842490)
19 exp Mineral/ (6830)
20 exp Lipid/ (507543)
21 exp Antilipemic Agent/ (85172)
22 or/5-21 (4763456)
23 4 and 22 (1451)
24 limit 23 to (human and english language and yr="2003 - 2008") (444)
25 Randomized Controlled Trial/ (150503)
26 exp Randomization/ (24258)
27 exp RANDOM SAMPLE/ (826)
28 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).ti,mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (77576)
29 Double Blind Procedure/ (67017)
30 exp Triple Blind Procedure/ (8)
31 exp Control Group/ (1076)
32 exp PLACEBO/ (105770)
33 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (389627)
34 or/25-33 (515753)
35 24 and 34 (77)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to October Week 3 2007>
Search Strategy:

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1 exp Pressure Ulcer/ (4966)
2 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, subject heading word, abstract, instrumentation] (5618)
3 bedsore$.mp. (70)
4 or/1-3 (5632)
5 exp NUTRITION/ (32637)
6 exp Diet Therapy/ (6433)
7 exp FOOD/ (26691)
8 (nutri$ or diet$ or food$).mp. [mp=title, subject heading word, abstract, instrumentation] (78659)
9 (enteral or parenteral or protein$ or vitamin$ or mineral$).mp. [mp=title, subject heading word, abstract, instrumentation] (31657)
10 exp Amino Acids/ (4396)
11 exp Peptides/ (11963)
12 exp DIETARY PROTEINS/ or exp PROTEINS/ (32219)
13 exp Dietary Supplements/ (1903)
14 exp ANTIOXIDANTS/ (2750)
15 exp Growth Substances/ (5659)
16 exp VITAMINS/ (9680)
17 exp Enzymes/ (7839)
18 exp COENZYMES/ (374)
19 exp Enzyme Inhibitors/ (11330)
20 exp MINERALS/ (1674)
21 exp LIPIDS/ (17434)
22 exp Antilipemic Agents/ (3902)
23 or/5-22 (149452)
24 4 and 23 (678)
25 limit 24 to (english and yr="2003 - 2007") (250)
26 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (61139)
27 RCT.mp. (741)
28 exp Meta Analysis/ (5741)
29 exp "Systematic Review"/ (3348)
30 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (20170)
31 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (11627)
32 exp PLACEBOS/ (3830)
33 or/26-32 (79660)
34 25 and 33 (31)

Appendix 4: Search Strategy for Repositioning

Search date: April 18, 2008
Databases searched: MDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to April Week 2 2008>
Search Strategy:

1	exp Pressure Ulcer/ (3534)
2	((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (4336)
3	1 or 2 (4336)
4	(reposition$ or re-position$ or position$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (160069)
5	(mobiliz$ or mobilis$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (24127)
6	exp Posture/ (19236)
7	exp Prone Position/ (1470)
8	exp Supine Position/ (2456)
9	(turn$ adj3 (patient$ or schedul$ or interval$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1630)
10	or/4-9 (194918)
11	3 and 10 (412)
12	limit 11 to (english language and humans and yr="2000 - 2008") (259)
13	limit 12 to (case reports or comment or editorial or letter) (30)
14	12 not 13 (229)

Database: EMBASE <1980 to 2008 Week 15>
Search Strategy:

1	exp Decubitus/ (3909)
2	((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3181)
3	1 or 2 (4770)
4	(reposition$ or re-position$ or position$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (243757)
5	(mobiliz$ or mobilis$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (45414)
6	(turn$ adj3 (patient$ or schedul$ or interval$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (2735)
7	exp Patient Positioning/ (7098)
8	exp Body Posture/ (15566)
9	or/4-8 (300588)
10	3 and 9 (542)

11 limit 10 to (human and english language and yr="2000 - 2008") (226)
12 limit 11 to (editorial or letter or note) (36)
13 Case Report/ (985499)
14 11 not (12 or 13) (170)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to April Week 2 2008>
Search Strategy:

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1 exp Pressure Ulcer/ (5186)
2 ((decubitus or bed or pressure) adj1 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (5871)
3 1 or 2 (5871)
4 (reposition$ or re-position$ or position$).mp. [mp=title, subject heading word, abstract, instrumentation] (22332)
5 (mobiliz$ or mobilis$).mp. [mp=title, subject heading word, abstract, instrumentation] (2522)
6 (turn$ adj3 (patient$ or schedul$ or interval$)).mp. [mp=title, subject heading word, abstract, instrumentation] (678)
7 exp Patient Positioning/ (4230)
8 exp Posture/ (6653)
9 or/4-8 (29902)
10 3 and 9 (521)
11 limit 10 to (english and yr="2000 - 2008") (289)

Appendix 5: Search Strategy for Incontinence Management

Search date: April 25, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, CINAHL, and INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to April Week 3 2008>
Search Strategy:

1	exp Pressure Ulcer/ (3538)
2	exp Skin Ulcer/ (12680)
3	exp Wound Healing/ or exp Wound Infection/ (34511)
4	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (7005)
5	(bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1445)
6	or/1-5 (45985)
7	exp Incontinence Pads/ or exp Fecal Incontinence/ or exp Urinary Incontinence/ or exp Feces/ or exp Urine/ (36994)
8	(incontinen$ or continen$ or diaper$ or toilet$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (61681)
9	exp Diaper Rash/ (146)
10	or/7-9 (85691)
11	6 and 10 (555)
12	limit 11 to (english language and humans and yr="2000 - 2008") (377)
13	*Diabetic Foot/ (2601)
14	*Burns/ (7358)
15	*Venous Ulcer/ (1089)
16	*Ischemia/ (8464)
17	*Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (37790)
18	or/13-17 (56875)
19	12 not 18 (346)
20	limit 19 to (case reports or comment or editorial or letter) (37)
21	19 not 20 (309)
22	limit 21 to medline records [Limit not valid in: Ovid MEDLINE(R); records were retained] (309)

Database: EMBASE <1980 to 2008 Week 17>
Search Strategy:

1	exp Decubitus/ (3919)
2	exp Skin Ulcer/ (18030)
3	exp Chronic Wound/ (244)
4	exp Wound Healing/ or exp Wound Infection/ (51059)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject

headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9510)
6 bedsore$.mp. (158)
7 or/1-6 (67664)
8 exp Incontinence/ or exp Urine/ or exp Feces/ (52601)
9 exp diaper/ or exp diaper dermatitis/ (699)
10 (incontinen$ or continen$ or diaper$ or toilet$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (43062)
11 or/8-10 (69761)
12 7 and 11 (941)
13 limit 12 to (human and english language and yr="2000 - 2008") (574)
14 limit 13 to (editorial or letter or note) (34)
15 Case Report/ (987264)
16 13 not (14 or 15) (498)
17 *Burns/ (12467)
18 *Varicosis/ (3652)
19 *MICROVASCULAR ISCHEMIA/ (47)
20 *Diabetic Foot/ (1990)
21 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10663)
22 or/17-21 (28794)
23 16 not 22 (487)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to April Week 3 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (5204)
2 exp Skin Ulcer/ (10309)
3 exp Wound Healing/ or exp Wound Infection/ (9655)
4 exp Wounds, Chronic/ (848)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6621)
6 bedsore$.mp. (76)
7 or/1-6 (18545)
8 exp Incontinence/ or exp Urine/ or exp Feces/ (6728)
9 exp Diapers/ or exp Diaper Rash/ (270)
10 exp Incontinence Aids/ (605)
11 (incontinen$ or diaper$ or toilet$ or continen$).mp. [mp=title, subject heading word, abstract, instrumentation] (9065)
12 or/8-11 (10718)
13 7 and 12 (518)
14 limit 13 to (english and yr="2000 - 2008") (368)
15 limit 14 to (brief item or commentary or editorial or letter) (21)

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Management of Chronic Pressure Ulcers

An Evidence-Based Analysis

Presented to the Ontario Health Technology Advisory Committee in October 2008

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About the Medical Advisory Secretariat

The Medical Advisory Secretariat (MAS) is part of the Ontario Ministry of Health and Long-Term Care. The mandate of MAS is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The MAS also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The MAS conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, MAS systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The MAS makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practicing medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact MAS: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Table of Contents

Abbreviations

AH	Amorphous hydrogel
AHRQ	Agency for Healthcare Research and Quality
Al	Aluminum
AP	Alternating pressure
As	Arsenide
BFGF	Basic fibroblast growth factor
BID	Twice daily
C	Collagenase
CI	Confidence interval
D	Dextranomer paste
DDCT	Decubitus direct current treatment
DIME	Debridement, infection control, moist wound environment, and edge effect
DNAase	Deoxyribonuclease
FDA	Food and Drug Administration
FGF	Fibroblast growth factor
GA	Gallium
GM-CSF	Granulo macrophage-colony stimulating factor
GRADE	Grading of Recommendation Assessment, Development, and Evaluation
He	Helium
HINF	High Intensity Fund
HR	Hazard ratio
kJ	Kilojoule
LAL	Low-air-loss
LLL	Low-level laser
LOS	Length of stay
LP	Low pressure
LTC	Long-term care
MCSF	Macrophage-colony stimulating factor
MD	Medical doctor
μg	Microgram
mg	Milligram
mL	Millilitre
MVP	Moisture vapour permeable
NA	Not applicable
NCNT	Noncontact normothermic therapy
NE	Neon
NGF	Nerve growth factor
NPUAP	National Pressure Ulcer Advisory Panel

NPWT	Negative pressure wound therapy
NS	Not statistically significant
OR	Odds ratio
PBO	Placebo
PDGF	Platelet-derived growth factor
PMN	Polymorphonuclear neutrophils
PSST	Pressure Sore Status Tool
PT	Physical therapist
PUSH	Pressure Ulcer Scale for Healing
RCN	Royal College of Nurses
RCT	Randomized controlled trial
RD	Registered dietician
rhPDGF	Recombinant human platelet-derived growth factor
RN	Registered nurse
RR	Relative risk
RR	Relative risk
SATA	Spacial and temporal averaged
SCI	Spinal cord injury
SD	Standard deviation
TGF	Transforming growth factor
Tx	Treatment
UCV	Ultraviolet C
US/UVC	Ultrasound/ultraviolet C
VA	Veterans Administration
VAC	Vacuum-assisted closure
WMD	Weighted mean difference

In April 2008, the Medical Advisory Secretariat began an evidence-based review of the literature concerning pressure ulcers.

Please visit the Medical Advisory Secretariat Web site, http://www.health.gov.on.ca/english/providers/program/mas/tech/tech_mn.html to review these titles that are currently available within the Pressure Ulcers series.

1. *Pressure ulcer prevention: an evidence based analysis*
2. *The cost-effectiveness of prevention strategies for pressure ulcers in long-term care homes in Ontario: projections of the Ontario Pressure Ulcer Model (field evaluation)*
3. *Management of chronic pressure ulcers: an evidence-based analysis*

Executive Summary

Objective

The Medical Advisory Secretariat (MAS) conducted a systematic review on interventions used to treat pressure ulcers in order to answer the following questions:

- Do currently available interventions for the treatment of pressure ulcers increase the healing rate of pressure ulcers compared with standard care, a placebo, or other similar interventions?
- Within each category of intervention, which one is most effective in promoting the healing of existing pressure ulcers?

Background

A pressure ulcer is a localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in conjunction with shear and/or friction. Many areas of the body, especially the sacrum and the heel, are prone to the development of pressure ulcers. People with impaired mobility (e.g., stroke or spinal cord injury patients) are most vulnerable to pressure ulcers. Other factors that predispose people to pressure ulcer formation are poor nutrition, poor sensation, urinary and fecal incontinence, and poor overall physical and mental health.

The prevalence of pressure ulcers in Ontario has been estimated to range from a median of 22.1% in community settings to a median of 29.9% in nonacute care facilities. Pressure ulcers have been shown to increase the risk of mortality among geriatric patients by as much as 400%, to increase the frequency and duration of hospitalization, and to decrease the quality of life of affected patients. The cost of treating pressure ulcers has been estimated at approximately $9,000 (Cdn) per patient per month in the community setting. Considering the high prevalence of pressure ulcers in the Ontario health care system, the total cost of treating pressure ulcers is substantial.

Technology

Wounds normally heal in 3 phases (inflammatory phase, a proliferative phase of new tissue and matrix formation, and a remodelling phase). However, pressure ulcers often fail to progress past the inflammatory stage. Current practice for treating pressure ulcers includes treating the underlying causes, debridement to remove necrotic tissues and contaminated tissues, dressings to provide a moist wound environment and to manage exudates, devices and frequent turning of patients to provide pressure relief, topical applications of biologic agents, and nutritional support to correct nutritional deficiencies. A variety of adjunctive physical therapies are also in use.

Method

Health technology assessment databases and medical databases were searched from 1996 (Medline), 1980 (EMBASE), and 1982 (CINAHL) systematically up to March 2008 to identify randomized controlled trials (RCTs) on the following treatments of pressure ulcers: cleansing, debridement, dressings, biological therapies, pressure-relieving devices, physical therapies, nutritional therapies, and multidisciplinary wound care teams. Full literature search strategies are reported in appendix 1. English-language studies in previous systematic reviews and studies published since the last systematic review were included if they had more than 10 subjects, were randomized, and provided objective outcome measures on the healing of pressure ulcers. In the absence of RCTs, studies of the highest level of evidence available were included. Studies on wounds other than pressure ulcers and on surgical treatment of pressure ulcers were excluded. A total of 18 systematic reviews, 104 RCTs, and 4 observational studies were included in this review.

Data were extracted from studies using standardized forms. The quality of individual studies was assessed based on adequacy of randomization, concealment of treatment allocation, comparability of groups, blinded assessment, and intention-to-treat analysis. Meta-analysis to estimate the relative risk (RR) or weighted mean difference (WMD) for measures of healing was performed when appropriate.
A descriptive synthesis was provided where pooled analysis was not appropriate or not feasible. The quality of the overall evidence on each intervention was assessed using the grading of recommendations assessment, development, and evaluation (GRADE) criteria.

Findings

Findings from the analysis of the included studies are summarized below:

Cleansing

- There is no good trial evidence to support the use of any particular wound cleansing solution or technique for pressure ulcers.

Debridement

- There was no evidence that debridement using collagenase, dextranomer, cadexomer iodine, or maggots significantly improved complete healing compared with placebo.
- There were no statistically significant differences between enzymatic or mechanical debridement agents with the following exceptions:
    - Papain urea resulted in better debridement than collagenase.

- Calcium alginate resulted in a greater reduction in ulcer size compared to dextranomer.
- Adding streptokinase/streptodornase to hydrogel resulted in faster debridement.
- Maggot debridement resulted in more complete debridement than conventional treatment.

- There is limited evidence on the healing effects of debridement devices.

Dressings

Hydrocolloid dressing was associated with almost three-times more complete healing compared with saline gauze.

- There is evidence that hydrogel and hydropolymer may be associated with 50% to 70% more complete healing of pressure ulcers than hydrocolloid dressing.
- No statistically significant differences in complete healing were detected among other modern dressings.
- There is evidence that polyurethane foam dressings and hydrocellular dressings are more absorbent and easier to remove than hydrocolloid dressings in ulcers with moderate to high exudates.
- In deeper ulcers (stage III and IV), the use of alginate with hydrocolloid resulted in significantly greater reduction in the size of the ulcers compared to hydrocolloid alone.
- Studies on sustained silver-releasing dressing demonstrated a tendency for reducing the risk of infection and promoting faster healing, but the sample sizes were too small for statistical analysis or for drawing conclusions.

Biological Therapies

- The efficacy of platelet-derived growth factors (PDGFs), fibroblast growth factor, and granulocyte-macrophage colony stimulating factor in improving complete healing of chronic pressure ulcers has not been established.
- Presently only Regranex, a recombinant PDGF, has been approved by Health Canada and only for treatment of diabetic ulcers in the lower extremities.
- A March 2008 US Food and Drug Administration (FDA) communication reported increased deaths from cancers in people given three or more prescriptions for Regranex.
- Limited low-quality evidence on skin matrix and engineered skin equivalent suggests a potential role for these products in healing refractory advanced chronic pressure ulcers, but the evidence is insufficient to draw a conclusion.

Adjunctive Physical Therapy

- There is evidence that electrical stimulation may result in a significantly greater reduction in the surface area and more complete healing of stage II to IV ulcers compared with sham therapy. No conclusion on the efficacy of electrotherapy can be drawn because of significant statistical heterogeneity, small sample sizes, and methodological flaws.
- The efficacy of other adjunctive physical therapies [electromagnetic therapy, low-level laser (LLL) therapy, ultrasound therapy, ultraviolet light therapy, and negative pressure therapy] in improving complete closure of pressure ulcers has not been established.

Nutrition Therapy

- Supplementation with 15 grams of hydrolyzed protein 3 times daily did not affect complete healing but resulted in a 2-fold improvement in Pressure Ulcer Scale for Healing (PUSH) score compared with placebo.
- Supplementation with 200 mg of zinc three times per day did not have any significant impact on the healing of pressure ulcers compared with a placebo.
- Supplementation of 500 mg ascorbic acid twice daily was associated with a significantly greater decrease in the size of the ulcer compared with a placebo but did not have any significant impact on healing when compared with supplementation of 10 mg ascorbic acid three times daily.
- A very high protein tube feeding (25% of energy as protein) resulted in a greater reduction in ulcer area in institutionalized tube-fed patients compared with a high protein tube feeding (16% of energy as protein).
- Multinutrient supplements that contain zinc, arginine, and vitamin C were associated with a greater reduction in the area of the ulcers compared with standard hospital diet or to a standard supplement without zinc, arginine, or vitamin C.
- Firm conclusions cannot be drawn because of methodological flaws and small sample sizes.

Multidisciplinary Wound Care Teams

- The only RCT suggests that multidisciplinary wound care teams may significantly improve healing in the acute care setting in 8 weeks and may significantly shorten the length of hospitalization. However, since only an abstract is available, study biases cannot be assessed and no conclusions can be drawn on the quality of this evidence.

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Objective

The objective of this analysis is to review a spectrum of pressure ulcer treatments to identify whether there are any treatment modalities that are more effective than others in promoting complete closure of pressure ulcers in the various health care settings. This evidence-based analysis reviews local wound care (cleansing, debridement, topical agents, dressings, and biological therapies), pressure relieving supportive surfaces, adjunctive physical therapies, nutrition therapy, and multidisciplinary wound care teams.

Background

Pressure Ulcers

Definition and Location

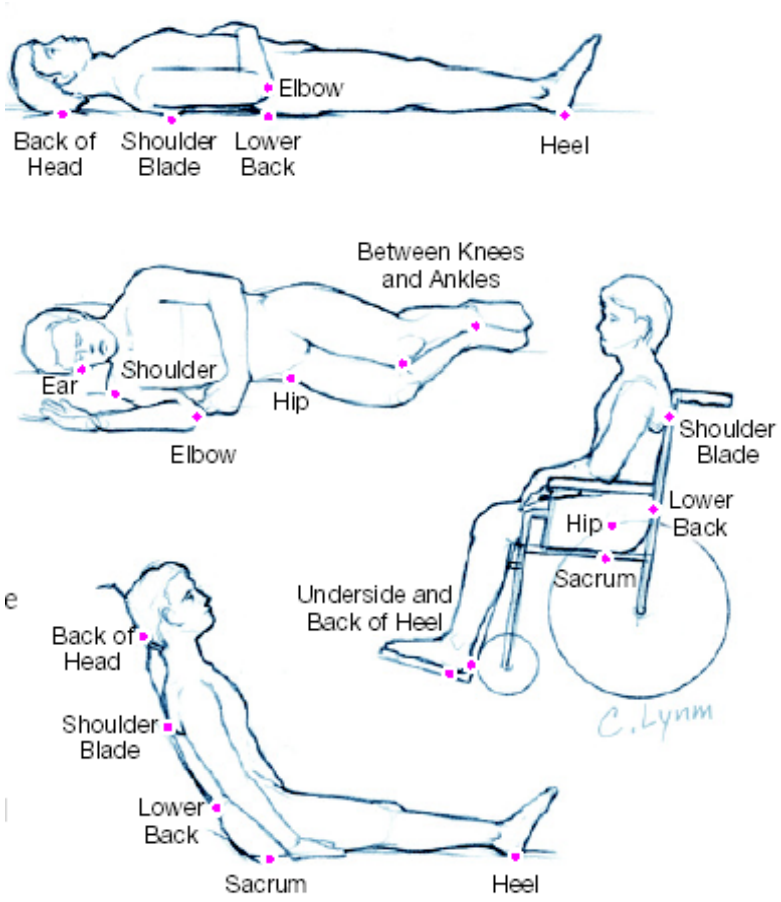
According to the National Pressure Ulcer Advisory Panel (NPUAP), (1) a pressure ulcer is defined as a localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear and/or friction. The sacrum and heel are the most common location of pressure ulcers. Other areas that are prone to the development of pressure ulcers are shown in Figure 1.

Risk Factors for Developing Pressure Ulcers

Prolonged, uninterrupted pressure is the main cause of pressure ulcers and impaired mobility is the most common reason that people are exposed to unrelieved pressure. People with impaired mobility such as stroke patients, patients with spinal cord injury, or unconscious patients, are at risk of developing pressure ulcers as they are not able to shift their position to relieve pressure. Many of these patients also have other conditions that contribute to poor tissue viability including loss of loss of muscle and adipose due to immobility and poor nutrition, poor sensation, urinary and fecal incontinence, and poor overall physical and mental health.

Many tools have been developed to assess individuals' risks of developing a pressure ulcer. These tools are generally based on an assessment of the above-mentioned risk factors. The most often used tool is the Braden scale.

Figure 1: Common Locations of Pressure Ulcers



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Classification of Pressure Ulcers

There are different systems for classifying a pressure ulcer based on their severity, taking into consideration the surface area and depth of the ulcer, the tissues affected, and presence or absence of necrosis, exudate, and slough. The most commonly used system is the North American National Pressure Ulcer Advisory Panel(NPUAP) system and the European Pressure Ulcer Advisory Panel System (Appendix 1). Characteristics of the stages are summarized in Table 1. Stage I usually refers to a change in the skin without breakage. Stage II refers to a shallow ulcer with partial thickness skin loss. Stages III and IV are considered advanced ulcers with full thickness skin loss affecting tissues beneath the dermis. A new category was recently added to represent damage of underlying soft tissues while the skin remained intact.

Since pressure ulcers do not heal by regeneration and various strata (e.g., muscle, fascia, subcutaneous) are not replaced, pressure ulcers should not be reverse staged (e.g., from stage IV to stage III) as they heal.

Table 1: Characteristics of Stages of Pressure Ulcers

Stage	Suspected Deep Tissue Injury	I	II	III	IV	Unstageable
Skin	Intact Purple or maroon localized discoloration or blood-filled blister	Intact Localized unblanchable redness	Partial thickness loss of dermis Shallow open ulcer	Full thickness tissue loss	Full thickness tissue loss	Full thickness tissue loss
Tissues involved	Damage of underlying soft tissue from pressure/shear	Epidermis	Dermis	Sub-cutaneous fat; may include undermining/ tunneling	Exposed bone, tendon, or muscle; often include undermining/ tunneling	True depth of ulcer cannot be determined
Slough/ eschar present?	No	No	No	Slough may be present	May be present on part of ulcer	Covered by slough and/or eshcar

Based on 2007 National Pressure Ulcer Advisory Panel Classification System. (1)

Two other tools are often used to assess the status of a pressure ulcer. The Pressure Sore Status Tool (PSST) assesses a pressure ulcer condition based on 13 parameters each measured on a Likert scale of 1 to 5. The total score ranges from 13 to 65 with the score of 13 indicating a healed ulcer. The 13 parameters are as follows:

- Size (length times width)
- Depth
- Edges
- Undermining
- Necrotic tissue type
- Necrotic tissue amount
- Exudate type
- Exudate amount
- Skin color surrounding wound
- Peripheral tissue edema
- Peripheral tissue induration
- Granulation tissue
- Epithelialization

The PUSH scores a pressure ulcer based on its surface area, amount of exudates, and the type of tissue present (e.g., granulation). The total score ranges from 0 (healed ulcer) to 17 (> 24cm^2 with heavy exudates and necrosis).

Prevalence of Pressure Ulcers

Woodbury et al. (2) conducted a systematic review to determine the prevalence of pressure ulcers in health care settings across Canada. The review combined data that surveyed more than 14,000 patients from 45 health care institutions across Canada. The results of the review are summarized in Table 2. On the average, 1-in-4 patients across Canadian health care settings suffered from a pressure ulcer (median prevalence regardless of health care setting = 26%).

Table 2: Prevalence of Pressure Ulcers in Canada and Ontario by Health Care Setting

	Median Prevalence (range) (%)	
Setting	**Canada**	**Ontario**
Acute care hospitals	25.1 (24–26)	27 (23.9–29.7)
Nonacute care facilities*	29.9 (28–31)	34.6 (30.0–53.3)
Mixed health care facilities†	15.1 (21–23)	13.2 (based on 1 study)
Community care	22.1 (13–17)	21.6 (13.1–25.7)

*Included subacute, complete continuing care, chronic care, long-term care, and nursing home.
†Included a mixture of acute, nonacute, and community care settings.

Burden of Illness

The impact of pressure ulcers can be seen in human and economic terms. In human terms, the geriatric patient who develops a pressure ulcer has a four-fold increased risk of death. (3) Pressure ulcers also affect quality of life and lead to more frequent hospitalization. In economic terms, the cost of healing a pressure ulcer is likely high because it often involves a multitude of prolonged complex treatments and hospitalization. Once a pressure ulcer reaches stage III or IV, it may take as long as 6 months to heal. Experts advise that some ulcers may not be healable because of existing comorbidities and may require ongoing treatment and care. (Campbell) In a 2004 case study, Allen and Houghton (4) estimated that the total cost for 3 months of care of a person with a stage III pressure ulcer in the community was $27,500 per patient. This amount included reimbursement for professional and support staff, wound care supplies, electrical stimulation, rental of equipment, and loss of potential income.

In Ontario, the Ministry of Health and Long-Term Care provides a claims-based supplementary High Intensity Fund (HINF) to long-term care facilities to help finance care for medically complex residents. Of the $31.9 million HINF provided to long-term care facilities in 2006, 65% were claimed for wound care. (E-mail communication, 2007)

In the United States, the national expenditure for costs related to the care of patients with pressure ulcers in 1998 were estimated to be more than $1.3 billion per year. (5) This number is expected to increase at a high rate as the population over age 85 will increase from 4 million to 17 million over the 15 years since this cost study. (6)

Process of Wound Healing

There are three phases in wound healing:

- Inflammatory Phase – This phase begins the moment the tissue is injured as blood components spill into the site of injury, triggering platelets to release clotting factors, essential growth factors, and

- Proliferative Phase – This phase begins once the wound site is cleaned out and is marked by migration of fibroblasts, proliferation of new tissues, and deposition of extracellular matrix.
- Remodelling Phase – In this final phase, the new collagen matrix becomes cross-linked and organized through numerous cell-signalling events. (6)

In nonhealing pressure ulcers, the above process is lost and the ulcers are locked into a state of chronic inflammation that prevent them from healing. (6)

Pressure Ulcer Prevention

Pressure ulcer prevention aims to eliminate or reduce factors that predispose a person to pressure ulcer development. The prevention strategies commonly used include regular risk assessment, use of special pressure relieving support surfaces, regular repositioning and turning, local skin care, and nutrition support. Pressure ulcer prevention is addressed in a separate MAS systematic review.

Factors Influencing Healing

Many variables that can affect ulcer healing, including patient demographics, pressure ulcer size and severity, and pressure ulcer management practices. Retrospective multivariate regression analysis of databases had been performed to identify factors that influence healing of pressure ulcers (Appendix 2).

Based on these studies, patient-related variables that were significantly associated with improved healing included higher body weight and lower body temperature, (7) whereas comorbid cardiovascular disease, incontinence, and immobility were associated with decreased odds of pressure ulcer healing. (8;9)

The size of the ulcer also has an impact on likelihood of healing. Vu et al. (10) found that for every 1 mm increase in the width of the wound at enrolment, the chance of healing decreased by 4.0% [RR 0.96 (95% confidence interval (CI) 0.95–0.98), $P = .000$]. Deep wounds had a 60% reduced chance of healing compared with superficial wounds [RR 0.40 (95% CI, 0.25–0.62), $P = .000$]. (10) Graumlich et al. (11) also reported that deep ulcers at randomization decrease the chance of healing compared with superficial ulcers [odds ratio (OR) = 0.56 (95% CI, 0.38–0.81), $P = .002$].

Several treatment variables were identified to be significantly associated with improved healing of pressure ulcers:

- Moist dressing (in stage II and stage III/IV ulcers) (12)
- Receiving sufficient enteral feeding (> 30 kcal/kg) (12)
- Use of exudate management dressing (8)
- Rehabilitation services (9)

Treatment variables associated with decreased odds of pressure ulcer healing were:

- Frequent changes in dressing types with indications of inappropriate changes (8)
- Failure to use exudate management dressing in ulcers with large to moderate amount of exudate (8)
- Lack of debridement in pressure ulcers with yellow slough (8)

Technology

Pressure ulcers are marked by excessive infiltration of neutrophils, which are believed to be responsible for the chronic inflammation characteristics of nonhealing pressure ulcers. (6) The neutrophils release significant amounts of enzymes that destroy the connective tissue matrix and an elastase that is capable of destroying important healing factors. Chronic pressure ulcers will not respond to treatment until the wound bed is properly prepared. (6) Experts suggest that adequate wound bed preparation consists of four main components represented by the acronym DIME: debridement of necrotic tissues, control of infection, providing a moist wound environment, and dealing with the edge effect (when the edge fails to close). Hence local wound care is the cornerstone for the treatment of pressure ulcers. (13)

Present treatment of pressure ulcers focuses on:

- Treating the underlying disease and addressing patient-centred concerns
- Local wound care (DIME) including cleansing, debridement of necrotic tissues, appropriate dressing to provide a moist environment for healing, and topical biological therapies (e.g. topical growth factors) to facilitate healing
- Adjunctive physical therapies such as electrical stimulation, electromagnetic stimulation, LLL therapy, ultrasound therapy, ultraviolet radiation, and negative pressure therapy
- Providing nutrition support to correct nutritional deficiencies
- Providing pressure relief using special support beds, mattresses, overlays, cushions, and regular turning schedules
- Integration of wound care through multidisciplinary wound care teams
- Surgical repair

This MAS systematic review includes all of the above with the exception of treatment for underlying diseases, turning, and surgical repair. Drug treatment for infection control is also outside the scope of this review.

Literature Search

Objectives

To systematically assess the evidence for the effectiveness of interventions used in the treatment of pressure ulcers.

Questions

- Do currently available interventions for the treatment of pressure ulcers increase the healing rate of pressure ulcers compared with standard care, placebo, or another similar intervention?
- Within each category of interventions, which one is most effective in promoting healing of existing pressure ulcers?

Method

Search Strategy

Initially, 1 search was run on August 6, 2007, to capture all treatment modalities. This search covered the literature published between January 1996 and August 2007. Separate search strategies were then developed to address each category of intervention included in the systematic review (see inclusion criteria) for the period of January 2003 to March 2008. The detailed search strategies are shown in Appendix 3. All final searches were run between March 10 and March 30, 2008 in the following databases: OVID MEDLINE, OVID MEDLINE In-Process and Other Nonindexed Citations, OVID EMBASE, OVID CINAHL, Cochrane Library, and the INAHTA/CRD database. All searches were limited to human subjects and English-language articles. Additional searches of websites and references of publications were also performed to ensure comprehensiveness.

Selection of Articles

One researcher screened the citations and abstracts from the literature search and selected articles according to the following inclusion and exclusion criteria. Full text reports were obtained if there were no abstracts or when the abstract was unclear.

Inclusion Criteria

- English language systematic reviews and RCTs that meet the following description:
  - Patients: in any setting, with one or more pressure ulcers
  - Interventions: nondrug and nonsurgical treatments for pressure ulcers including:
    - *Local wound therapy* – cleansing agents, topical treatments, debridement agents and devices, dressings, and biological therapy
    - *Adjunctive physical therapies* – hydrotherapy, electrical stimulation, electromagnetic therapy, ultrasound therapy, LLL therapy, and negative pressure therapy
    - *Pressure relieving support surfaces* – beds, mattresses, overlays, and cushions
    - *Nutrition therapy* – supplementation of macro or micronutrients alone or in combination
    - *Multidisciplinary wound care teams*
  - Comparison: an intervention versus a placebo, a sham treatment, or another intervention
  - Outcome of interest: proportion of ulcers that healed completely (closed), percent change in surface area/volume, rate of change in surface area (cm^2/day or week), mean time to achieve complete healing, change in the amount of exudate, granulation, PSST score, PUSH score, treatment-related adverse events, and absorbency and ease of removal (for dressings)
- Clinical controlled trials or other observational studies only if RCTs are not available
- Sample ≥ 10 ulcers

Exclusion Criteria

- Studies on acute wounds or chronic wounds other than pressure ulcers
- Studies with only subjective outcomes
- Nonsystematic reviews or case reports (except where indicated)
- Opinion articles or letters to the editor that provided no primary data
- Studies for which results have already been reported or for which a more current update is available
- Full text articles in a language other than English
- Studies on surgical reconstruction of pressure ulcers

Results

The results of the literature searches are summarized in summarized in Table 3.

The number of studies from previous systematic reviews and studies identified from this literature search are summarized in Table 4.

Table 3: Results of Literature Searches

Treatment Intervention	Search Date	No. of Citations Retrieved
General Search	August 6, 2007	2,120
Multidisciplinary Teams	March 10, 2008	926
Dressings	March 16, 2008	371
Growth Factors	March 19, 2008	446
Cleansing	March 19, 2008	586
Debridement	March 22, 2008	190
Electrical Stimulation	March 24, 2008	217
Electromagnetic Therapy	March 24, 2008	55
Laser Therapy	March 24, 2008	183
Ultrasound	March 25, 2008	149
Nutrition	March 26, 2008	537
Positioning	March 29, 2008	335
Support Surfaces	March 30, 2008	543

Table 4: Level of Evidence of Included Studies*

Study Design	Level of Evidence	Number of Studies From Previous Reviews	Number of Studies From Current Search
Systematic reviews of RCTs	1		18
Large RCT	1	9	
Large RCT unpublished but reported to an international scientific meeting	1(g)†		1
Small RCT	2	77	17
Small RCT unpublished but reported to an international scientific meeting	2(g)		
Non-RCT with contemporaneous controls	3a		4
Non-RCT with historical controls	3b		
Non-RCT presented at international conference	3(g)		
Surveillance (database or register)	4a		
Case series (multisite)	4b		
Case series (single site)	4c		
Retrospective review, modeling	4d		
Case series presented at international conference	4(g)		

*MAS indicates Medical Advisory Secretariat; RCT, randomized controlled trial.
†For each included study, levels of evidence were assigned according to a ranking system based on a hierarchy proposed by Goodman. (14) An additional designation “g” was added for preliminary reports of studies that have been presented at international scientific meeting.

Quality Assessment and Data Abstraction

One researcher reviewed the full-text reports and extracted data using data extraction tables. For RCTs, the quality of studies was assessed using the following criteria:

- Method of randomization described and adequate
- Concealment of allocation described and adequate
- Inclusion and exclusion criteria described
- A priori sample size calculation described
- Blinded assessment of outcomes employed
- Attrition reported and explained
- Intention-to-treat analysis conducted

The quality of observational studies was evaluated based on method of patient selection, sample size, statistical analysis, and completeness of follow-up. The quality assessment of the included studies is summarized in Appendix 4.

Analysis and Synthesis of Evidence

When appropriate, Revman 4.2 (the Cochrane meta-analysis software) was used to test for heterogeneity and to estimate the RRs for complete healing of pressure ulcers. Weighted mean differences were estimated for mean reduction in ulcer size and mean time to achieve complete healing. A point estimate with the 95% CI was generated when appropriate. A descriptive synthesis was provided when statistical analysis was not feasible.

Grading Quality of Evidence

The overall quality of evidence was examined according to the GRADE Working Group criteria (15;16). This system rates the overall quality of evidence based on the assessment of 4 key elements:

- Study design – broadly categorized as randomized trials and observational studies.
- Quality of included studies – refers to whether there were limitations relating to the methods and exaction that may result in biases. The assessment is based on appropriate criteria such as adequacy of allocation concealment, blinding, and follow-up.
- Consistency of outcomes – refers to similarity of estimates of effect across studies. If there is important unexplained inconsistency in the result, confidence in the estimate of effect for that outcome decreases. Differences in the direction of effect, the size of differences in effect, and the significance of the differences guide the decision about whether important inconsistency exists.
- Directness – refers to the extent to which the subjects, interventions, and outcome measure are similar to those of interest.

As stated by the GRADE Working Group, the following definitions were used in grading the quality of evidence:

- High: further research is very unlikely to change our confidence in the estimate of effect,
- Moderate: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate,
- Low: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate, and
- Very low: any estimate of effect is very uncertain.

The GRADE quality of evidence is summarized in Appendix 5.

Reporting of Findings

The studies are summarized in detail in Appendix 6.

Analyses of findings are reported in the following order:

Local pressure ulcer treatment:
- Wound cleansing
- Debridement
  - Chemical (enzymatic) debridement
  - Mechanical debridement
  - Autolytic debridement (compared with the above)
  - Biological debridement – maggot debridement
  - Devices for debridement
- Topical treatment
- Dressing
  - Modern dressings versus traditional dressings
  - Modern dressings versus modern dressings

Biological therapies
- Growth factors
- Engineered skin equivalents and skin matrix

Pressure-relieving support services

Adjunctive physical therapies
- Hydrotherapy
- Electrotherapy
- Electromagnetic therapy
- LLL therapy
- Ultrasound therapy
- Negative pressure therapy

Nutrition therapy
- Protein supplement
- Zinc supplement
- Ascorbic acid supplement
- Multi-nutrient supplements

Multidisciplinary wound care teams

Summary of Literature Review Findings

Local Wound Care

Cleansing of Pressure Ulcers

Cleansing of the pressure ulcer is assumed to be an important component of pressure ulcer care. In a 2005 systematic review, Moore and Cowman (17) assessed the effects of wound cleansing solutions and wound cleansing techniques on the healing rates of pressure ulcers. The review included RCTs and controlled clinical trials in the absence of RCTs. No studies comparing cleansing with no cleansing were found. Three studies that addressed cleansing of pressure ulcers were found and these are summarized in Table 5. The MAS literature search did not find any other studies on this subject.

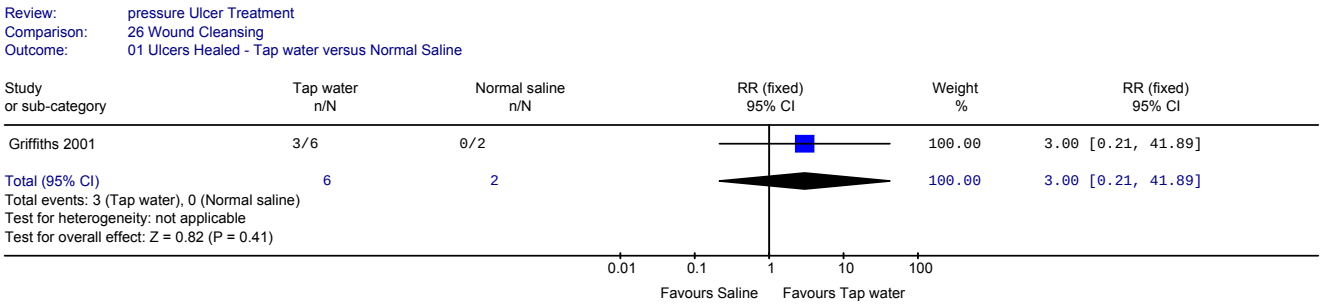
Table 5: Randomized Controlled Trials on Cleansing of Pressure Ulcers*

	Griffiths 2001 (18)	Bellingeri 2004 (19)	Burke 1998 (20)
Design	RCT Pressure ulcer N = 6/2 All wounds N = 49	Multicentre RCT, N = 59/74	RCT, N = 24 vs. 18
Pressure ulcers	Grade 2 or 3	> Grade 1	Grade 3 or 4
Mean age (years)	Tap water 76.6 (range 40–90) Saline 81.16 (range 56–100)	74 vs. 73	Not reported
Comparison	Tap water vs. saline Hydrocolloid for both	Vulnopur spray (saline w/aloe vera, silver chloride and decyl glucoside) vs. isotonic saline	Whirlpool 20 min/day vs. No whirlpool
Duration (wks)	6	2	≥ 2
Outcomes	Pressure ulcers healed Tap water 3/6 Saline 0/2 All wounds = NS	No statistically significant difference in healing % <down> in PSST score from baseline 27.8 (31.3) (Vulnopur) vs. 20.5 (24.1) (Saline) *P* = .025	Ulcers improved Whirlpool 14/24 Control 5/18 P = .08

*NS indicates not statistically significant; PSST, Pressure Sore Status Tool; RCT, randomized controlled trial.

Two of the 3 RCTs compared different cleansing solutions. Griffiths et al. (18) compared 20 patients whose wounds were cleansed with tap water to 23 patients whose wounds were cleansed with normal saline solution for a period of 6 weeks. Only 6 of the wounds in the tap water group and 2 of the wounds in the saline group were pressure ulcers. The wounds were grade 2 (partial thickness skin loss) and grade 3 (full thickness skin loss down to the fascia) according to Carville's definition. Wound cleansing in both groups were achieved using a 30 mL syringe and a 20 g canola. Hydrocolloid and or gel and a clean dressing were applied after the wound was patted dry. After 6 weeks, 3 of the 6 pressure ulcers cleansed with tap water had healed but neither of the pressure ulcers cleansed with saline had healed. The difference in complete healing between the two groups was not statistically significant (Figure 2). Moore and Cowman (17) stated that the sample size was too small to draw any conclusion.

Figure 2: Forest Plot of Ulcers Healed – Tap Water Versus Normal Saline Cleansing*



*CI indicates confidence interval; RR, relative risk.

In another RCT, Bellingeri compared cleansing with Volnopur® (contains saline, aloe vera, silver chloride, and decyl glucoside) to cleansing with isotonic saline spray in patients with pressure ulcers greater than grade 1 in the NPUAP scale. The Volnopur group consisted of 39 subjects with a mean PSST score of 34 (standard deviation [SD] 11.5) and the 74-subject saline group had a mean baseline PSST score of 33 (SD 10.3). After 2 weeks and withdrawal of 7 patients, the mean percentage change from baseline in PSST score was –27.8% (SD 31.3%) in the Volnopur group compared with –20.5% (SD 24.1%) in the isotonic saline group. Bellingeri et al. reported that the difference in change of PSST scores between the groups was statistically significant in favour of Volnopur (P = .025). Moore and Cowman stated that since the data from this study were skewed, the nonparametric tests used in the study could not be reproduced without the raw data. It is not appropriate to compare the groups using RevMan since this software assumes a normal distribution.

In the third RCT, 24 grade 3 or 4 pressure ulcers treated with 20 minutes per day of whirlpool were compared with 18 pressure ulcers that did not receive whirlpool treatment. At the end of 2 weeks, 14 of the whirlpool group versus 5 of the control group showed improvement. The author reported a statistically significant difference (P = .0435). However, as reported by Moore and Cowman, RevMan analysis showed that the difference between the 2 groups was not statistically significant [RR 2.10 (95% CI, 0.93–4.76), P = .08]. This study will be discussed in greater detail in the hydrotherapy section.

Based on the above studies, Moore and Cowman concluded that overall, there is no good trial evidence to support the use of any particular wound cleansing solution or technique for pressure ulcers.

Debridement

Debridement refers to the removal of necrotic or infected tissues and excess moisture from a wound that may impair proper wound healing. Necrotic tissues must be removed in order for granulation and re-epithelialization to occur. (21) Debridement may also control infection and stimulate a nonadvancing wound edge. Debridement may be selective, removing only necrotic tissues, or nonselective, removing or damaging healthy tissues as well as necrotic tissues. Traditionally, debridement was achieved by applying a mesh gauze dressing to the ulcer, moistened with saline, povidone-iodine, or Dakin's solution, and then removing the dressing after drying. This nonselective method of debridement can damage granulation tissue and new epithelium in the wound and the process can be painful. Presently, there are a variety of approaches to debridement, summarized in Table 6.

Table 6: Comparison of Debridement Methods

Type of Debridement	Debridement Agent	Examples	Advantages	Disadvantages
Autolytic	Phagocytic cells and endogenous proteolytic enzymes of the wound – moist environment created by use of an occlusive dressing	Occlusive dressing with hydrocolloid, hydrogel, or alginate	Selective Slow process Painless Useful in wound with minimal debris	Slow process Contraindicated for infected wounds
Chemical	Exogenous Proteolytic enzymes	Collagenase, streptokinase/ streptodornase, papain-urea (enzyme from papaya, rendered more effective by urea; active in pH of 3 to 12)	Selective Slow process Painless Useful for noninfected wounds where other methods are contraindicated	May cause irritation of surrounding tissue Slow process Enzymes may be inactivated by the wound's pH or other topical agents being used Need to cross-hatch eschar if present prior to application of enzymes
Mechanical	Water jets Certain dressings Debridement polysaccharides	Wet-to-dry gauze dressings Hydrotherapy (whirlpool or high pressure irrigation devices) Dextranomer beads or paste Cadexomer iodine	Easy to perform Faster than autolytic and chemical debridement Useful in wounds with necrotic material and moderate to large amount of exudate	Nonselective May remove viable tissue May damage surrounding tissue Can be painful
Surgical (sharp)	Using surgical instruments	Scissors* Scalpels* Dermatomes* Curettes *	Immediate results Selective Indicated in ulcers with large amount of necrosis and eschar	Invasive Requires a skilled clinician May cause bleeding and pain Need for analgesia
Biological	Maggots	Maggot therapy	Highly selective Maggots produce antimicrobial factors	Use is confined to selected cases

* Alvarez 2002. (22)
Adapted from Falabella, 2006. (23)

MAS Review of Debridement

This review focused on nonsurgical debridement techniques. No new studies on nonsurgical debridement were found in the MAS literature search. Studies from previous systematic reviews are discussed. These are shown in Table 7 and reviewed in the following sections.

Table 7: Studies Comparing Debriding Agents*

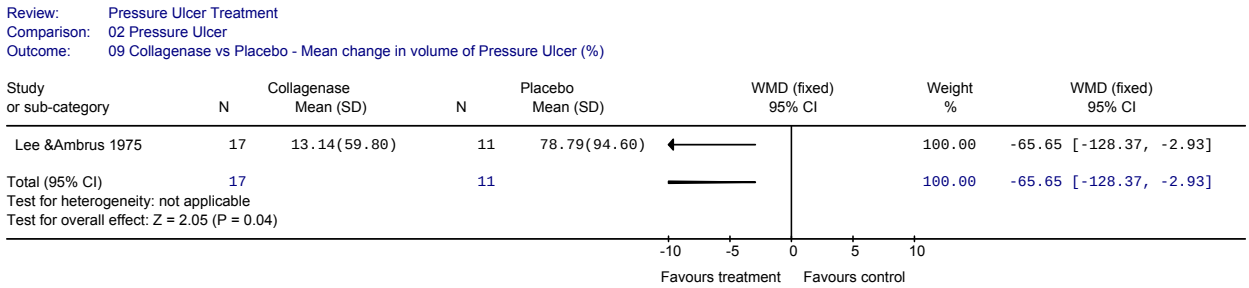
Comparison	Studies	Outcome Measure	Outcome Measure
Collagenase vs. placebo	Lee and Ambrus 1975 (24)		Mean % <down> in volume
	Parish and Collins 1979 (25)	Complete healing	
Collagenase vs. hydrocolloid dressing	Burgos 2000 (26)	Complete healing	Mean % <down> in area
	Muller 2001 (27)	Complete healing	Mean time to complete healing
Collagenase vs. fibrinolysin/DNAase	Pullen 2002 (28)		Decrease in necrotic area
Collagenase vs. papain urea	Alvarez 2002 (22)		Decrease in wound area Decrease in necrotic area Increase in granulation
Collagenase vs. dextranomer	Parish and Collins 1979 (25)	Complete healing	
Streptokinase.streptodonase vs. hydrogel	Agren and Stromberg 1985 (29)		% median change in surface area
Dextranomer vs. placebo	Parish and Collins 1979 (25)		
Dextranomer vs. Eurosl and paraffin gauze dressing	Nasar and Morley 1982 (30)		Clean and granulating wounds less than 25% of original size
Dextranomer vs. saline dressing	Ljungberg 1998 (31)		Decrease in necrotic area Increase in granulation and epithelialization
Dextranomer vs. amorphous hydrogel	Collins 1996 (32)		Complete debridement Decrease in ulcer area
	Thomas 1993 (33)		Complete debridement
Dextranomer vs. calcium alginate	Sayag, 1996 (34)		Decrease in ulcer area rate of healing
Cadexomer iodine vs. standard therapy	Moberg 1983 (35)		Complete healing Decrease in ulcer area Increase epithelialization
Maggot debridement vs. conventional therapy	Sherman 2002 (36)		Complete healing Mean time to complete healing

*DNAase indicates deoxyribonuclease.

Chemical (Enzymatic) Debridement: Collagenase Versus Placebo

Two studies compared collagenase debridement to a placebo treatment. Lee and Ambrus (24) compared the treatment of 17 advanced pressure sores using a topical collagenase preparation (250 units per gram of white petroleum) to 11 pressure sores treated with a placebo (deactivated collagenase in the same concentration) for 4 weeks. Both arms showed an increase in the mean volume of the pressure ulcer but the increase was significantly smaller in the collagenase arm than in the placebo arm (Figure 3).

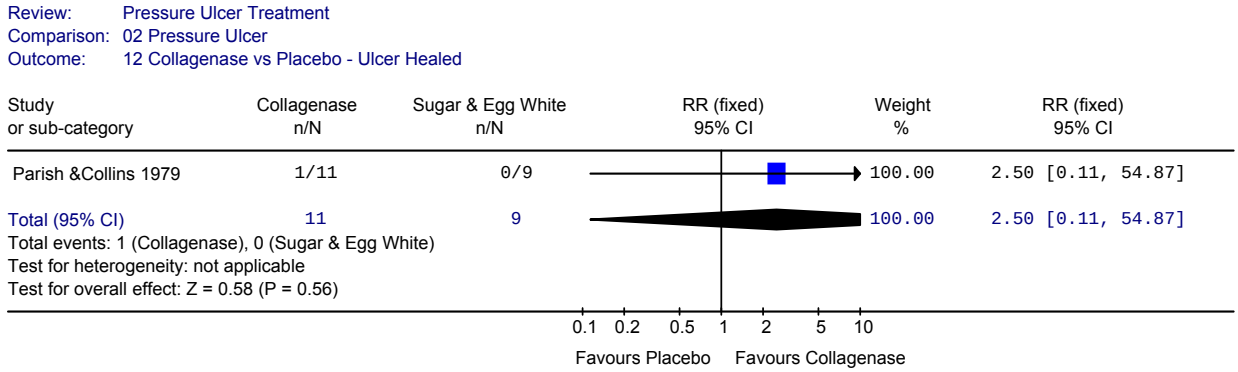
Figure 3: Forest Plot of Mean Percentage Change in Volume of Ulcers – Collagenase Versus Placebo*



*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

In a 3-arm study, Parish and Collins (25) included a comparison of collagenase debridement of 11 pressure ulcers for 4 weeks to treatment of 9 pressure ulcers with a placebo (sugar and egg white). At follow-up, no significant difference was detected in the proportion of ulcers healed between the collagenase group and the placebo group (Figure 4).

Figure 4: Forest Plot of Ulcers Healed – Collagenase Versus Placebo*



*CI indicates confidence interval; RR, relative risk.

Chemical (Enzymatic) Debridement: Collagenase Versus Hydrocolloid Dressing (Autolytic Debridement)

Two small RCTs (26;27) were found. Both studies compared debridement of advanced pressure ulcers (stage III in one study and stage IV in the second study) using topical collagenase to autolytic debridement using an occlusive hydrocolloid dressing in elderly hospitalized patients. These studies are summarized in Table 8.

Table 8: Randomized Studies Comparing Collagenase With Hydrocolloid Dressing for the Debridement of Pressure Ulcers*

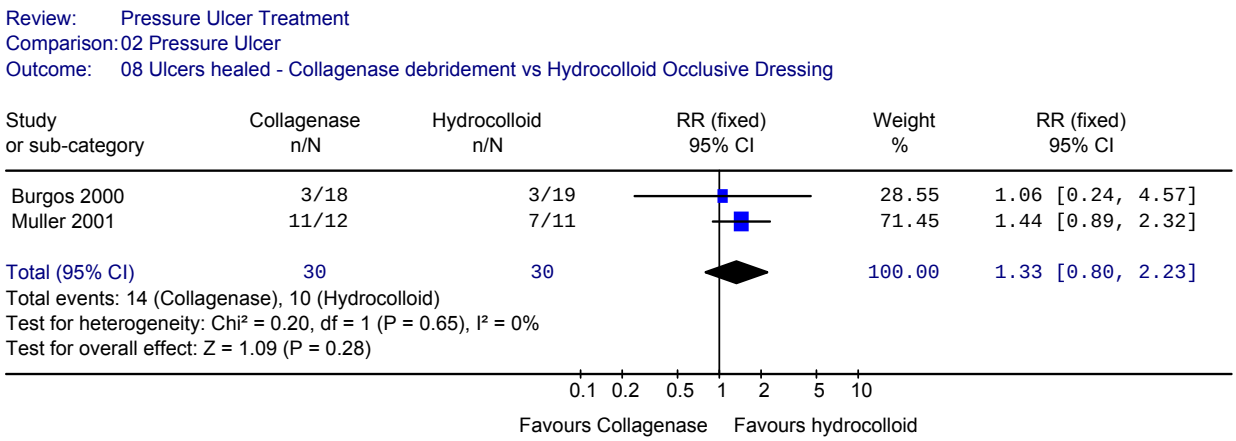
Study	Sample Size Patients (pressure ulcers)	Mean Age Treatment vs. Control, Years SD)	Ulcers Stage	Debriding Agent	Comparator	Results
Burgos et al., 2000 (26)	RCT 37 pats 43 ulcers	81.9 (12.7) vs. 78.6 (10.4)	III	Collagenase	Occlusive hydrocolloid dressing	Complete healing: Collagenase = 3/18 Hydrocolloid = 3/19 (*P* = .451) <down> in area of ulcer after 12 weeks (cm^2): Collagenase 9.1 (SD, 12.7) = 44.2% Hydrocolloid 6.2 (SD, 9.8) = 27.9% (*P* = .369)
Muller et al., 2001 (27)	RCT 24	74.6 72.4	IV	Collagenase	Hydrocolloid dressing	Complete healing: Collagenase = 11/12 (91.7%) Hydrocolloid = 7/11 (63.6%) (*P* < .005) Mean time to complete healing (weeks): Collagenase 10 (range 6–12) Hydrocolloid 14 (11–16) (*P* < .005)

*mL indicates millilitre; RCT, randomized controlled trial; SD, standard deviation

Neither of the studies reported a significant difference in the proportion of ulcers with complete healing, and Burgos et al. (26) also reported no significant difference in the reduction of the size of stage III ulcers between the two arms (44.2% for collagenase vs. 27.9% for hydrocolloid dressing, $P = .369$). Muller et al., (27) who studied patients with stage IV ulcers, reported that even though there was no statistically significant difference in complete healing between the collagenase arm and the hydrocolloid arm, ulcers debrided with collagenase healed faster compared with patients treated with hydrocolloid dressing (mean time to achieve complete healing: 10 weeks vs. 14 weeks, $P < .05$). Burgos et al. (26) reported that collagenase debridement resulted in lower mean global cost for each centimetre reduction in ulcer area, and Muller reported that collagenase debridement resulted in a lower average cost for each successfully treated patient.

A pooled analysis of the proportion of ulcers with complete closure was conducted for the two studies. The test for heterogeneity is insignificant ($I^2 = 0\%$). The pooled estimate for RR showed no evidence of a significant difference between the 2 debridement methods (RR 1.33 in favour of hydrocolloid; 95% CI, 0.80–2.23) (Figure 5).

Figure 5: Forest Plot of Ulcers Healed – Collagenase Versus Hydrocolloid*



*CI indicates confidence interval; RR, relative risk.

Enzymatic Debridement: Collagenase Debridement Versus Other Topical Debriding Agents

Three studies (22;28) compared topical collagenase treatment to 3 other topical debriding agents. (Table 9).

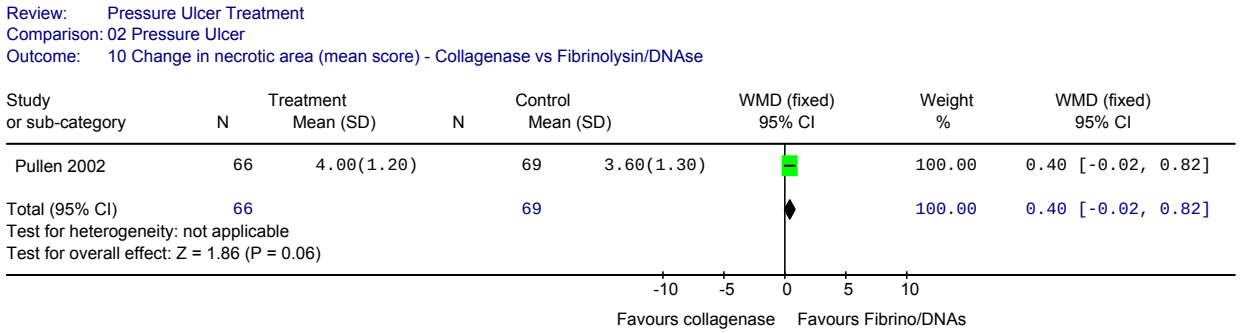
In an RCT, Pullen et al. (28) compared 66 patients with stage II to III pressure ulcers treated with collagenase ointment twice daily to 69 similar patients treated with fibrinolysin/deoxyribonuclease ointment twice daily. After 4 weeks of treatment, Pullen et al. (28) found no significant difference in the reduction in necrotic wound area either by intention-to-treat analysis or by protocol analysis (Figure 6).

Table 9: Randomized Controlled Trials Comparing Collagenase Debridement to Other Debriding Agents*

Study	Sample Size	Debriding Agent	Comparator	Ulcer Stage	Baseline	Mean Age, Years (SD)	Study Duration (weeks)	Results
Pullen et al., 2002 (28)	RCT 135	Topical collagenase (N = 66)	Fibrinolysin/DNAase (N = 69) (Enzyme)	II, III, and IV	Stage III and IV Collagenase 73% Fibrinolygsin/ DNAse 71%	Collagenase 78.4 (8.9) Fibrinolysin /DNAse	4	No significant difference in <down> in necrotic wound area or wound (ITT or protocol analysis)
Alvarez et al., 2002 (22)	RCT 26	Topical collagenase (N = 12)	Papain-urea ointment (N = 14) (Enzyme)	II, III, and IV	Stages III and IV Collagenase 67% Papain-urea 50% Nonviable tissue Collagenase 66.7% Papain-Urea 70%	Collagenase 76 (Range 25–97) Papain-Urea 74 (Range 21–101)	4	Papain-urea group showed significantly greater Decrease in nonviable area , higher degree of granulation and greater <up> in epithelial tissue than collagenase No significant difference in <down> in wound area or overall wound condition
Parish and Collins, 1979 (25)	RCT 17 patients 34 ulcers	Collagenase	Dextranomer Placebo (Mechanical)	Advanced	Mean ulcer surface area Collagenase 3.2 cm^2 Dextranomer 4.5 cm^2 Placebo 2.4 cm^2 Difference not significant	Range of age: Collagenase 28–59 years Dextranomer 29–57 years Sugar and egg white 32–70 years	4	Ulcers healed Collagenase 9% (1/11) Dextranomer 43% (6/14) Placebo 0% (0/9) Dextranomer vs. collagenase (NS) Dextranomer vs. placebo $P < .05$ Collagenase vs. placebo (NS)

*ITT indicates intention-to-treat; NS, not statistically significant; RCT, randomized controlled trial; SD, standard deviation.

Figure 6: Forest Plot of Mean Change in Necrotic Area – Collagenase Versus Fibronolysin/DNAase*

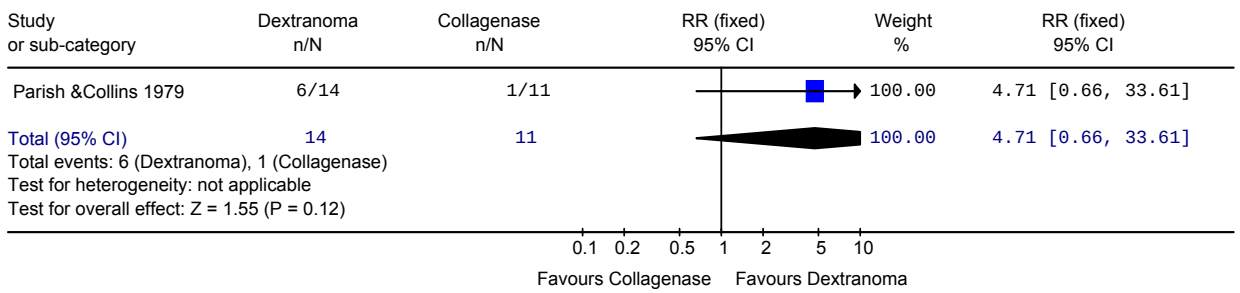


*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

In another RCT, Alvarez et al. (22) compared 14 patients treated with papain-urea ointment for 4 weeks to 12 patients treated with topical collagenase for the same period of time. The primary endpoint was reduction of area covered by nonviable tissue as a percentage of the area at baseline. After 4 weeks of treatment, Alvarez et al. (22) reported that compared with treatment with collagenase, treatment with papain-urea resulted in significantly greater reduction in area covered with nonviable tissues (99% vs. 25%, $P = .0053$), a higher degree of granulation (75%–100% vs. < 25%, $P < .0167$), and a greater increase in the amount of epithelial tissue; however, there was no significant difference in the area of the wound and in the overall wound condition between the two arms.

In a placebo-controlled study, Parish and Collins (25) compared debridement using collagenase to debridement using dextranomer and treatment with a placebo (sugar and egg white). The study included 17 residents of a nursing home with a total of 34 pressure ulcers among them. After wound cleansing with saline, 11 of the pressure ulcers were treated a daily application of a collagenase enzyme (Santyle®) and covered with a dry dressing while 14 of the ulcers were treated with dextranomer polysaccharide beads applied 1 to 3 times and covered with a dry dressing. Nine other ulcers were treated with the mixture of sugar and egg whites After 4 weeks, none of the wounds treated with the placebo had healed. The ulcers treated with dextranomer showed better healing than those treated with collagenase, but the difference was not statistically significant (Figure 7).

Figure 7: Forest Plot of Ulcers Healed – Dextranomer Versus Collagenase*



*CI indicates confidence interval; RR, relative risk.

Table 10: Summary of Results on Debridement Using Collagenase

Study	No. of Ulcers	Debriding Agent	Comparator	Ulcer Stage	Mean Age Treatment vs. Control, Years	Study Duration (weeks)	Necrotic Area (collagenase vs. comparator)	Impact on Healing (collagenase vs. comparator)
Lee and Ambrus, 1975 (24)	28	Collagenase	Placebo	Advanced	67.6	4	Not reported	Collagenase less increase in ulcer area
Burgos 2000 (26)	37	Collagenase	Hydrocolloid dressing	III	81.9 71.6	12	Not reported	No significant difference
Muller 2001 (27)		Collagenase	Hydrocolloid dressing	IV	All females 74.6 72.4	Till healing	Not reported	Collagenase more healed ulcers and faster
Pullen et al., 2002 (28)	135	Collagenase	Fibrinolysin/DNAse	II – IV	78	4	No significant difference	No significant difference
Parish and Collins, 1979 (25)	34	Collagenase	Dextranomer Placebo (egg white and sugar)	Advanced	Range 28–59 29–57 32–70	4	Not reported	Dextranomer significantly more ulcers healed than placebo No significant difference vs. collagenase
Alvarez et al., 2002 (22)	26	Collagenase	Papain-urea	II – IV	76 74	4	Greater <down> with Papain-urea	Papain-urea more granulation and epithelialization

Enzymatic Debridement: Streptokinase/Streptodornase

Streptokinase/streptodornase (Varidase®) consists of two enzymes believed to have two separate modes of action. Streptokinase acts directly upon a substrate of fibrin or fibrinogen by activating a fibrinolytic enzyme in human serum. Streptodornase liquefies the vicious nucleoprotein of dead cells or pus.

Agren and Stromberg (29) randomized 28 elderly patients with one or more necrotic pressure sores to either streptokinase/streptodornase enzymatic debridement (Varidase Topical) or zinc oxide applied to a sterile gauze compress dressing (Table 11). No surgical debridement was performed but loose necrotic material was removed prior to initiation of treatment. Wound area was assessed through tracing and photograph and evaluated by a surgeon blinded to treatment allocation. At the end of the treatment period, ulcers treated with streptokinase/streptodornase had a median increase of 18.7% in surface area whereas ulcers treated with zinc oxide had a median decrease of 2.4% in surface area. Three patients withdrew from the enzymatic debridement group because of skin reaction or increase in necrotic area.

Table 11: Streptokinase/Streptodornase Versus Traditional Dressing

Study	No. of Ulcers	Debriding Agent	Comparator	Ulcers Stage	Median Age, Enzyme vs. Control	Duration of Study (weeks)	Necrotic Area (enzyme vs. comparator)	Change in Area of Pressure Ulcer (enzyme vs. control)
Agren and Stromberg, 1985 (29)	14/14 In- or outpatient	Streptokinase/ streptodornase (Varidase Topical ®) applied to sterile gauze dressing – changed 2x/day	Zinc oxide (400 mg /cm^2) applied to sterile gauze dressing changed 1x/day	Necrotic pressure ulcers	86 vs. 81 years	8	Not reported	+ 18.7% vs. −2.4%

Enzymatic Debridement: Streptokinase/Streptodornase Debridement in Hydrogel Versus Hydrogel Alone

One small double-blind RCT by Martin et al. (21) compared debridement using enzymes streptokinase and streptodornase mixed with hydrogel to debridement using hydrogel alone. The study consisted of 17 patients (mean age 81 years) with 21 stage IV necrotic pressure sores. Martin et al. (21) reported that there were no statistically significant differences in the mean time to eschar removal between the two groups (11.8 [SD 2.9] days for the enzyme plus hydrogel group vs. 8.1 [SD 1.8] days for hydrogel alone). The author concluded that if the results were confirmed, using hydrogel alone would be equally effective as using streptokinase/streptodornase in combination with hydrogel, and the cost of debriding agents would be £2.40 instead of £85.80. (21)

Mechanical Debridement

Mechanical Debridement: Dextranomer Versus Collagenase or Advanced Dressings

Dextranomer paste contains polysaccharide beads that are highly hydrophilic, drawing moisture away from the wound surface by capillary action and is capable of drawing nonviable debris from the wound bed. (32) Six RCTs on the use of debridement were found. One study compared dextranomer paste with another debriding enzyme (collagenase), 2 with a traditional dressing, and 3 with autolytic debridement using advanced moisture retentive dressings (Table 12).

Table 12: Randomized Controlled Trials Comparing Dextranomer Paste With Other Treatments for Pressure Ulcers*

Study	Sample Size Patients (pressure ulcers)	Debriding Agent	Comparator	Ulcers Stage	Mean Age Treatment vs. Control Years (SD)	Duration of Study (weeks)	Impact on Necrotic Area (dextranomer vs. comparator)	Impact on Wound Healing (dextranomer vs. comparator)
Parish and Collins, 1979 (25)	17 (37)	Dextranomer paste	Collagenase Placebo (sugar and egg white)	Not stated	Range D, 29–57 C, 28–59 PBO, 32–70	4	Not reported	Ulcers healed: vs. Placebo 6/14 vs. 0/9 (*P* <.05) vs. collagenase 6/14 vs. 1/11 (NS)
Nasar and Morley, 1982 (30)	18	Dextranomer paste (Debrisan®) 2x/day first 3 days then daily	Eusol and paraffin dressing 3x/day first 3 days then 3x daily	Unclear	83.2 vs. 77.4 Ulcers mostly on foot and heel	13.4	Not reported	Ulcers clean, granulating and <25% of original size 67% (6/9) vs. 56% (5/9) Mean time to reach endpoint 39.3 days vs. 62 days
Ljungberg, 1998 (31)	23 (30) Males with spinal cord injury	Dextranomer paste	Saline dressing	II – IV†	Median 54	2.1 (15 days)	≥25% improved drainage 73% vs.13% (*P* < .01) No necrosis 80% vs. 27%	No significant difference in granulation and epithelialization
Collins et al., 1996 (32)	135 (135)	Dextranomer paste	Amorphous hydrogel	Sloughy Grade 2–4, Majority stage III	D, 81 AH, 79	3	Complete debridement – no significant difference	Hydrogel significantly higher median <down> in ulcer area
Thomas et al., 1993 (33)	20/19	Dextranomer paste	Amorphous hydrogel	Sloughy Grade 3 or 4	D, 81.0 AH, 83.5	4	Complete debridement at 14 days D, 1/20 (5%) AH, 8/19 (42%) (*P* = .008) at day 28 D, 5/20 (20%) AH, 8/19 (42%) (*P* = not reported)	Not reported
Sayag et al., 1996 (34)	92 (92)	Dextranomer paste	Calcium alginate	III ~2/3 IV ~1/3	D, 80.4 (9.1) A, 81.9 (8.9)	8		Greater <down> in wound area and higher rate of healing with calcium alginate

*AH indicates amorphous hydrogel; C, collagenase; D, dextranomer paste; NS, not statistically significant; PBO placebo; RCT, randomized controlled trial; SD, standard deviation.
† Eltorai grading system.

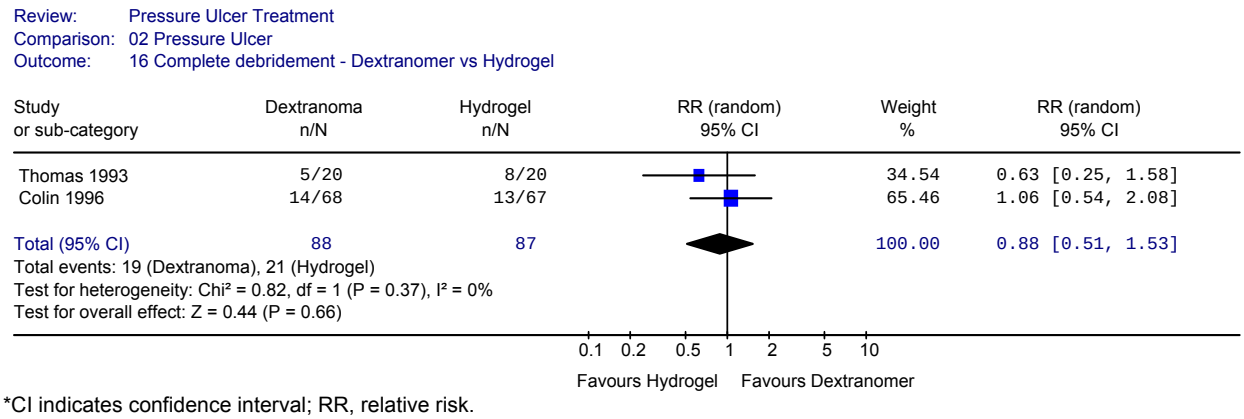
Parish and Collins (25) compared dextranomer debridement with another debriding enzyme collagenase and with a placebo. This study reported that dextranomer debridement resulted in a higher proportion of completely healed ulcers compared with debridement with collagenase (43% vs. 9%) or with placebo (43% vs. 0%). The study, however, consisted of only 17 patients and 37 ulcers.

Nasar and Morley (30) compared dextranomer debridement in 9 patients with deep pressure ulcers to Eusol and paraffin dressing in 9 controls. Eusol is a disinfectant solution containing chlorinated lime and boric acid. Hardened slough present in the pressure ulcer was cut off before initiation of the treatment. The only other concurrent treatment was ultraviolet light. After a maximum treatment period of 94 days, there was no significant difference in the percent of ulcers that reached the endpoint (a clean and granulating wound less than 25% of the original size). The mean time to reach endpoint was shorter for dextranomer compared with Eusol (39.3 days vs. 62 days). Three ulcers in the Eusol group were switched to dextranomer. It should be noted that Eusol may cause irritation to skin surrounding the ulcer and thus protection of the periwound area with soft paraffin or vaseline has been recommended.

Ljungberg et al. (31) compared dextranomer paste with saline dressing (no debridement) in stage II to IV ulcers. There was a significant improvement in drainage and decrease in necrosis in the dextranomer group without any significant difference in granulation or epithelialization of the wounds.

Two studies compared dextranomer debridement with autolytic debridement using topical amorphous hydrogel. In the first study, Collins et al. (1996) compared dextranomer paste with an amorphous hydrogel in the debridement of 64 sloughy grade 2 to grade 4 pressure ulcers. After 3 weeks, both treatments were found to be equally efficacious in reducing the area of nonviable tissues (74% for amorphous hydrogel vs. 62% for dextranomer, $P = .20$). The proportion of ulcers with complete debridement was similar (14/68 in dextranomer vs. 13/67 in hydrogel). However, amorphous hydrogel was found to have a greater impact in reducing the wound area compared with dextranomer paste (35% vs. 7%, $P = .03$). The second study (33) compared 20 pressure ulcers debrided using dextranomer to 19 ulcers debrided using an amorphous hydrogel. The proportion of ulcers with complete debridement was also not significantly different between the 2 groups (5/20 vs. 8/20). A pooled analysis of the two studies showed that both hydrogel and dextranomer paste were equally effective in achieving complete debridement (Figure 8) but more patients reported leakage through the dressing in the group treated with hydrogel. Cost analysis showed that cost of using hydrogel was substantially less than that of dextranomer paste. (33)

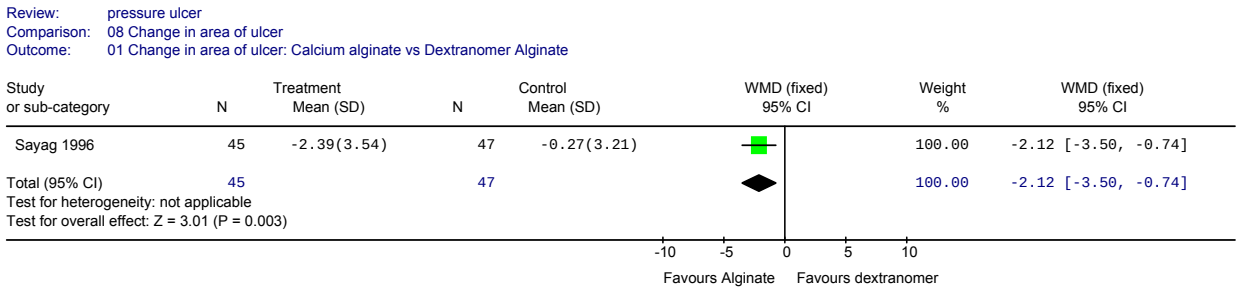
Figure 8: Forest Plot of Complete Debridement – Dextranomer Paste Versus Topical Hydrogel*



*CI indicates confidence interval; RR, relative risk.

In a prospective randomized study involving 92 patients and 92 stage III to IV established pressure ulcers in a high-risk population (with immobilization, poor metal status, poor health status, and a high proportion of urinary and fecal incontinence), Sayag et al. (34) compared 47 ulcers treated with calcium alginate dressing with 45 ulcers treated with dextranomer paste. The authors reported that after 8 weeks of treatment, calcium alginate dressing performed significantly better than dextranomer paste in achieving a minimum of 40% reduction (relative to baseline) in the wound area (74% vs. 42%, $P = .002$) and in the rate of wound healing (3.55 cm^2/week vs. 2.15 cm^2/week, $P = .024$) (Figure 9). Adverse events associated with dextranomer paste debridement included pain upon application, local infection, slight bleeding on removal, and hypergranulation. These events generally did not require termination of treatment. (34)

Figure 9: Forest Plot of Ulcer Area Reduction – Calcium Alginate Versus Dextranomer*



*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

The limited evidence available suggests that the use of dextranomer paste is likely better than the use of traditional dressing alone. There is no significant difference between dextranomer paste and collagenase in terms of ulcers healed. Autolytic debridement of stage II to IV pressure ulcers using amorphous hydrogel or calcium alginate was shown to be as effective as debridement using dextranomer paste and resulted in significantly greater and faster reduction in the wound area compared with dextranomer paste. Calcium alginate was also shown to be effective in debriding even sloughy pressure ulcers.

Antimicrobial Mechanical Debridement: Cadexomer Iodine Versus Standard Treatment

Cadexomer iodine consists of spherical microbeads with a three-dimensional network of modified starch. The microbeads contain iodine within its matrix. When applied to the wound, the highly hydrophilic microbeads absorb exudate from the wound surface, swelling to form a gel, and progressively release iodine at the wound surface. One gram of powder can absorb as much as 7 mL of fluid. Cadexomer iodine promotes an acid pH that favours the antimicrobial activity of the iodine. (35)

One RCT (35) on cadexomer iodine was found. In this study, 16 patients that received treatment of pressure ulcers using daily application of cadexomer iodine were compared with a control group of 18 patients who received the standard treatment in their hospital, including saline dressing, enzyme-based debridement, and nonadhesive dressings. Within 3 weeks of treatment, cadexomer iodine treatment resulted in a significantly greater re-epithelialization and greater absolute and percentage reduction of ulcer area. This advantage was maintained at 8 weeks and healing was also significantly better with cadexomer iodine (8/16 vs. 1/18, $P < .01$). People treated with cadexomer iodine also had significantly greater reduction in pain and pus/debris compared with standard treatments. (35)

Maggot Debridement Therapy

No RCTs on maggot debridement of pressure ulcers were found. In a nonrandomized study, Sherman et al. (36) compared pressure ulcers treated with maggot debridement to those treated with only conventional therapy (Table 13). Patient allocation to maggot therapy was based on the decision of the physician and the patient. Patients in the intervention group received, in addition to conventional therapy, two 48-hour debridement treatments each week using sterile maggots. The controlled group received only conventional therapy prescribed by their primary care provider or the hospital's wound care team, which included topical antimicrobial therapy (35%), hydrogel (10%), chemical debridement (8%), saline moistened or wet-to-dry dressings (8%), hydrocolloid and alginates (6%), growth factors (4%), and combinations of nonsurgical treatments (12%). Almost 12% of the control group also received bedside or intraoperative surgical debridement. (36)

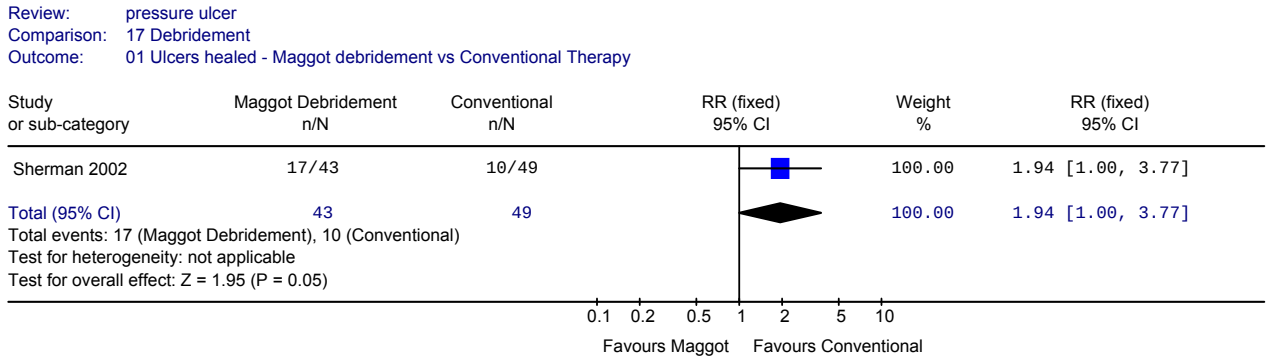
Table 13: Nonrandomized Controlled Study on Maggot Debridement Compared With Conventional Therapy*

Study	No. of Ulcers	Comparison	Ulcer	Mean Age (years)	Duration (weeks)	Complete Debridement at week 5	Impact on Wound Healing
Sherman, 2002 (36) (Nonrandomized controlled trial – the only study available)	Enrolled 61/84 Reported 43/49	MDT vs. conventional therapy MDT = two 48-hr cycles per week for 8 weeks	MDT stage III 58% stage IV 42% Control stage III 92% stage IV 8%	MDT 62 (26–85) Control 66 (32–91)	8	MDT 80% Control 48% (*P* = .021) Necrotic tissue at 3 weeks MDT = .033 of Control (*P* = .05)	Complete healing MDT, 39% (17/43) Control 21% (10/49) (*P* = .058) % of wounds that <down> in surface area 4 wks MDT = 79% Control = 44% (*P* < .05) Average time to complete healing MDT = 12.0 weeks (7–17) Control = 13.4 (8–19) (NS)

*MDT indicates maggot debridement therapy; NS, not statistically significant.

Sherman et al. (36) reported that after 8 weeks, the rate of complete healing was higher in the maggot debridement group compared with the conventional group (RR 1.94); the difference was close to but did not reach statistical significance since the lower limit of the 95% CI overlapped with 1 (Figure 10). The percentage reduction in surface area of the wound at 4 weeks was significantly higher in the maggot debridement group (79% vs. 44%, $P < .05$). The average time taken to completely heal a pressure ulcer was not significantly different between the two groups (12 weeks for maggot debridement therapy vs. 13.4 weeks for the control). (36)

Figure 10: Forest Plot of Ulcers Healed – Maggot Debridement Versus Conventional Therapy*



*CI indicates confidence interval; RR, relative risk.

Devices for Debridement

Devices for debridement include syringes, dental irrigation systems, pulsed lavage systems, and high power water jet systems. The available evidence is shown in Table 14.

Table 14: Studies on Devices for Debridement*

Study	Study Design	Comparison	No. of Ulcers	Ulcer Stages	Treatment Duration	Results
Burke, 1998 (20)	RCT	Whirlpool 20 minutes daily vs.no whirlpool	42	III or IV	2 weeks	Number of ulcers improved 14/24 vs. 5/18 RR = 2.10 (95% CI, 0.93, 4.76) (*P* = .08)
Diekmann, 1984 (37)	RCT	Irrigation with saline using a dental device vs. standard care	16	III or IV	2 weeks	Post-treatment ulcer area (mm^2) 831.25 (SD, 667.88) vs. 801.25 (SD, 631.70) (*P* = .06)
Granick, 2006 (38)	Retrospective, comparative study	High pressure waterjet (Versajet) vs. surgical debridement	45 vs. 22 (67)	Chronic (30% were pressure ulcers)		Odds ratio that Versajet decreased the number of debridement procedures OR = 6.97 (95% CI, 1.59 to 30.67) (*P* = .01)

*CI indicates confidence interval; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk; SD, standard deviation.

Summary of Analysis – Debridement

Table 15: Impact of Debridement on Complete Healing*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stages	Relative Risk (95% CI)	I^2 (%)	*P* Value
Collagenase vs. placebo	1	20	Advanced	2.5 (0.11, 54.87)	NA	.56
Collagenase vs. hydrocolloid	2	61	III, IV	1.33 (0.80, 2.23)	0	.28
Collagenase vs. dextranomer	1	25	Advanced	4.71 (0.66, 33.61)	NA	.12
Dextranomer vs. placebo	1	23	Advanced	8.64 (0.55, 137.33)	NA	.13
Cadexomer iodine vs. standard care	1	34		6.75 (0.91, 50.23)	NA	.60
Maggot debridement vs. conventional therapy	1 CCT	82	III, IV	1.94 (1.00, 3.77)	NA	.50

*CCT indicates clinical controlled trial; CI, confidence interval; I^2, test for heterogeneity.

Table 16: Impact of Debridement on Necrotic Area or Area of Pressure Ulcer*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stages	Weighted Mean Difference (95% CI)	I^2 (%)	*P* Value
Collagenase vs. fibrnolysin/DNAase	1	66	II–IV	Difference in score 0.4 (–0.02, 0.32)	NA	.06
Collagenase vs. papain urea	1	26	II–IV	<down> in necrotic area 25% vs. 99%	NA	.0167
Dextranomer vs. hydrogel	2	174	Sloughy II–IV	Complete debridement (RR) 0.88 (0.51, 1.53)	0	.66
Maggot debridement vs. conventional therapy	1	82	III, IV	Complete debridement at 5 weeks 80% vs. 52%	NA	.021
Calcium alginate vs. dextranomer	1	92	III, IV	<down> in wound area (cm^2/week) –2.12 (–3.50, –0.74)	NA	.003
Streptokinase/streptodornase hydrogel vs. hydrogel alone	1	21	IV necrotic	Days to eschar removal (WMD) 3.7 (1.66, 5.74) favours hydrogel	NA	.0004

*CI indicates confidence interval; DNAase, deoxyribonuclease; I^2, test for heterogeneity; WMD, weighted mean difference; NA, not applicable; RR, relative risk.

Summary Statements – Debridement

There was no evidence that debridement using collagenase, dextranomer, cadexomer iodine, or maggots significantly improved complete healing compared with placebo

There were no statistically significant differences between enzymatic or mechanical debriding agents with the following exceptions:

- Papain urea resulted in better debridement than collagenase.
- Calcium alginate resulted in a greater reduction in ulcer size compared with dextranomer.
- Adding streptokinase/streptodornase to hydrogel resulted in faster debridement.
- Maggot debridement resulted in more complete debridement than conventional.
- There is limited evidence on the healing effects of debriding devices.

Expert Opinion

- Regular debridement is necessary to convert a chronic wound to an acute wound in order to initiate healing.
- Surgical debridement is the most effective debridement technique especially in pressure ulcers with much necrosis.
- Enzymatic debridement and autolytic debridement are slow and are only effective in wounds with minimal necrosis. They can be used in adjunct to surgical debridement.

Topical Agents

Topical Phenytoin Versus Traditional Dressing or Advanced Dressing

Phenytoin is an antiepileptic agent. Topically applied, phenytoin has been shown to accelerate the healing process in ulcers of various etiology. (39) Proposed actions of phenytoin include accelerated fibroblast proliferation, formation of granulation tissue, deposition of connective tissue components, reduction in collagenase activity, and bacterial contamination of the ulcer. (40) A common and frequent adverse effect of phenytoin sodium anticonvulsant therapy is gingival hyperplasia.

The review update found two studies that explored the efficacy of topical phenytoin treatment on pressure ulcers (Table 17). Hollisaz et al. (41) compared a hydrocolloid dressing to phenytoin cream and a simple saline dressing in an 8-week randomized controlled study. Hydrocolloid dressing resulted in a higher percentage of complete healing only in stage I ulcers compared with phenytoin cream (85% vs. 22%, $P < .005$), whereas in stage II ulcers the difference in percent complete healing between phenytoin cream and hydrocolloid dressing did not reach statistical significance (67% vs. 48%, $P > .05$).

Subbanna et al. (40) compared stage II pressure ulcers treated for 15 days with sterile gauze soaked in a phenytoin solution with pressure ulcers treated with saline gauze. At the end of the 15 days, no statistically significant differences were detected between the two groups in the reduction in PUSH scores (19.53 vs. 11.39, $P = .261$), reduction in the size of the ulcers (47.83% vs. 36.03%, $P = .132$), or in reduction of volume (53.94% vs. 55.76%, $P = .777$). No patients withdrew because of adverse events.

Pooling the two studies was not appropriate or feasible because of differences in patient populations, comparators, and reported outcomes.

Table 17: Randomized Controlled Trials Comparing Topical Phenytoin With Traditional or Advanced Dressing*

Study	Sample size Patients (pressure ulcers)	Patient Mean Age Treatment vs. Control Years (SD)	Ulcers Stage	Mean Baseline Ulcer Size, Treatment vs. Control (cm^2)	Study Duration	Comparison	Reported Outcomes
Subbanna et al., 2007 (40)	28	34.25 (18.12) 31.64 (12.27)	II		15 days	Phenytoin solution vs. saline gauze	%<down> in PUSH scores and ulcer size
Hollisaz et al., 2004 (41)	83 men (91 ulcers)	36.64 (6.04)	I and II	5.12 (SD, 3.63) 10.27 (15.32) (P > .10)	8 weeks	Phenytoin cream vs. hydrocolloid dressing	Complete healing Stage I ulcers Hydrocolloid 85% (11/13) Phenytoin cream 22% (2/9) (*P* < .005) Compared with hydrocolloid Stage II ulcers Hydrocolloid 67% (12/18) Phenytoin cream 48% compared with hydrocolloid (*P* > .005)

*PUSH indicates Pressure Ulcer Scale for Healing; SD, standard deviation.

Topical Collagen Versus Hydrocolloid Dressing

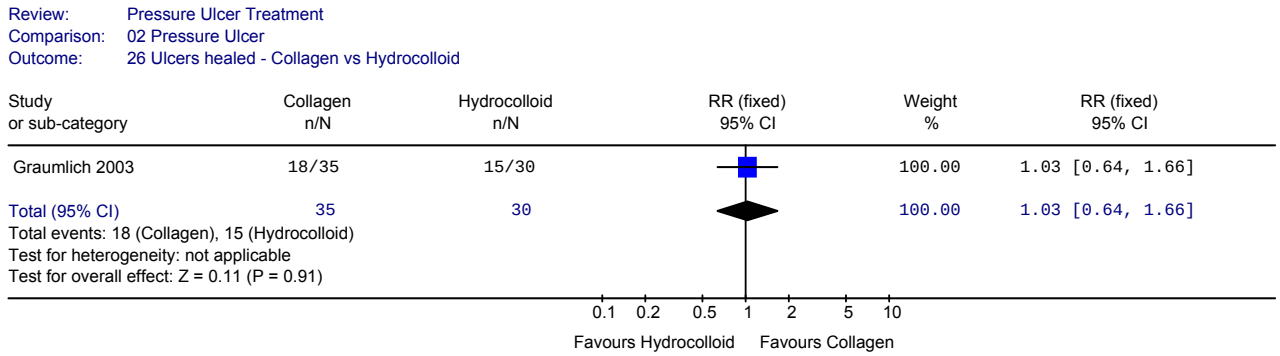
In a single-blind RCT, Graumlich et al. (11) compared 35 stage II and III pressure ulcers treated with topical collagen to 30 pressure ulcers treated with hydrocolloid dressing (Table 18). There were no statistically significant differences in age, area and depth of ulcers, stage of ulcers, or duration of ulcers at randomization. After 8 weeks of treatment, no significant differences in complete healing (Figure 11), area healed per day, or in time required to achieve complete healing could be detected between the study groups. However, collagen was applied daily compared with two changes of hydrocolloid dressing per week. The average cost per patient was higher in the collagen group compared with the hydrocolloid group ($627.56 vs. $222.36 US).

Table 18: Randomized Controlled Study – Topical Collagen Versus Hydrocolloid*

Study	Sample Size (pressure ulcers)	Comparison	Patient Mean Age Treatment vs. Control Years (SD)	Ulcers Stage	Mean Baseline Ulcer Size, Treatment vs. Control (mm^2)	Study Duration (weeks)	Reported Outcome at 8 weeks Collagen vs. Hydrocolloid
Graumlich et al., 2003 (11)	35/30	Daily topical collagen vs. hydrocolloid dressing	82 vs. 80.6	Stage II and III	121 vs. 174 (NS)	8	Complete healing 18/35 (51%) vs. 15/30 (50%) *P* = .893 Time to heal 5 weeks vs. 6 weeks (*P* = .409) Mean area healed/day 6mm^2 vs. 6 mm^2 (*P* = .942) Mean cost per patient $627.56 vs. $222.36 (US)

*NS indicates not statistically significant; SD, standard deviation.

Figure 11: Forest Plot of Pressure Ulcers Healed – Topical Collagen Versus Hydrocolloid Treatment*



*CI indicates confidence interval; RR, relative risk.

Dressings

As described in an earlier section, wound healing is a complex and progressive systemic process. The dressing used on the wound should intensify the body's natural response to wound healing and utilize its own enzymes to augment healing.(42)

The choice of dressing needs to be tailored to the characteristics of the pressure ulcer such as size, stage, depth/undermining, amount of exudate or eschar, and presence or absence of infection.

Primary dressings (including beads, powder, gels, cream, and bordered dressings) are placed in or on the wound surface. If the primary dressing does not have an adhesive border, then a secondary cover dressing is used to secure the primary dressing. Secondary dressings are designed to provide additional support, absorption, compression, and protection, when needed.

Traditional dressings include gauze moistened with saline (wet-to-dry or wet-to-wet) and paraffin impregnated gauze.

Major types of advanced dressing include hydrocolloid, polyurethane foam, hydropolymer, hydrocellular, and alginate. The characteristics of the various dressings are summarized in Table 19.

Hydrocolloid

Polyurethane Foam: The polyurethane foam dressing consists of a soft foam sheet with a hydrophilic wound contact surface that has low adherence. The middle portion of the dressing consists of hydrophilic foam that absorbs and contains the exudate. The foam backing layer is moisture-vapour permeable but impermeable to water and bacteria. (43)

Hydropolymer: Hydropolymer adhesive dressings (TIELLE, Johnson and Johnson) consisting of a polyurethane adhesive backing, a centre hydropolymer island, and a nonwoven layer in between. As the dressing absorbs exudate, the hydropolymer central island swells and fills any irregular contours to the wound, minimizing exudate build-up and the chance of maceration. Excess moisture is held in the wicking layer next to the polyurethane backing. The vapour-permeable backing allows excess moisture to evaporate through the back of the dressing, allowing the dressing to manage additional exudate. (44)(Thomas 1997, J of Wound Care 1997; 6(8): 1997)

Hydrocellular: The hydrocellular dressing (Allevyn Hydrocellular, Smith and Nephew Medical, Hull, England) consists of a layer of soft, hydrophilic polyurethane foam about 4 mm thick boned to semi-permeable polyurethane film. The wound contact surface is covered with apertured three-dimensional plastic net (43) This dressing is available in both adhesive and nonadhesive format.
Alginate: Alginate is a dressing made from seaweed.

Table 19: Characteristics of Major Types of Dressings

Dressing	Primary / Secondary	Material	Form	Adherent to Wound?	Adhesive to Healthy Tissue?	Permeable?	Absorbency	Protection Against Bacteria?
Gauze	Primary	Cotton polyester	Pad	Yes	No	Yes	Medium to high	Not adequate
Paraffin gauze	Primary contact layer	Cotton polyester with soft paraffin	Pad	No	No	Yes	None	Not adequate
Transparent film	Primary or secondary	Polyurethane	Film	No	Yes	Semi*	No	Yes
Hydrogel	Primary (gel– requires a secondary dressing)	Cross-linked polymer high water content	Amorphous gel, bundle, or sheet	No	No	Oxygen -yes	Low	Yes
Hydrocolloid	Primary – interact with exudate to form a gel	Carboxy-methlcellulose gelatin, pectin, eslastomer and adhesives	Wafer with outer film or foam layer Interact with exudate to form a gel	No	Yes	No when intact Semi in gel form	Moderate	Yes
Polyurethane foam	Primary or secondary	Polyurethane	Different shapes and sizes	No	Yes	Semi	Moderate to heavy	Yes
Hydropolymer	Primary	Polyurethane adhesive backing with a hydropolymer central island and a nonwoven layer in between	Different sizes	No	Yes	Semi	High	Yes
Hydrocellular	Primary	Polyurethane foam bonded to polyurethane film with a 3-dimensional plastic net wound contact surface		No	Yes and No	Semi	High	Yes
Alginates	Primary–needs secondary dressing	Nonwoven fibers containing calcium alginate derived from sea weed	Sheet, rope, ribbon, or powder Interact with exudate to form a gel -Ideal for cavities	No	No	Semi	Moderate to high (contraindicated for dry wounds)	No

*Semi permeable: Not permeable to water and exudate, but permeable to gases and vapour.

Existing Systematic Reviews on Efficacy of Dressings in the Treatment of Pressure Ulcers

Four systematic reviews on wound dressings were identified. These are summarized in Table 20.

Table 20: Previous Systematic Reviews on Wound Dressings*

	Singh et al., 2004 (45)	Royal College of Nurses, 2005 (46)	Bouza, 2006 (47)	San Miguel et al., 2007 (48)
Period of literature search	Up to 2001	Up to August 2004	Up to January 2003	January 1986 – August 2006
Type of wounds covered	Pressure ulcer, venous leg ulcer, excised pilonidal sinus wound	Pressure ulcers	Type II–IV pressure ulcers	Pressure ulcers
Purpose	Compared hydrocolloid vs. gauze in healing chronic wounds	Efficacy of dressings in the treatment of pressure ulcers	Efficacy of advanced dressings in the treatment of types II –IV pressure ulcers	Efficacy and economics of modern vs. traditional dressing in pressure ulcer care
Types of comparisons	Hydrocolloid vs. gauze (soaked with saline or antiseptics)	Modern vs. traditional Modern vs. modern (multiple comparisons)	Advanced dressings† vs. conventional dressings; Advanced dressing vs. advanced dressing	Modern vs. traditional gauze dressings; Modern vs. modern dressing
Type of studies included	RCTs (English language)	RCTs	RCTs Quasi-randomized studies Controlled clinical trials	RCTs Comparative studies Economic studies Meta-analysis (Not restricted to English language)
Outcome measures	Complete healing	Complete healing	Complete healing Time to heal	Effectiveness (complete healing, time to heal, change in area); Cost information
Method of analysis	Meta-analysis	Meta-analysis	Meta-analysis	Descriptive synthesis
Studies (RCTs) on treatment of pressure ulcers included in the review	Gorse 1987; Alm 1989 Xakellis 1992 Colwell 1993 Kim 1996	Alm 1989 Xakellis 1992 Colwell 1993 Matzen 1999 Barrois 1992 Kraft 1993 Sebern 1986 Thomas 1998 Whitney 2001 Kloth 2000 plus 16 trials that compared modern to modern dressing	Gorse 1987 Alm 1989 Xakellis Colwell 1993 Matzen 1999 Kim 1996 Ljungberg 1998 Nasar 1982 Sebern 1986 Thomas 1998 plus 10 trials that compared modern to modern dressings	Gorse 1987 Alm 1989 Xakellis 1992 Colwell 1993 Karft 1993 Sebern 1986 Kim 1996 Thomas 1998 Hollisaz 2004 Kaya 2005 plus 9 nonrandomized studies

Table 20: Previous Systematic Reviews on Wound Dressings (continued)*

	Singh et al., 2004 (45)	Royal College of Nurses, 2005 (46)	Bouza, 2006 (47)	San Miguel et al., 2007 (48)
Conclusions	More chronic wounds healed completely with hydrocolloid than with gauze OR = 1.72 (1.23 to 2.41, P = .00) (Fixed effect)	Varied results in modern dressing vs. traditional dressings No statistically significant differences detected in modern vs. modern dressings	Confirmed the efficacy of hydrocolloid dressings over moistened conventional dressings in healing pressure ulcers. There were insufficient data to establish with any certainty that other types of advanced dressings have greater efficacy over conventional ones or over one another.	There is evidence to support the use of modern dressing as opposed to reverting to traditional methods that would seem clinically and economically unsound.

*OR indicates odds ratio; RCT, randomized controlled trial.
†Included topical debriding agent (dextranomer) in advanced dressings.

Three of the reviews (46-48) only included studies on pressure ulcers whereas one review (45) also included studies on other types of wounds. Two of the reviews (45;47) concluded that hydrocolloid was superior to gauze dressing for healing pressure ulcers and wounds. One review (48) supported the use of modern dressing. The most recent review concluded that results of comparisons between modern and traditional dressings varied and that there were no statistically significant differences between modern dressings. (46)

The MAS literature search identified five additional studies (41;49-52) on dressings that have not been included in the Royal College of Nurses (RCN) review. These studies will be reviewed along with studies included in previous reviews.

MAS Review on Dressing

Modern Dressing Compared With Traditional Dressing

Comparisons of modern dressings with traditional dressings (gauze, paraffin gauze) were performed including studies identified from previous systematic reviews and new studies from literature search. The following comparisons between advanced and traditional dressings were performed.

Advanced Dressing	Traditional Dressing
Hydrocolloid	Saline gauze
Hydrocolloid	Gauze soaked with an antimicrobial solution
Polyurethane (moisture vapour permeable)	Saline gauze
Hydrogel	Saline gauze
Hydrogel	Gauze soaked with an antimicrobial solution

Comparison 1: Hydrocolloid versus Saline Gauze

Seven RCTs compared hydrocolloid with saline gauze in the treatment of pressure ulcer (Table 21). With the exception of a single study, (41) the other studies were included in the review by the RCN (46) (2005). These studies are described in Table 21 and Appendix 4

Heterogeneity was found among the studies. Settings of the studies included long-term care facilities, community care, and acute care. Most of the patients were elderly with the exception of one study that was conducted on patients with spinal cord injury. Six of the studies included stage II and III ulcers and one did not specify the stage of the ulcer. Duration of treatment ranged from 6 weeks to 6 months. The outcomes of these studies are summarized in Table 22.

Only 5 of these studies provided data on complete healing (Alm 1989, (53) Xakellis 1992, (54) Colwell 1993, (55) Matzen 1999, (56) and Hollisaz 2004 (41)). Because the study by Xakellis (54) had much longer treatment duration compared with the other 4 studies (6 months vs. 6–12 weeks), it was analyzed separately from the other 4 studies.

Table 21: Summary of Randomized Controlled Trials Comparing Hydrocolloid With Saline Gauze*

Study	No. of Ulcers/Setting	Mean Age (years)	Ulcer Stage	Comparison	Traditional Dressing	Treatment Duration	Outcome Measures
Alm et al., 1989 (53)	31/25 ulcers 50 LTC in-patients	83.6 (SD, 9.2) vs. 83.4 (SD, 9.4)	Not reported	Hydrocolloid (Comfeel) different forms	Wet saline gauze	up to 10 weeks	Ulcers healed
Xakellis et al., 1992 (54)	18/21 (1) LTC facility	77.3 (SD 16.9) vs. 83.5 (SD, 10.6)	II (93%) and III	Hydrocolloid (sheet)	Saline gauze	6 months	Ulcers healed Median time to healing
Colwell et al., 1993 (55)	48/49 Acute care	68 vs. 68	II and III	Hydrocolloid (Duoderm) sheet	Saline gauze	8 weeks	Ulcers healed Surface area <down>
Matzen et al., 1999 (56)	17/15 Community	82 vs. 84	III or IV	Hydrocolloid (Amorphous)	Saline gauze	12 weeks	Ulcers healed Percent change in wound volume
Hollisaz et al., 2004 (41) Iran	31/30 Male Spinal cord injury	36.64 (6.04)	Equivalent II and III in NPUAP scale	Hydrocolloid	Wet saline dressing	8 weeks	Ulcers healed
Mulder 1993 (57)	23/21	63.1 vs. 57.2	II or III	Hydrocolloid	Saline gauze	8 weeks	Percent <down> in surface area / week
Chang et al., 1998 (58) Kuala Lumpur	17/17 Neurological /malignancy	57.6 (range 20–85)	II or III	Hydrocolloid	Saline gauze	8 weeks	Mean change in surface area: Hydrocolloid <down>34% Saline Gauze <down>8%

*LTC indicates long-term care; NPUAP, National Pressure Ulcer Advisory Panel; SD, standard deviation.
Xakellis: Multivariate analysis :Presence of exudate at baseline <down> healing rates by 2/3. Cox proportional HR: exudate vs. no exudate = 0.34 (*P* = .009). Saline gauze vs. hydrocolloid, HR = .6 (*P* = .17)

Table 22: Outcomes of Randomized Controlled Trials Comparing Hydrocolloid With Saline Gauze*

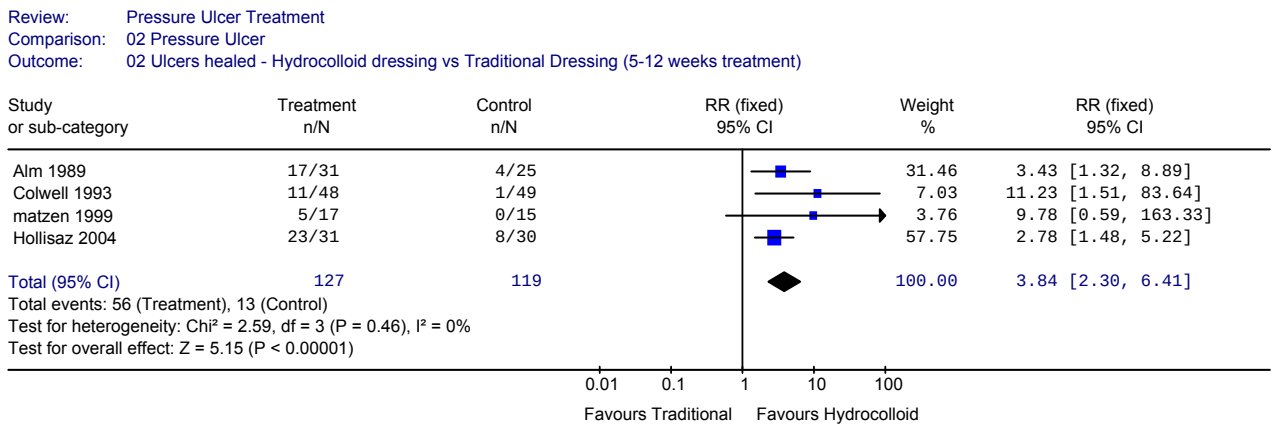
Study	Study Duration	Proportion of Ulcers Healed		Change in Surface Area of Ulcer	
		Hydrocolloid	Saline Gauze	Hydrocolloid	Saline Gauze
Alm et al., 1989 (53)	6 weeks	17/31 (55%, range 50%–60%)	4/25 (15%, range 10%–20%)	NR	NR
Xakellis et al., 1992 (54)	6 months	16/18 (89%) (All stage II)	18/21(86%) (Stages II and III)	NR	NR
Colwell et al., 1993 (55)	8 weeks	11/48	1/49	Decrease 31.9%	<up> 28.3%
Matzen et al., 1999 (56)	12 weeks	5/17 (29%)	0/15 (0%)	Final wound volume 26 (SD, 20)%	Final wound volume 64 (SD, 16)%
Hollisaz et al., 2004 (41)	8 weeks	23/31 Stage I: 11/13 (85%) Stage II: 12/18 (67%)	8/30 Stage I: 5/11 (45%) Stage II: 3/19 (16%)	NR	NR
Mulder et al., 1993 (57)	8 weeks	NR	NR	Mean percent decrease per week 3.3 (SD, 32.7)	Mean percent decrease per week 5.1 (SD, 14.8) (NS)
Chang et al., 1998 (58)	8 weeks	NR	NR	Mean change in surface area decrease 34%	Mean change in surface area increase 8%

*NR indicates not reported; NS, not statistically significant; SD, standard deviation.

The Forest plot of the studies that compared treatment with hydrocolloid dressing with treatment with gauze dressing soaked in saline solution for 6–12 weeks showed a similar trend in complete healing favouring hydrocolloid. The use of hydrocolloid dressing increased the likelihood of complete healing by almost three-fold compared with saline gauze dressing (RR 2.84 [95% CI, 2.30–6.41], $P < .00001$). The test for heterogeneity was not significant ($I^2 = 0\%$, $P = .46$) (Figure 12). Most of the studies also showed a greater reduction in the mean surface area of the ulcer in the hydrocolloid-dressing group compared with the saline gauze group.

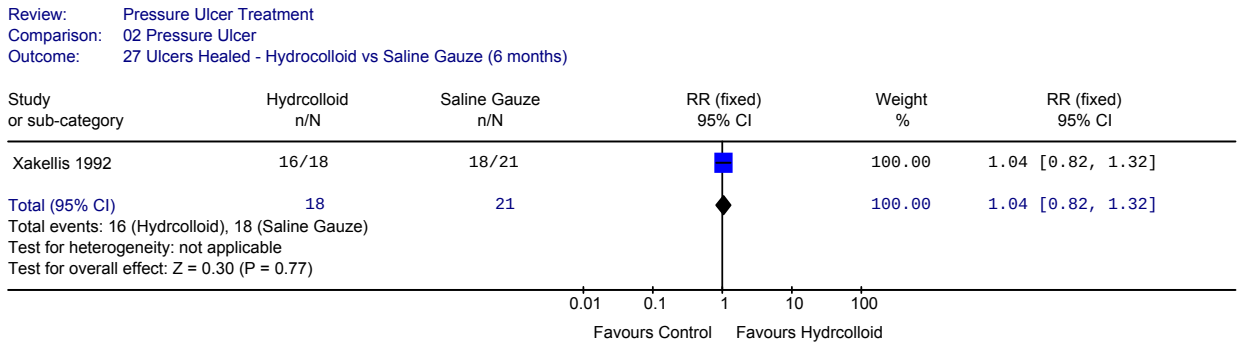
The study (54) that compared 6-month treatment with hydrocolloid dressing to 6-month treatment with saline gauze showed a similar proportion of complete healing at the end of the treatment period (RR 1.04, 95% CI [0.82–1.32], $P = .77$) (Figure 13). Besides having longer duration in treatment, it should be noted that the mean surface area of the ulcers at baseline was smaller (< 1 cm^2) than those in the other studies.

Figure 12: Forest Plot of Ulcers Healed – Hydrocolloid Dressing Versus Saline Gauze (6–12 Weeks Treatment)*



*CI indicates confidence interval; RR, relative risk.

Figure 13: Forest Plot of Ulcers Healed – Hydrocolloid Dressing Versus Saline Gauze (6 Months Treatment)*

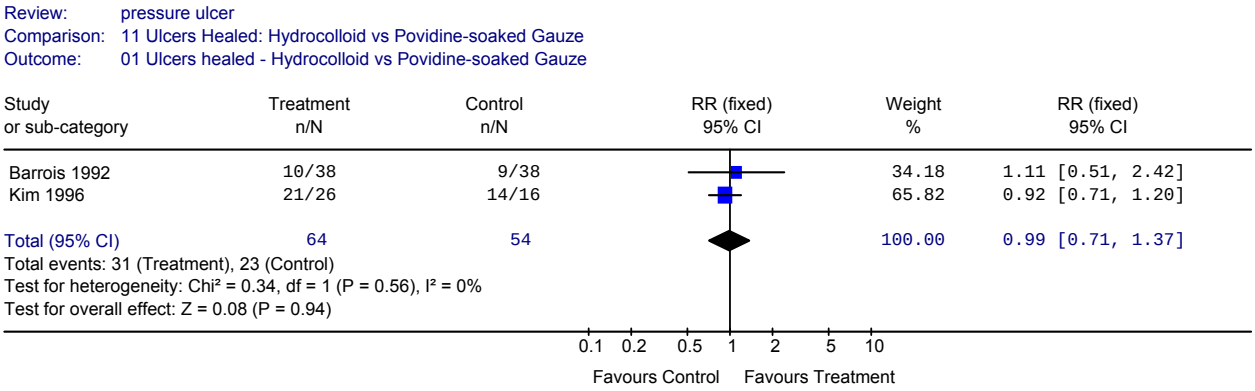


*CI indicates confidence interval; RR, relative risk.

Comparison 2: Hydrocolloid versus Gauze Soaked in an Antimicrobial Solution

Two studies compared treatment with hydrocolloid dressing with treatment with gauze dressing soaked in povidone (Table 23). A third study that compared hydrocolloid with gauze soaked in Dakin's solution was excluded because allocation to treatment arms was not randomized. Based on the 2 included studies (59), it appears that the advantage of hydrocolloid dressing over gauze dressing in promoting complete healing was lost when the gauze dressing was soaked in povidone. A Forest plot of the 2 studies showed no statistically significant difference in proportions of ulcers healed between the 2 treatments (RR 0.99, 95% CI [0.71–1.37], P = .94). Test for heterogeneity was not significant (I^2 = 0%, P = .56) (Figure 14).

Figure 14: Forest Plot of Ulcers Healed – Hydrocolloid versus Gauze Soaked in Antiseptic Solution*



*CI indicates confidence interval; RR, relative risk.

Comparison 3: Polyurethane (Moisture Vapour Permeable) Dressing versus Saline Gauze

Sebern et al. (60) compared a transparent moisture vapour permeable (MVP) polyurethane adhesive dressing with gauze moistened with saline in home care patients with grade 2 or 3 pressure ulcers. The RCT compared 37 pressure ulcers treated with MVP and 40 pressure ulcers treated with saline gauze dressing (Table 24).

At the end of the 8-week treatment, no significant difference in complete healing or median percent reduction in surface area was found between the study groups, though complete healing of grade 2 ulcers was significantly higher in the MVP treated group compared with the saline gauze group. Notably, the sample size was small and there is much uncertainty about the point estimate in the meta-analysis because of the wide CI (Figure 15). The median percentage reduction in surface area was also significantly higher in grade 2 ulcers treated with MVP compared with grade 2 ulcers treated with gauze dressing (100% vs. 52%, P < .01). The authors concluded that MVP dressing improved the rate of healing in the treatment and was more cost effective in the treatment of grade 2 pressure ulcers, but there was no significant difference in the healing rate or cost for the grade 3 ulcers.

Table 23: Randomized Controlled Studies Comparing Hydrocolloid Dressing With Povidine-Soaked Gauze*

Study	No. of Ulcers Advanced vs. Traditional	Mean Age, Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Traditional Dressing	Study Duration (weeks)	Results: Advanced Dressing	Results: Traditional Dressing
Barrois et al.,(61)	38/38 ulcers	Not reported	Not reported	Hydrocolloid	Tulle dressing impregnated with Povidone-iodone	8	Healed ulcers: Hydrocolloid 10/38	Tulle with Povidone-iodine 9/38
Kim et al., 1996 (59)	Inpatients at a rehabilitation ward 26/18	50.5 (SD, 18.3) vs. 46.9 (SD, 16.8)	I and/or II	Occlusive hydrocolloid	Povidone soaked gauze, wet to dry	Mean 18.9 vs. 24.3	Complete healing Hydrocolloid 21/26 (80%) Mean treatment duration: 18.9 (SD, 8.2) days Speed of healing 9.1 (SD, 5.4) mm^2/day	Complete healing Povidone soaked gauze 14/18 (77.8%) Mean treatment duration: 24.3(SD, 11.2) days (NS) Speed of healing 7.9 (SD, 4.7) mm^2/day (NS)

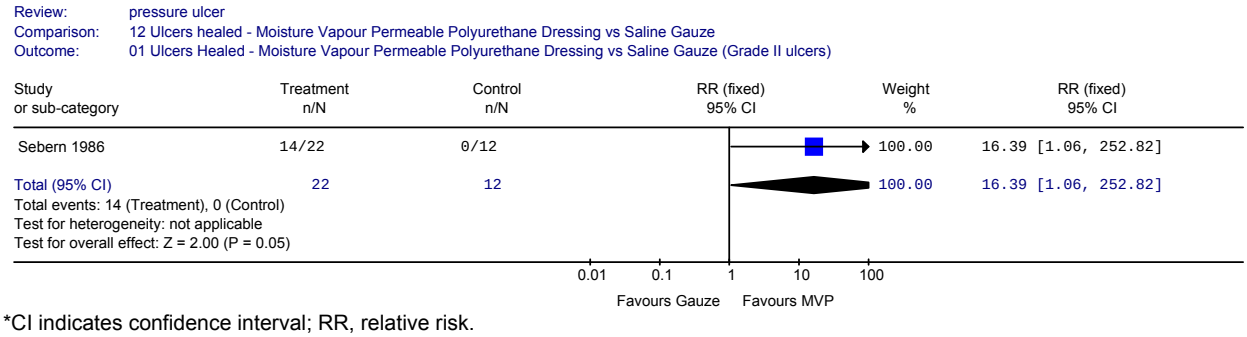
*NS indicates not statistically significant; SD, standard deviation.

Table 24: Randomized Controlled Study Comparing Polyurethane Dressing With Saline Gauze*

Study	No. of Ulcers Advanced vs. Traditional	Mean Age, Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Traditional Dressing	Study Duration (weeks)	Results: Advanced Dressing	Results: Traditional Dressing
Sebern et al., 1986 (60)	37/40 Setting = Home care	76.3 (SD, 17.6) vs. 72.4 (SD, 17.0)	II or III	Polyurethane (transparent moisture vapour permeable adhesive)	Saline gauze	8	Healing status of grade 3 ulcers not significantly different between the 2 groups For stage II ulcers MVP Healed 14/22 (64%) Progress 4/22 (18%) No change 1/22 (5%) Deteriorated or discontinued 3/22 (14%) *χ^2 test (P <.01)	Saline Gauze 0/12 * 4/12 (33%) 1/12 (8%) 7/12 (58%)

*MVP indicates moisture vapour permeable; SD, standard deviation.

Figure 15: Forest Plot Comparing Healing of Grade 2 Pressure Ulcers – Polyurethane Dressing Versus Saline Gauze*



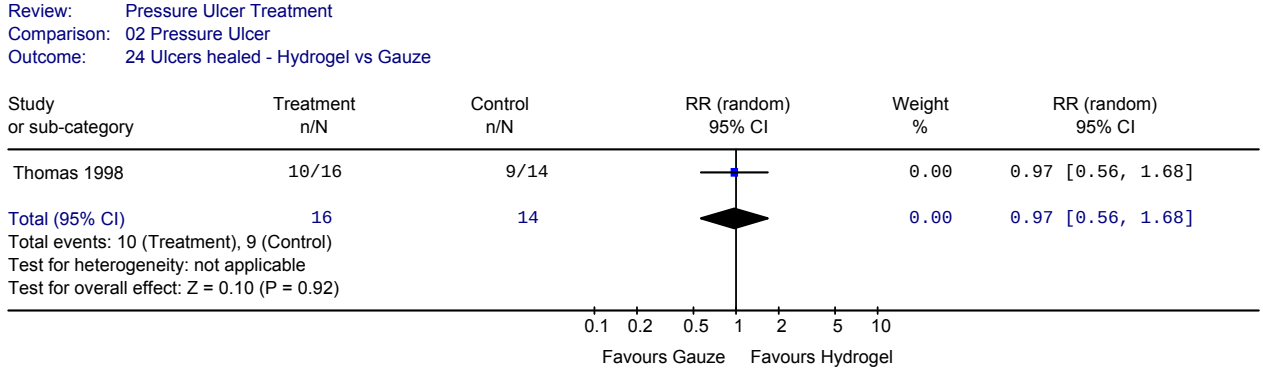
*CI indicates confidence interval; RR, relative risk.

Comparison 4: Hydrogel versus Gauze

Two studies compared hydrogel with gauze dressing. These are summarized in Table 25.

Thomas et al. (62) compared hydrogel derived from the aloe plant with gauze moistened with saline solution in 41 elderly nursing home residents and home care recipients with stage II to stage IV pressure ulcers with surface area equal to or greater than 10 cm^2. After 10 weeks treatment, 11 patients dropped out because of death, ulcer deterioration, hospitalization, or protocol violation. Analysis based on the 30 remaining ulcers showed no statistically significant differences in complete healing of ulcers (RR 0.97, 95% CI [0.56–1.68)] (Figure 16). The average time needed to achieve complete healing was also similar between the 2 treatment groups (5.3 weeks for hydrogel vs. 5.2 weeks for gauze). (62)

Figure 16: Forest Plot of Ulcers Healed – Hydrogel versus Traditional Dressing*



*CI, confidence interval; RR, relative risk.

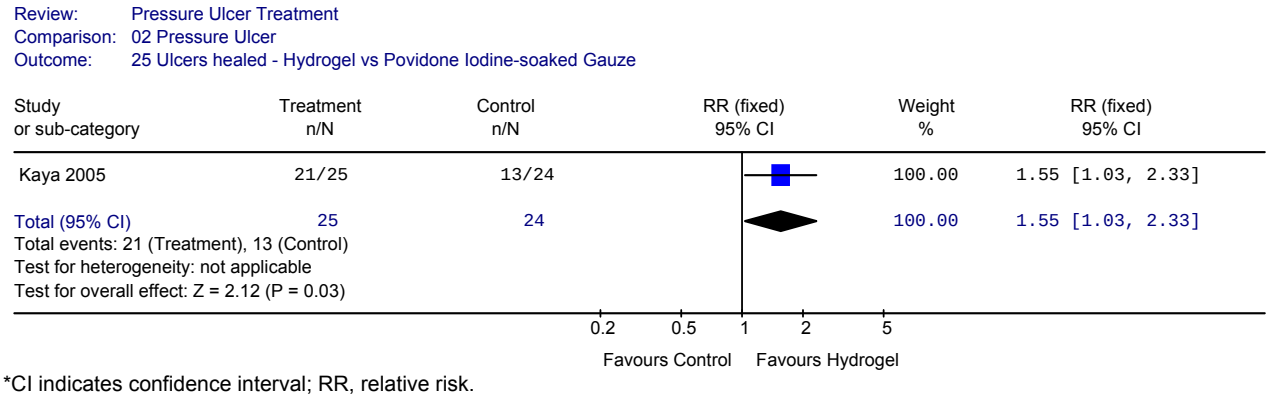
A more recent study by Kaya et al. (63) compared an occlusive hydrogel-type dressing with gauze soaked in povidone-iodine in the treatment of 49 stage I to stage III pressure ulcers in 27 patients with spinal cord injury. Kaya et al. (63) reported that the rate of healing was not significantly different between the two treatment groups (0.12 [SD 0.16] cm^2/day for hydrogel vs. 0.09 [SD 0.05] cm^2/day for povidone-iodine gauze, P = .97); however, the percentage of ulcers that have epithelialized was significantly higher in the hydrogel group (Figure 17). This difference was marginal since the lower limit of the 95% CI was very close to 1.

Table 25: Randomized Controlled Trials Comparing Hydrogel With Saline Gauze*

Study	No. of Ulcers Advanced vs. Traditional	Mean Age Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Traditional Dressing	Study Duration (weeks)	Results: Advanced Dressing	Results: Traditional Dressing
Thomas et al., 1998 (62)	Hydrogel 16 Gauze 14 Nursing home and home care	Hydrogel 79 (SD, 9) Gauze 72 (SD, 13)	II, III, or IV ≥10 cm^2	Amorphous hydrogel from aloe plant (Carrasyn® gel)	Saline dressing	10	Ulcers Healed 10/16 (63%) Time to healing 5.3 (SD, 2.3) weeks Ulcers healed regardless of treatment:	Ulcers healed 9/14 (64%) Time to healing 5.2 (SD, 2.4) weeks Stage II 93%, Stage III 46%, Stage IV 0%
Kaya et al., 2005 (63)	Hydrogel 25 Povidone Gauze 24 Spinal cord injury patients	Hydrogel 35.3 (SD, 14.57) Povidone gauze 29.7 (SD, 6.4)	NPUAP I, II, and III Grade 3 8% vs. 4.2%	Occlusive Hydrogel-type dressing (Elasto-Gel®)	Povidone-soaked gauze	Until healed	Rate of healing 0.12 (SD, 0.16) (cm^2/day) 84% of ulcers epithelialized	Rate of healing 0.09 (SD, 0.05) (cm^2/day) (*P* = .97) 54% of ulcers epithelialized

*NPUAP indicates National Pressure Ulcer Advisory Panel; SD, standard deviation.

Figure 17: Forest Plot of Percent Epithelialization – Hydrogel versus Gauze Soaked in Providone Iodine*



*CI indicates confidence interval; RR, relative risk.

Modern Dressing Compared With Modern Dressing

Studies were available for the following comparisons between advanced dressings (Table 26).

Table 26: Comparisons of an Advanced Dressing With Another Advanced Dressing

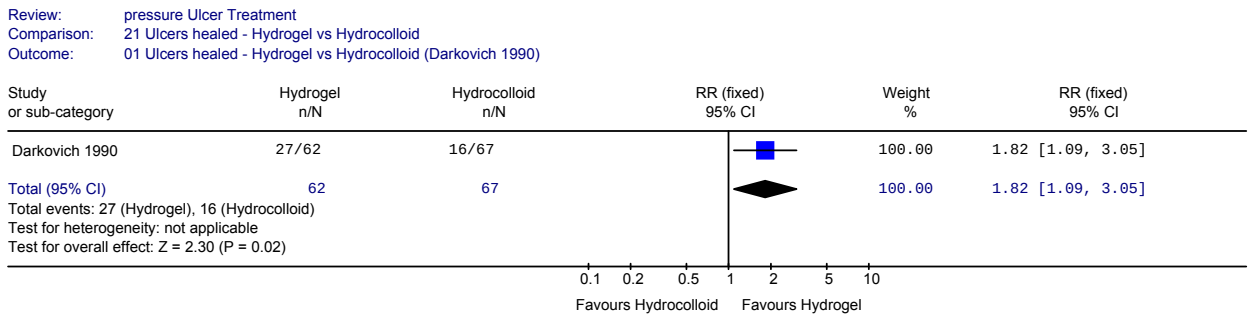
Comparison	Studies	Outcome Measure
Hydrogel vs. hydrocolloid	Darkovich 1990 Mulder 1993 (57) Motta 1999 (64)	Complete healing 60 days Complete healing Decrease in ulcer area
Hydrogel vs. hydrogel	Bale 1998 (a) (65)	Complete healing at 4 weeks
Polyurethane foam vs. hydrocolloid	Bale 1997 (66) Banks 1994a (67) Banks 1994b (68)	Complete healing at 4 weeks Complete healing at 6 weeks Complete healing at 6 weeks
Polyurethane foam vs. hydrocellular	Banks 1997 (43)	Complete healing at 6 weeks
Hydropolymer vs. hydrocolloid	Thomas 1997 (44) Honde 1994 (69)	Complete healing at 6 weeks
Hydrocellular vs. hydrocolloid	Seeley 1999 (70) Bale 1998 (71)	Complete healing at 8 weeks
Sequential calcium alginate plus hydrocolloid vs. hydrocolloid	Belmin 2002 (72)	Surface area reduction at 4 weeks
Silver releasing dressing vs. alginate dressing or other advanced dressings	Meaume 2005 (49) Munter 2006 (50)	Decrease in ulcer area Decrease in ulcer area
Honey dressing vs. ethoxy dianoxide	Gunes 2007 (51)	Complete healing at 5 weeks
Noncontact normothermic dressing vs. another advanced dressing or hydrocolloid	Kloth 2000, 2002 (73) Whitney 2001 (74)	Complete healing at 12 weeks Complete healing at 8 weeks
Radiant heat dressing vs. another advanced dressing	Price 2000 (75) Thomas 2005 (52)	Complete healing at 6 weeks Complete healing at 12 weeks

Comparison 1: Hydrogel Dressing versus Hydrocolloid Dressing

Hydrocolloid and hydrogel are two commonly used modern dressings. Three randomized studies compared hydrogel with hydrocolloid in the treatment of stage II to III pressure ulcers (see Table 27)

Darkovich et al. (76) compared BioFilm® hydrogel dressing (BF Goodrich Company; now known as Flexigel®, Smith and Nephew, Largo, Florida) with the DuoDERM® hydrocolloid dressing (Bristol-Myers Squibb, Princeton, New Jersey) in the healing of grade 1 (ulceration or skin breakdown limited to superficial epidermis and dermal layer) and 2 ulcers (ulceration extending through the dermis but not through adipose tissue) based on the Enis and Sarmienti classification system (equivalent to stage II and III in the NPUAP system). The BioFilm dressing consists of a polyurethane top film and foam bonded to a fabric containing the hydrogel with an adhesive on the underside. DuoDERM hydrocolloid dressing is composed primarily of pectin, gelatin, and carboxymethyl cellulose. After 60 days treatment, a significantly higher proportion of pressure ulcers healed in the hydrogel group compared with the hydrocolloid group (RR 1.82 [95% CI, 1.09–3.05], P = .02) (Figure 18).

Figure 18: Forest Plot of Ulcers Healed – Hydrogel versus Hydrocolloid*



*CI indicates confidence interval; RR, relative risk.

Ninety percent of the ulcers in the hydrogel group healed or improved compared with 78% in the hydrocolloid group. Mean percent of wound area healed was 68% in the hydrogel group and 40% in the hydrocolloid group. The difference in the percent of area healed between the 2 groups was not significant for stage I ulcers, but the mean percent of area healed was significantly higher for stage II wounds treated with hydrogel (64% vs. 34%, P < .025). (76)

Two randomized studies compared sheet hydrogel dressing with hydrocolloid dressing in the healing of stage II and III pressure ulcers. Motta et al. (64) compared the AcryDerm polymeric sheet wound dressing (AcryNed, Portland, Oregon) with the DuoDerm CGF hydrocolloid dressing in 10 patients. Standardized wound care included light debridement, cleansing, and sterile saline irrigation as required before the application of the dressing. After 8 weeks of treatment, complete healing occurred in 2 out of 5 patients in each group. The overall healing rates of ulcers from the study groups were not significantly different and no significant differences were noted between the dressing performances, with the exception that the use of the polymeric hydrogel dressing was more often associated with desirable levels of autolytic debridement than the hydrocolloid dressing.

Table 27: Hydrogel Dressing Versus Hydrocolloid Dressing*

Study	No. of Ulcers	Mean Age Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Advanced Dressing	Study Duration	Outcome Measures	Results		
Darkovich et al., 1990 (76)	Patients 41/49 Wounds 62/67 Acute care and extended care	Overall 75 (range 30-98) Acute care 69 Extended care 83	I or II† Equival-ent to stage II and III in the NPUAP scale	Hydrogel (BioFilm, multilayer) (56% stage II ulcers)	Hydrocolloid (DuoDerm) (54% stage II ulcers)	60 days Mean treat-ment days 12.0 vs. 11.3 days.	% wound area healed; % area healed per day	Overall: Healing Complete (all ulcers) Stage II Improved Same Worse Mean % area closed Stage I ulcers Stage II ulcers Stage II >2 cm^2 and <20 cm^2 Stage II and Acute care 	Hydrogel 27/62 (43%) (34%) 47% 7.5% 1.5% 72% 64% 72% 8.1%/d 80% 10.6%/d	Hydrocolloid 16/67 (24%) (16%) 54% 12% 10% 44% (NS) 34%‡ 38%§ 3.1%/d§ 15%‖ 1.3%/d‖
Motta et al., 1999 (64)	5/5 Home care	34-76 (range) mean age 60	II or III	Hydrogel polymer sheet (AcryDerm, now called Flexigel)	Hydrocolloid (DuoDerm)	8 weeks	Complete healing; perform-ance	Healed Absorption Moist Environment Autolytic Debridement Clinical Performance (1 = most favourable, 5 = least favourable) NS except autolytic debridement	Hydrogel 2/5 1.62 1.28 1.17 1.42	Hydrocolloid 2/5 1.56 1.24 2.01 1.60

Table 27: Hydrogel Dressing Versus Hydrocolloid Dressing* (continued)

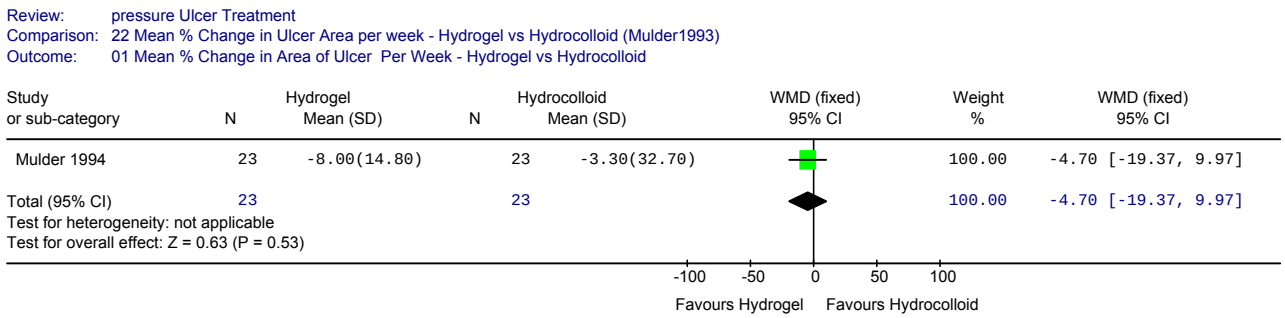
Study	No. of Ulcers	Mean Age Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Advanced Dressing	Duration of Study (weeks)	Outcome Measures	Results
Mulder et al., 1993 (57)	3-arm 23/23/21 Acute care, In and outpatients	56.7/63.1/57.2 (*P* = .49)	II or III	Hydrogel sheet (Clearsite®)	Hydrocolloid (Duoderm)	8	Median percent change in wound area from baseline per week	Mean % change per week in surface area from baseline Hydrogel 8.0% (SD, 14.8) Hydrocolloid 3.3 (SD, 32.7) Standard 5.1 (SD, 14.8) Not significantly different Median % reduction in surface area per week Hydrogel 5.6% Hydrocolloid 7.4% Standard 7.0% Compared to each other (*P* = .89)

*d indicates day; NPUAP, National Pressure Ulcer Advisory Panel; NS, no significant difference; SD, standard deviation.
†Defined by Enis and Sarmienti
‡*P* < .025
§*P* < .01
‖*P* < .001
In the Motta et al:study, clinical performance included ease of use, slippage, conformability, patient comfort, and dressing debris remaining in the wound area after dressing removal.

Mulder et al. (57) also compared a Clearsite hydrogel sheet dressing (New Dimensions in Medicine, Dayton, Ohio) with a DuoDERM hydrocolloid dressing (ConvaTec/Bristol Myers-Squibb, Princeton, New Jersey) and wet-to-moist gauze dressing in a multisite randomized study. Clearsite is composed mainly of water, plasticizer/humectant, and propylene glycol, and has an adhesive border. After 8 weeks treatment, the median and mean percentage change per week in wound surface area of stage II and III ulcers was not significantly different between the hydrogel and the hydrocolloid groups [weighted mean difference:– 4.70 (95% CI, 19.37–9.97), P = .53] (Figure 19). No data on complete healing of pressure ulcers were reported and there were no significant differences in qualitative outcomes. The transparency of the hydrogel sheet dressing allowed visualization of the wound through the dressing.

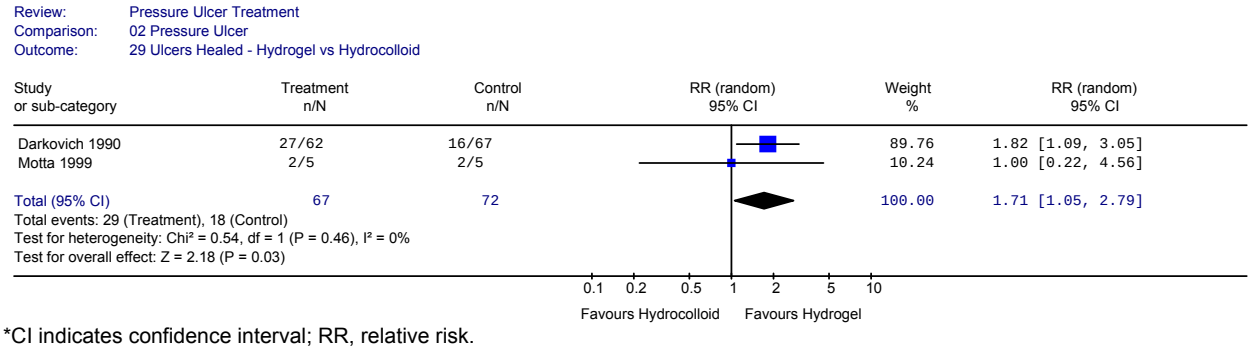
A Forest plot of ulcers healed showed a statistical significant difference in ulcers treated with hydrogel compared with hydrocolloid [RR 1.71, (95% CI, 1.05–2.79), P = .03] (Figure 20).

Figure 19: Percent Change per Week in Surface Area of Ulcer – Hydrogel Versus Hydrocolloid*



*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

Figure 20: Forest Plot of Ulcers Healed – Hydrogel Dressing Versus Hydrocolloid Dressing*



*CI indicates confidence interval; RR, relative risk.

Comparison 2: Polyurethane Foam Dressing Versus Hydrocolloid Dressing

Three randomized studies compared polyurethane foam dressing with hydrocolloid dressing in the healing of stage II and III pressure ulcers (summarized in Table 28). The studies were small with the number of ulcers ranging from 29 to 60. Two were performed in hospitals and one in a community setting. Methodological limitations included no concealment of allocation, no a priori power calculation, lack of blinded outcome assessment, and lack of intention-to-treat analysis despite high withdrawal rates.

Table 28: Polyurethane Dressing Versus Hydrocolloid Dressing

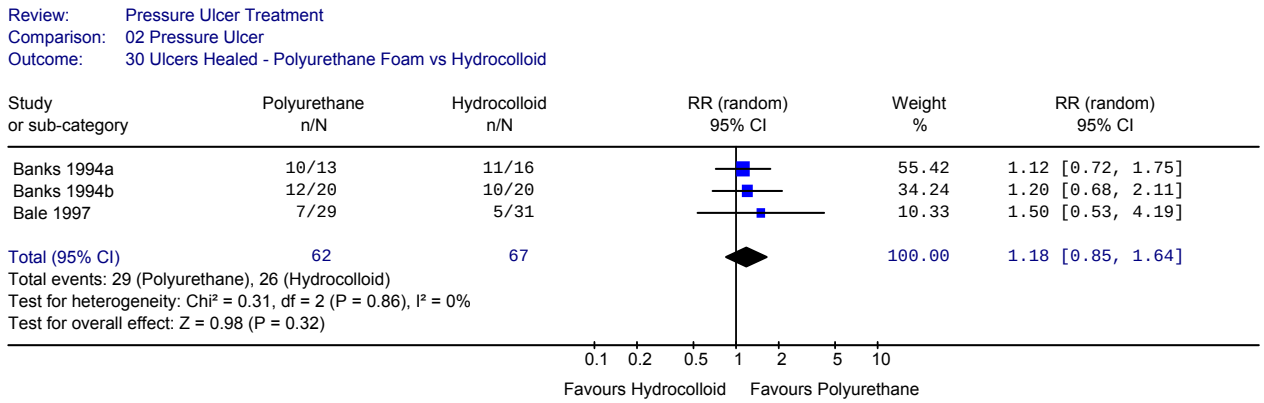
Study	No. of Ulcers	Comparison	Ulcer Stage	Mean Age Treatment vs. Control (years)	Treatment Duration (weeks)	Results: Polyurethane Foam vs. Hydrocolloid
Bale 1997 (66) (Hospitals)	29/31*	Allevyn adhesive polyurethane foam vs. Granuflex hydrocolloid	II or III**	Median 73 vs. 74	4.3	Complete healing 7/29 vs. 5/31 Ease of application similar Conforming to wound: Polyurethane foam better (*P* = .018) Absorbency: polyurethane better; soled clothing 4% vs. 25% (*P* = .002) Wear time 3.8 days vs. 3.2 days Damage to surrounding skin 2% vs. 7%
Banks 1994a (67) (Hospital)	13/16	Spyrosorb polyurethane vs. Granuflex hydrocolloid	II or III	Median 73 vs. 74	6	Complete healing by 6 weeks 10/13 vs. 11/16 Median time to healing (days) 13.36 vs. 12.69 (*P* value not reported)
Banks 1994b (68) (Community)	20/20	Spyrosorb polyurethane vs. Granuflex hydrocolloid	II or III	Median 71(range 40–100) vs. 73 (range 46–93)	6	Complete healing by 6 weeks 12/20 vs. 10/20 Healed or greatly improved 18/20 vs. 10/20

Bale et al. (66) (1997) compared the performance of the Allevyn® Adhesive polyurethane foam dressing to the Granuflex® hydrocolloid dressing (ConvaTec, Bristol-Myers Squibb, UK). The Granuflex dressing consisted of a semi-permeable polyurethane film bonded to a wound contact surface coated with a hydrocolloid matrix. The patient groups were balanced for age, sex, and stage and site of pressure ulcers. After 4.3 weeks of treatment, the proportion of wounds that healed between the groups was not significantly different [RR 1.50, (95% CI, 0.53–4.19)]. Both had similar ease of application and wear time, but the polyurethane foam dressing was found to conform better to the wound and have better absorbency and hence less soiled clothing (4% vs. 25%, *P* = .002).

Banks et al. (68) conducted two open, single-centre, randomized studies to compared the Spyrosorb® dressing (C.Y. Laboratories Ltd) with the Granuflex hydrocolloid dressing in stage II and III pressure ulcers in hospital (29 ulcers) and community settings (40 ulcers). The Spyrosorb dressing is a vapour-permeable dressing with a microporous polyurethane membrane for absorption and a pressure-sensitive wound contact surface. Both studies lasted for 6 weeks, after which no significant difference in complete healing was observed between the dressings in either the hospital or community setting.

A pooled analysis of the 3 studies yielded a RR of 1.18 in favour of polyurethane dressing, but the difference was not statistically significant [95% CI (0.85– 1.64), P = .32]. The test for heterogeneity was not significant (I^2 = 0%, P = .86) (Figure 21).

Figure 21: Forest Plot of Complete Healing – Polyurethane Dressing Versus Hydrocolloid Dressing*



*CI indicates confidence interval; RR, relative risk.

Comparison 3: Hydropolymer Dressing Versus Hydrocolloid Dressing

Two studies compared hydropolymer dressing to hydrocolloid dressing (summarized in Table 29). Thomas et al. (44) conducted an open, 2-centre randomized trial to compare the Tielle hydropolymer dressing to the Granuflex hydrocolloid dressing in the healing of stage II and III pressure ulcers and venous leg ulcers. Only the outcomes of pressure ulcers are discussed in this review. The Tielle dressing consisted of three layers: a polyurethane adhesive backing, an absorbent island of a hydrophilic polyurethane foam, and a nonwoven fabric layer in between. No significant differences were found between dressing groups in the number of pressure ulcers that completely healed during the course of the study. Mean wear times were also not significantly different. The hydropolymer dressing was significantly more absorbent as indicated by less leakage (P = .007) and also had less difficult removal compared with the hydrocolloid dressing.

Honde et al. (69) compared an amino acid copolymer membrane dressing (Inerpan ™, Synthelabo) to the Comfeel™ hydrocolloid dressing (Coloplast) in the healing of grade 2 to 4 ulcers with a diameter less than 10 cm in 168 elderly hospital patients. There were no significant differences between the dressings in mean wear time (4.0 vs. 3.8 days) or mean number of dressings used (15 vs. 14). A higher proportion of patients treated with hydropolymer dressing achieved complete healing (RR 1.47), but this difference did not reach statistical significance (95% CI, 0.94–2.29). Ulcers treated with hydropolymer dressing achieved complete healing faster than those treated with hydrocolloid dressings (mean of 32 days vs. 38 days, P = .044).

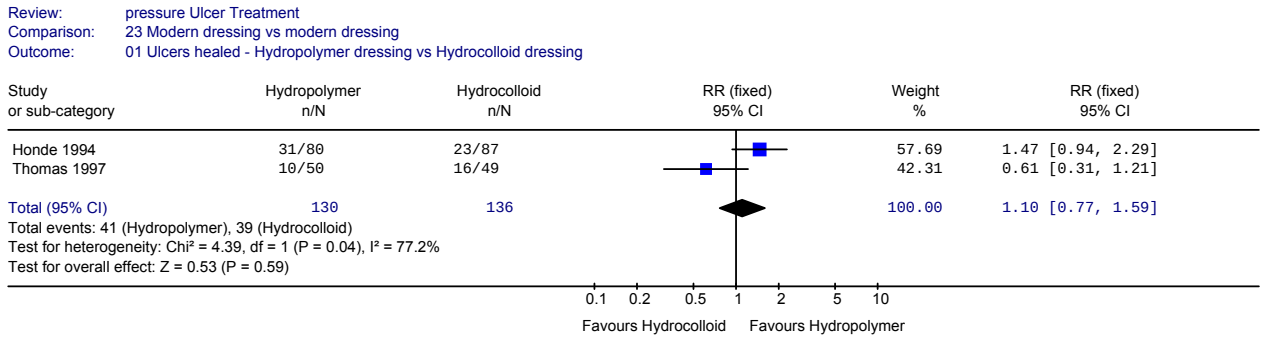
Pooled analysis of the proportion of ulcers healed showed no statistical significant differences between polymer dressings and hydrocolloid dressings [RR 1.10, (95% CI, 0.77– 1.59), P = .59]. The test of heterogeneity showed significant heterogeneity (I^2 = 77.2, P = .04) (Figure 22).

Table 29: Hydropolymer Dressing Versus Hydrocolloid Dressing*

Study	No, of Pressure Ulcers	Comparison of Dressings	Ulcer Stage	Mean Age (SD) Treatment vs. Control (years)	Maximum Treatment Duration	Results: Polyurethane Foam vs. Hydrocolloid
Thomas, 1997 (44) Community	Pressure ulcer 50/49†	Tielle® hydropolymer vs. Granuflex hydrocolloid	II or III	80.1 (10.2) vs. 78.6 (14.3)	6	Complete healing: 10/50 vs. 16/49Improved not healed 29/50 vs. 23/49 -Mean wear time: 2.4 days vs. 2.7 days Leakage 4/50 vs. 15/49 (*P* = .007) Difficult to remove 11/537 vs. 85/509
Honde, 1994 (69) Hospital	80/88	Inerpan® amino acid copolymer vs. Comfeel™ hydrocolloid	II, III, or IV <10 cm in diameter	80.4 (8.2) vs. 83.5 (7.8) (*P* < .05)	8	Complete healing: 31/80 vs. 23/87 Mean time to achieve complete healing (days): 32 vs. 38 (*P* = .044) Mean number of dressings used: 15 vs. 14 Mean wear time (days) = 4.0 vs. 3.8 1 patient excluded from control group

*SD indicates standard deviation.
†Previously presented by at 1996 Symposium on Advanced Wound Care and Medical Research Forum on Wound Care, Banks, 1996. (77)
Study also included leg ulcers 50/50 (only results on pressure ulcers were included in table).

Figure 22: Forest Plot of Ulcers Healed – Hydropolymer Dressing Versus Hydrocolloid Dressing*



*CI indicates confidence interval; RR, relative risk.

Comparison 4: Hydrocellular Dressing Versus Hydrocolloid Dressing

Two randomized studies compared a hydrocellular dressing with a hydrocolloid dressing (summarized in Table 30). Bale et al. (71) compared the Allevyn hydrocellular dressing (Smith and Nephew Medical, Hull, England) with the Granuflex hydrocolloid dressing in an open-label, single-centre, randomized study. The study included stage II or III ulcers with moderate to high exudates and leg ulcers of any etiology. Only outcomes pertaining to pressure ulcers (32 out of a total of 100 ulcers) are reported in this review. Complete healing after 8 weeks was not statistically different, neither was mean wear time. The percent of dressing changes due to leakage was significantly higher with the hydrocolloid dressing and more wounds treated with hydrocolloid dressing also required cleansing at dressing change.

In another open, randomized study by Seeley et al. (70), 20 stage II or III pressure ulcers were treated with the Allevyn hydrocellular dressing and 20 were treated with the DuoDERM CGF Boarder hydrocolloid dressing (ConvaTec, Princeton, New Jersey). The ulcers in both groups were predominantly stage III ulcers (85% vs. 89%). At the end of the 8-week treatment period, there were no statistically significant differences in complete healing or in the mean reduction of ulcer area; however, the hydrocellular dressings were associated with less leakage of exudates and less difficult removals. The proportion of ulcers healed was similar for the two groups.

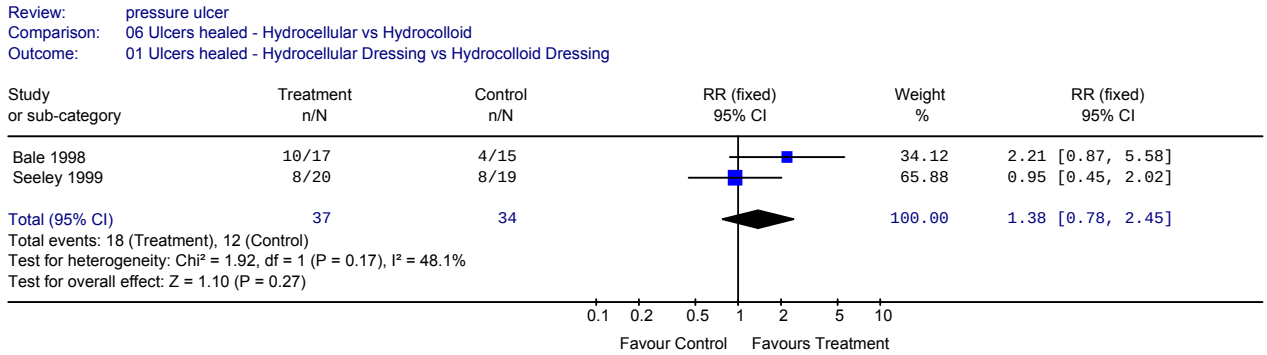
A meta-analysis of the two studies showed no significant differences in complete healing between the dressing groups after 8 weeks treatment (Figure 23).

Table 30: Randomized Studies – Hydrocellular Dressing Versus Hydrocolloid Dressing*

Study	Sample Size	Comparison	Ulcer Stage	Mean Age Treatment vs. Control (years)	Treatment Duration (weeks)	Results: Polyurethane Foam vs. Hydrocolloid
Bale., 1998 (71)	17/15	Allevyn hydrocellular dressing vs. Granuflex hydrocolloid dressing	II or III with moderate to high exudate†	76 vs. 76	8	Completely healed 10/17 vs. 4/15 Mean wear time 3.5 vs. 4.1 (.15) days Dressing change due to leakage 56% vs. 63% (*P* = .037) Wound cleansing required 48% vs. 75% (*P* < .001)
Seeley et al., 1999 (70) LTCs and Wound Centre out-patients	20/19	Allevyn hydrocellular dressing vs. DuoDERM CGF border hydrocolloid dressing	II or III	75.7 (SD, 18.6) vs. 76.7 (SD, 19.5)	8	Complete healing 8/20 vs. 8/19 Mean reduction in ulcer area 50% vs. 52% (*P* = .31) Improved pressure ulcers 12/20 vs. 11/19 (*P* = 1.0) Difficult application 1/20 vs. 4/19 (*P* = .18) Difficult dressing removal 5% vs. 62% (*P* < .001) Leakage 4 vs. 23 (*P* = .04)

*LTC indicates long-term care, SD, standard deviation.
†also included leg ulcers of any etiology.

Figure 23: Ulcers Healed – Hydrocellular Dressing Versus Hydrocolloid Dressing*



*CI indicates confidence interval; RR, relative risk.

Comparison 5: Sequential Calcium Alginate Dressing and Hydrocolloid Dressing Versus Hydrocolloid Alone

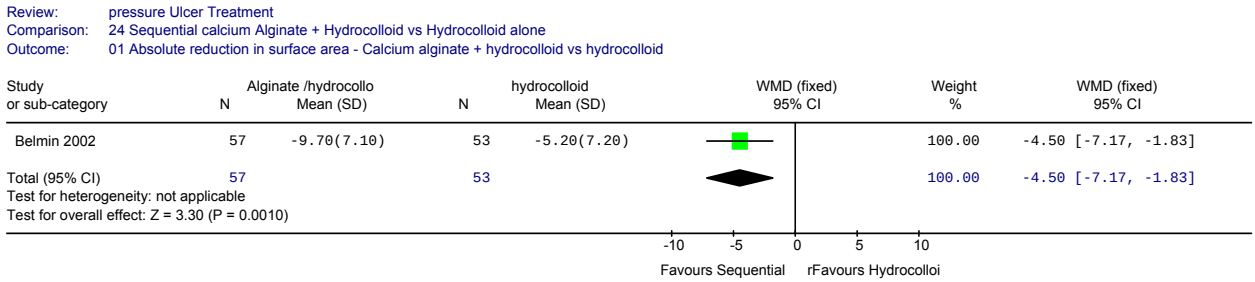
In a randomized study by Belmin et al. (72), 57 stage III or IV pressure ulcers were treated with UrgoSorb® calcium alginate (Urgo, France) for 4 weeks followed by the AlgoPlaque® HealthPoint hydrocolloid dressing (Urgo, France) for 4 weeks while 53 controlled ulcers were treated with the DuoDERM hydrocolloid dressing alone for 8 weeks (Table 31).

Table 31: Sequential Calcium Alginate Dressing and Hydrocolloid Dressing Versus Hydrocolloid Dressing Only

Study	Sample Size	Mean Age Treatment vs. Control (years)	Ulcer Stage	Advanced Dressing	Advanced Dressing	Study Duration (weeks)	Results: Sequential Alginate + Hydrocolloid vs. Hydrocolloid
Belmin et al., 2002 (72) 20 geriatric hospital wards in France	57/53	85 vs.82	III or IV	Calcium alginate for 4 weeks followed by hydrocolloid for 4 weeks	Hydrocolloid dressing for 8 weeks	8	Absolute surface area reduction (cm^2) at 4 weeks 7.0 (5.7) vs. 1.6 (4.9) at 8 weeks 9.7 (7.1) vs. 5.2 (7.2) (P < .001)

After the 8-week treatment, ulcers treated with the sequential strategy showed a significantly greater mean absolute and relative reduction in the surface area compared with ulcers treated with hydrocolloid alone (Figure 24). The sequential use of calcium alginate and hydrocolloid was also associated with fewer dressings used per week, less pain during removal, and less odour. (72)

Figure 24: Absolute Reduction in Ulcer Area (cm^2) – Sequential Calcium Alginate and Hydrocolloid Versus Hydrocolloid*



*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

Comparison 6: Antimicrobial Dressings versus Another Modern Dressing

Silver-Releasing Dressings

Two RCTs explored the effect of silver-releasing dressings on chronic wounds at high risk of infection, including pressure ulcers (Table 32). Pressure ulcers constituted 29% and 7%, respectively, of the study populations (49;50).

Meaume et al. (49) reported that pressure ulcers treated with a silver-releasing alginate dressing appear to have a greater wound reduction after 4 weeks (31.6% vs. 13.9%) and greater reduction in wound severity score (30.7% vs. 17.5%) compared with ulcers treated with an alginate dressing. No statistical analysis can be performed, however, because of the small sample sizes (statistical significance is, therefore, also unknown). Munter et al. (50) found that at the end of 4 weeks of treatment, the silver-releasing foam dressing had greater reduction in ulcer area (58.5% vs. 33.3%), less maceration, better exudate handling, and faster reduction of malodour compared with dressings in standard practice. However, the sample was too small to perform statistical analysis. The mean wear time was significantly longer for silver-releasing foam dressing (3.1 days vs. 2.1 days, $P < .0001$).

Table 32: Randomized Controlled Studies Comparing Silver-Releasing Advanced Dressing Compared With Another Modern Dressing in Standard Practice*

Study	Sample Size (NCNT/ standard care)	Mean Age Treatment vs. Control (years)	Mean Baseline Ulcer Size, Treatment vs. Control (cm^2)	Standard Care	Duration of Study (weeks)	Outcome Measures	Results: Silver-Releasing Dressing (SD)	Results: Traditional Dressing (SD)
Meaume et al., 2005 (49)	28 Stage III and IV	74.9 (9) 77.5 (10.9)	22.5 22.4	Alginate dressing	2	Percent <down> area of ulcer	31.6	13.9†
Munter et al., 2006 (50)	46 (out of 619) Multi-centre	69.8 (13.7) 68.8 (14.1)	52.9 (90.0) 36.6 (64.4)	Different dressings including other silver dressing	4	Percent <down> area of ulcer	58.5	33.3†

* NCNT indicates noncontact normothermic therapy; SD, standard deviation.
†P value not reported.

Topical Honey Dressing

There is growing interest in using honey as a wound dressing material. Clinical studies in other types of wounds (e.g. leg ulcers) suggest that honey may facilitate wound healing by providing a moist healing environment, preventing excessive bacterial growth, and by reducing inflammation, pain, and swelling. (51)

Gunes et al. (51) studied the effect of dressings with unprocessed honey on the healing of Stage II and III pressure ulcers. Twenty-five ulcers in 15 patients treated with honey dressing were compared with 25 ulcers (11 patients) treated with nitrofurazone cream and gauze soaked with ethoxydiaminoacridine solution. At the end of 5 weeks, the honey-treated ulcers had significantly lower ulcer severity scores (6.55 vs. 12.62, $P < .001$), four times the rate of pressure healing (56% decrease in ulcer size vs. 13%, $P < .001$), and a higher percentage of completely healed ulcers (20% vs. 0%, $P < .05$). Yapacu et al. suggested that additional studies are required to compare honey dressing with alginate, hydrocolloid, and hydrogel dressings, and in patients with stage IV ulcers.

Comparison 7: Noncontact Normothermic Dressing/Radiant Heat Dressing Versus Modern Dressings

Applying heat to local wounds has been shown to increase capillary flow by 3-fold, increase tissue oxygen tension, and reduce the growth of bacteria. (73) It has been suggested that preventing hypothermia and maintaining a normothermic state in a pressure ulcer might improve wound healing (52). Noncontact normothermic wound therapy using a noncontact sterile dressing and a warming unit that gives constant radiant heat at 38^{o}C to restore periwound and wound temperatures toward normothermia. Therapy consisted of three 1-hour treatments daily.

Four RCTs compared thermal wound therapy with moisture retentive modern dressings in the treatment of stage III and IV pressure ulcers. (73);(74);(75)) Two of the studies used noncontact normothermic dressing as the heat source (73;75), while the other two studies (52;74) used radiant heat dressings. Sample size ranged from 29 to 41 patients. Two of the studies included a variety of moisture retentive dressings in the control group (73-75), whereas Thomas et al. (52) limited the comparison to hydrocolloid dressing with the addition of alginate filler as needed. The duration of the studies ranged from 8 to 12 weeks. (Table 33) None of the studies reported blinding of the assessor and only 1 of the studies reported intention-to-treat analysis.

Meta-analysis showed that there is no statistically significant difference in the proportion of ulcers healed between groups at the end of the study period, [RR 1.29 (95% CI, 0.84–1.97, $P = .24$)] (Figure 25). Although there is no significant difference in the number of wounds healed, Price et al.(75) and Kloth et al., (73) reported greater reduction is surface area (by 140% and 40% respectively) in the thermal dressing group compared with the control group. Whitney et al. (74) reported that the liner rate of healing was 0.012 (SD 0.008) cm per day for normothermic patients compared with 0.004 (SD 0.006) cm per day for control patients ($P = .01$), but the 95% CI of the two rates overlapped.

Table 34 shows reported adverse events of noncontact normothermic therapy.

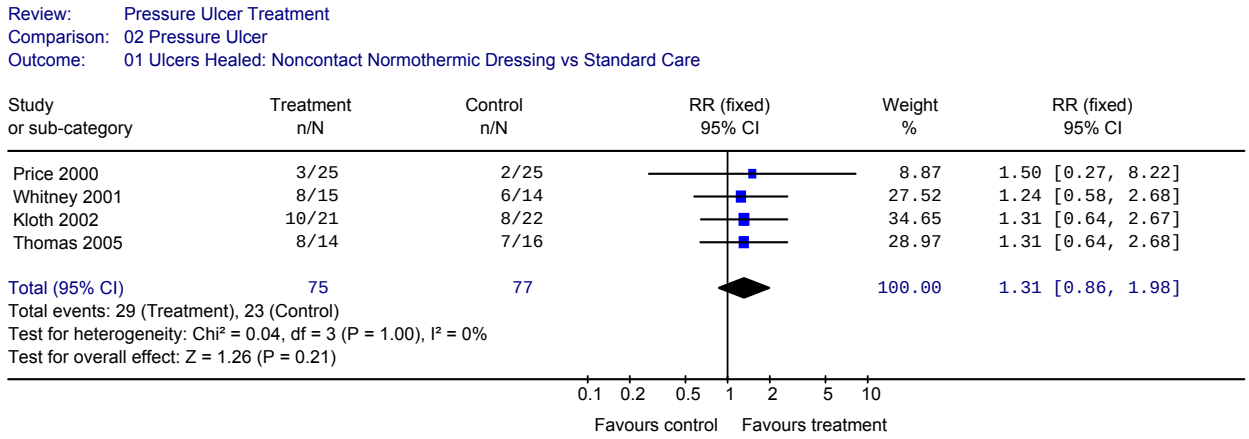
In summary, thermal dressings such as noncontact normothermic dressings or radiant heat dressings were associated with greater improvement in stage III and IV pressure ulcers; however, this did not translate into more wound closure. There is no evidence at present to conclude that thermal dressings will result in more complete healing in stage III or IV pressure ulcers.

Table 33: Studies on the Use of Thermal Dressings to Treat Stages III and IV Pressure Ulcers*

Study	Sample Size (NCNT/ standard care)	Mean Age Treatment vs. Control (years)	Mean Baseline Ulcer Size, Treatment vs. Control (cm^2)	Comparison	Study Duration (weeks)	Outcome Measures	Results: Treatment Group (SD)	Results: Standard Care (SD)
Price et al., 2000 (75)	25/25	75.7 (SD, 16.8) 69.76 (SD, 16.2)	7.3 (SD, 7.0) 9.8 (SD, 12.0) Stage III or IV	Noncontact normothermic vs. standard usually alginate	6	Healed at 6 weeks	12% (3/25)	8% (2/25)
						Mean ulcer area decrease (cm^2)	4.03 (SD, 4.3)	3.89 (SD, 8.1)
						Percent ulcer area decrease	54.62 (SD, 39.9)	22.84 (SD, 75)
						Time to achieve 75% decrease in ulcer area (days) (ITT)	32.8	37.7
Kloth et al., 2002 (73)	21/22 VA nursing home	78.1 (SD, 3.0) 77.9 (SD, 4.0)	5.4 (SD, 1.7) 4.1 (SD, 0.8) Stage III or IV	Noncontact normothermic vs. moisture retentive dressing	12	Healed at 12 weeks	All 48% (10/21) Stage III 50%† Stage IV 25%†	All 36% (8/22) Stage III 38%† Stage IV 0%†
						Percent decrease ulcer area	69	50‡
						Mean rate of decrease in ulcer area (cm^2/week)	0.52	0.23§
Whitney et al., 2001 (74)	15/14 Home care, LTC or acute care	63 (SD, 21) 53 (SD, 19)	10 (SD, 10) 7 (SD, 9) Stage III or IV	Radiant heat dressing vs. moisture retentive dressing	8	Healed at 8 weeks	All 53% (8/15) Stage III 71% Stage IV 38%	All 43% (6/14) Stage III 54% Stage IV 0%
						Linear rate of healing (cm/day)	0.012 (SD, 0.008)	0.004 (SD, 0.006)
Thomas et al., 2005 (52)	21/20 Out-patients, nursing home and rehab patients	75.5 (SD, 12.6)	11.0 (SD, 9.5) vs. 12.1 (SD, 18.2) (P = .81) Stage III or IV	Radiant heat dressing vs. pydrocolloid +/– alginate filler	12	Healed at 12 weeks	All 54% (8/14) Stage III 80% (8/10) Stage IV 0% (0/4)	All 44%(7/16) Stage III 78% (7/9) Stage IV 0% (0/7)

*ITT indicates intention-to-treat; LTC, long-term care; NCNT, noncontact normothermic therapy; SD, standard deviation; VA, Veterans Administration.
†Based on Marario Wounds 2002; 14(3):9.–106
‡ Treatment vs. standard care (P = .11).
§ Treatment vs. standard care (P = .02).

Figure 25: Ulcers Healed: Noncontact Normothermic Dressing Compared With Moisture Retentive Dressing*



*CI indicates confidence interval; RR, relative risk.

Table 34: Reported Adverse Events of Thermal Dressings*

Study	Treatment	Hospitalization	Complications	Deterioration in Condition	Deaths
Kloth 2002 (73)	NCNT Standard care	NR	NR	NR	
Thomas 2005 (52)	NCNT Standard care	2 3	NR	NR	2 1
Whitney 2001 (74)	NCNT Standard care	NR	Periwound maceration (1) Infection (unrelated to treatment (1) 0	NR	
Price 2000 (75)	NCNT Standard care	NR	NR	4 (1 device-related) 1	3

*NCNT indicates noncontact normothermic therapy, NR-adverse events for category not reported

Summary of Analysis – Dressings

Findings of the analysis are summarized in Tables 35 through 38.

Table 35: Summary of Findings on Complete Healing – Modern Dressings Versus Traditional Dressings*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stages	Relative Risk (95% CI)	I^2 (%)	*P* Value	Quality of Evidence
Hydrocolloid vs. saline gauze (6 – 12 weeks)	4	246	Mostly II – III	2.91 (1.52, 5.57)	23.1	.001	Moderate
Hydrocolloid vs. saline gauze (6 months)	1	39	II – III	1.04 (0.82, 1.32)	NA	.77	NE
Hydrocolloid vs. gauze soaked in antimicrobial	3	248	II – IV	1.21 (0.96, 1.51)	8.2	.10	NE
Moisture vapour permeable vs. saline gauze	1	34	II – III	16.39 (1.06, 252.02)	NA	.05	NE
Hydrogel sheet dressing vs. saline gauze	1	30	II – IV	0.97 (0.56, 1.68)	NA	.92	NE
Hydrogel vs. Povidone soaked gauze	1	49	I – III	1.55 (1.03. 2.33)	NA	.03	Low

*CI indicates confidence interval; I^2, test for heterogeneity; NA, not applicable; NE= not evaluated

Table 36: Summary of Findings on Complete Healing – Modern Dressings Versus Modern Dressings*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stages	Relative Risk (95% CI)	I^2 (%)	*P* Value	Quality of Evidence
Hydrogel vs. hydrocolloid	2	139	II–III	1.71 (1.05, 2.79)	0	.03	Low
Hydropolymer vs. hydrocolloid	2	267	II–III	1.53 (1.05, 2.22)	0	.03	Low
Polyurethane foam vs. hydrocolloid	3	129	II–III	1.18 (0.85, 1.64)	0	.32	NE
Hydrocellular vs. hydrocolloid	2	71	II–III	1.38 (0.78, 2.45)	48.1	.27	NE
Noncontact normothermic/radiant heat dressing vs. other modern	4	152	III–IV	1.31 (0.86, 1.98)	0	.21	NE

*CI indicates confidence interval; I^2, test for heterogeneity; NE= not evaluated

Table 37: Summary of Reduction in Ulcer Size – Modern Dressings Versus Modern Dressings*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stages	Mean Weighted Difference	*P* Value	Quality of Evidence
Sequential calcium alginate plus hydrocolloid vs. hydrocolloid	1	110	III–IV	Mean change in ulcer area (cm^2) – 4.5 (–1.73, –7.17)	.001	Moderate
Silver releasing dressing vs. alginate dressing	1	28	III–IV	Decrease in wound area 31.6% vs. 13.9%	Not reported	NE
Silver releasing polyurethane foam vs. other modern dressing	1	46	III–IV	Decrease in wound area 58.5% vs. 33.3%	Not reported	NE

* NE= not evaluated

Table 38: Summary on Absorbency and Ease of Removal – Modern Dressings Versus Modern Dressings*

Comparison	No. of Studies	No. of Ulcers	Absorbency	Removal	Other
Polyurethane foam vs. hydrocolloid	1	60	Soiling of clothes 4% vs. 25% *P* = .002	Difficult removal 3% vs. 27%	Mean wear time (days) 3.8 vs. 3.2 (NS)
Hydropolymer vs. hydrocolloid	1	99	Leakage 8% vs. 31% *P* = .007)	Difficult removal 2% vs. 17%	Not reported
Hydrocellular vs. hydrocolloid	1	39	Leakage 4 vs. 23 (NS)	Difficult removal 5% vs. 62% (*P* < .001)	Not reported
Hydrocellular vs. hydrocolloid (Moderate to high exudates wounds)	1	32	Leakage 56% vs. 63%	Not reported	Required wound cleansing 48% vs. 75% (*P* < .001)
Sustained silver releasing dressing vs. other modern dressings	1	28	Silver dressing had better exudates management Faster reduction of malodour	Not reported	Risk of infection index at 2 weeks 81.8 vs. 115.3 (lower score represents lower risk)

*NS indicates not statistically significant.

Summary Statements – Dressings

- Hydrocolloid dressing was associated with almost 3 times more complete healing compared with saline gauze.
- There is evidence that hydrogel and hydropolymer may be associated with 50% to 70% more complete healing of pressure ulcers than hydrocolloid dressing.
- No statistically significant differences in complete healing were detected among other modern dressings.
- There is evidence that polyurethane foam dressings and hydrocellular dressings are more absorbent and easier to remove than hydrocolloid dressings in ulcers with moderate to high exudates.

- In deeper ulcers (stage III and IV), the use of alginate with hydrocolloid resulted in significantly greater reduction in the size of the ulcers compared with hydrocolloid alone.
- Studies on sustained silver-releasing dressings demonstrated a tendency for reducing the risk of infection and promoting faster healing, but the sample sizes were too small for statistical analysis and for drawing firm conclusions.

Integrating Findings on Dressings With Expert Panel Input

- No single dressing can meet the needs of all pressure ulcers.
- Dressings need to provide a moist environment and selection depends on:
  - An assessment of the ulcer: size, depth, amount of exudate, amount of necrotic tissue and eschar, and signs of infection (malodour, bacterial load). Adjust selection as condition of ulcer changes.
  - Staffing: gauze dressings – changed 2–3 times per day; modern dressing – changed every ≥ 4 days.
  - Cost – Modern dressings more costly than gauze; antimicrobial dressing even more so.
- An example of a guide for the selection of dressings based on characteristic of the ulcer, evidence, and Expert Panel input is shown in Table 39.

Table 39: Selection of Dressings

Pressure Ulcer	Dressing Need	Possible Choice of Dressing
All ulcers (type ≥ stage II)	Impermeable to bacteria; provides a moist environment; easily removed; keep periwound area dry	Occlusive or semi-occlusive dressing Nonadhesive to wound surface
Superficial; no or low exudates	See above	Film, hydrocolloid
Moderate to high draining/exudate	Plus high absorbency	Foam (e.g., polyurethane foam) Plus alginate as necessary
Dry/eschar present	Provides extra moisture and promote autolytic debridement	Hydrogel (calcium alginate contraindicated)
Deep with cavity or undermining	Packing of cavity	Calcium alginate or hydrofibre
High bacterial count or malodour	Antimicrobial	Sustained silver-releasing or gauze impregnated with antimicrobial agent
	Secondary dressing for hydrogel or hydrofibre or for extra absorbency	Gauze

Biological Therapies

Topical Growth Factors

Growth factors are cytokines (chemical signals) that control cell growth, cell migration, matrix production, enzyme expression, and differentiation. They play fundamental roles in the wound repair process. Most growth factors are multifunctional and the roles of some growth factors in promoting healing of chronic pressure ulcer have been explored. The origin and mode of action of these growth factors are summarized in Table 40.

The RCN review identified 7 small clinical trials comparing different topical growth factors to placebo 4 of which are included in this review (see Table 41). No new studies were found since the RCN review.

Table 40: Growth Factors Studied in the Healing of Pressure Ulcers

Growth Factor	Cell Tissue of Origin	Selected Target Cells or Tissue	Selected Stimulatory or Inhibitory Functions
Platelet-derived growth factor (PDGF)	Platelets, macrophages, neutrophils, smooth muscle cells	Fibroblasts, smooth muscle cells	Stimulates: - Proliferation of smooth muscle cells and fibroblasts - Migration of neutrophils, macrophages and fibroblasts - Chemotaxis - Extracellular cell matrix (production of fibronectin, hyaluronan, and proteases by fibroblasts);
Granulocyte macrophage colony-stimulating factor (GM-CSF)	T-lymphocytes, macrophage, fibroblasts, endothelial cells	Hematopoietic, inflammatory cells; neutrophils; fibroblasts	Stimulates: - Chemotaxis of endothelial cells and inflammatory cells - Proliferation of keratinocyt; - Activation of neutrophils
Fibroblast growth factor (FGF)	Monocytes; macrophages; endothelial cells	Endothelium; fibroblasts; keratinocytes	Stimulates: - Proliferation of endothelial cells, keratinocytes, and fibroblasts (give rise to granulation tissue) - Chemotaxis - Angiogenesis - Extracellular cell matrix
Transforming growth factor (TGF)	Platelets, leukocytes, and fibroblasts	Fibroblasts; endothelial cells; keratinocytes; lymphocytes; monocytes	Stimulates: - Extracellular matrix - Chemotaxis - Angiogenesis Inhibits: - Proliferation of keratinocytes, endothelial cells
Nerve growth factor (NGF)	Endothelial cells, circulating monocytes,		Neuropeptide modulation Stimulates: - Growth of endothelial cells - Release of other growth factors - Angiogenesis
Interleukin-1B	Lymphocytes; macrophages; keratinocytes	Monocytes; neutrophils; fibroblasts; keratinocytes	Stimulates: - Monocytes, neutrophils - Macrophage chemotaxis

Table 41: Studies Comparing Topical Growth Factor With Placebo in Treating Pressure Ulcers*

Study	Comparison	Sample Size	Mean Age, Years (SD)	Ulcer Stage	Mean Baseline Ulcer Volume (mL)	Treatment Duration (weeks)	Results: Growth Factor vs. Placebo
Mustoe 1994 (78)	Recombinant human PDGF vs. placebo	PDGF 100 μg/mL (16)	73.5 (15.0)	III or IV	5.5 (6.1)	4	Completely healed during treatment (regardless of recurrence): 100 μg/g PDGF = 2/16 300 μg/g PDGF = 0/14 Placebo = 1/14
		PDGF 300 μg/mL (14)	67.5 (17.7)		7.1 (8.8)		
		Placebo (14)	73.4 (17.7)		10.8 (13.2)		Completely healed during treatment or follow-up: 100 μg/g PDGF = 6/16 (37.5%) 300 μg/g PDGF = 3/14 (21.4%) Placebo = 4/14 (28.6%) Percent decrease in median ulcer volume compared with baseline: 100 μg/g PDGF = 71% 300 μg/g PDGF = 60% Placebo = 17% Ulcer volume adjusted for baseline volume: rPDGF treated ulcers smaller volume than placebo (P = .056)
		Total 41pts 44 ulcers					
Rees 1999 (79)	Recombinant human PDGF (becaplermin gel) vs. placebo	PDGF 100 μg/g (31)	48 (13.1)	III or IV	16.6 (15.1)	16	Completely healed ulcers: Placebo = 0/31 = 0%
		PDGF 300 μg/g (32)	49 (12.5)	NPUAP	17.2 (19.7)		PDGF 100 μg = 23% (7/31) vs. 0%§ PDGF 300 μg = 19% (6/32) vs. 0%‖
		PDGF 100 μg BID (30)	51 (18.3)		17.6 (33.8)		PDGF 100 μg BID = 3% (1/30) vs. 0%¶
		Placebo (31)	50 (13.6)		19.6 (21.9)		≥ 90% healing; PDGF vs. Placebo (58% vs. 29%, P = .021) and 59% vs. 29% (P =.014)

(continued)

Table 41: Studies Comparing Topical Growth Factor With Placebo in Treating Pressure Ulcers* (continued)

Study	Comparison	Sample Size	Mean Age Years, (SD)	Ulcers Stage	Mean Baseline Ulcer Volume (mL)	Treatment Duration (weeks)	Results: Growth Factor vs. Placebo
Robson 2000 (80)	Sequential GM-CSF/bFGF vs. bFGF vs. GM-CSF vs. placebo	GM-CSF/bFGF(16) bFGF (15) GM-CSF (15) Placebo (15) Total = 61	51.3 (11.2) 51.7 (11.3) 48.8 (11.8) 47.1(10.8)†	III or IV	38.16 (38.3) 33.81 (26.12) 32.77 (21.06) 45.19 (34.79)†	5	At 5 weeks: i) None healed ii) **Percent of ulcers ≥ 85% healed** 3/15(GMCSF) vs. 6/15(bFGF) vs. 4/16 (GM-CSF/bFGF) vs. 0/15(placebo) **Percent decrease in ulcer area**: bFGF 75% (26.57 cm^3) GM-CSF 67% (20.75 cm^3) GM-CSF/bFGF 68% (21.33 cm^3) Placebo 71% (30.95 cm^3) (No significant difference)
Payne 2001 (81) (1 year follow-up of Robson 2000 RCT)							**Completely healed at 6 weeks** GM-CSF 7/14 bFGF 8/14 GM-CSF/bFGF GF 7/15 Placebo = 3/14
						1 year	**Completely healed at I year** 27/41 (growth factor) vs. 10/13 (placebo) No significant difference in % complete closure and time to complete closure
Landi 2003 (82) Nursing home	NGF vs. standard therapy	NGF solution (18) Placebo solution (18)	80.2 (3.0) 80.2 (4.7)	Pressure ulcer of foot 2 – 5‡	1012 (633) mm2 1012 (655) mm2	6	Complete healing NGF 8/18 vs. Placebo 1/18 Percent decrease in surface area of ulcer: Nerve GF = 738 (393) mm^2 Placebo = 485 (384) mm^2 (P = .034)

*BID indicates twice daily; bFGF, basic fibroblast growth factor; GM-CSF, granulocyte macrophage colony-stimulating factor; MCSF, macrophage-colony stimulating factor; NGF, nerve growth factor; NPUAP, National Pressure Ulcer Advisory Panel; PDGF, platelet-derived growth factor; rPDGF recombinant platelet-derived growth factor; SD, standard deviation.
†Placebo group.
‡Based on Yarkony-Kirk Scale.
§100ug/g becaplermin vs. placebo (P = .005).
‖300 μg/g becaplermin vs. placebo (P = .008).
¶100 μg/g becaplermin BID vs. placebo (not statistically significant).

Platelet-Derived Growth Factor

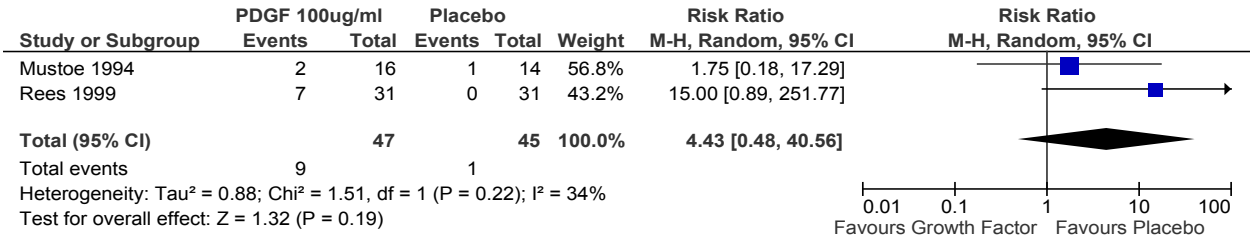
Platelet-derived growth factor is a dimeric protein composed of two disulfilde-linked polypeptide chains. It exists in three different isoforms, the heterodimer PDGF-AN (consisting of an A chain and a B chain), and two homodimers, consisting of 2 A chains (PDGF-AA) or 2 B chains (PDGF-BB). PDGF-BB has been shown in preclinical and clinical studies to promote the formation of granulation tissues at the wound site and to stimulate wound healing. (79) Becalpermin is a recombinant PDGF-BB produced using recombinant DNA technology and formulated in a sodium carboxymethycellulose-based gel for topical administration. This preparation was used in two clinical studies on pressure ulcers. (78;79)

Mustoe et al. (78) compared a placebo group with a group of elderly patients treated in a hospital or nursing home with either 100 μg/mL or 300 μg/mL of topical platelet-derived growth factor (rhPDGF-BB). At the end of the treatment period, patients in both rhPDGF-BB groups had smaller ulcer volumes compared with the placebo group (P = .009, 2-sided t-test), but the number of ulcers healed and the time to achieve 50% healing were not significantly different between the study groups. It was also reported that 14.3% of the ulcers in the placebo group healed during treatment but recurred during follow-up.

Rees et al. (79) also compared a group of patients with chronic pressure ulcers treated with a placebo gel to 3 groups treated with topical rhPDGF (becalplemin) (100 μg/mL or 300 μg/mL once daily, or 100 μg/mL twice daily). Once daily rhPDGF treatment at concentrations of 100 μg/g and 300 μg/g significantly increased the incidence of complete healing (23% vs. 0%, and 19% vs. 0%, respectively) and of ≥ 90% healing (58% vs. 29%, and 59% vs. 29%, respectively). Treatment with rhPDGF at a concentration of 100 μg/g once daily was equally efficacious as treatment with rhPDGF at a concentration of 300 μg/g. There was no significant difference in the incidence of complete healing or ≥ 90% healing between the group treated with 100 μg/g rhPDGF twice daily and the placebo group. Kallianinen et al. (83) conducted a follow-up analysis at 1 of the study sites on patients who underwent salvage surgery after failing to heal. The analysis compared post-surgery healing rates of 3 unhealed ulcers in the placebo group with 12 unhealed ulcers that had previously received some rhPDGF treatment. Statistical analysis showed that a greater proportion (11/12) of the ulcers of patients who were treated with rhPDGF (any dose) and salvage surgery healed completely compared with placebo and salvage surgery (0/3) (P < .05). There were no significant differences in wound healing noted between different dosages of rhPDGF. (83)

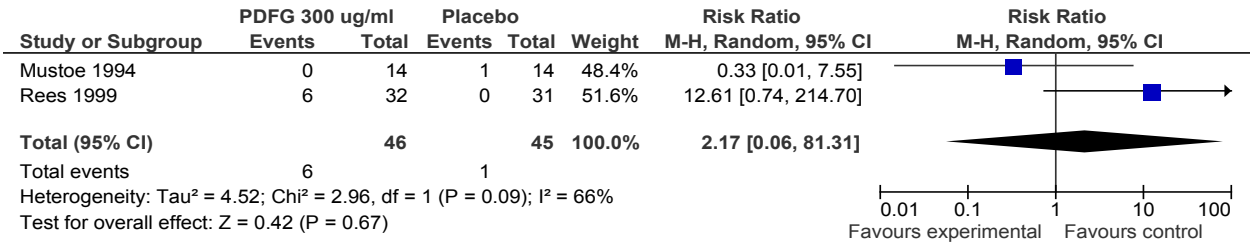
Pooled analysis of above studies showed different trends in complete healing and no significant difference in healing between the rhPDGF and placebo arms at either at dosing concentration (Figures 26–28).

Figure 26: Forest Plot of Complete Healing – Recombinant Platelet-Derived Growth Factor (100 μg/ml) Versus Placebo at 4 Weeks*



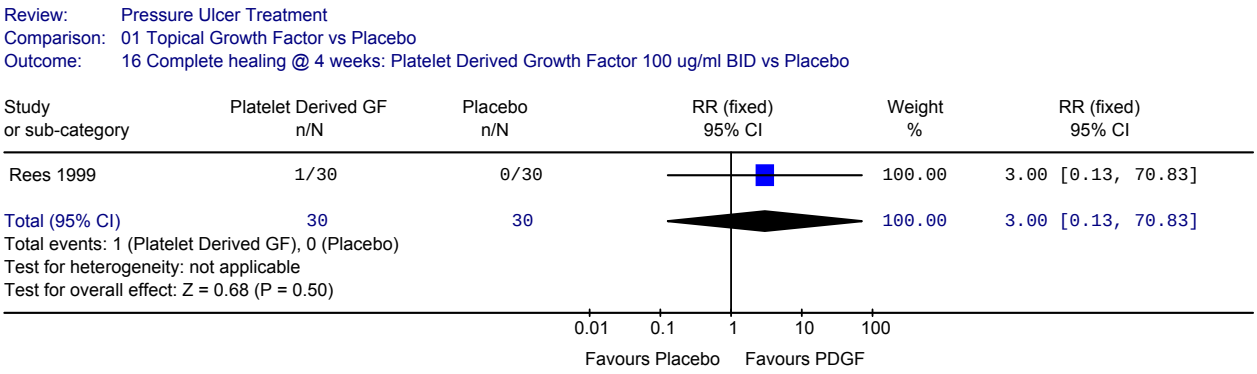
*CI indicates confidence interval; PDGF, Platelet Derived growth factor;

Figure 27: Forest Plot of Complete Healing – Recombinant Platelet-Derived Growth Factor (300 μg/ml) Versus Placebo at 4 Weeks*



*CI indicates confidence interval; PDGF, Platelet Derived growth factor

Figure 28: Forest Plot of Complete Healing – Recombinant Platelet-Derived Growth Factor (100 μg/ml BID) Versus Placebo at 4 Weeks*



*BID indicates twice daily; CI, confidence interval; GF, growth factor; RR, relative risk.

Safety of Platelet-Derived Growth Factor

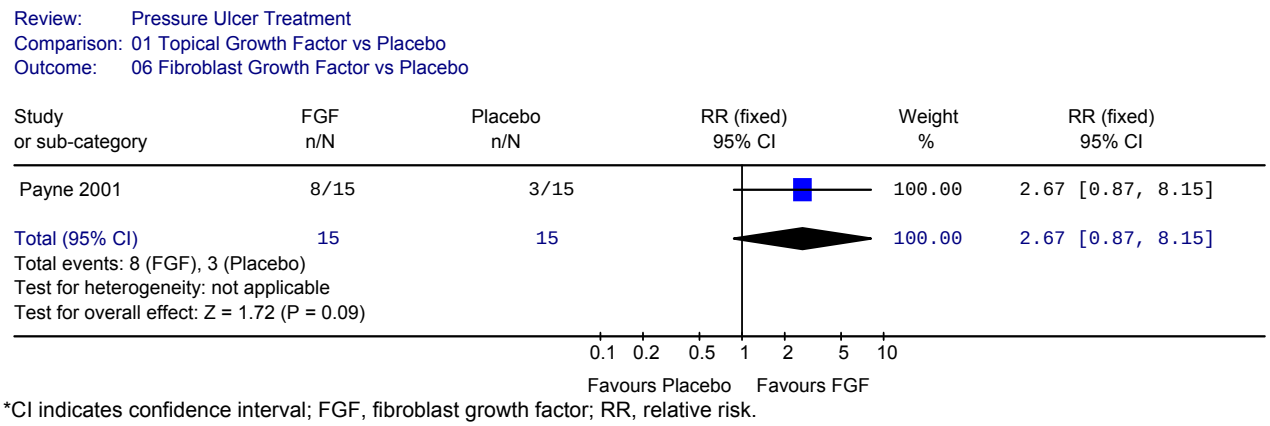
On March 27, 2008, the US FDA (84) issued a communication regarding the safety of Regranex, a recombinant PDGF approved for the treatment of diabetic leg ulcer. The FDA communication stated that a long-term safety study by the manufacturer completed in 2001 reported more cancers in people who used Regranex (recombinant PDGF) than in those who did not use it. In addition, an analysis of a health insurance database (1998–2003) showed that deaths from cancer (all types combined) were higher for patients who were given ≥ 3 prescriptions for Regranex than those who were not treated with Regranex. The FDA urges health care professionals to promptly report serious and unexpected adverse reactions associated with Regranex to the FDA MedWatch. (84)

Fibroblast Growth Factor and Granulo Macrophage Colony-Stimulating Factor

Robson et al. (80) compared patients treated sequentially with granulocyte macrophage colony-stimulating growth factor (GM-CSF) and basic fibroblast growth factor (BFGF) with patients treated with each of the growth factors alone, and with patients treated with a placebo. The mean change in volume of the pressure ulcers at 35 days did not differ significantly among the groups. At 6 weeks, 50% of the 44 patients treated with growth factor achieved complete closure of the ulcer compared with 3

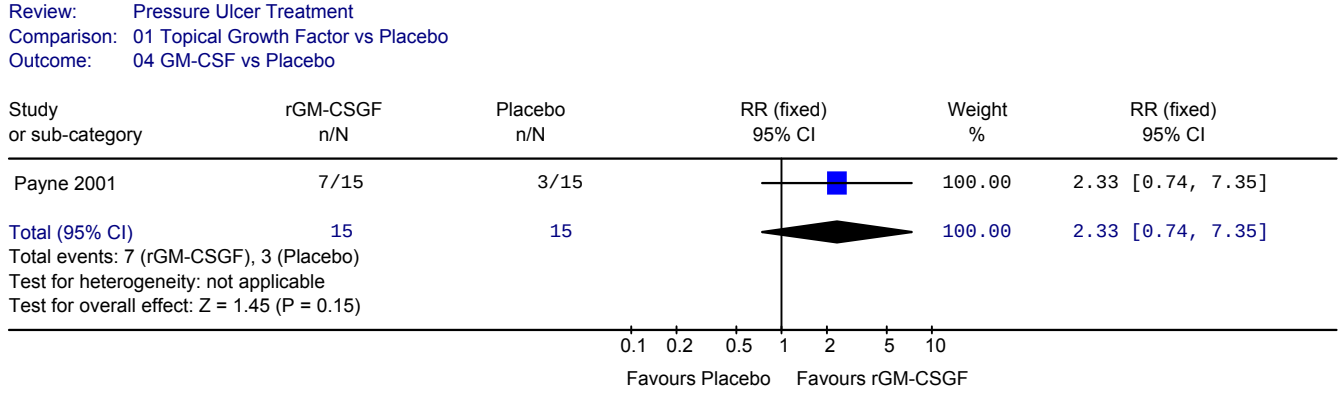
out of 13 patients treated with placebo. This difference did not achieve statistical significance. Payne et al. (81) reported that at 1-year follow-up there were no significant differences among the percentage of patients healed across the four treatment groups at any follow-up visit ($P > .05$) (Figures 29–31). There was a trend for BFGF treated patients to achieve healing faster than the other groups, but the difference did not reach statistical significance (log-rank $P = .18$, Wilcoxon $P = .25$)

Figure 29: Forest Plot of Complete Healing – Fibroblast Growth Factor Versus Placebo at 6 Weeks*



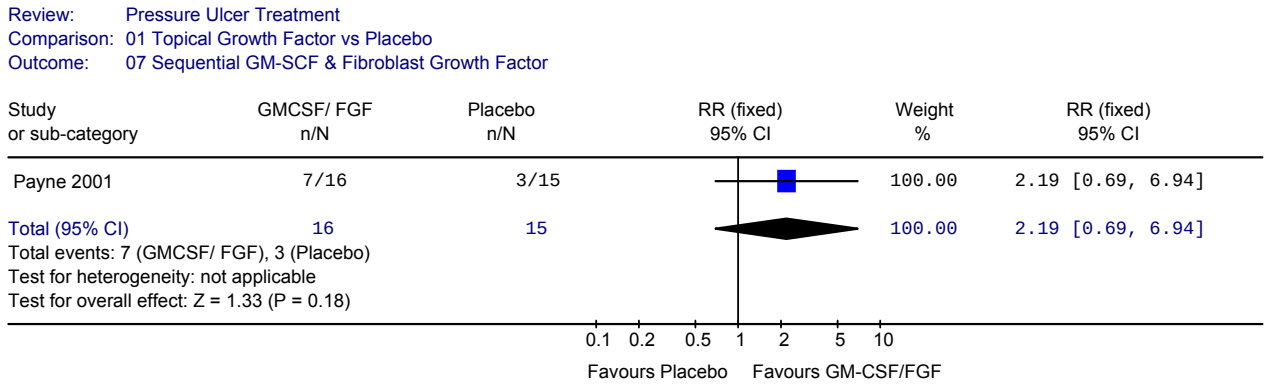
*CI indicates confidence interval; FGF, fibroblast growth factor; RR, relative risk.

Figure 30: Forest Plot of Complete Healing – Granulo Macrophage Colony Stimulating Factor Versus Placebo at 6 Weeks*



*CI indicates confidence interval; GM-CSF, granulo macrophage-colony stimulating factor; RR, relative risk.

Figure 31: Forest Plot of Sequential Fibroblast Growth Factor and Granulo Macrophage Colony Stimulating Factor Versus Placebo at 6 Weeks*



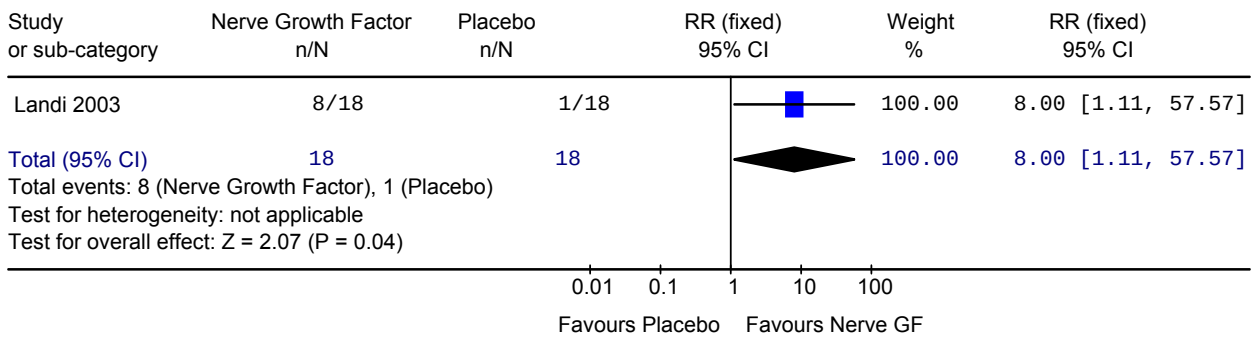
*CI indicates confidence interval; FGF, fibroblast growth factor; GMCSF, granulo macrophage-colony stimulating factor; RR, relative risk.

Nerve Growth Factor

Nerve growth factor is a polypeptide that has been shown to promote the regeneration of injured cells that express nerve growth factor receptors in the peripheral and central nervous systems. Observational studies suggest that nerve growth factors speeded recovery from skin ulcer in humans. (82)

Landi et al. (82) compared 18 patients with pressure ulcers of the foot randomly assigned to receive topical nerve growth factor daily for 6 weeks with 18 patients assigned to receive a balanced salt solution (vehicle control) without nerve growth factor. The pressure ulcers healed completely in 8 patients in the nerve factor treated group compared with 1 patient in the control group (Figure 32). None of the ulcers in the control group improved by 3 stages or more during the treatment period.

Figure 32: Forest Plot of Complete Healing – Nerve Growth Factor Versus Placebo at 6 Weeks*

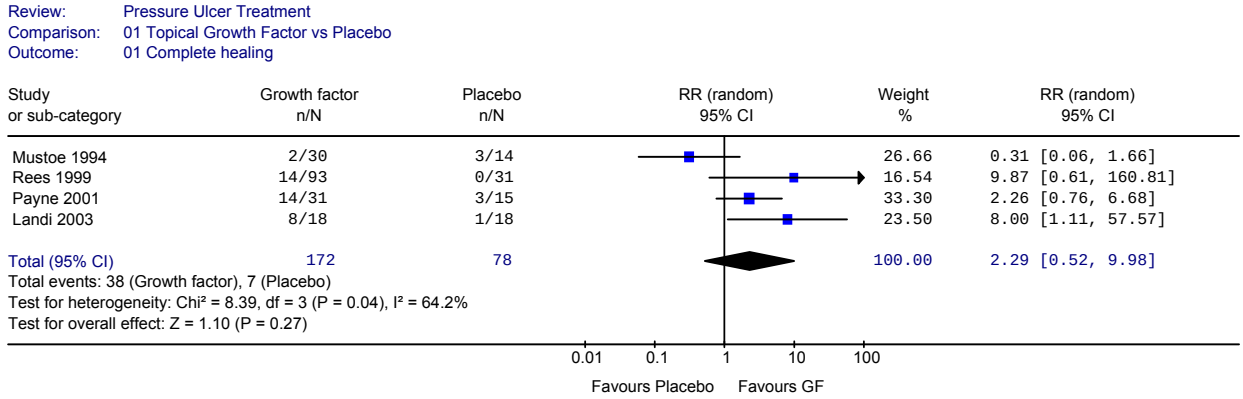


*CI indicates confidence interval; RR, relative risk.

In addition to the above studies, Hirchberg et al. (85) reported on a subset analysis of data from a randomized, blind, parallel, placebo controlled trial involving 14 patients with stage III or stage IV ulcers located on the trunk. The analysis compared patients who received topical recombinant transforming growth factor (TGF-β3) (1 μg/cm^2 or 2.5 μg/cm^2) with patients who received topical placebo. Patients who received 2.5 μg/cm^2 of TGF-β3 exhibited an increased rate of wound healing at the fourth visit ($P < .05$), but there was no significant difference in the healing rate among the groups at the end of the 16-week follow-up period. No conclusion can be drawn from this study because of its small sample size (14) and high attrition (43%).

A pooled analysis was performed that included the four studies with available data. The analysis compared complete healing in patients that received any growth factor with patients that received placebo. The results showed an RR of 2.29 in favour of growth factors; however, this did not reach statistical significance (95% CI, 0.52–9.98), and the test for heterogeneity showed much heterogeneity ($I^2 = 64.2\%$) (Figure 33). Note that in the figure below, that the study by Mustoe et al. (78) had the shortest treatment period (4 weeks) which may explain its deviation in results from the other studies.

Figure 33: Forest Plot of Complete Healing – Growth Factor Versus Placebo (All Studies)*



*CI indicates confidence interval; RR, relative risk.
Payne 2001 (81) – Complete healing at 6 weeks.

Engineered Skin Equivalents and Skin Matrix

Besides having decreased growth factors, chronic wounds may have impaired cell migration and insufficient angiogenesis to support complete wound closure. There may be an imbalance of matrix metalloproteases and their inhibitors, favouring tissue destruction. Cellular therapies being investigated include autologous epidermis, allografts, and engineered living skin equivalents and skin matrix. Autografts involves having a patient's own skin removed from one area of the body and applied to the wound and can be partial or full thickness. Heterografts are tissues derived from an external source and applied to another (e.g., bovine skin or cadaver skin as a temporary covering). (Woo 2007, Advances in Skin and Wound Care, Feb, 2007)

Tissue engineering aims to develop biological substitutes or synthetic skin equivalents that emulate normal skin functions to accelerate wound healing. An example is Apligraf, a composite bilayer product that uses a combination of bovine type I collagen gel and living neonatal fibroblasts from neonatal foreskin as the dermal component, with a cornified epidermal layer of neonatal keratinocytes. (86)

Dermal substitutes made from collagen matrix have also been investigated as artificial dermis in the treatment of deep wounds.

No randomized controlled studies were found on the use of engineered skin substitutes and skin matrix to treat pressure ulcers, although two observational studies were identified (Table 42).

Table 42: Studies in Engineered Skin Substitute and Skin Matrix

Study	Design	Comparison	No. of Ulcers	Ulcer Stage	Duration	Results
Brem 2000 (87)	Consecutive case series	Human skin equivalent Apligraf*	21	III and IV	Up to 10 months	13/21 (62%) of pressure ulcers healed in an average of 29 days with 1 application of Aligraf 5 stage IV ulcers failed to heal, 3 lost to follow-up
Ichioka 2003 (88)	Nonrandomized controlled trial	Collagen matrix substitute dermis (Terudermis®)†	15	IV	31.2 months	Time to epithelialization 84.1 days vs. 215.3 days Percent increase in vascular density 431.9% in experimental group Reported to be significant, *P* value not reported

*A layer of allogenic human keratinocytes on a layer of allogenic fibroblasts on type 1 collagen dispersed in a dermal layer matrix. Cells are grown from neonatal foreskin.
†Atelocollagen matrix with a silicone layer – act as scaffold for regeneration.

Ichioka et al. compared 9 patients with stage IV sacral ulcers treated with a collagen matrix substitute dermis (Terudermis, Terumo Corp., Tokyo, Japan) to 6 patients with grade 4 sacral ulcers treated with alginate dressing instead of Terudermis. Terudermis consists of an atelocollagen matrix with a silicone layer that acts as a scaffold for regeneration. Ulcers from both groups were thoroughly debrided and cleansed before treatment. After an average follow-up period of 31.2 months (SD 2.6, range 20–44 months), time to achieve complete epithelialization was significantly shorter in patients that received the substitute dermis compared with the conventional group (84.1 days vs. 215.3 days). Histological examination of the substitute dermis group showed a significant increase in post-treatment area vascular density (431.9% of pre-treatment density) and in length density (1,059% of pre-treatment density)
Brem et al. (87) treated 21 consecutive patients with stage III or IV pressure ulcers with Apligraf. After one application of Apligraf, 62 % of the patients achieved complete healing of the ulcer in a mean healing time of 29 days. Ichioka et al. (88) reported a nonrandomized study that found much shorter time to epithelialization and greater increase in vascular density in patients given a collagen matrix substitute compared with patients treated with conventional therapy.

Summary of Analysis – Biological Therapies

Table 43: Summary of Impact of Biological Therapy on Complete Healing of Pressure Ulcers*

Comparison	Study	No. of Ulcers	Ulcer Stages	Relative Risk (95% CI)	I^2 (%)	*P* Value	Quality of Evidence
Nerve growth factor vs. placebo (pressure ulcer of foot)	Landi 2003(82)	36	II – IV	8.00 (1.11, 57.57)	NA	.04	Low
Platelet-derived GF vs. placebo (100 μg/g) meta-analysis	Mustoe 1994(78) Rees 1999(79)	92	III, IV	2.48 (0.08, 80.77)	78.3	.61	NE
(300 μg/g) meta-analysis		91	III, IV	1.35 (0.02, 111.25)	79.0	.89	NE
(100 μg/g BID)	Rees 1999(79)	60	III, IV	3.0 (0.13, 70.83)	NA	.50	NE
Granulo macrophage colony-stimulating GF vs. placebo	Payne 2001(81)	30	III, IV	2.33 (0.74, 7.35)	NA	.15	NE
Fibroblast GF vs. placebo		30	III, IV	2.67 (0.87, 8.15)	NA	.09	NE
Sequential GM-CSF/FGF vs. placebo		31	III, IV	2.19 (0.69, 6.94)	NA	.18	NE
GFs vs. placebo (meta-analysis)	Mustoe 1994(78) Rees 1999(79) Payne 2001(81) Landi 2003(82)	250	Mostly III or IV	2.29 (0.52, 9.98)	64.2	.27	Low
Transforming growth factor	Hirchberg 2001 (85)	14	III, IV	No significant difference in healing	NA	Not reported	NE

*BID indicates twice daily; CI, confidence interval; FGF, fibroblast growth factor; GF, growth factor; GM-CSF, granulo macrophage colony stimulating factor; I^2, test for heterogeneity; NA, not applicable, NE, not evaluated

Summary Statements – Biological Therapies

- The efficacy of growth factors in improving complete healing of chronic pressure ulcers has not been established.
- Presently only Regranex, a recombinant PDGF has been approved by Health Canada and only for treatment of diabetic ulcers in the lower extremities.
- A March 2008 FDA communication reported increased deaths from cancers in people given 3 or more prescriptions for Regranex.
- Limited low quality evidence on skin matrix and engineered skin equivalent suggests a potential role for these products in healing refractory advanced chronic pressure ulcers, but the evidence is insufficient to draw a conclusion.

Pressure-Relieving Support Surfaces

Support surfaces include special beds, mattresses replacements, mattress overlays, and seat cushions.

Classification of Pressure-Relieving Support Surfaces

Low Tech Devices

- Standard foam mattresses
- Alternative foam mattresses: high specification foam mattress (defined as a foam mattress with a two-way stretch vapour permeable cover), viscoelastic, convoluted foam, cubed foam
- Gel-filled, fluid-filled, fibre-filled, and air-filled mattresses and overlays

Constant Low-Pressure Devices

- Air-fluidized therapy: consist of a bed frame containing silicone-coated beads. This type of bed uses both air and fluid to provide support. Beads in the bed behave like a liquid when air is pumped through them. On this type of bed, the body is immersed in the warm, dry fluidized beads. Air-fluidized beds are recommended for patients with multiple large pressure ulcers. They are not recommended for patients with pulmonary disease or unstable spines or for patients who are ambulatory. Because so much air is needed to fluidize the total bed, dehydration (from heat escaping from the body) is a risk.
- Low- air-loss beds: patients are supported on air-filled sacs inflated at a constant pressure, through which air can pass.
- Air-fluidized and low-air-loss (LAL) beds are designed to conform to the body contours. In addition to providing pressure relief, these specialty beds also eliminate shear and friction and, decrease moisture.

Alternating Pressure Systems

- Alternating pressure (AP) mattress overlays
- AP mattress replacements
- Turning beds/frames (kinetic or profiling beds): beds that either aid manual repositioning of the patient or reposition the patient by motor-driven turning and tilting

Previous Systematic Reviews on Pressure-Relieving Support Surfaces

Three previous systematic reviews examined the evidence on pressure relieving support surfaces as treatments for pressure ulcers (Table 45). These reviews found some evidence that air-fluidized beds may improve the rate of healing of pressure ulcers compared with AP beds or mattresses, but found no conclusive evidence on the influence of other beds and surfaces on the healing of pressure ulcers.

Table 44: Classification of Pressure Relieving Devices for Pressure Ulcer Treatment

Class	Examples
Static surfaces	- Standard foam - Alternative foam (High specification, cubed, convoluted) - Gel-filled, water-filled, fibre-filled, and air-filled - Sheepskin - Foam wheelchair cushion
Constant low pressure devices	- Low-air-loss - Air-fluidized mattresses
Alternating pressure devices	- Alternating pressure mattresses and overlays
Other features	
Mattress	Replacement vs. overlays
Bed frames	Profiling vs. flat-based
Power	Powered vs. nonpowered

Table 45: Systematic Reviews on Pressure Relieving Support Surfaces*

	Cullum et al., 2001 (89)	ECRI/AHRQ, 2001 (90)	Royal College of Nurses 2005 (46)
Literature search up to:	June 1998	2001	August 2004
Type of wounds covered	Pressure sores	Stage III or IV pressure ulcers	Pressure ulcers of any grade
Purpose	Influence on prevention and treatment of pressure sores	Determine effectiveness of air–fluidized beds in treating stage III or IV pressure ulcers	Determine whether pressure relieving surfaces increase the rate of healing of pressure ulcers
Setting	Any setting	Home environment	Any setting
Comparison	Standard support surfaces or among special support surfaces	Air-fluidized beds vs. group II surfaces (low-air-loss beds and low pressure mattresses	Special support surfaces vs. standard support surfaces Special support surfaces vs. special support surfaces
Type of studies included	RCTs, no language restrictions	Parallel controlled studies with >10 patients in each group	Randomized controlled studies
Outcome measures	Objective measures of wound healing: change in would area or volume	Complete healing, number with reduction in size of ulcers, mean time to heal, time to 50% healing, mean area reduction, number requiring hospitalization, length of stay during treatment	Healing rates of existing ulcers by objective measurement Costs of support surfaces Patient comfort Durability Reliability Acceptability
Method of analysis	Descriptive and meta-analysis	Descriptive	Description and meta-analysis

(continued)

Table: 45: Systematic Reviews on Pressure Relieving Support Surfaces (continued)*

	Cullum et al., 2001 (89)	ECRI/AHRQ, 2001 (90)	Royal College of Nurses 2005 (46)
Studies (RCTs) on treatment of pressure ulcers included in the review	-Between constant low-pressure support Groen 1999 -Air-fluidized bed vs. other surfaces Allman 1987, Munro 1989, Strauss 1991 -Low-air-loss beds Ferrell 1993, Mulder 1994, Caly 1994 -Alternating pressure devices Devine 1995, Evans 2000, Russell 2000 -Special seat cushion Clark 1999	-Air-fluidized bed studies Allman 1987 Strauss 1991 -Group II surfaces Ferrell 1993 Mulder 1994 Day 1993 Groen 1999	Strauss 1991; Allman 1987 Clark 1999; Day 1993; Devine 1995; Evans 2000; Ferrell 1993; Groen 1999; Munro 1989; Caley 1994; Keogh 2001; Mulder 1994; Russell 2000; Russell 2004 Ewing 1964
Conclusions	There is evidence from 1 high-quality trial that air-fluidized therapy may improve pressure sore healing rates. There is insufficient evidence to draw conclusion about the value of other beds, mattresses, and seat cushions as pressure sore treatment.	-1 RCT in home setting difficult to interpret results because of bias in treatment -1 RCT in hospital setting found significantly greater reduction in ulcer size with air-fluidized beds but no specific information on stage III and IV ulcers and study performed >10 years ago -Evidence on group 2 support surfaces in hospitals or nursing homes was not conclusive	-There is some evidence that air flotation supports reduce the size of established pressure ulcers compared with a modified alternating pressure support or standard care -There is no conclusive evidence to support the superiority of either alternating pressure support surfaces or continuous low-pressure supports in the treatment of existing ulcers -Confidence regarding conclusion tempered by poor quality of many of the trials and lack of replication of most comparisons

*RCT indicates randomized controlled trial

MAS Review of Evidence

The MAS reviewed the updates to the 2005 RCN review on support surfaces since it is the most current and comprehensive review available. The MAS literature search yielded 2 additional RCTs (Rosenthal 2003 and Nixon 2006). (91;92) One retrospective comparative study (93) was included because of the large sample size. A total of 16 studies were included in the analysis (Table 46). Detailed description of the studies is provided in Appendices to 4 .

Table 46: Studies on Support Surfaces for Treatment of Pressure Ulcers*

Comparison	No. of Studies	Studies
Nimbus AP mattress replacement vs. another AP mattress replacement	3	Devine 1995 (Nimbus 1 vs. Airwave AP mattress) (94) Evans 2000 (95) (Nimbus 3 vs. another AP mattress) Russell 2000 (96) (Nimbus 3 vs. Cairwave)
Nimbus 3 AP multicell mattress vs. RIK static, fluid overlay mattress	1	Russell 2003 (97)
AP overlay vs. AP mattress replacement	1	Nixon 2006 (91)
Air-fluidized bed vs. standard care	3	Allman 1987 (98) Munro 1989 (99) Strauss 1991 (100)
Low-air-loss bed vs. convoluted foam mattress	3	Ferrell 1993 (101) Mulder 1994 (102) Day 1993 (103)
Low air-loss bed vs. low air-loss overlay	1	Caley 1994 (unpublished)
Air suspension bed vs. foam mattress overlay	1	Day 1993 (103)
Foam mattress vs. water mattress	1	Goren et al., 1999 (104)
Static vs. low-air-loss and AP vs. air fluidized beds	1	Ochs 2005 (93) large retrospective study
Electric profiling bed vs. flat-based bed	1	Keogh 2001 (105)
AP seat cushion vs. static air seat cushion	1	Clark 1999 (106)
Generic total contact seat vs. low-air-loss bed or low pressure mattress overlay	1	Rosenthal et al., 2003 (92)

*AP indicates alternating pressure.

Comparison 1: Air-Fluidized Bed with Other Support Surfaces

Three RCTs compared the air-fluidized bed with other support surfaces (Table 47).

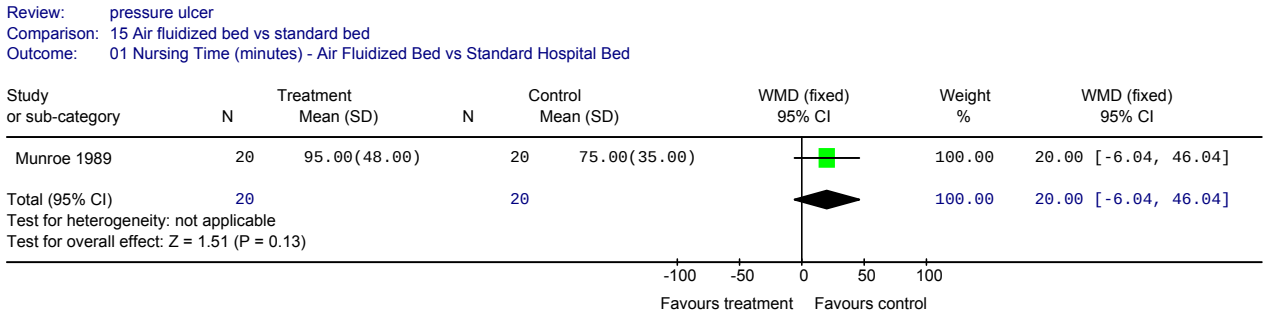
Munroe et al. (99) compared treatment of grade 2 and 3 ulcers using air fluidized bed with treatment using a standard hospital bed and sheep skin or gel pads placed underneath the ulcer. At the end of the 2-week treatment, the 20 patients that received an air fluidized bed had a 44% reduction in the surface area of the ulcer, whereas the other 20 patients that received a standard hospital bed had a 40% increase in the area of the ulcer. Mean nursing time per patient was higher in the group that used air-fluidized bed, but the increase in nursing time was not statistically significant (Figure 34).

Table 47: Randomized Controlled Trials Comparing Air-Fluidized Bed With Other Support Surfaces*

Study	Patients	Comparison	Ulcer Stage	Mean Age (years)	Duration (weeks)	Outcome Measures: Air-Fluidized Bed vs. Comparator
Munro et al., 1989 (99)	Hospital in patient All males N = 20/20	Air-fluidized bed (Clinitron®) vs. standard bed + sheep skin or gel pads placed beneath ulcer	Grade 2 or 3	67.2 (range 48–88)	2	Average reduction in diameter of ulcer 1158–2660 mm^2 vs. 1464–2051 mm^2 Final ulcer area as % of baseline area 44% vs.140% Mean nursing time (minutes per 8 hour shift 95 (SD, 48) vs. 75 (SD, 35) Patient satisfaction score (for 18 pts) 57.5 (SD, 6.1) vs. 48.6 (SD, 12.3) *P* = .067
Allman et al., 1987 (98)	Hospital inpatient Age >18 N = 32/34 Attrition 32% vs. 24%	Air-fluidized bed (Clinitron) + turning every 4 hours vs. AP air mattress (Lapidus Air Float system) covered with 19 mm foam pad + turning every 2 hrs + use of heel and elbow protection	All stages Stage III or IV 48% vs. 41%	65.5 (SD, 15.6) vs. 67.6 (SD, 18.3)	Mean 13 days (4–77)	Proportion with improved ulcer† All ulcers 22/32 vs. 16/34 Largest ulcers ≥ 7.8 $cm^{2)}$ 10/16 vs. 5/17 Median change in total surface area (cm^2) –1.2 (–38.0 to 15.5) vs. +0.5 (–55.1 to +94.7) For ulcers ≥ 7.8 cm^2 –5.3 (–38.0 to +15.5) vs. 4.0 (–55.1 to +94.7) (*P* = .01)
Strauss et al., 1991 (100)	Home N = 58/54 Completed study 50% vs. 56%	Air-fluidized bed vs. conventional (AP pads, air support, water mattresses, or high density foam)	Stage III or IV	65 vs. 63	36	Proportion of ulcers improved based on independent Nurse Reviewers' assessment‡ 19/22 vs. 9/13 Total hospital days per patient 3.6 (SD, 8.7) vs. 16.9 (SD, 30.6) LOS each hospitalization (days) 11.5 (SD, 8.8) vs. 21.5(SD, 23.8) (*P* < .05)

*AP indicates air pressure; LOS, length of stay; SD, standard deviation.
†Improved ulcers included = Healed ulcers + much improved ulcers + little improved ulcers.
‡Improved ulcer = progressed to a lower stage or reduced surface area or less inflammation or less eschar.

Figure 34: Nursing Time per Patient (Minutes) – Air Fluidized Bed Versus Standard Hospital Bed*

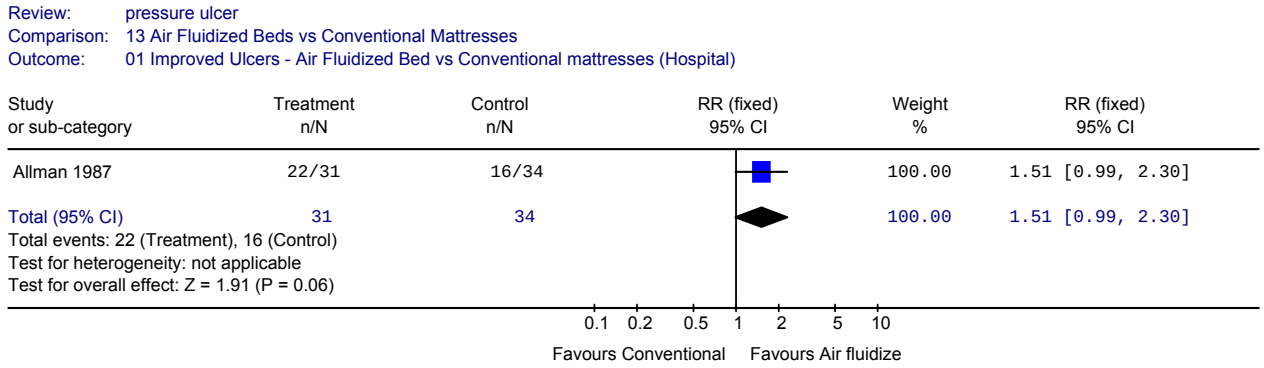


*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

Two studies compared air-fluidized beds with low-pressure support surfaces. Allman et al. (98) randomized 32 patients to receive air-fluidized beds and repositioning every 4 hours and 24 patients to be given an AP air mattress covered with a 19 mm foam pad. Patients in the control group were turned every 2 hours and allowed to use heel or elbow protection. Physicians were allowed to order a plastic surgery consult, topical therapy with saline or povidone-iodine, enzymatic debridement, sterile gauze dressing, and whirlpool treatment as needed. Approximately 90% of the ulcers in each arm were stage II or higher. The proportion of patients that had either healed or improved ulcers was higher in the group that received air-fluidized beds compared with the AP air mattress, but the difference did not reach statistical significance (Figure 35). There were also no significant differences in the proportion of improved ulcers between the two arms when only ulcers equal to or larger than 7.8 cm^2 were considered (Figure 36).

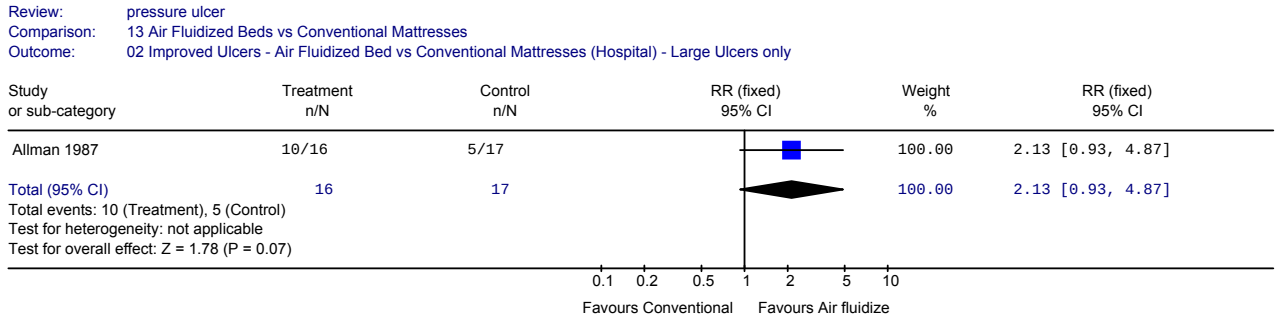
The authors reported a mean reduction of 1.2 cm^2 in the surface of ulcers in the air-fluidized bed arm compared with an increase of 0.5 cm^2 in the control arm. This difference was more pronounced (–5.3 cm^2 vs. +4.0 cm^2) and statistically significant (P = .01) for large ulcers (≥ 7.8 cm^2).

Figure 35: Forest Plot of Improved Ulcers – Air-Fluidized Bed versus Conventional Therapy (Hospital) All Ulcers*



*CI indicates confidence interval; RR, relative risk.

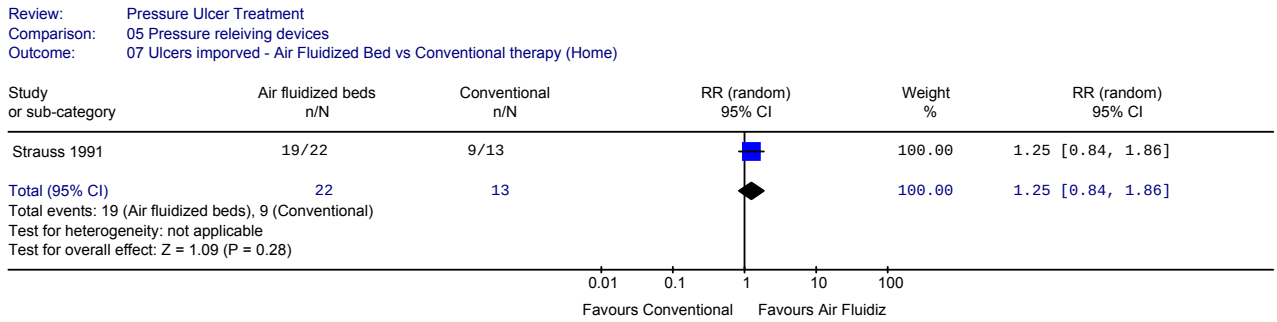
Figure 36: Forest Plot of Improved Large Ulcers (>7.8 cm^2) – Air-Fluidized Bed versus Conventional Mattresses (Hospital)*



*CI indicates confidence interval; RR, relative risk.

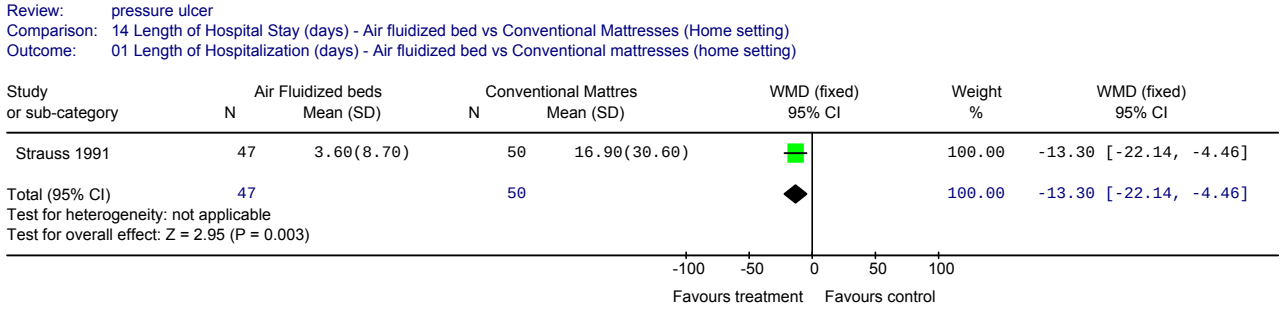
Strauss et al. (100) compared 58 home care patients that received air-fluidized beds with 54 that received other low pressure support surfaces (AP pads, air support mattresses, water filled mattresses, or high-density foam mattresses). Only patients with stage III or IV ulcers were included. Virtually all patients in both groups had moist or wet-to-dry dressing. Only 50% of the air-fluidized bed group and 56% of the control group completed the study. The proportion of improved ulcers was not significantly different between the two arms (Figure 37); however, the mean hospital stay per patient during the study was 13 days shorter for patients that received air-fluidized bed therapy (Figure 38).

Figure 37: Forest Plot of Improved Ulcers – Air-Fluidized Bed Versus Conventional Therapy*



*CI indicates confidence interval; RR, relative risk.

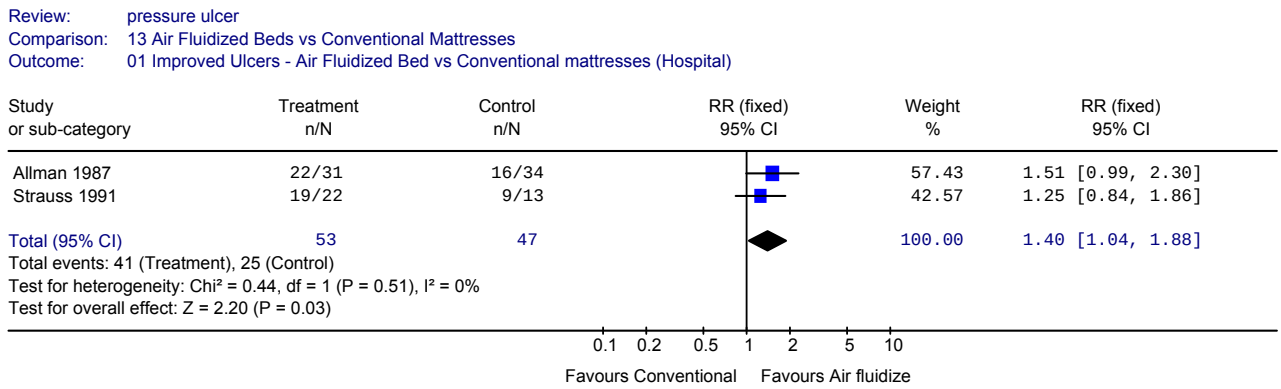
Figure 38: Pressure Ulcer Related Hospital Days – Air-Fluidized Bed Versus Conventional*



*CI indicates confidence interval; SD, standard deviation; WMD, weighted mean difference.

Pooled analysis of the studies showed a significantly higher proportion of improved ulcers in patients treated with air-fluidized beds compared with other low pressure support surfaces [RR 1.36, 95% CI (1.02–1.82), P = .01] and the test for heterogeneity was not significant (I^2 = 0%, P = .51) (Figure 39).

Figure 39: Forest Plot of Improved Ulcers – Air-Fluidized Bed Versus Conventional (Hospital and Home Setting)*



*CI indicates confidence interval; RR, relative risk.

Ochs et al. (93) conducted a large retrospective study to compare the air-fluidized beds with other categories of support surfaces using existing data from the National Pressure Ulcer Long-Term Care Study (NPULS) in the United States (Table 48).

The study included 664 residents of 109 long-term care facilities that had at least 1 pressure ulcer. The 3 groups of support surfaces compared were:

Group 1: Overlays and replacement dry pressure mattresses, gel pressure pads, and air and water pressure overlays.

Group 2: Powered LAL overlays and mattresses, powered LAL-reducing beds, and AP surfaces.

Group 3: Air-fluidized beds.

There were no statistically significant differences in the mean weight among the groups, but patients in Group 3 were sicker, had significantly larger ulcers, and more stage III/IV/eschar ulcers. The analysis showed that residents in Group 3 (air-fluidized beds) had significantly greater healing rate compared with Group 1 and 2 respectively. groups (5.2 cm^2/week vs. 1.5 cm^2/week or 1.8 cm^2/week; P = .007), particularly for stage III/IV ulcers. Patients in Group 2 had significantly more hospitalization and emergency room visits (19%) compared with Group 1 (10.2%) and Group 3 (7.3%) (P = .01).

There are limitations to this study because of the retrospective nature. Patients were not allocated randomly and there was an imbalance of sample size among the 3 groups. There were differences in the baseline characteristics of the patients and their ulcers. Moreover, due to limitation of the databases, some factors that may influence healing such as debridement, level of continence, pressure ulcer infection, effects of different dressings, and baseline nutritional status (e.g., pre-albumin level) were not available. The strength of this study is in its size since there is no prospective study on support surfaces that is close to the size of this study. (93)

Table 48: A Large Retrospective Study Comparing Air – Fluidized Beds, Low-Air-Loss Beds, and Static Beds

Study	Population	Comparator	Ulcer Stage	Mean Age (years)	Duration	Outcome Measures: Impact on Wound Healing
Ochs 2005 (93)	Nursing homes (National Pressure Ulcer Long-Term Care Study) With 1 documented pressure ulcer N = 664	(1) Static (N = 463) (2) Low-air-loss and AP (N = 119) (3) Air-fluidized beds (N = 82)	All stages Percent III and IV 19.6% vs. 43.7% vs. 70.8% Initial ulcer size (cm^2) 11.3 vs. 22.2 vs. 56.5 *P* < .0001	79.3 vs. 77.4 vs. 67.6	3 months	Healing rate: Group 1 = 1.5 cm^2/wk Group 2 = 1.8 cm^2/wk Group 3 = 5.2 cm^2/wk Group 3 significantly greater rate *P* = .007 Difference more pronounced for group III and IV ulcers Hospitalization and emergency room visits Group 1 = 10.2% Group 2 = 19% Group 3 = 7.3% Group 2 higher than groups 1and3 (*P* < .05) Even after controlling for severity of illness

Comparison 2: Low-Air Loss Mattresses With Convoluted Foam Mattresses

An LAL bed consists of multiple inflatable fabric pillows attached to a modified hospital bed frame. An electrical blower (fan) maintains comfortable buoyancy of the pillow as the heated air escapes from the fabric air sacks. This design allows subjects to assume a variety of elevated foot, knee, and head positions. Two RCTs compared LAL beds to convoluted foam mattress overlays in the treatment of pressure ulcers (Table 49).

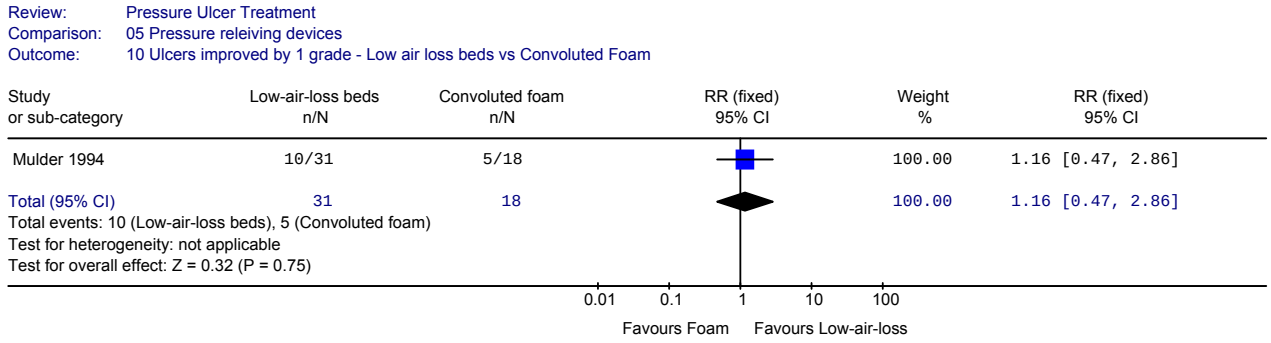
Table 49: Randomized Controlled Trials Comparing Low-Air-Loss Mattress With Convoluted Foam Mattresses

Study	Patients	Comparison	Ulcer Stage	Mean Age (years)	Duration	Outcome Measures: LAL Bed vs. Comparator
Ferrell et al., 1993 (101)	Nursing home N = 43/41	Low-air-loss bed (Kinair) vs. 10 cm Convoluted foam mattress overlay	II, III, or IV On trunk, buttock or trochanters	85 vs. 4	Until ulcers healed Median 33 vs. 40 days	Ulcers healed Median rate of decrease in ulcer size 9.0 vs. 2.5 (*P* = .0002)
Mulder et al., 1994 (102)	Nursing home N = 31/18	Pulsating low air loss (Therapulse) vs. convoluted foam mattress overlay (Geomatt)	III or IV	Not reported	Maximum 12 weeks	Ulcers healed Proportion of ulcers Improved by 1 grade: 10/31 vs. 5/18 % change in area from baseline Percent change was 77% higher for the Low-air-loss
Day and Leonard 1993(103)	Hospital N = 44/39	Air suspension bed (Therapulse®) vs. geometric foam (GeoMatt®)	II, III, or IV	75.09 vs. 77.13	Unclear	No statistical between-group difference in healing of pressure ulcers (*P* > .05)

Ferrell et al. (101) compared a LAL bed and 10-inch convoluted foam mattress overlay in the treatment of stage II to IV pressure ulcers. Forty-three elderly nursing home residents were given an LAL bed while 41 residents were given the convoluted foam mattress overlay. All patients were turned every 2 hours and provided with nutritional support and infection control as needed. There were no significant differences in the stage and size of the ulcer at baseline. After a follow-up period of up to 90 days (median 33 days for LAL beds and 40 days for foam overlay), no significant differences were found in the proportion of patients with complete closure of their ulcers. Patients given an LAL bed had a significantly higher median rate of reduction in ulcer size compared with patients who received a convoluted foam overlay (median 9.0 mm^2/day vs. 2.5 mm^2/day). The improvement in healing rate was observed in both shallow ulcers (stage II) and in deep ulcers (stages III and IV). Cox regression modeling that adjusted for fecal continence and depth of pressure ulcer yielded a hazard ratio of 2.66 [likelihood to heal was 2.66 (95% CI, 1.34–5.17); P = .004] in favour of LAL.

In another RCT by Mulder et al. (102), 41 nursing home residents were given a LAL bed consisting of cushions that provide pulsating air suspension by alternately partially inflating and deflating cushions in the bed. Control patients (N = 18) were given a convoluted foam mattress overlay. Patients were well matched in age, nutritional status, mobility, and stage of ulcers. Ten patients were excluded from the analysis. At the end of the 12-week study period, there were no significant differences in complete healing (16% vs. 17%) or in proportion of ulcers that improved from stage IV to stage III (32% vs. 28%) (Figure 40). After adjusting for the differences in initial stage, decrease in area of the ulcer from baseline was 77% higher in the LAL group compared with the control group (P < .042), but there were no significant differences in the percentage change in volume between the groups (P = .17).

Figure 40: Forest Plot of Ulcers Improved by One Grade – Low-Air-Loss Mattress versus Convoluted Foam Mattresses*

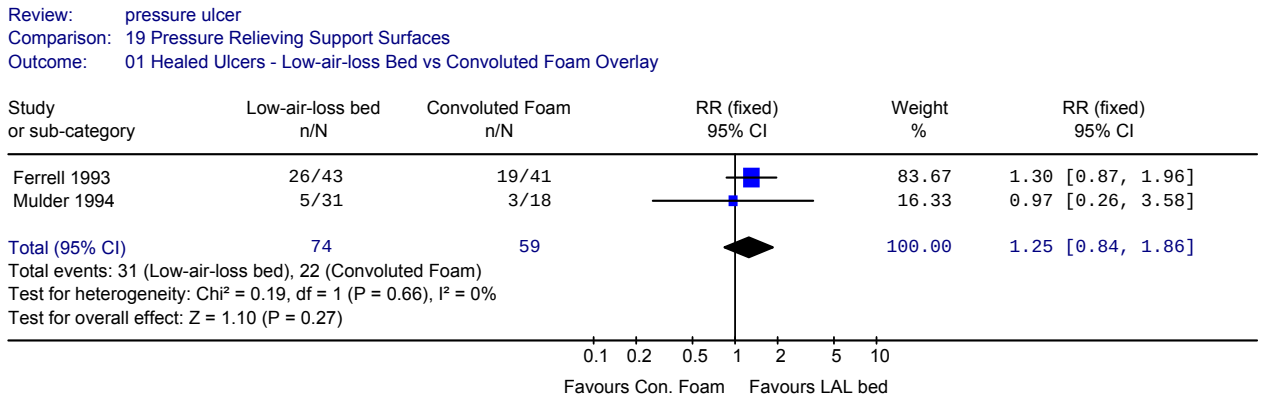


*CI indicates confidence interval; RR, relative risk.

Day et al. also compared air suspension beds to a geometric foam mattress in 83 hospital patients with stage II to stage IV ulcers. The outcome measure was reduction in the area of the ulcer. For all ulcers, covariance analysis showed no statistically significant difference in the healing of pressure ulcers between groups. Analysis by ulcer stage showed that the proportion of stage III or IV ulcers with healing greater than 10 cm^2 was significantly higher in the air-suspension bed group compared with the foam mattress overlay group.

The Forest plot of the 2 studies that reported complete healing showed no statistically significant differences in the proportions of ulcers with complete closure at 12 weeks [RR 1.25 (95% CI, 0.84–1.86); P = .27]. The test for heterogeneity was significant.

Figure 41: Forest Plot of Ulcers Completely Healed at 12 Weeks – Low-Air-Loss Beds Versus Convoluted Foam Mattresses*



*CI indicates confidence interval; RR, relative risk.

Despite a lack of statistical heterogeneity, there was clinical heterogeneity as one study included only deep ulcers (stage III and IV) whereas the other study also included stage II ulcers. There were limitations in the quality of both studies. Despite randomization in the study by Mulder et al., (102) the number of patients in the control group was about 60% of that in the LAL group. Twenty percent of patients were excluded from analysis in this study and the distribution of the excluded patients between groups was not reported. In the study by Ferrell et al., 9 patients were prematurely removed from the assigned treatment in the control group because of failure to heal in a reasonable time. (101)

In summary, the use of LAL beds was associated with greater and faster reduction in ulcer surface area but did not result in a significant improvement in complete healing of ulcers compared with treatment on convoluted foam mattress overlays.

Comparison 3: Alternating Pressure Mattress, Replacements, and Overlays

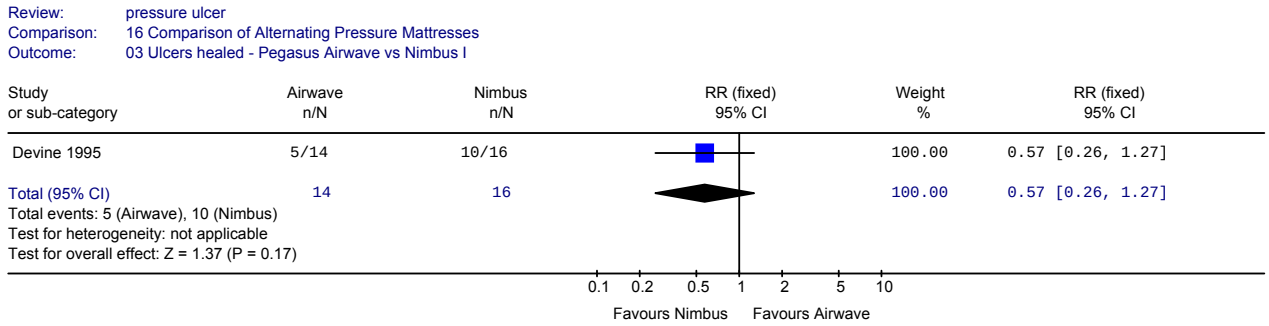
Three RCTs compared the Nimbus AP mattresses with other AP mattresses (Table 50). Two studies (94;96) compared the Pegasus AP mattresses with the Nimbus AP mattress in treating pressure ulcers (≥ stage II) in hospitals. In a 1995 RCT, Devine et al. (94) compared the healing rate of pressure ulcers in 19 patients given a Pegasus Airwave AP mattress with that of 22 patients assigned to a Nimbus I Dynamic Floatation AP mattress. The Pegasus AP mattress consists of double layers with a 3-cell alternating cycle of 7.5 minutes. The Nimbus I Dynamic Floatation AP mattress consists of rows of figure of 8 shaped cells with the two alternating sets of cell inflated and deflated over a 10-minute cycle. Standardized protocol for the use of wound dressings was reported but no details were provided. The withdrawal rate was 26% for the Pegasus group and 27% for the Nimbus group. No statistical significant differences were detected in the overall complete healing rates between the study arms after 4 weeks (Figure 42).

Table 50: Randomized Controlled Trials Comparing Alternating Pressure Mattresses*

Study	Population	Comparator	Ulcer Stage	Mean Age (years)	Duration	Outcome Measures: Impact on Wound Healing
Devine 1995 (94)	Hospital N = 19/22	Airwave AP vs. Nimbus AP	≥ II	84 (SD, 8) vs. 81 (SD, 5)	4 weeks	Ulcers healed Airwave 5/14 Nimbus 10/16 Ulcers healed or improved based on patients who completed the study Airwave 11/14 Nimbus 14/16
Russell 2000a (96)	Hospital N = 71/70	Cairwave AP plus Proactive cushion vs. Huntleigh Nimbus 3 AP plus Aura cushion	≥ II	84.6 (SD, 6.2) vs. 83.9 (SD, 5.9)	18 months	Overall improvement (patients) Cairwave = 65/71 Nimbus = 65/70 Sacral ulcers healed Cairwave = 32/71 Nimbus = 36/70 Heel ulcers healed Cairwave = 19/58 Nimbus = 30/55 Sacral and heel ulcers healed Cairwave = 51/129 Nimbus = 66/125
Evans et al., 2000 (95)	Hospital N = 12 (7/5) Nursing home N = 20 (10/10)	Nimbus 3 AP vs. Another AP	III or II plus mobility problem	68 (SD, 3.4) vs. 78 (SD, 3.2)	Unclear-varied	Ulcers healed Absolute and relative decrease in ulcer size/day Comfort

*AP indicates alternating pressure; SD, standard deviation.

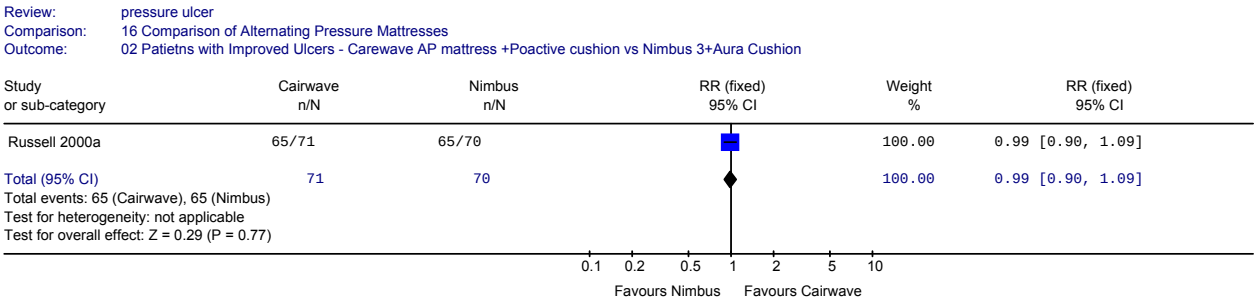
Figure 42: Forest Plot of Ulcers Healed – Airwave Alternating Pressure Mattress versus Nimbus I Alternating Pressure Mattress*



*CI indicates confidence interval; RR, relative risk.

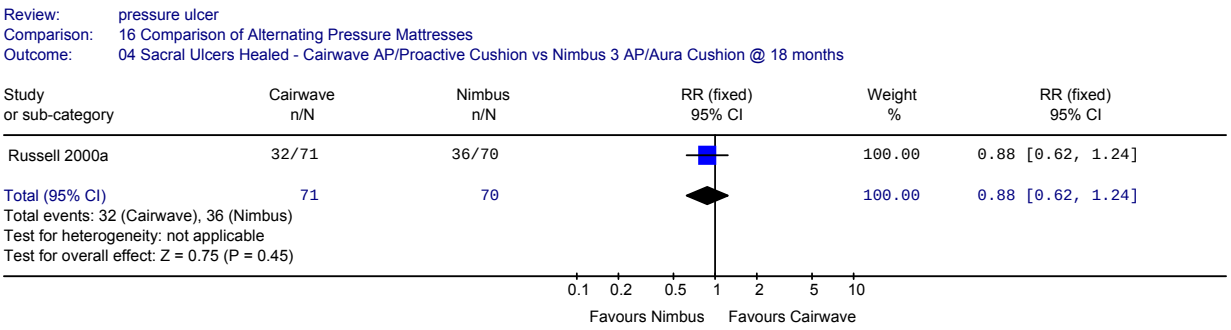
Russell et al. (96) compared the Pegasus Cairwave AP mattress combined with the Proactive cushion to the Nimbus 3 AP mattress combined with the Aura cushion. The Nimbus 3 mattress is similar to the Nimbus I but includes 5 heel-guard cells that are powered down during deflation. One-hundred and forty-one patients completed the 18-month study but its unclear how many ulcers were included as only the number of sacral and heel ulcers were reported. Both groups achieved overall improvement of ulcers in 90% of the patients (Figure 43) and complete healing of approximately 50% of sacral ulcers (Figure 44). There were no significant differences in the length of stay or patient comfort score. The Nimbus 3 used in conjunction with the Aura cushion resulted in a significantly higher healing rate of heel ulcers compared with the Cairwave AP mattress and Proactive cushion combination (Figure 45).

Figure 43: Forest Plot of Patients With Overall Improvement in Pressure Ulcer – Cairwave Alternating Pressure Mattress Plus Proactive Cushion Versus Nimbus 3 Alternating Pressure Mattress Plus Aura Cushion*



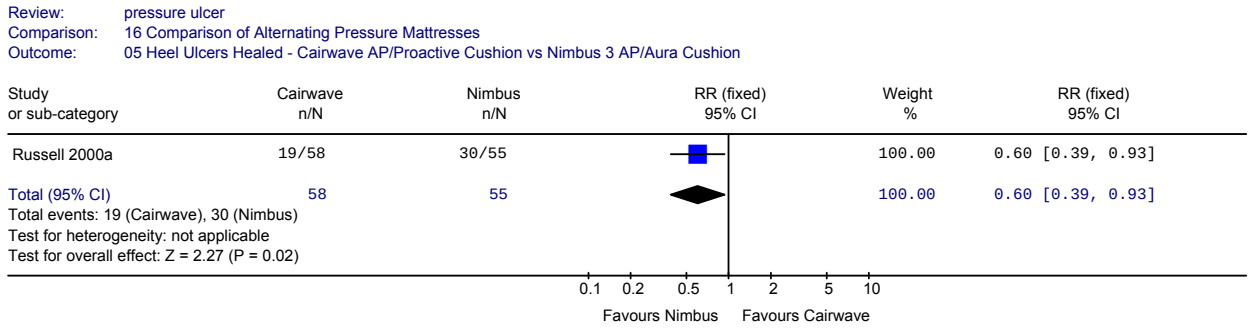
*CI indicates confidence interval; RR, relative risk.

Figure 44: Forest Plot of Sacral Ulcers Healed – Cairwave AP/Proactive Cushion Versus Nimbus 3 AP/Aura Cushion*



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

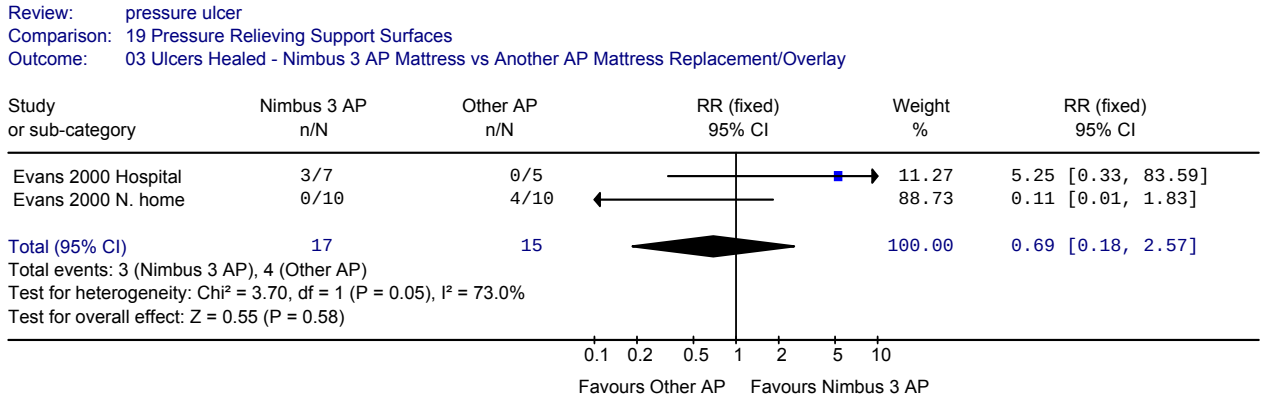
Figure 45: Forest Plot of Heel Ulcers Healed – Cairwave AP/Proactive Cushion Versus Nimbus 3 AP/Aura Cushion*



*CI indicates confidence interval; RR, relative risk.

Evans et al. (95) compared the Nimbus 3 AP mattress replacement with other AP support surfaces. Twelve patients in a hospital were randomly allocated to a Nimbus 3 AP mattress replacement or another AP mattress replacement and 20 nursing home residents were randomly assigned to a Nimbus 3 or an AP mattress overlay. The included subjects must have a grade 3 pressure ulcer or a grade 2 with impaired mobility. The same protocol for wound dressing was followed for all 4 groups. At the end of the treatment period, No significant differences were found in complete healing in either the hospital patients (3/7 vs. 0/5) or nursing home patients (0/10 vs. 4/10) (Figure 46). The median absolute or relative decrease in the area of the ulcers was not significantly different between the Nimbus 3 AP group and control group in the hospital setting or the nursing home setting.

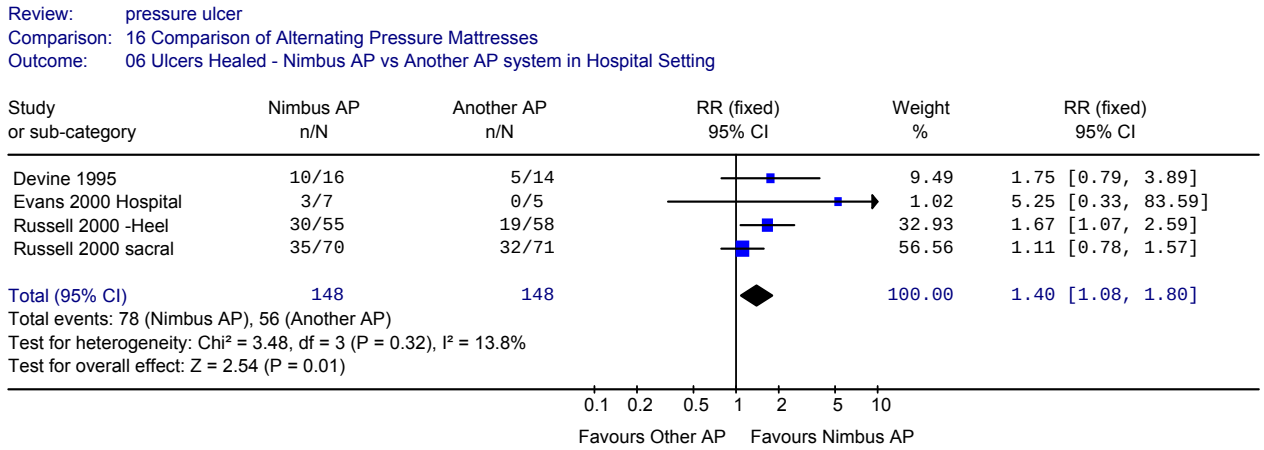
Figure 46: Forest Plot of Healed Ulcers – Nimbus 3 Alternating Pressure Mattress Versus Another Alternating Pressure Mattress Replacement or Overlay*



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

A pooled analysis of the three studies was performed to compare complete healing on Nimbus mattresses to complete healing of another AP system in the hospital setting (Figure 47). The Forest plot showed an RR of 1.40 (95% CI, 1.08–1.80) in favour of Nimbus AP mattresses (P = .02). The test for heterogeneity is not significant (I^2 = 20.2, P = .29). The advantage of the Nimbus 3 mattress appears to be mainly due to improved complete healing in heel ulcers.

Figure 47: Nimbus Alternating Pressure Mattresses Versus Another Alternating Pressure Mattress Replacement or Overlay in Hospital Setting*



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Comparison 4: RIK Static Fluid Overlay Versus Nimbus 3 Alternating Pressure Mattresses

In another RCT, Russell et al. (97) compared the RIK mattress with the Nimbus 3 AP mattress in the treatment of pressure ulcers at stage I or higher (Table 51). The Nimbus 3 has a 10 minute cycle time , modified heel cells and is equipped with a sensor pad that continually adjusts pressure to the individual patient's position, weight, and size. The RIK mattress is a nonpowered static fluid-filled overlay system that distributes pressure evenly by allowing the patient to sink into a fluid surface. Patients with at least a stage I pressure ulcer were randomized to receive either a Nimbus 3 AP mattress (N = 83) or to the RIK static mattress (N = 75). There were no statistically significant differences in baseline parameters. Patients in both groups were turned at least once every 4 hours. No additional pressure relieving equipment was used under any pressure area during the study. Ulcers were assessed and photographed weekly. At trial completion, the difference in ulcer improvement was not statistically significant, whether measured based on all ulcers or on the worst ulcers (Figures 48–49). Thirteen patients in the RIK group were transferred to a Nimbus 3 AP mattress.

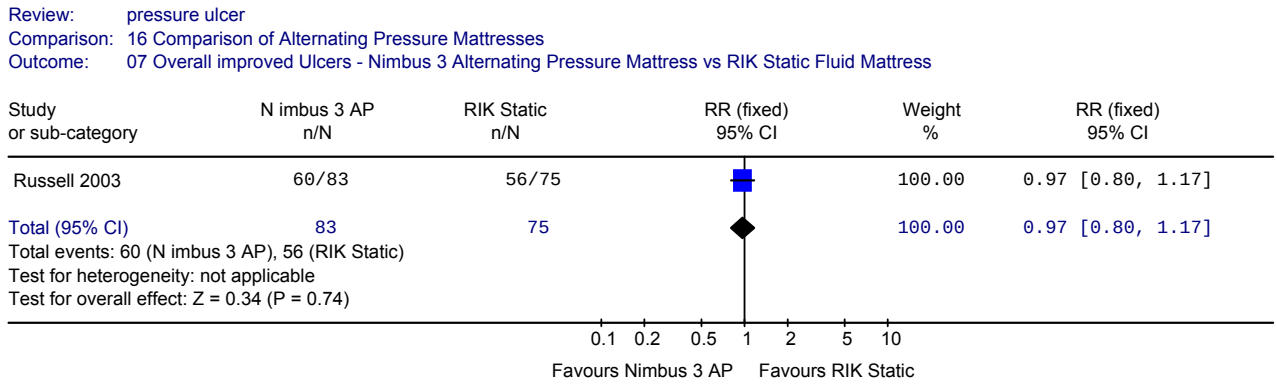
In summary, the Nimbus 3 AP system does not appear to be superior to other AP systems in promoting complete healing of stage II to IV pressure ulcers with the exception that it is appears to be more efficacious in healing heel ulcers. There is evidence to suggest that static fluid-filled mattresses may be as effective as a Nimbus 3 AP mattress in promoting heeling of pressure ulcers.

Table 51: Randomized Controlled Trial Comparing Nimbus 3 AP Mattresses With RIK Static Fluid-Filled Mattresses*

Study	Population	Comparator	Ulcer Stage	Mean Age, Years (SD)	Study Duration	Outcome Measures: Impact on Wound Healing
Russell 2003 (97)	Hospital inpatient 83/75	Nimbus 3 AP mattresses vs. RIK Static fluid-filled mattresses	≥ Stage I Change to alternative mattress if worsened to grade 3	80.39 (9.95) vs. 79.76 (9.74)	Not reported	Improved ulcer – overall 60/83 (72.3%) vs. 56/75 (74.7%) *P* = .74 Improved – worst ulcer 63/83 (75.9%) vs. 63/75 (84.0%) *P* = .20 Control upgraded to AP system : 17.3% Average length of stay 22.17 days vs. 20.05 days; *P* = .23

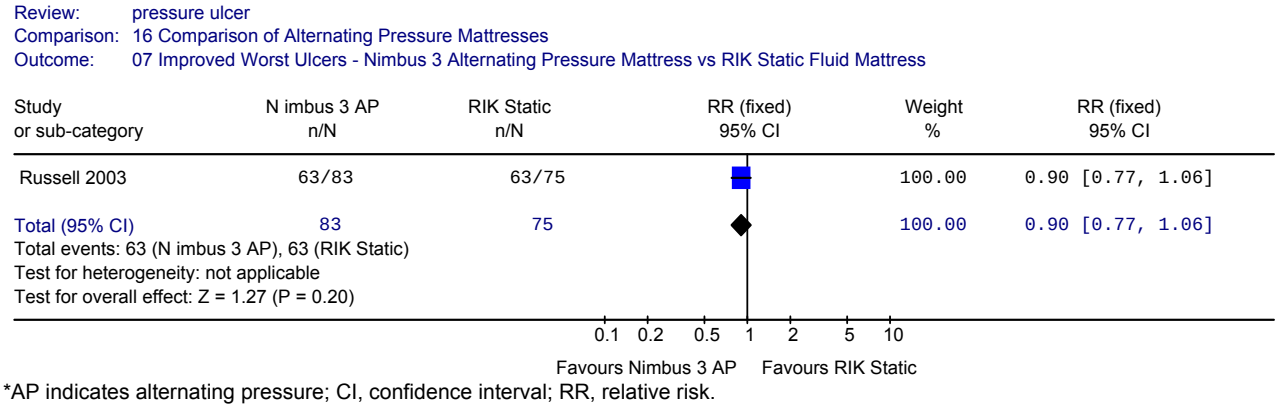
*AP indicates alternating pressure; SD, standard deviation.

Figure 48: Overall Improved Ulcers – Nimbus 3 Alternating Pressure Mattress Versus RIK Static Fluid Mattresses*



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 49: Improved Worst Ulcers – Nimbus 3 Alternating Pressure Mattress Versus RIK Static Fluid Mattresses*



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Comparison 5: Alternating Pressure Mattress Overlays Versus Alternating Pressure Mattress Replacements

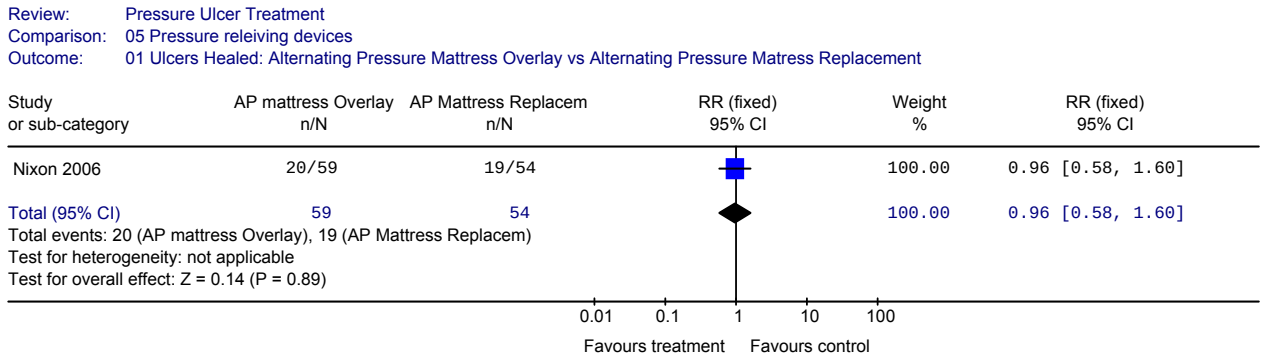
Nixon et al. (91) conducted an open RCT that randomized 1,972 patients who were completely immobile or had very limited mobility and/or had a pre-existing grade 2 ulcer to either an AP mattress overlay (N = 989) or to an AP mattress replacement (N = 982). Patients were followed for a maximum duration of 60 days after randomization. The secondary end of this study was the number of patients with pre-existing grade 2 ulcers that healed (Table 52). At randomization, a pre-existing ulcer was present in 59 patients in the AP mattress overlay group and in 54 of the AP mattress replacement group. At the end of the study period, the existing pressure ulcer in 33.9% (20/59) in the AP mattress overlay group and 35.2% (19/54) of the AP mattress replacement group had healed. This difference is not statistically significant [RR 0.96 (95% CI, 0.58–160), *P* = .89] (Figure 50). Median time to healing was 20 days for both groups. The development of new grade 2 ulcers, the primary endpoint, was also not significantly different between the 2 groups (10% vs. 9.3%, *P* = .58). (91)

Table 52: Randomized Controlled Trial Comparing Alternating Pressure Mattress Overlays With Alternating Pressure Mattress Replacements in the Treatment of Pressure Ulcers*

Study	No. of Patients With Existing Ulcer(s)	Ulcer	Mean Age (years)	Mean Baseline Ulcer Size (cm^2)	Duration (weeks)	Outcome Measures:
Nixon et al., 2006 (91)	Overlay vs. replacement N = 59/54 (Entire study 989/982)	Grade 2	AP mattress overlay = 75.4 (SD, 9.7) AP mattress replacement 76.0 (SD, 9.2)	Overlay = 2.3 (SD, 4.4) Replacement = 3.9 (SD, 7.9)	= 8.6 (60 days)	Complete healing 20/59 vs. 19/54 Mean time to healing: 20 (12 not estimable) vs. 20 (12 not estimable)

*AP indicates alternating pressure; SD, standard deviation

Figure 50: Forest Plot of Ulcers Healed – Alternating Pressure Mattress Overlay Versus Alternating Pressure Mattress Replacement



*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

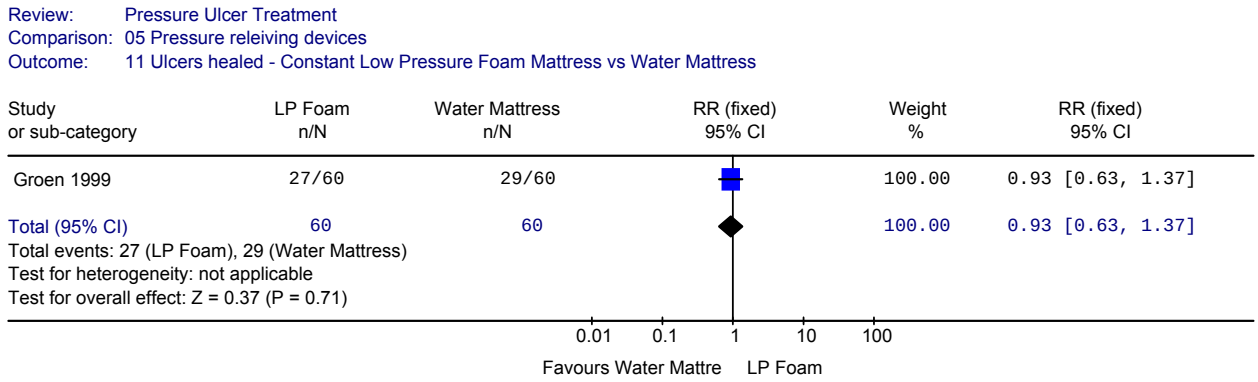
Comparison 6: Constant Low Pressure Mattress versus Water Mattress

Groen et al. (104) compared a constant low-pressure foam mattress replacement with a water mattress in the healing of stage III and IV pressure ulcers (Table 53). In this multicentre RCT, 60 nursing home residents were treated on the TheraRest constant low-pressure foam replacement mattress consisting of three layers of polyurethane foam with adjustable angle. Another 60 residents were given the Secutex water mattress consisting of three PVC sections, each holding 26 litres of water with heating elements (this mattress cannot be adjusted at an angle). The ulcers in both groups were treated in accordance with hospital guidelines including turning every 2 hours. At the end of the 4-week treatment period, complete healing occurred in 45% of the residents on the constant low pressure foam mattress replacement and in 48% of residents on the water mattress. The difference in healing rates did not reach statistical significance [RR 0.93, (95% CI, 0.63–1.37), P = .71] (Figure 51). (104)

Table 53: Randomized Controlled Trial Comparison: Foam Mattress versus Water Mattress*

Study	Population	Comparator	Ulcer Stage	Mean Age (years)	Duration (weeks)	Outcome Measures: Impact on Wound Healing
Groen 1999 (104)	Nursing homes (3) Age ≥60 yrs. N = 60/60	TheraRest vs. water mattress	III or IV	81.9 vs. 83.5	4	Complete healing 45% vs. 48% Adverse events Slight pain at start 40% vs. 20%

Figure 51: Forest Plot of Ulcers Healed – Constant Low Pressure Foam Mattress versus Water Mattress*



*CI indicates confidence interval; LP, low pressure; RR, relative risk.

Comparison 7: Electric Profiling Bed versus Flat-Based Beds

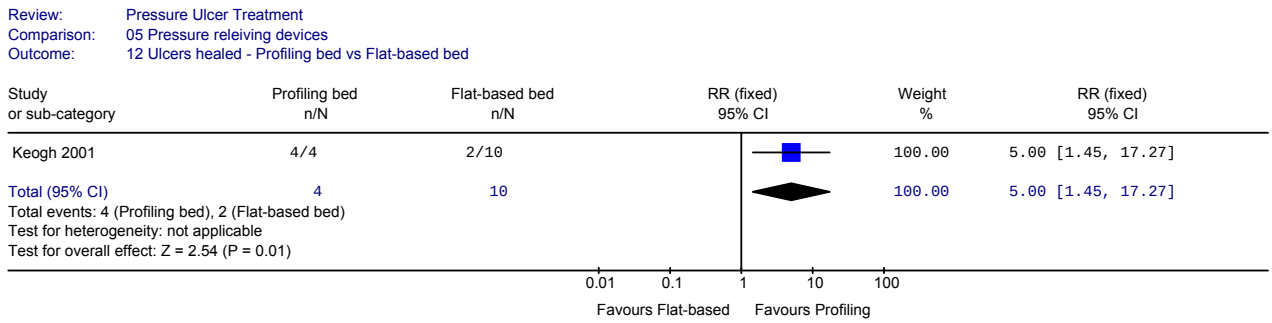
Electrically operated profiling beds were compared to standard flat hospital beds in one RCT examining the prevention and treatment of stage I pressure ulcers (Table 54). Keogh et al. (105) randomized 70 hospital inpatients to either the electrically operated beds (Contoura 880, Huntleigh Health Care) (N = 35) or to standard hospital beds (N = 35). A pressure reducing foam mattress was used in both groups. The standard hospital bed was a hydraulic, foot-pumped device with a flat base and a pull out backrest. Patients sitting on these beds tend to slide down the bed and often have difficulty adjusting their position or the height of the bed without help. The 4-section profiling bed facilitates the movement of patients, reducing the need for manual handling. (105) When out of bed, all patients in the study sat on a pressure-redistributing cushion or seat according to hospital policy. An existing stage I pressure ulcer was found in 4 subjects in the group that received a profiling bed and in 10 patients that received a flat-based bed.

At the end of the maximum period of 10 days, all 4 ulcers in profiling bed group and 2 in the flat-based bed groups had healed. This difference was statistically significant (RR = 5.0; *P* = .01), but there was much uncertainty around the RR because of the wide CI (95% CI, 1.45–17.27) as a result of the small sample size. No new grade 1 ulcers developed in either group. (105)

Table 54: Randomized Controlled Trials Comparing Electric Profiling Bed With Flat-Based Beds in the Treatment of Pressure Ulcers

Study	Population	Comparator	Ulcer Stage	Mean Age (years)	Duration (days)	Outcome Measures: Impact on Wound Healing
Keogh 2001 (105) Prevention and treatment study	Hospital Patients with ulcer N = 70 (35/35)	Electrically operated 4-section profiling bed vs. standard flat hospital bed Both with pressure relieving mattress	I	68.7 (40–90) vs. 71.3 (42–86)	Maximum 10	Incidence of new ulcers 0% in both groups Complete healing of existing stage I ulcers 4/4 vs. 2/10

Figure 52: Forest Plot of Ulcers Healed – Profiling Bed Versus Flat-Based Bed*



*CI indicates confidence interval; RR, relative risk.

Comparison 8: Pressure-Relieving Seat Cushions

Three RCTs on pressure redistributing seat cushions were found. In a 1999 RCT, Clark et al. investigated the effect of seat cushions on the healing of stage II to stage IV pressure ulcers (Table 55). (106) Thirty-three elderly patients from acute care hospitals were randomized to receive either a four-cell alternating air pressure cushion (Pro-Active 2®, Pegasus Airwave Ltd.) or to a static air-filled cushion (ROHO Quadtro, Raymar Ltd). The Pro-Active Cushion had four inflatable air sacs powered electrically to inflate and deflate in 12-minute cycles. Eight patients (24%) were withdrawn from the study.

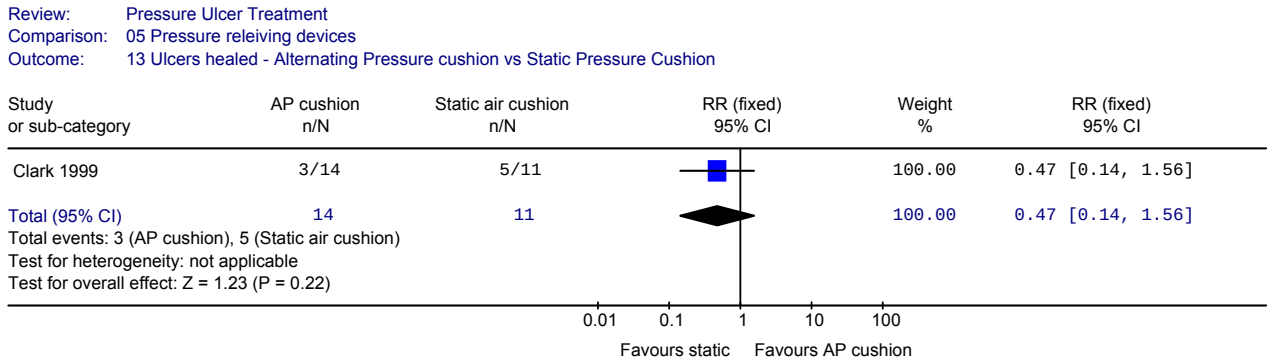
Analysis of the data on the 25 remaining subjects found no statistically significant differences in the occurrence of complete healing or the rate of healing between the study groups (Figures 53–55).

Table 55: A Randomized Controlled Trial Comparing Alternating Pressure Seat Cushion With Static Air Seat Cushion in the Treatment of Pressure Ulcers*

Study	Population	Comparison	Ulcer Stage	Mean Age (years)	Study Duration (days)	Outcome Measures: Impact on Wound Healing (AP cushion vs. static air cushion)
Clark 1999 (106)	Hospital and nursing homes N = 25 (14/11)	AP air seat cushion (N = 14) vs. static air seat cushion	II, III, or IV	AP = 84.78 (SD, 1.27) Static = 80.00 (SD, 2.34) Percent of ulcers stages II:III:IV AP = 50:14:36 Static = 64:9:27 (No significant difference)	Until ulcers healed or patient died or was discharged	Ulcers healed AP = 3/14 Static = 5/11 Rate of <down>in area of ulcer (cm^2/day) 0.13 (SE, 0.10) vs. 0.27 (SE, 0.17) Percent change in ulcer area/day 2.56 (SE, 2.10) vs. 5.7 (SE, 1.68) Rate of reduction in volume of ulcer (cm^3/day) 0.56 (SE, 0.23) vs. 0.56 (SD, 0.26)

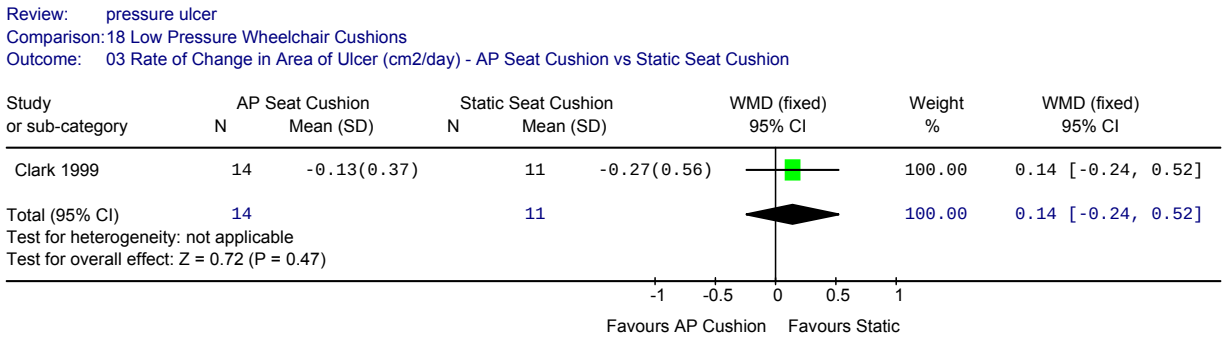
*AP indicates alternating pressure; SD, standard deviation; SE, standard error.

Figure 53: Forest Plot of Ulcers Healed – Alternating Pressure Seat Cushion Versus Static Seat Cushion*



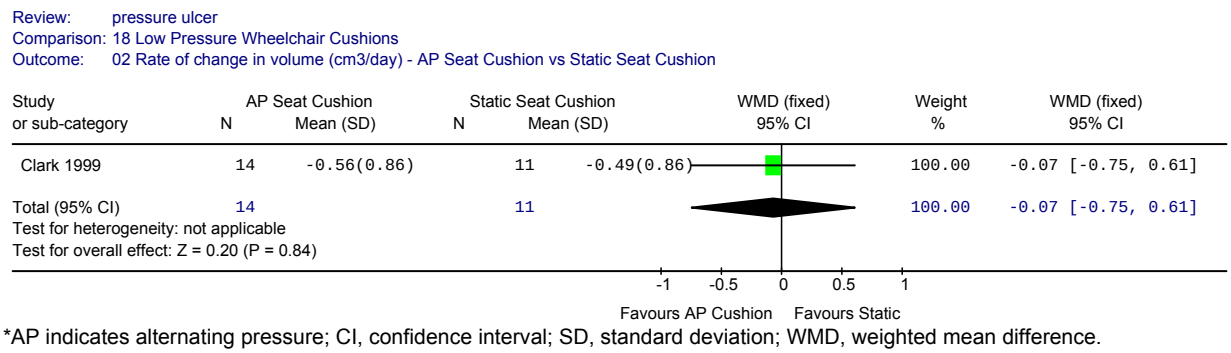
*AP indicates alternating pressure; CI, confidence interval; RR, relative risk.

Figure 54: Forest Plot of Rate of Change in Area of Ulcer – Alternating Pressure Seat Cushion Versus Static Air Seat Cushion*



*AP indicates alternating pressure; CI, confidence interval; SD, standard deviation; WMD, weighted mean difference.

Figure 55: Forest Plot of Rate of Change in Volume of Ulcer – Alternating Pressure Seat Cushion Versus Static Air Seat Cushion*



*AP indicates alternating pressure; CI, confidence interval; SD, standard deviation; WMD, weighted mean difference.

Comparison 9: Generic Total Contact Seat Versus a Low-Air-Loss Bed and Versus a Low Pressure Mattress Overlay

Rosenthal et al. (92) conducted two separate RCTs of stage III and IV pressure ulcers that compared wound healing on three different support surfaces: a total contact seat, a LAL bed, and a low pressure mattress overlay (Table 56).

Table 56: Randomized Controlled Trial Comparing a Generic Total Contact Seat With a Low-Air-Loss Bed and a Mattress Overlay*

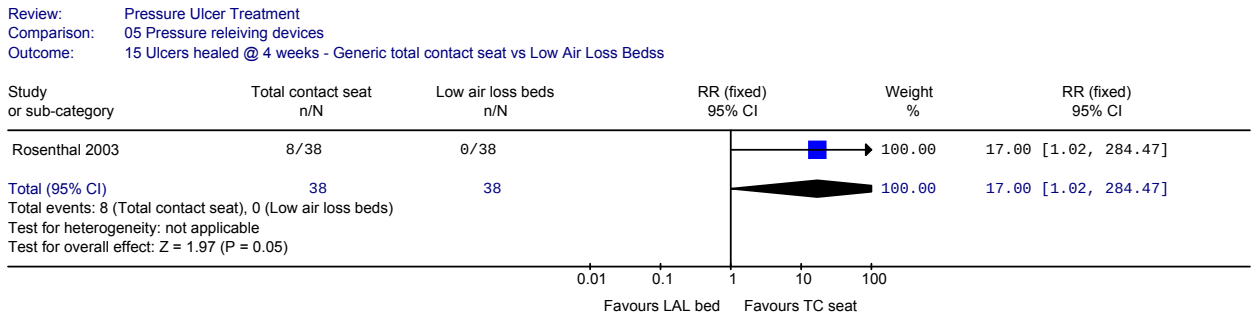
Study	Population	Comparison	Ulcer Stage	Mean Age (years)	Study Duration	Outcome Measures: Impact on Wound Healing
Rosenthal 2003 (92) (Study 1)	LTC	Total contact seat vs. low–air-loss bed vs. LP foam overlays N = 38/38/38	III or IV	70.4 (4.5) vs. 69.0 (4.1) vs. 68.6 (3)	6 months	Primary: Median time to total healing (months) 3.33 (0.12) vs. 4.38 (0.14) vs. 4.55 (0.22) Total contact seat shorter time ($P < .001$) Complete healing at 4 weeks better with total contact seat 8/38 vs. 0/38 vs. 0/38 PSST score at 4 weeks 9.65 (7.73) vs. 25.39 (11.98) vs. 36.00 (12.15) ; ($P < .001$) Functional outcome (Katz ADL score)
Rosenthal 2003 (92) (Study 2)	LTC	Total contact seat vs. low-air-loss bed N = 47/47	III or IV	68.0 (3.8) vs. 68.7 (3.9)	4 weeks	PSST score at 4 weeks: 24.17 (11.08) vs. 39.30 (12.19)

*ADL indicates activities of daily living; LP, low pressure; LTC, long-term care; PSST, Pressure Sore Status Tool.

In the first study, Rosenthal et al. (92) randomized 108 patients to either sitting on a generic total contact seat (maximum 4 hours) or to an LAL suspension bed (TheraPulse) preset for body weight, height, girth, and optimum air-flow, or to a pressure reducing 8.89 cm medium density open-cell polyurethane foam overlay (Geo-Matt). The generic total contact seat redistributed the weight from pressure sensitive bony prominences (ischial tuberosities and the coccyx) onto less pressure sensitive areas (thighs and lateral pelvis). The seat was individually fitted to each subject's anatomy. The LAL bed consisted of a rack of inflatable fabric pillows attached to a modified bed frame to provide pulsating air support. In the second study, 47 patients that received the same generic total contact seat were compared with 47 residents that received the LAL bed.

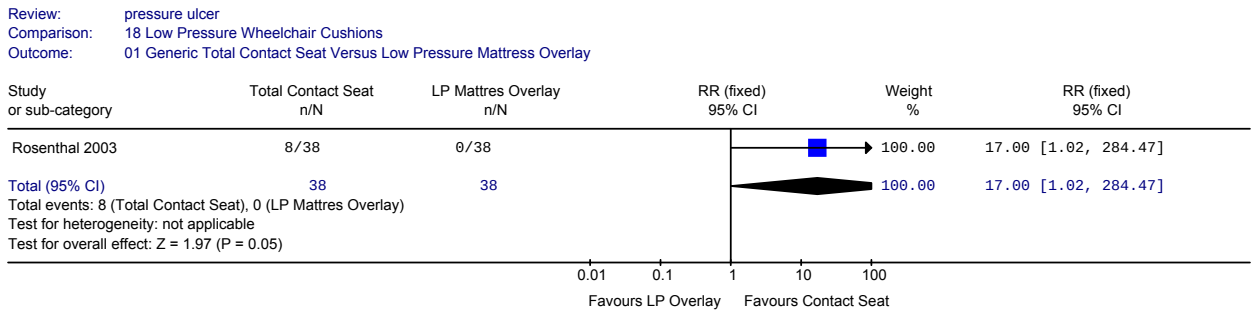
Treatment groups did not differ significantly in baseline parameters. In Study 1, contrast estimates showed that PSST scores on the total contact seat were significantly lower (better) than on the LAL bed ($P < .001$) or on the low pressure foam overlay ($P < .001$) (Table 56). PSST improvement on the generic seat was also significantly greater than that in the other 2 support surfaces ($P < .001$ for both contrasts). The generic contact seat was also associated with significantly better PSST compared with the LOL beds in Study 2. In Study 1, 8 subjects that received the total contact seat had a completely healed pressure ulcer after 4 weeks treatment while no complete healing occurred in the other 2 groups (Figure 56). The RR of 17 is only marginally statistically significant and the wide CI (1.02–284.47) precludes any firm conclusion on the impact of generic total contact seat on complete healing (Figures 56 and 57). (92)

Figure 56: Forest Plot of Ulcers Healed – Total Contact Seat Versus Low-Air-Loss Bed*



*CI indicates confidence interval; RR, relative risk.

Figure 57: Forest Plot of Ulcers Healed – Total Contact Seat Versus Low Pressure Foam Mattress Overlay*



*CI indicates confidence interval; LP, low pressure; RR, relative risk.

The patients from the 2 studies were combined for analysis of time to total healing. Eight patients in the overlay group were withdrawn from Study 1 because of worsened condition. Kaplan-Meier analysis showed that the median time to complete healing was significantly shorter in the total contact seat group compared with the LAL bed (3.33 months vs. 4.38 months, log rank = 28.03, $P < .001$) and with low pressure foam overlay (3.33 months vs. 4.55 months, log rank = 20.64, $P < .001$). Functional outcomes measured using the 12-point Katz score at 4 weeks were significantly better with the total contact seat (6.6, SD 1.85) compared with the LAL bed (3.1, SD 1.23) and with the low pressure foam overlay (1.9, SD 0.62) ($P < .001$ for both comparisons). (92)

Comparison 8: Pressure Relieving Devices for the Heel

Pressure ulcer of the heel is one of the most common pressure ulcers for bed-ridden patients. Only 1 RCT examined the influence of special beds and surfaces on the healing of heel ulcers. Russell et al. (96) reported that the Nimbus 3 AP bed with a heel guard that can be powered down resulted in a statistically significant increase in completely healed heel ulcers at 18 months compared with the Pegasus Cairwave mattress that did not have a heel guard [RR 1.67 (95% CI, 1.07–2.59), $P = .02$].

Other special devices have also been designed to relieve pressure from the heel. These are mainly ankle-foot orthoses such as sheepskin boots and special heel protectors that essentially float the heel, eliminating contact with the support surface. These devices can be used in conjunction with stabilizer wedges; however, the literature searches failed to identify comparative studies that explored the influences of these devices on the healing of heel ulcers. (96)

Table 57: Alternating Bed With Heel Guard Versus Alternating Bed Without Heel Guard*

Study	Population	Comparison	Ulcer Stage	Mean Age (years)	Study Duration	Outcome Measures: Impact on Wound Healing
Russell et al., 2000 (96)	Hospital N = 70/71	Nimbus 3 AP plus Aura cushion vs. Cairwave AP plus Proactive cushion	≥ II	84.6 (SD, 6.2) vs. 83.9 (SD, 5.9)	18 months	All ulcers healed Sacral ulcers healed Heel ulcers healed

*AP indicates alternating pressure; SD, standard deviation.

Summary of Analysis –Pressure Relieving Support Surfaces and Devices

Table 58: Summary of Impact of Pressure Relieving Devices on Complete Healing of Pressure Ulcers*

Comparison	No. of Studies	No. of Ulcers	Relative Risk (95% CI)	I^2 (%)	*P* Value	Quality of Evidence
†Nimbus AP mattress vs. another AP mattress	3	214	1.27 (0.75, 2.13)	33%	.37	NE
Nimbus 3 AP vs. another mattress on Heel ulcers	1	111	1.67 (1.07, 2.59)	NA	.02	Low
AP mattress overlay vs. AP replacement	1	113	0.96 (0.58, 1.60)	NA	.89	NE
Low-air-loss bed vs. convoluted foam mattress	2	133	1.25 (0.84, 1.86)	0%	.27	NE
CLP Foam vs. water mattress	1	120	0.93 (0.63, 1.37)	NA	.71	NE
Profiling bed vs. flat-based bed	1	14	5.0 (1.45, 17.27)	NA	.01	Moderate
AP Seat cushion vs. static cushion	1	25	0.47 (0.14, 1.56)	NA	.22	NE

*AP indicates alternating pressure; CI, confidence interval; I^2, test for heterogeneity; LP, low pressure; NA, not applicable, NE, not evaluated
† meta-anlaysis not shown in report, includes Devine 1995, Russell 200a, and Evans 2000 reported in table 50.

Table 59: Summary of Impact of Pressure Relieving Devices on Improved Ulcer Healing*

Comparison	No. of Studies	No. of Ulcers	Relative Risk (95% CI)	I^2 (%)	*P* Value
Air-fluidized bed vs. AP mattress	2	105	1.40 (1.04, 1.88)	0%	.03
Rate of healing: AP air seat cushion vs. static air cushion (cm^2/day)	1	25	–0.14 (–0.25, –0.63)	NA	.02

*AP indicates alternating pressure; CI, confidence interval; I^2, test for heterogeneity; NA, not applicable.

Summary Statements – Pressure-Relieving Support Surfaces

- There were no comparisons between specialized beds with standard foam mattresses as treatment.
- An AP mattress with a heel guard that can be powered down was associated with significantly more closure of heel pressure ulcers than AP beds without a heel guard [RR 1.67 (95% CI, 1.07–2.59)].
- A profiling bed was associated with a significantly higher percentage of healed stage I pressure ulcers than a flat-based bed [RR 5.0 (95% CI, 1.45–17.27)].
- Patients ambulated to a generic total contact seat for up to 4 hours per day had better healing of stage III or IV ulcers compared with patients confined to a LAL bed or a medium density foam mattress overlay [RR 17 (95% CI, 1.02–284.47)] .
- Support from air-fluidized beds was associated with significantly more improved ulcers than AP beds or mattresses.
- The studies failed to detect a statistically significant difference in complete closure of pressure ulcers (≥ stage II) between the following treatments:
    - A LAL bed and a convoluted foam mattress
    - A constant low pressure foam and a water mattress
    - An AP mattress replacement and an AP mattress overlay
    - One AP mattress and another AP mattress

An AP seat cushion and a static cushion (although the rate of healing was significantly higher with the AP seat cushion).

Adjunctive Physical Therapies

Hydrotherapy

Only one randomized controlled study on the use of whirlpool as an adjuvant therapy for pressure ulcer was identified (Table 60). The study compared patients from the medical wards of two acute care hospitals that presented with one or more stage III or stage IV ulcers. After sharp debridement of necrotic tissues and confirmation of no symptoms of wound infection, the 24 patients randomized to hydrotherapy received 20 minutes of whirlpool therapy at 96°F to 98°F daily in addition to conventional therapy. The 18 patient control group received only conventional therapy consisting of irrigation with normal saline, wet-to-wet cotton dressing, air mattresses, turning every 2 hours, and Roho seat cushions. (20)

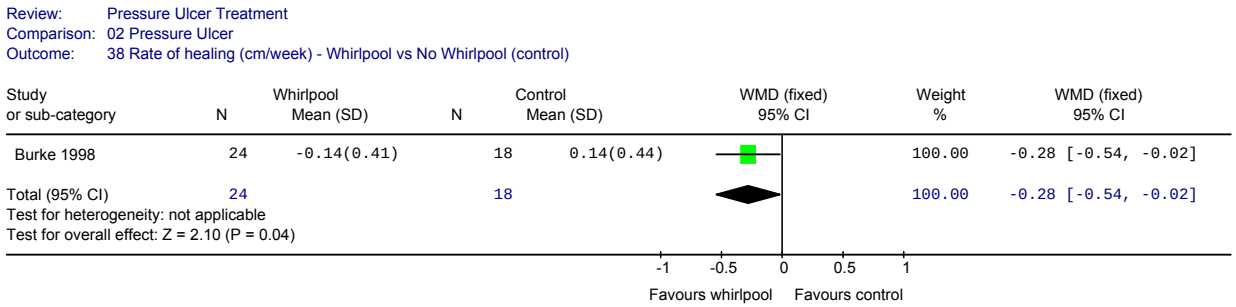
Table 60: Summary of a Randomized Controlled Trial on Whirlpool Therapy*

Study	Population	Comparison	Ulcer Stage	Mean Age	Duration	Outcome Measures: Impact on Wound Healing (AP cushion vs. static air cushion)
Burke, 1998 (20)	Hospital patients N = 24/18	Adjuvant whirlpool therapy (20 minutes/day) vs. conventional therapy only	III or IV	Not reported	≥ 2	Rate of change in size of ulcer measured by change in sum of maximum length and width of ulcer per week = change in (max length + max. width)/duration of treatment in weeks Improved 14/24 vs. 5/18 No change 1/24 vs. 2/18 Deteriorated 9/24 vs. 11/18

*AP indicates alternating pressure.

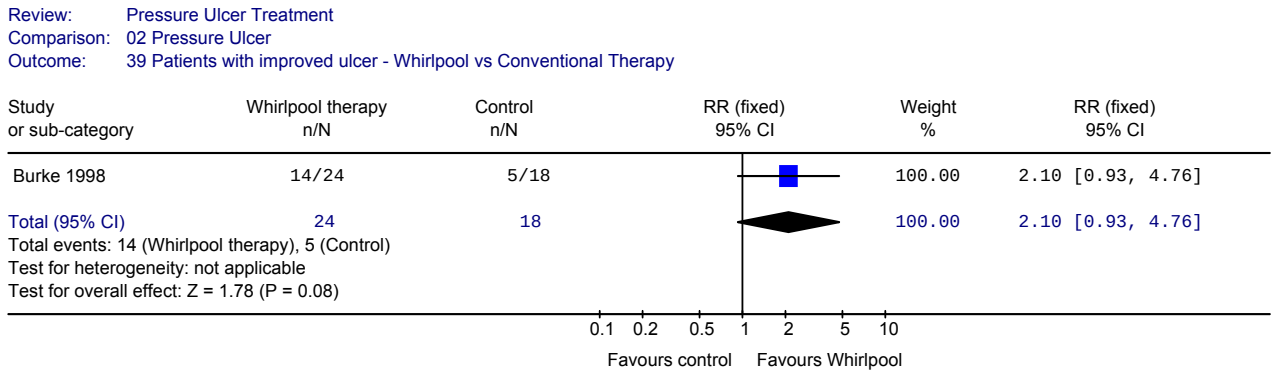
The outcome measure was the weekly change in ulcer size represented by the sum of their maximum length and width. The mean weekly change in ulcer size and SD for each group was calculated using the patient-level data. A Forest plot of the mean and SD showed that patients that received adjuvant hydrotherapy had a significantly higher mean rate of reduction in ulcer measurements compared with patients that received only conventional therapy [WMD = –0.28 cm/week, 95% CI (–0.54 to –0.02), P = .04] (Figure 58). The proportion of ulcers with a mean weekly reduction in the size was also higher in the hydrotherapy group compared with the controls (14/24 vs. 5/18), but the difference was not statistically significant (Figure 59). The proportion of ulcers that deteriorated during the study was not significantly different between the two groups (Figure 60).

Figure 58: Mean Weekly Change in Ulcer Size – Whirlpool Versus Conventional Therapy*



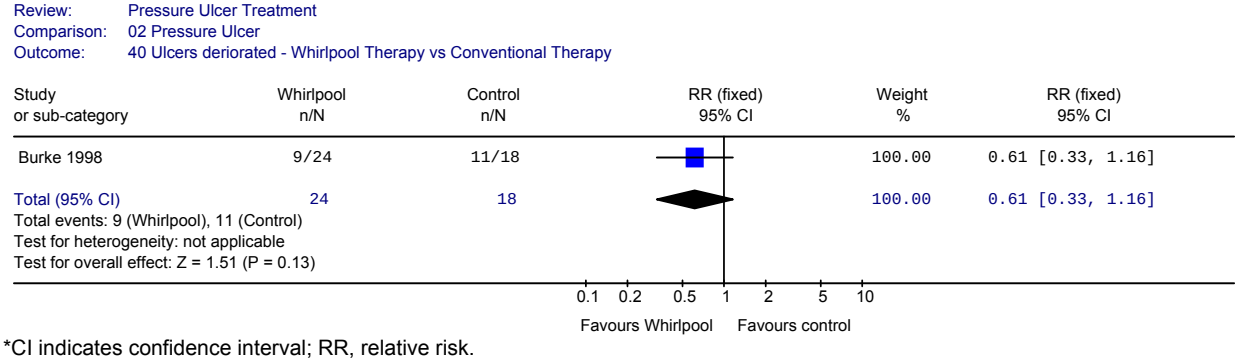
*CI indicates confidence interval; SD, standard deviation, WMD, weighted mean difference.

Figure 59: Proportion of Patients That Experienced a Mean Reduction in Ulcer Measurements per Week – Whirlpool Versus Conventional Therapy*



*CI indicates confidence interval; RR, relative risk.

Figure 60: Forest Plot of Ulcers That Deteriorated During the Study – Whirlpool Therapy Versus Conventional Therapy*



*CI indicates confidence interval; RR, relative risk.

There were, however, quality limitations in the above study. The method of randomization was not described and there was no mention of concealment of allocation. No baseline data on the patients or ulcers were provided and, it was thus not possible to determine whether the patient groups were similar at baseline. The minimum follow-up was 2 weeks but the mean and maximum follow-up periods were not reported.

Electrical Stimulation Therapy

Pressure ulcers are characterized by abnormally low electrical potentials, resulting in voltage gradients compared with the surrounding healthy tissue (Bradock et al., 1999) This forms the basis for the use of electrical stimulation to treat pressure ulcers. Early research suggests that electrical stimulation may initiate or accelerate the wound healing process through different mechanisms. Electrical stimulation devices can provide a direct current (monopolar or bipolar) or both direct and alternating currents. Therapeutic electric currents can be delivered into the wound and/or periwound tissue through electrodes applied directly to the patient's skin (Table 61).

Table 61: Types of Electric and Electromagnetic Stimulation*

	Low Voltage Direct Current	Pulsed Direct Current	Low Voltage Alternating Current	Pulsed Electromagnetic Therapy
Voltage magnitude available	Low (< 8 volts)	High (6–200 v)	Low (<10 volts)	NA
Current type	Direct current	Direct current	Alternating current	Alternating current
Average current intensity	20–999 uA	0.3–2.5 mA	15–25 mA	750 mA
Waveform	Monophasic rectangular	Monophasic with sharp high peaks	Unbalances biphasic with sharp high peaks	Biphasic
Pulse duration	100 uS	45–100 uS	250 uS	65 uS
Pulse frequency per second	<60	80–130	40–85	80–600
Treatment regimen (hour/day)	2–4	0.75–1	2	1
Electrode proximity placement	In wound	In wound	Edge of wound	Above wound
Electrode reversal	Yes	Yes	No	No

*NA indicates not applicable.; From Sheffet et al., 2000 (107)

Regulatory Status

At the time of this review, Health Canada has licensed the devices listed in Table 62 for electrotherapy of wounds including pressure ulcers.

Table 62: Electrotherapy Devices Licensed in Canada for Wound Therapy (as of November 12, 2007)

Company	Name of Device	License Number	Medical Device Classification	Type of Wounds Targeted
Biomation, ON, CA	Genistim 330™ Portable electrical stimulators	70759	2	Did not specify (wound healing)
	PulseStim 240™ Portable electrical stimulators		2	
Lifewave Ltd, Ill., USA	Lifewave BST Wound Treatment Devices	75468	2	Stage II–IV wounds, including pressure ulcers

From e-mail communications.

Systematic Reviews of Electrical Stimulation Therapy

Four previous systematic reviews examined the evidence on the effectiveness of electrical stimulation as an adjunctive therapy for chronic pressure ulcers. These systematic reviews are summarized in Table 63. The current review updated the most recent systematic review (RCN 2005). This review included three of the studies from the RCN review (Gentzkow 1991, Griffin 1991, Wood 1993) and an additional study published since the last review (Adunsky 2005). One study (Ritz 2002) in the RCN review was excluded because it did not involve the use of electrical current. Another study by Adgoke and Badmos (2001) was also excluded as it involved only 3 subjects in each group. The studies are summarized in Table 64.

Table 63: Previous Systematic Reviews on Electrical Stimulation Therapy on Wound Healing*

	Gardner et al. 1999 (108)	Cullum et al. 2001 (89)	Royal College of Nurses 2005 (46)	Blue Cross Blue Shield 2005
Literature search up to	Not reported	December 1999	September 2005	Not reported
Scope	Electrical stimulation on pressure ulcers	Comprehensive review of wound care therapies	Comprehensive review of wound care therapies	Electrical and electromagnetic
Type of wounds covered	Chronic wounds	Chronic wounds	Pressure ulcers	Chronic wounds
Type of studies included	RCTs and other controlled studies	RCTs	RCTs	RCTs
Outcome measures	Mean percent healing rate per week	Percent complete healing or mean % of area healed	% complete healing or Mean % area healed	Percent complete healing or percent <down> ulcer size
Method of analysis	Meta-analysis	Descriptive plus meta-analysis	Descriptive	Descriptive
RCTs on pressure ulcers included	Gentzkow 1991 Griffin 1991 Wood 1993 Kloth and Feeder 1998 Prantz (unpublished)	GentzKow 1991 Griffin 1991 Wood 1993	GentzKow 1991 Griffin 1991 Wood 1993 Ritz 2002 (radiofrequency)	GentzKow 1991 Griffin 1991 Wood 1993
Conclusions (for pressure ulcers)	May be effective for healing pressure ulcers Net effect 13.3% Further research needed	Pooled RR 7.91 (95% CI, 3.32–18.85) Suggest benefit but insufficient evidence to draw conclusion	No evidence of improved healing over sham therapy. Interpret results with caution	Not sufficient evidence to permit conclusion on efficacy

*CI indicates confidence interval; RCT, randomized controlled trial; RR, relative risk

Table 64: Randomized Controlled Trials Comparing Electrical Stimulation With Placebo*

Study	No. of Patients (pressure ulcers)	Patient Population	Mean Age Treatment vs. Control (years)	Ulcer Stage	Mean Baseline Ulcer Area Treatment vs. Control (cm^2)	Type of Electrical Stimulation	Comparator	Study Duration (weeks)
Gentzkow et al., 1991 (109)	55 ulcers	Hospital and community	63.3 62.3	II–IV	19.2 (SD, 23.2) 12.5 (SD, 11.9)	Pulsed Alternated polarity 2x 30 min/day	Sham stimulation	4
Griffin et al., 1991 (110)	17 (17)	Male spinal cord injury patients	Median 32.5 26.0	II –IV (Dlisa system)	234.1 mm^2 271.8 mm^2	Pulsed stimulation 1 hour per day	Sham electrical stimulation	2.9
Wood et al., 1993 (111)	71 (74)		75.6 74.9	II or III	2.61 2.91 $P < .5$	Pulsed – low intensity direct current + standard treatment	Sham pulsed direct current + standard treatment	8.0 8.0
Adunsky et al., 2005 (112)	63 (63) 38 completed	Geriatric or rehab facilities (11 facilities)	71.8 71.4	III	7.6 (1.1) 7.5 (2.1)	DDCT plus conservative treatment	Placebo DDCT plus conservative treatment	8.0 wks treatment (plus 90 days follow-up)

* DDCT indicates decubitus direct current treatment; SD, standard deviation.

All four studies compared electrotherapy with sham electrotherapy (placebo). The studies were conducted mostly in institutional setting including hospitals and rehabilitation facilities, with the exception of one that included community patients. Three of the studies included mostly elderly patients except the study by Griffin et al., which included male spinal cord patients with average ages of 32.5 and 26 years. Two of the studies included stages II to grade 4 ulcers; one included stages II and III ulcers; and one included only stage III ulcers. Three studies used pulsed electrical stimulation and three used direct current while one used alternating current. Two of the studies reported treatment duration to be 1 hour per day. Duration of the studies (active treatment period) varied from 20 days to 8 weeks.

In the more recent study, Adunsky et al. (112) treated 35 patients with stage III pressure sores with decubitus direct current treatment (DDCT) adjunctive to conservative therapy including debriding and hydrocolloid or collagen dressings for 8 weeks while a control group of 28 patients with stage III pressure ulcers received conservative treatment and sham direct current treatment. Progress of the wounds were assessed and documented during treatment and for a follow-up period of 90 days. Only 38 patients completed the study. The group treated with direct current exhibited a higher rate of absolute ulcer reduction during the first 45 days (–0.44 vs. –0.14). There were, however, no statistically significant differences between the groups in complete wound closure (DDCT 25.7% vs. 35.7% for placebo, $P = .28$) or in the mean time to complete closure [63.4 (SD 15.1) days for DDCT group vs. 89.7 (SD 9.2) days for the placebo group, $P = .016$]. Per protocol analysis of the 38 patients that completed the study showed that complete healing was better in the DDCT group (5 vs. 1) and the time needed for wound closure at the end of the follow-up period was 52% longer for the placebo group compared with the DDCT group (102 vs. 67 days, $P = .0329$). (112) The results of the studies are summarized in Table 65.

Table 65: Outcomes of Randomized Controlled Trial Comparing Electrotherapy With Sham Therapy*

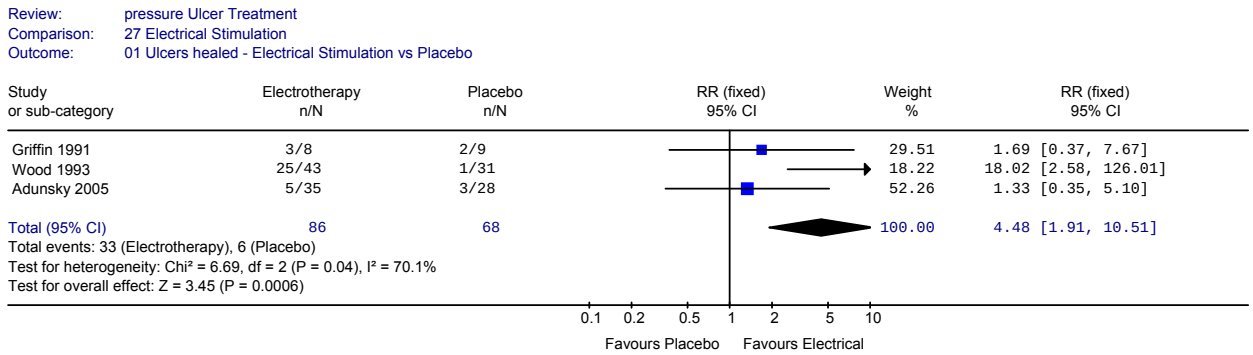
Study	Treatment Duration (weeks)	Ulcers Completely Healed	% Decrease in Area of Ulcer (Treatment vs. Placebo)	Time to Complete Healing (Treatment vs. Placebo)
Gentzkow et al., 1991 (109)	4	Not reported	49.8 (SD, 30.9)% vs. placebo 23.4 (SD, 47.4)% ($P = .042$)	Rate of healing 12.5 %/week vs. 5.8 %/week
Griffin et al., 1991 (110)	2.9	At 20 days 3/8 vs. 2/9	(Median) 80% (range 52% 100%) vs. 52% (14%100%); ($P = .05$)	NA
Wood et al., 1993 (111)	8	At 8 weeks 25/43 vs.1/31	Ulcers with >80% <down> in ulcer area: 31/43 vs. 4/31; (P < .0001)	NA
Adunsky et al., 2005 (112)	8 wks treatment (plus 90 days follow-up)	At 8 weeks 5/35 vs. 3/28	NA	ITT: 63.4 (SD15.1) days vs. 89.7 (SD, 9.2) days ($P = .16$) Logistic regression OR for complete healing = 1.6 (95% CI, 0.4–4.73) in favour of electrotherapy

*CI indicates confidence interval; ITT, intention-to-treat; OR, odds ratio; SD, standard deviation, NA-not applicable

Gentzkow et al. and Griffin et al. (110) reported significantly greater reduction in the mean area of ulcers treated with electrotherapy compared with sham therapy. Wood et al. (111) reported that significantly more ulcers treated with electrotherapy achieved a greater than 80% reduction in the area of the ulcer compared with sham therapy.

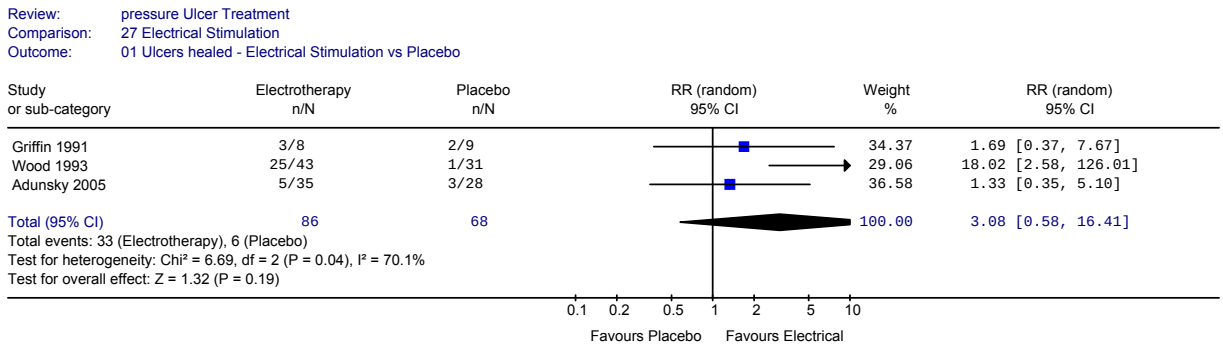
Three studies (110-112) provided information on complete ulcer closure. These were included in a pooled analysis. All three showed a higher proportion of complete healing in the electrotherapy group compared with the sham therapy group, but the difference in complete healing was statistically significant only in one of the studies (Wood et al., 1993). The Forest plot of complete healing of ulcers during treatment showed that electrotherapy was more than 4 times as effective as sham treatment in healing ulcers [RR 4.48, (95% CI, 1.91–10.51), P = .0006]; however, the there was significant heterogeneity among the studies (I^2 = 70.1%, P = .04) (Figure 61). When the Forest plot was repeated using the random effects model, the difference in complete healing between the electrical stimulation group and the placebo group was not statistically significant and the test for heterogeneity was still significant (Figure 62).

Figure 61: Forest Plot of Ulcers Healed – Electrotherapy Versus Sham (ITT data) – Fixed Effects Model*



*CI indicates confidence interval; RR, relative risk.

Figure 62: Forest Plot of Pressure Ulcer Healed – Electrotherapy Versus Sham Electrotherapy (Random Effect Model)*



*CI indicates confidence interval; RR, relative risk.

Summary

There is evidence to suggest that electrical stimulation is associated with greater relative reduction in area of pressure ulcers and may increase the healing of pressure ulcers compared with sham therapy. However, because of the small sample size of the studies and the significant heterogeneity, the results need to be interpreted with caution.

Electromagnetic Stimulation

Electromagnetic therapy of pressure ulcers involves the use of pulsed electromagnetic fields in the radiofrequency band without thermal effects. It is different from electrical stimulation therapy in that it does not involve the use of current, leads, or electrodes. The therapy is believed to stimulate blood flow and promote cell proliferation for wound healing. Contraindications for electromagnetic therapy of pressure ulcers include infection, necrosis, pacemakers not identified as RF-compatible, immature bone development, pregnancy, metal implants at the ulcer site, and documented or suspected malignancy at the ulcer site (CIGNA Health Care coverage position November 15, 2006).

At the time of this review, the ROMA 3 Electrotherapeutic Signal Generator (T.H.E. Medicals) was the only electromagnetic device licensed for wound therapy in Canada. No published studies on this device were found in the literature search. Three RCTs were found using electrotherapy devices licensed in other countries.

Of note, the FDA has approved PROVANT, a short wave diathermy device that applies electromagnetic energy to the body in the radiofrequency bands of 13 megahertz to 27.12 megahertz. (113)

Three previous systematic reviews on electromagnetic therapy for treating pressure ulcers were found: Cullum et al., 2001,(89) Royal College of Nursing and National Institute for Clinical Excellence 2006, (46) and Olyaee Manesh et al., 2006 (114)). These reviews and their conclusions are summarized in Table 66. All three reviews included the same two RCTs (Comorosan 1993 and Salsberg 1995). These studies were thoroughly reviewed and analyzed including quality assessment. The characteristics of these studies are summarized in Table 67 and the results are summarized in Table 68.

Table 66: Summary of Systematic Reviews on Electromagnetic Therapy as a Treatment of Pressure Ulcers*

	Cullum et al., 2001 (89)	Royal College of Nurses 2005 (46)	Olyaee Manesh 2006 Cochrane (114)
Literature search up to	1998	June 2004	October 2005
Type of wounds covered	Venous leg ulcers and pressure ulcers	Pressure ulcers	Pressure ulcers
Type of studies included	RCTs	RCTs	RCTs
Comparisons	Versus sham therapy or standard therapy	Versus sham therapy or standard therapy	Versus sham therapy, no electromagnetic therapy, or standard treatments
Outcome measures	Ulcers healed **Decrease** in size of ulcers	Ulcers healed Decrease in size of ulcers	Ulcers healed Rate of change in ulcer area Time to complete healing
Method of analysis	Meta-analysis	Descriptive – could not combine for meta-analysis	Meta-analysis
RCTs on pressure ulcers included	Comorosan, 1993 Salzberg 1995	Comorosan, 1993 Salzberg 1995	Comorosan, 1993 Salzberg 1995
Conclusions (for pressure ulcers)	No clear evidence of benefit	Results should be viewed as unreliable; further research needed	No reliable evidence of benefit

*RCT indicates randomized controlled trial.

Table 67: Characteristics of the Randomized Controlled Trials on Electromagnetic Therapy of Pressure Ulcers

Study	Sample Size Patients (pressure ulcers)	Patient	Mean Age Treatment vs. Control (years)	Ulcer Stage	Mean Baseline Ulcer Size (cm^2)	Type of Electromagnetic Stimulation	Study Duration (weeks)	Quality Limitations
Comorosan, 1993 (115)	Conventional plus electro-magnetic N = 20 Conventional plus sham N = 5 Conventional only N = 5	Social care unit for elderly	Diapulse: 72.05 Sham: 69.4 Conventional: 74.4	II or III	Diapulse: 4.46 Conventional: 5.4 Sham: 10.7	Diapulse Peak power 6 (117V, 27.12 MHz) for 30 minutes 2x daily + peak power 4x 20 min 1x daily	2	Difference in baseline ulcer size Unbalanced samples, No info on -method of randomization -conceal-ment -blinded assessment
Salzberg, 1995 (116)	Electro-magnetic N = 15 Sham N = 15	Male spinal cord injury patients	58 vs. 50	II and III	Median area Electromagnetic: 15 Sham: 33 *P* = .089	12 MHz, pulse repetition 80-600 pps 30 min 2x daily	12	-See above -Reported complete healing at 12 weeks only for stage III ulcers
Ritz 2002 (117)	Radio-frequency N = 16 Sham N = 18	In hospital	Electromagnetic Stage II: 72 Stage III: 75 Sham Stage II: 69 Stage III: 63	II or III	Electromagnetic Stage II: 3.0 Stage III: 11.3 Sham Stage II: 4.4 Stage III: 4.4	PROVANT ® Radiofrequency No information provided	12	None

Table 68: Results of Randomized Controlled Trials on Electromagnetic Therapy of Pressure Ulcers*

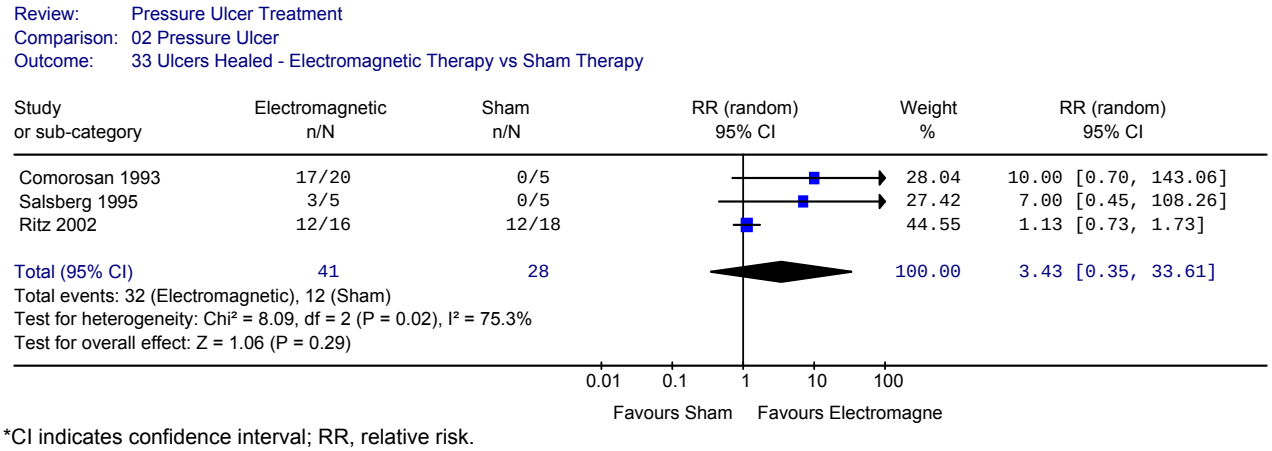
Study	Outcome – Complete Healing of Pressure Ulcers		Other Outcomes
Comorosan, 1993 (115)	At 2 weeks Electromagnetic = 17/20 (8/10 stage II + 9/10 stage III) Sham = 0/5 (0/2 stage III) Standard treatment = 0/5		
Salzberg, 1995 (116)	At 12 weeks: Grade 3 ulcers Electromagnetic 3/5 Sham 0/5		At 1 week – median percent of ulcer surface healed for grade 2 ulcers: Electromagnetic = 84% Placebo = 40% (*P* =.01)
Ritz et al., 2002 (117)	At 6 weeks Stage II Electromagnetic = 8/8 Sham = 4/11	At 12 weeks: Stage III Electromagnetic = 4/8 Placebo = 1/7 (*P* ≤ .01) Stages II and III Electromagnetic = 12/16 Placebo = 12/18	Mean surface area reduction Electromagnetic 87% Sham 56% (*P* ≤ .05) Rate of wound closure Stage II Ulcers Electromagnetic 11.92 (SD, 2.0) mm^2/day Sham 6.8 (SD, 1.7) mm^2/day Stage III Ulcers Electromagnetic 12.9 (SD, 4.1)mm^2/day Sham 3.6 (SD, 2.2) mm^2/day

*SD indicates standard deviation.

Impact on Complete Healing

Salsberg et al. (116) only reported on complete healing for grade 3 ulcers while the other 2 studies reported on complete healing for both grade 2 and grade 3 ulcers. A Forest plot that compared electromagnetic therapy with sham therapy with respect to ulcers healed (grade 2 and 3) showed significant heterogeneity (I^2 = 75.3%, *P* = .02) (Figure 63).

Figure 63: Comparison of Complete Healing – Electromagnetic Therapy Versus Sham Therapy*



*CI indicates confidence interval; RR, relative risk.

Impact on Healing Process

The above analyses suggest that electromagnetic stimulation does not appear to have a beneficial effect on complete healing of pressure ulcers.

Of note, Comorosan et al. (115) reported that in the electromagnetic therapy group, 85% of the patients achieved complete healing and the remaining 15% experienced very good healing (75% to 95% healed), whereas the placebo group and the conventional treatment group exhibited either poor healing or no improvement. Ritz et al. (117) reported that the radiofrequency treatment group had a significantly greater mean reduction in ulcer surface area (87% vs. 56%, $P = .05$) and that the rate of wound closure was greater than in the sham cohort. It was unclear whether this difference was statistically significant.

Low-Level Laser Therapy

Lasers have been used for surgery, relief of pain, treatment of soft-tissue injuries, and control of inflammation. It was believed that lasers might favour wound healing because it has been shown to promote fibroblast proliferation, collagen production, and epithelialization. Moreover, lasers enhance succinic dehydrogenase activity and alter prostaglandin levels at the cellular level.

Low-level laser (LLL) therapy or cold lasers use radiation intensities so low that it is thought that any biological effects that occur are due to the direct effect of radiation rather than the result of heating. Energies delivered are typically about 10 joules per cm^2, using lasers operating at powers of 50 mW or less. Low-level lasers include the gallium aluminum (GaAl), gallium-arsenide (GaAs), gallium-aluminum-arsenide (GaAlAs), and helium-neon (He-Ne) lasers. Lasers are primarily defined by wavelength, energy, energy density, and power density. Wavelengths of lasers from helium neon are in the visible light range, and those from GaAlAs and GaAs are in the infrared region of the light spectrum. (118) Several devices have been licensed by Health Canada to provide laser therapy for wound healing. These are summarized in Appendix 7.

Previous Systematic Reviews

No systematic reviews on the use of laser therapy to promote healing of pressure ulcers alone were found. The literature search identified three previous systematic reviews (118-120) on the use of LLL to treat wounds (Table 69) (all three reviews included studies on chronic wounds). Studies on pressure ulcers only accounted for 25% to 33% of all the studies in the reviews. None of the above systematic reviews found any evidence that the addition of LLL therapy would improve the healing of chronic wounds including pressure ulcers. The literature search for the present review identified an additional study on LLL treatment of pressure ulcers. (121) The four studies specifically evaluating the application of LLL therapy for the treatment of pressure ulcers are summarized in Table 70 and Appendix 4 .

All 5 studies reporting on the treatment of laster therapy (4 for LLL, one for laser therapy) reported in Table 70 are RCTs with sample sizes ranging from 16 to 86 ulcers. Three of the studies included elderly patients (mean age > 80 years) in hospitals or nursing homes and two included patients with spinal cord injuries. The 2000 study by Lucas et al. (122) was a preliminary exploration prior to the larger study published by the same group in 2003. Three of the studies compared LLL to conventional therapy. Taly et al. (121) compared LLL to sham therapy while Nussbaum et al. compared LLL to a combination of ultrasound and ultraviolet C radiation. The quality of the studies ranged from high to low. Two of the studies reported on the method of randomization; concealment of allocation was reported by one study and all but one study had independent assessors of outcomes blinded to treatment allocation. Results of the studies are summarized in Table 71. Low-level laser therapy appears to be safe; no adverse events were reported in any of the studies.

Table 69: Summary of Previous Systematic Reviews on Laser Therapy of Pressure Ulcer*

	Lucas et al., 2000 (119)	Simon (AHFMR), 2004 (118)	Samson et al., 2004 (AHRQ) (120)
Studies published	1975 – 1998	1996 – 2004	1966 – June 14, 2004
Type of wounds covered	Chronic wounds	Chronic wounds	Chronic wounds
Studies included	4 RCTs (1 on pressure ulcer)	9 RCTs (3 on pressure ulcers)	11 RCTs (3 on pressure ulcers)
Studies on pressure ulcers included	Nussbaum 1994	Lucas 2000 (systematic review) Schubert 2001 Lucas 2003	Nussbaum 1994 Lucas 2000 (RCT) Lucas 2003
Intervention	LLL therapy	Infra-red LLL therapy	LLL therapy
Outcome measures	Percent of wounds still open at end of trial	Complete healing Healing rates **decrease** in wound size	Primary: incidence of complete wound closure; time to complete closure, adverse events Secondary: facilitating surgical closure; need for debridement; infections; pain
Method of analysis	Meta-analysis	Descriptive	Descriptive
Conclusions (for mostly chronic wounds)	No scientific arguments for routine use of LLL therapy in chronic ulcers including decubitus ulcers	Efficacy of LLL therapy has not been established Limit use to research in patients resistant to conventional therapy	Poor quality evidence; No definitive conclusions Data suggest addition of laser therapy does not improve wound healing Type 2 error unlikely - no trends or patterns of outcomes favouring laser group

* AHFMR indicates the Alberta Heritage Foundation for Medical Research; AHRQ, Agency for Healthcare Research and Quality; LLL, low-level laser; RCT, randomized controlled trials.

Table 70: Characteristics of the Randomized Controlled Studies on Laser Therapy for Treatment of Pressure Ulcer*

Study	No. of Pressure Ulcers	Comparison	Ulcer Stage	Type of Laser	Duration of Study (weeks)	Outcome Measure
Nussbaum 1994 (123)	22 SCI pts	Ultrasound +UVC vs. Laser vs. Standard wound care Mean age 40 yrs (range 15–61)	Not stated	Cluster probe Power density 120mW/cm^2; 5,000 Hz; energy density 4J/cm^2, 3x/week	Until wound losure	Ulcers healed – from graph Mean weekly healing rate
Schubert 2001 (124)	74 (37/37) Hospital In-pts	LLL therapy + conventional vs. conventional Mean age 85 vs. 85 Yrs	II or III	Infrared + pulsed monochromatic light 1–5x/wk for 10 wks till ulcer heals	Up to 10	Mean weekly healing rate <down> in ulcer size at week 4
Lucas 2000 (122)	16 (8/8) Nursing homes	LLL therapy + consensus treatment vs Consensus treatment -mean age 87.5 vs. 88 yrs	III	Infrared GaAs diodes Monochromatic light 5x/week energy density 1 J/cm^2 Exposure time 125s	6	Median wound area at 6 weeks Median relative <down> in surface area
Lucas 2003 (125)	86 (39/47) Nursing homes	LLL therapy + conventional vs. conventional Mean age 81 vs. 84 yrs	III	Infrared GaAs diodes Monochromatic light, 5x/week 532mW, 1 J/cm^2; pulse Frequency 830; Exposure time 125s	6	Ulcers healed <down> in surface area
Taly 2004 (121)	64 (35/29) SCI pts	LLL therapy vs. Sham Mean age 31.71 (SD, 1.23) yrs	II, III, or IV	Multiwavelength Ga-Al-As laser: 1.5J/cm^2 14 treatments	14 treatment + 2-week follow-up	Complete healing -Mean time to heal

* Al indicates aluminum; As, Arsenide; GA, gallium; J, joule; LLL, low-level laser; SCI, spinal cord injury; SD, standard deviation; UVC, ultraviolet C.
Spacial and temporal averaged (SATA) intensity 0.10 W/cm2.

Table 71: Outcomes of Randomized Controlled Trials on the Use of Low-Level Laser Therapy to Treat Pressure Ulcers*

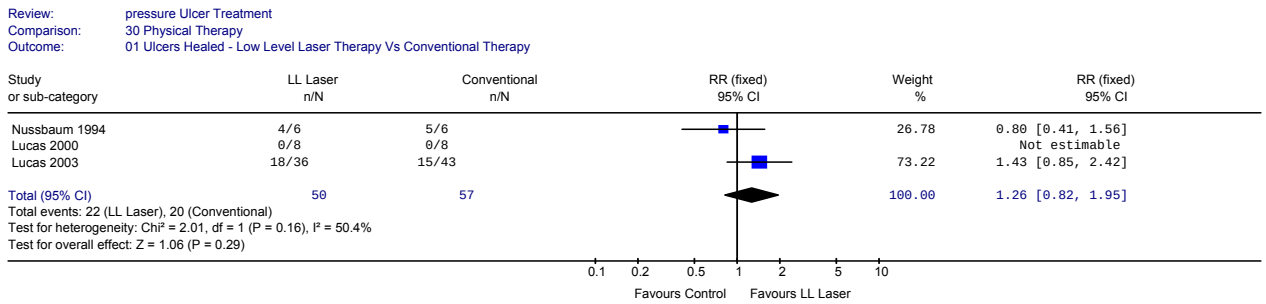
Study	Complete Healing	Reduction in Wound Size (absolute or relative)	Others
Nussbaum 1994 (123)	Ulcers healed at 12 weeks (from graph) US/UVC = 6/6 (100%) Conventional = 5/6 (>80%, < 100%) Laser = 4/6 (about 75%)	Relative decrease US/UVC vs. LLL therapy 53.5% vs. 23.7%, *P* = .032 Control 32.4% NS	Time for all ulcers to healed US/UVC 6 weeks Control 13 weeks Laser 20 weeks
Schubert 2001 (124)	Not reported	Rate of decrease LLL therapy = 0.298 cm^2 per week Control = 0.200 cm^2 per week (*P* < .05) Relative decrease after 4 wks 79% vs. 57% (*P* < .05)	Time to reduce ulcer area to 10% of baseline Laser 5 weeks Control = 9 weeks
Lucas 2000 (122)	Laser = 0/8 Consensus = 0/8	Median relative decrease in area LLL therapy plus consensus treatment = 83% Consensus treatment = 95% (not significant)	No treatment-related adverse effect
Lucas 2003 (125)	Laser 18/36 Conventional 15/43	Mean absolute wound reduction 48 (SD, 394) mm^2 vs. 138 (SD, 270) mm^2 Mean relative wound reduction LLL therapy plus standard care vs. standard care Mean = 5% (SD, 194) vs. 34% (SD, 204) Median = 97% vs. 80%	Developed stage IV ulcers Laser = 8% Standard care = 11%
Taly 2004 (121)	Laser 18/35 Sham 14/29 (*P* = .802)	For stage III and IV ulcers at randomization, PSST score at end of follow-up LLLT 16.8 (SD, 3.5) Sham 22.4 (SD, 3.9), (*P* = .049)	Mean time to heal (weeks) Laser 2.45 (SD, 2.06) Sham 1.78 (SD, 2.13) (*P* = .33) Mean time stage III and IV ulcers to reach stage II (weeks) Laser 2.25 (SD, 0.5) vs. sham 4.33 (SD, 1.53) (*P* = .047)

*LLL indicates low-level laser; PSST, Pressure Sore Status Tool; SD, standard deviation; US, ultrasound; UVC, ultraviolet C.

Impact on Complete Healing

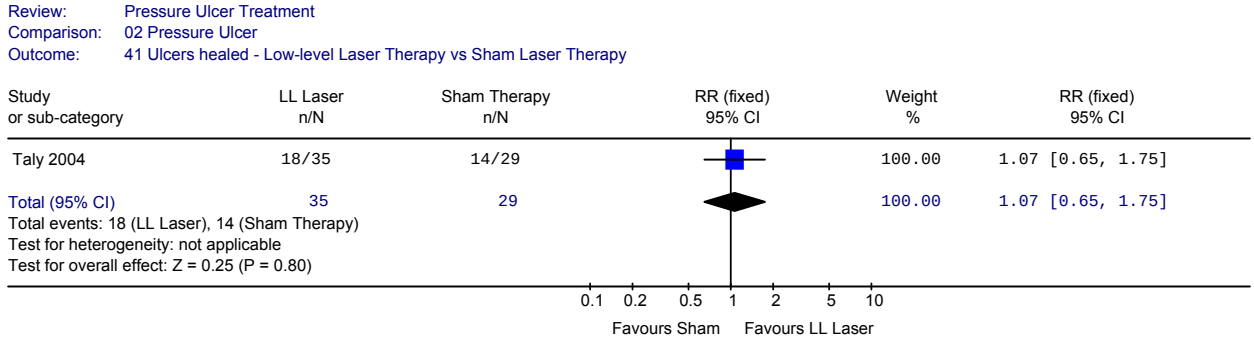
Three of studies (121;122;125) reported data on complete healing and complete healing was estimated from a graph in a third study. (123) A Forest plot comparing complete healing in the laser therapy group with that in the conventional therapy group showed moderate heterogeneity ($I^2 = 50.4$) and no statistical significant difference between groups in the proportion of ulcers that completely healed [RR 1.26, (95% CI, 0.82–1.95), $P = .29$] (Figure 64). There was also no statistically significant difference in complete healing between LLL therapy and sham laser therapy reported in 1 of the 4 studies (Figure 65). A Forest plot of studies that compared LLL therapy with either conventional therapy or sham therapy also failed to show any statistically significant benefit from adjuvant laser therapy on complete healing (Figure 66).

Figure 64: Forest Plot of Ulcers Healed – Low-Level Laser Therapy Versus Conventional Therapy*



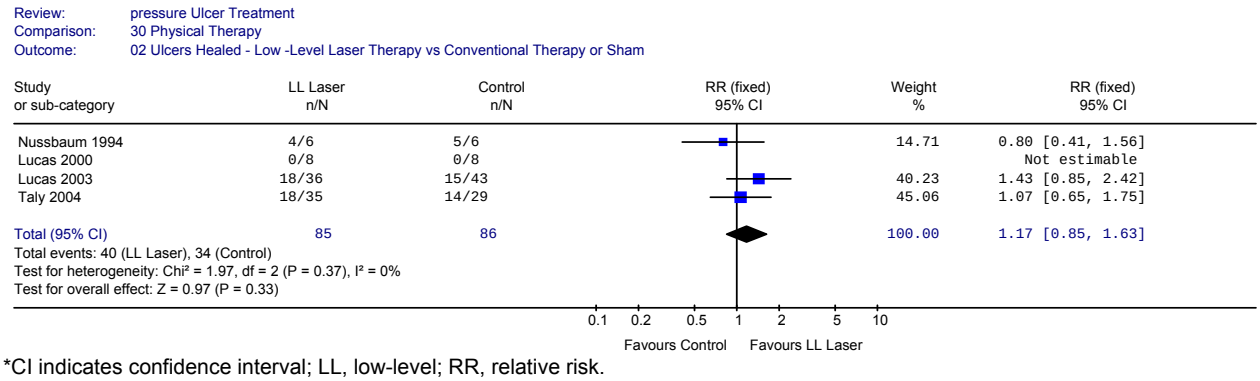
*CI indicates confidence interval; LL, low-level; RR, relative risk.

Figure 65: Forest Plot of Ulcers Healed – Low-Level Laser Therapy Versus Sham Laser Therapy*



*CI indicates confidence interval; LL, low-level; RR, relative risk.

Figure 66: Forest Plot of Ulcers Healed – Low-Level Laser Therapy Versus Sham Therapy or Standard Care*



*CI indicates confidence interval; LL, low-level; RR, relative risk.

Impact on Ulcer Size

The studies reported conflicting results on the impact of LLL therapy on the size of pressure ulcers. Nussbaum et al. (123) and Lucas et al. (122;125) reported no statistically significant difference in the mean absolute or relative reduction in ulcer area between the laser treated group and the group treated with conventional therapy alone; however, Shubert et al. (124) reported significantly greater mean weekly reduction in ulcer size and a greater relative reduction in ulcer size at week 4 for patients treated with LLL. Taly et al. reported better PSST scores for the stage III and IV ulcers that received LLL treatment compared with similar ulcers that received sham therapy. (121) Only Shubert et al. reported a significantly shorter time to achieve healing in patients that received LLL treatment. (124)

Ultrasound Therapy

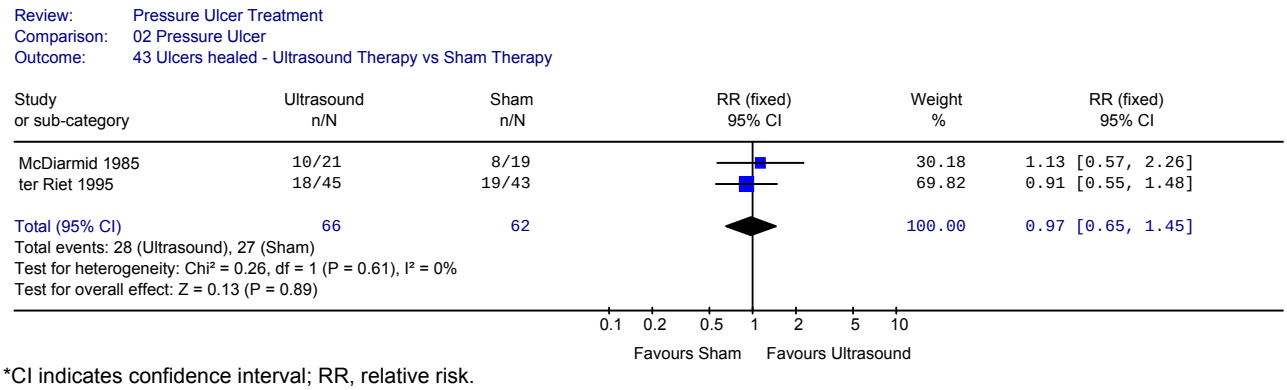
One 2006 Cochrane systematic review on ultrasound therapy for pressure ulcers was found. (126) This review included all randomized controlled studies that were published up to May 2006 and compared the use of ultrasound for pressure ulcer treatment with sham ultrasound, no ultrasound, or alternative treatments. There was no restriction to the age of patients, care setting, or severity of the pressure ulcer. Primary outcomes included any objective measures of healing and secondary outcomes included costs, quality of life, pain, and acceptability. Three RCTs met the inclusion criteria and were included in the systematic review and are summarized in Table 72 and Appendix 4. (123;127),(128). No new studies were found in the current review.

Two of the studies(127;128) compared therapeutic ultrasound with sham ultrasound, while the third study compared combined ultrasound/ultraviolet C (US/UVC) therapy with laser therapy and conventional therapy. The latter study has been described in the previous section. All three studies used ultrasound with frequency of approximately 3 MHz for 3 to 5 treatments per week. There was some heterogeneity in the special and temporal averaged (SATA) intensity, effective radiation area, and treatment duration. The duration of the study ranged from 60 days to 12 weeks. One of the studies included ulcers equivalent to NPUAP stage II while the study by ter Riet et al., (128)included stages III and IV. The third study by McDiarmid et al., (127) did not clearly state the stage of the ulcers included in the study. Results of the RCTs are summarized in Table 73.

Ultrasound Therapy Versus Sham Ultrasound

A Forest plot of the 2 studies that compared ultrasound therapy with sham ultrasound therapy found no significant between-group differences in the proportion of ulcers that completely healed [RR 0.97, 95% CI (0.65–1.45), $P = .89$]. The test for heterogeneity was negative ($I^2 = 0\%$, $P = .61$) (Figure 67).

Figure 67: Forest Plot of Ulcers Healed – Ultrasound Therapy Versus Sham Therapy*



*CI indicates confidence interval; RR, relative risk.

Table 72: Randomized Control Trials on Ultrasound Therapy of Pressure Ulcers

Study	No. of Ulcers	Comparison	Ulcer Stage	Type of Ultrasound	Study Duration	Outcome Measure
Nussbaum 1994 (123)	22 SCI pts	Ultrasound +UVC vs. laser vs. Standard care Mean age 40 yrs (range 15–61)	Not stated	2–3 x per week; Frequency 3 MHz SATA intensity = 0.2 W/cm^2 Pulse ration 1.4 Treatment duration 5 minutes per 5 cm^2 of wound area	Until wound closure	Complete healing (from graph) Ultrasound/UVC 6/6 Laser 4/6 Control 5/6 Mean weekly healing rate
McDiarmid 1985 (127)	40 (21/19)	Ultrasound vs. sham ultrasound	Equivalent to NPUAP Stage II	3x per week; Frequency 3 MHz SATA intensity 0.16 W/cm^2 SATA peak intensity 0.8 W/cm^2 Pulse duration 2 ms Effective radiation area = 5.2 cm^2 Treatment duration ≥ 5 minutes for ulcer ≤3 cm^2 and +1 minute for each additional 0.5 cm^2	More than 60 days (8–9 weeks)	Ulcers healed Average healing time Healing rate
ter Riet et al., 1995 (128)	88 (45/43) Nursing home	Ultrasound vs. sham ultrasound	II, III, or IV	5x per week; Frequency 3.28MHz, SATA intensity 0.10 W/cm^2; Pulse duration 2 ms Pulse frequency 100Hz; Effective radiating area = 4 cm^2	12 weeks or until wound closure if sooner	Complete wound closure (18/45 vs. 19/43) Change in wound surface area and volume Linear healing per week Clinical assessment from slides of wounds No significant difference in any of the above

NPUAP indicates National Pressure Ulcer Advisory Panel; SATA, spacial and temporal averaged; SCI, spinal cord injury; ;UVC, ultraviolet C.

Table 73: Outcomes of Randomized Controlled Trials on Ultrasound Therapy of Pressure Ulcers*

Study	Complete Healing	Change in Wound Size From Baseline	Others
Nussbaum 1994 (123) 20% drop-out	Ulcers healed at 12 weeks US/UVC = 6/6 (100%) Standard care = 5/6 (>80%, <100%) Laser = 4/6	Relative decrease in wound area US/UVC vs. Laser therapy 53.5% vs. 23.7% (*P* = .032) US/UVC vs. Standard care 53.5% vs. 32.4% (NS)	Time for all ulcers to be healed: US/UVC 6 weeks Standard care 13 weeks
McDiarmid 1985 (127)	Ultrasound 10/21 Sham 8/19	Wound size as % of baseline (4 weeks) <u>Uninfected wounds:</u> No significant difference between 2 groups (~40%) <u>Infected wounds:</u> Ultrasound ~65%; Sham>100% (*P* < .02)	Average healing time: Ultrasound 32 days Sham 36 days (*P* = .8) Healing rate ratio of clean: infected sores = 2.7 (*P* = .04)
Ter Riet 1995 (128)	Ultrasound 18/45 Sham = 19/43	Difference in Mean surface reduction (ITT) Ultrasound vs. Control Adjusted difference = –0.12 cm^2 (95% CI, –0.27 to 0.03), (*P* = .09) Difference in relative surface reduction (ITT), US vs. sham Adjusted difference = 8.27% (95% CI –2.31 to 18.85), (*P* = .10) No statistically significant difference in volume change or in linear healing rate.	No significant difference in healing between ultrasound or sham groups based on per protocol analysis or subgroup analysis of infected wounds.

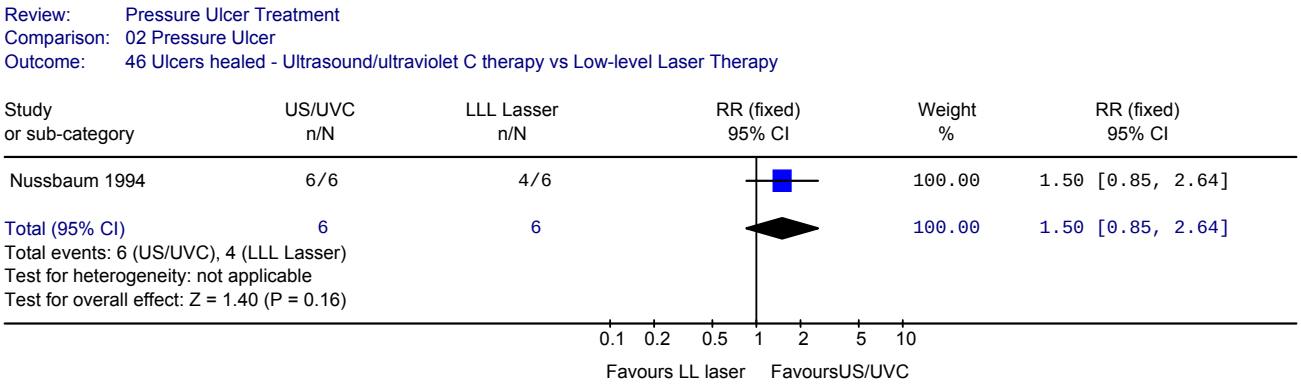
*ITT indicates intention-to-treat; NS, not statistically significant; US, ultrasound; UVC, ultraviolet C.

Ter Riet et al. (128) reported no statistically significant difference in the mean absolute or relative reduction in surface area or healing time of the ulcers between the ultrasound and the sham groups. McDiarmid et al. (127) reported similar relative reduction in wound size at 4 weeks for clean (uninfected) ulcers, but a significantly greater reduction in the ultrasound group compared with the sham group for infected ulcers. Ter Riet et al. conducted a subgroup analysis to compare the effect of ultrasound on infected and on uninfected ulcers, but failed to find any statistically significant difference in ulcer healing or healing time. It should be noted that the study by ter Riet et al. included stage III and stage IV ulcers in addition to stage II ulcers, whereas the study by McDiarmid included only stage II ulcers. This may partly account for the difference in findings between these studies.

Combined Ultrasound and Ultraviolet C Therapy Versus Standard Care

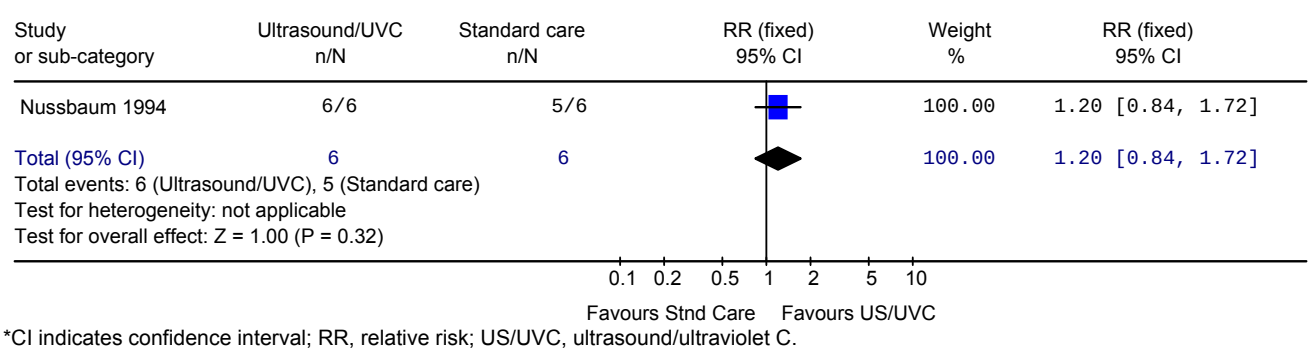
Nussbaum et al. (123) compared combined US/UVC with LLL therapy and with standard wound care. The number of subjects in each group was (9 in US/UVC, 7 in sham, and 6 in standard care). After 4 patients withdrew from the study, only 6 patients were left in each of the 3 arms. After 12 weeks of treatment, all 6 pressure ulcers had completely healed in the US/UVC group while 4 healed in the laser group and 5 healed in the standard care group. Forest plots of these results showed that US/UVC C therapy did not significantly improve complete healing compared with LLL therapy [RR 1.50 (95% CI, 0.865–2.64), P = .16] or with standard care [RR 1.2 (95% CI, 0.84–1.72), P = .32] (Figures 68 and 69).

Figure 68: Forest Plot of Complete Healing at 12 Weeks – Ultrasound/Ultraviolet C Therapy Versus Low-Level Laser Therapy*



*CI indicates confidence interval; LLL, low-level laser; RR, relative risk; US/UVC, ultrasound/ultraviolet C.

Figure 69: Forest Plot of Complete Healing at 12 Weeks – Ultrasound and Ultraviolet C Therapy Versus Standard Care*



*CI indicates confidence interval; RR, relative risk; US/UVC, ultrasound/ultraviolet C.

Nussbaum et al. (123) reported that combined US/UVC therapy resulted in a statistically significant higher relative reduction in ulcer area compared with laser therapy (53.5% vs. 23.7%, $P = .032$), but the difference in relative ulcer reduction between US/UVC and standard care (53.5% vs. 32.4%) was not statistically significant. Nussbaum et al. also reported that ulcers treated with US/UVC healed faster than those treated with standard care (mean healing time 6 weeks vs. 13 weeks) or with LLL therapy (6 weeks vs. 20 weeks); however, it is unclear whether this was statistically significant as no *P* value was provided.

Summary

This review confirmed the findings of Baba-Akbari Sari et al. (126) that there is presently no evidence of a benefit of using ultrasound therapy in the treatment of pressure ulcers and that the possibility of a beneficial or harmful effect cannot be ruled out due to the very small number of trials. Because of the small number of subjects in each trial, a type 2 error cannot be ruled out. The quality of the studies also needs to be considered. Although the study by ter Riet et al. (128) was very high quality, the other two studies had methodological limitations including an unclear method of randomization, concealment of allocation, and no intention-to-treat analysis. McDiarmid's finding suggests that ultrasound therapy may have a beneficial effect in the healing of infected wounds. This finding still needs to be confirmed, since ter Riet et al. were not able to reproduce this effect.

Ultraviolet Light Therapy

Ultraviolet light contains type A, B, and C wavelengths. Ultraviolet light has been investigated as a treatment for wounds. It is believed that ultraviolet light might increase epithelial cell turnover, remove slough, stimulate granulation and epithermal growth, and destroy bacteria. Only two studies have examined the impact of ultraviolet light on the healing of pressure ulcers (Table 74).

Table 74: Randomized Controlled Trials on Ultraviolet Light as a Treatment for Pressure Ulcer*

Study	No. of Ulcers	Comparison	Ulcer Stage	Type of Ultraviolet Light	Study Duration (weeks)	Outcome Measure (weeks)
Nussbaum 1994 (123)	22 SCI pts	Ultrasound +UVC vs. laser vs. standard care Mean age 40 yrs (range 15–61)	Not stated	2–3 x per week Ultraviolet C	Until wound closure	Complete healing Reduction in ulcer area Mean time to healing (see previous page)
Wills et al., 1983 (129)	16 extended care in-patients	Ultraviolet light therapy vs. sham ultraviolet therapy	Superficial < 5 mm deep	Predominantly A and B Kromayer lamp 2 x per week 2.5 MED increased from 2 seconds to 7 minutes 30 seconds in 8 weeks	8 weeks	Mean time to heal 6.25 vs. 8.38 ($P < .02$)

*SCI indicates spinal cord injury ;UVC, ultraviolet C.

Nussbaum e al. (123) reported that adding ultraviolet C therapy did not improve complete healing but resulted in significantly greater reduction in area of the ulcers compared with LLL therapy and shorter healing time compared with LLL therapy and standard care (see previous section).

In a small RCT involving 16 patients, Wills et al. (129) compared treatment of superficial pressure ulcers (< 5 mm deep) treated twice weekly with ultraviolet light (predominantly A and B) to similar pressure ulcers treated with sham ultraviolet light (a mica cap covers the quartz window in the lamp). Virtually all pressure ulcers in the study were infected. The only result reported was mean time to heal which was significantly shorter in the ultraviolet group than the control group (6.25 weeks vs. 8.38 weeks, $P < .02$). This difference persisted even when each patient's age and the initial size of the pressure ulcer were taken into account by covariance analysis. Yet, despite these promising results, there are concerns regarding ultraviolet radiation's mutagenic effect in causing skin cancer.

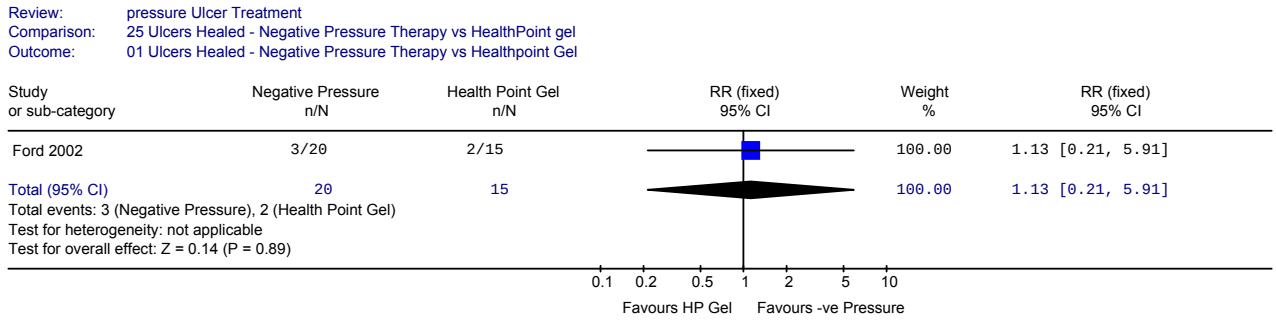
Negative Pressure Wound Therapy

Negative pressure wound therapy (NPWT), commonly known as vacuum-assisted wound therapy, uses negative pressure to create suction that removes exudate, while keeping the wound environment moist. This technique involves placing a large piece of foam over the wound with a drain tube. A large piece of transparent tape is then placed over the whole area including the surrounding healthy tissue. The drain tube is connected to a vacuum source to create negative pressure and fluid drawn from the wound is drained into a disposable canister. The system can be programmed to provide varying degrees of pressure either continuously or intermittently. (130)

A systematic review performed by MAS in 2006 examined the effectiveness of NPWT for healing wounds including pressure ulcers, diabetic ulcers, sternal wounds, and skin grafts. (130) The review concluded that, based on the evidence available at the time, the clinical effectiveness of NPWT for wound healing is unclear. As a result, OHTAC recommended that a field evaluation be performed to clarify the its effectiveness in this role. This field evaluation, coordinated and overseen by the Program for Assessment of Technology in Health (PATH) at McMaster University, is presently in progress. Of the six 6 RCTs included in the 2006 MAS review, two studies addressed pressure ulcers alone and one addressed nonhealing wounds that were predominantly pressure ulcers (Table 75). No additional randomized studies on the use of NPWT to treat pressure ulcers were found.

Ford et al. (2003) compared NPWT with HealthPoint gel in the treatment of stage III and IV ulcers. Forty-one patients were randomized to receive either vacuum-assisted closure (VAC) or a HealthPoint gel. Wounds in the control group that showed substantial exudates were treated with Indosorb or Indoflex gel (hydrophilic beads containing cadexomer iodine) while clean and granulating ulcers were treated with Panafil gel (a papin-urea-chlorophyllin-copper ointment). At the end of the 6-week trail (31 patients completed), no statistically significant differences were found between the study groups in the proportion of ulcers that healed completely (3/20 vs. 2/15) (Figure 70), mean percent reduction in ulcer volume (51.8% vs. 42.1%, $P = .46$), or the mean change in the number of polymorphonuclear neutrophils, lymphocytes, and capillaries per high power field.

Figure 70: Ulcers Healed – Negative Pressure Therapy Versus HealthPoint Gels*



*CI indicates confidence interval; RR, relative risk.

Table 75: Randomized Studies – Negative Pressure Therapy in the Treatment of Pressure Ulcers*

Study	No. of Ulcers	Comparison	Ulcer Stage	Type of Ultrasound	Study Duration (weeks)	Outcome Measure
Ford et al., 2002 (131)	41 (31 completed) 20/15	NPWT (VAC®) (N = 20) vs. (131) HealthPoint System gel products (HealthPoint) (N = 15)	III or IV	NPWT 41.7 Control 54.4	6 weeks (Follow-up 3–10 months)	Total healing 3/20 vs. 2/15 Mean volume reduction 51.8% vs. 42.1% (*P* = .46) Mean change in PMNs per high power field –37.0 vs. 22.7 (*P* = .13) Mean change in lymphocytes per high power field –6.2 vs. 45.0 (*P* = .41) Mean change in number of capillaries per high power field –5.1 vs. –7.6 (*P* = .75)
Wanner et al., 2003 (132)	22spinal cord injury patients	NPWT (N = 11) Vs. wet-to-dry/wet-to-wet gauze in Ringer's solution (N = 11)	≥ II in pelvic region	NPWT 49 (range 25–73) Control 53 (range 34–77)	Not reported	Mean time to 50% of initial wound volume NPWT 27 (SD, 10) days Control 28 (SD, 7) days
Joseph et al., 2000 (133)	36 chronic nonhealing wounds; 79% (28/36) ulcers	NPWT (N = 18) Vs. wet-to-moist gauze dressing (N = 18)	Nonhealing wounds 0f ≥ 4 weeks duration	NPWT 56 Control 49	6 weeks	Mean wound volume reduction NPWT 78% Control 30% (*P* = .038) NPWT significantly greater reduction in depth and width but not in length of the wound

*NPWT indicates negative pressure wound therapy; PMN, polymorphonuclear neutrophils;.SD, standard deviation; VAC, vacuum-assisted closure device.

Wanner et al. (2004) compared 11 pressure ulcers (≥ grade 2) treated with NPWT with 11 similar grade ulcers treated with wet-to-dry/wet-to-wet gauze dressing soaked in Ringer's solution. At the end of the study, no significant difference was found between the study groups in the mean time needed to achieve 50% reduction of the initial wound volume. No data on complete healing of wounds was reported.

Joseph et al. (2000) compared nonhealing chronic wounds of at least 4 weeks duration treated with NPWT with those treated with wet-to-moist gauze dressing. Of the 36 wounds in the study, 28 (79%) were pressure ulcers. After 6 weeks of treatment, wounds treated with NPWT were found to have a significantly greater reduction in the depth, width, and mean volume compared with the wounds treated with wet-to-moist dressing; however, no data on complete healing of wounds were reported. Histologically, granulation tissue formation was observed in 64% of wounds treated with NPWT, whereas 81% of the wounds treated with wet-to-moist dressing displayed inflammation and fibrosis.

The above studies showed conflicting results in the influence of NPWT in reducing the volume of wounds. None used complete healing as the primary outcome even though one study reported that NPWT did not result in a significantly higher proportion of complete wound closures compared with traditional gauze dressing. No study compared NPWT with the modern dressings presently used in Ontario. Moreover, all three studies had small sample size and methodological flaws including no a priori power calculation, no blinded assessment of outcomes, and no intention-to-treat analysis, despite patient withdrawal. Hence, the role of NPWT in the healing of chronic pressure ulcers is unclear at this time.

Summary Analysis – Adjunctive Physical Therapies

Table 76: Impact of Adjunctive Physical Therapies on Complete Healing*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stage	Relative Risk (95% CI)	I^2 (%)	*P* Value	Quality of Evidence
Electrotherapy vs. sham therapy (ITT)	3	154	II, III, IV	4.48 (1.91, 10.51)	70.1	.0006	Low
Electromagnetic therapy vs. sham therapy	2	59	II, III	2.75 (0.13, 56.06)	80.7	.51	Low
Electromagnetic therapy vs. conventional therapy	1	25	II, III	10.0 (0.70, 142.06)	NA	.09	Low
Low-level laser therapy vs. sham or standard care	2	143	II – IV	1.24 (0.86, 1.78)	0	.24	Low
Ultrasound vs. sham therapy	2	128	II	0.97 (0.65, 1.45)	0	.89	Moderate
Ultrasound/ultraviolet C vs. low level laser therapy	1	12	NR	1.50 (0.85, 2.64)	NA	.16	Low
Ultrasound/ultraviolet C vs. standard care	1 (same study for both comparisons)	12	NR	1.20 (0.84, 1.72)	NA	.32	Low
Negative pressure therapy vs. conventional gel products	1	35	III, IV	1.13 (0.21, 5.91)	NA	.89	Low

*CI indicates confidence interval; I^2, test for heterogeneity; ITT, intention-to-treat; NA, not applicable; NR, not reported.

Table 77: Impact of Adjunctive Physical Therapies on Reduction in Ulcer Size

Comparison	No. of Studies	No. of Ulcers	Ulcer Stage	Mean % Reduction in Area of Ulcer	*P* Value
Electrotherapy vs. sham therapy	1	55	II–IV	49.8% vs. 23.4%	.0042
Electrotherapy vs. sham therapy	1	17	II–IV	Median 80% vs. 52%	.05
Electrotherapy vs. sham therapy	1	74	II, III	Ulcer with >80% <down> in area 72% vs. 13%	< .0001
Negative pressure therapy vs. Healthpoint system gels	1	36	Non healing	78% vs. 30%	.038

Summary Statements – Adjunctive Physical Therapy

- There is evidence that electrical stimulation may result in a significantly greater reduction in the surface area and more complete healing of stages II to IV ulcers compared with sham therapy. These results need to be confirmed because of small sample sizes and presence of significant heterogeneity.
- The efficacy of other adjunctive physical therapies in improving complete closure of pressure ulcers has not been established.

Nutritional Therapy

Systematic Reviews

The search yielded three systematic reviews on the use of nutritional therapy in treating pressure ulcers. These are briefly summarized in Table 78.

Table 78: Systematic Reviews of Nutritional Therapy in Treating Pressure Ulcers*

	Langer et al. (Cochrane)2003 (134)	Royal College of Nurses 2005 (46)	Stratton et al., 2005 (135)
Literature search up to:	June 2003	August 2004	August 2004
Type of wound s covered	Pressure ulcer	Pressure ulcer	Pressure ulcer
Purpose	Treatment	Treatment	Prevention and treatment
Types of nutrition intervention reviewed	Supplementary nutrition Protein Zinc Ascorbic acid Mixed nutritional supplements	Supplementary nutrition: Protein Zinc Ascorbic Acid Multinutrient supplement	Multinutrient (>2 macronutrients as well as micronutrients) Oral nutritional supplements Enteral tube feeding
Type of studies included	RCTs Controlled trials if no RCT	RCTs Controlled trials if no RCT	RCTs Controlled trials if no RCT
Outcome measures	Primary Time to complete healing Secondary Acceptability, side effects, Costs Rates of complete healing Rate in change of size of ulcer Quality of life	Primary Proportion of participants developing new ulcers Time to complete healing Secondary Acceptability Side effects Rate of complete healing Rate in change of size of ulcers Quality of life	Pressure ulcer incidence Pressure ulcer healing Quality of life Complications Mortality Dietary intake Nutritional status
Method of analysis	Descriptive and meta-analysis	Descriptive and meta-analysis	Descriptive and meta-analysis
Studies (RCTs) on treatment of pressure ulcers included in the review	<u>Ascorbic acid supplement</u> Taylor 1974 ter Riet 1995 <u>Protein supplement</u> Chernoff 1990 <u>Zinc supplement:</u> Norris 1971 (Small, methodologically flawed)	<u>Ascorbic acid Supplement</u> Taylor 1974 ter Riet 1995 <u>Protein Supplement</u> Chernoff 1990 <u>Zinc Supplement</u> Norris 1971 Brewer 1967 (Small, methodologically flawed)	Enteral multi nutrient feedings Ek 1991 Benati 2001 Soriano 2004 (not RCT) Chernoff 1990 Breslow 1993 (not RCT) (Small, methodologically flawed)
Conclusions	It was not possible to draw firm conclusions on the effect of enteral or parenteral nutrition on the prevention and treatment of pressure ulcers. Need further trials of high methodological quality	Supplementation to correct the deficiencies may be indicated The effect of corrective nutritional supplementation on pressure ulcer healing remains unclear.	High protein/disease specific oral supplement or enteral nutrition feeding may improve healing of ulcers but needs to be confirmed in adequately powered, robust RCTs conducive to meta-analysis.

*RCT indicates randomized controlled trial.

Two of the systematic reviews are independent reviews addressing only nutritional therapy (134;135), while the third is a part of a comprehensive review of all treatments (RCN 2005). Two systematic reviews only included studies on treatment (Langer 2003, RCN 2005) and the third addressed both prevention and treatment of pressure ulcers. (Stratton 2005) Two reviews included only RCTs (Langer 2003 and RCN 2005), but one also included controlled trials (Stratton 2005). Langer et al. (2003) and RCN (2005) included studies using any form of nutritional supplement whereas Stratton 2005 focused on multinutrient oral supplements and enteral tube feedings.

The current review updates the two 2005 systematic reviews. Two new published RCTs on nutritional therapy were found (Lee 2006 and Desneves 2005). These studies, and those included in previous systematic reviews, are discussed below.

MAS Review of Studies in Nutritional Therapy

Protein Supplements

Two RCTs examined the effect of protein supplements on the healing of ulcer (Table 79).

Table 79: Comparison of Protein Supplements and Placebo*

Study	Sample Size Patients (pressure ulcers)	Patient Population	Ulcer Stage	Mean Baseline Ulcer Size, Treatment vs. Control (cm^2)	Type of Nutritional Therapy	Comparator	Study Duration (weeks)	Outcomes
Lee et al., 2006 (136) (Multicenter)	89 Tx = 44 C = 27 71 (108) completed study	Residents of 23 LTC facilities in 4 US states with pressure ulcers	II, III, IV	Baseline PUSH score (SD) 9.11 (4.15) 6.07 (2.65)	3 times daily: 15 g of concentrated fully hydrolyzed collagen protein supplement (Pro-stat)	3 times daily: 15 g of placebo	8	Mean improvement in PUSH score 5.56 vs. 2.85 (reported to be significant but *P* value not reported)

*LTC, long-term care; PUSH, Pressure Ulcer Scale for Healing; SD, standard deviation; Tx, treatment; US, United States.

In an RCT, Lee et al. (136) explored the effect of protein supplement on the healing of stage II, III, and IV pressure ulcers in long-term care residents. The trial compared 56 residents of long-term care facilities that received standard care plus a concentrated fortified collagen protein hydrolysate supplement for 8 weeks with 33 counterparts who received standard care and a placebo. Seventy-one of the subjects completed the study: 44 in the treatment group with 75 pressure ulcers and 27 in the placebo group with 33 pressure ulcers. At 8 weeks, the protein hydrolysate group showed twice the rate of pressure ulcer healing compared with the placebo group (mean improvement in PUSH score 5.56 for treatment vs. 2.85 for placebo). There were no significant differences among the groups in the rate of adverse events.

Zinc Supplementation

Zinc is a trace mineral that is an integral part of many body tissues and enzymes. It plays an important part in the synthesis of deoxyribonucleic acid and ribonucleic acid that foster tissue growth and healing, as well as collagen synthesis. Zinc deficiency is associated with hair loss, diarrhoea, poor appetite, decrease in sense of taste and smell, and lesions in the skin and eye. A study had shown that up to 88% of eating-dependent nursing home residents had dietary zinc intake below 50% of the recommended daily allowance. Hence dietary supplementation of zinc had been investigated as a treatment for pressure ulcers. (Posthauer 2005, Advances in Skin and Wound Care)

The previous systematic reviews included two studies relating to zinc supplementation in the healing of pressure ulcers (137;138) (Table 80). There have been no new studies since the 2005 systematic review and no new studies were found in the current review. The following is based on the 2005 RCN review.

Table 80: Randomized Controlled Trial Comparing Zinc Supplement With Placebo*

Study	Sample Size	Mean Age	Ulcer Stage	Median Ulcer Volume (mL)	Type of Nutritional Therapy	Comparator	Study Duration (weeks)	Outcome Measures
Norris et al., 1971 (137;138) Double blind, cross over	14 Only 3 completed 24 weeks Inpatient chronic disease hospital	59	NR	20 (range 1–110)	200 mg zinc sulphate x 3 daily x 12 weeks then placebo for 12 weeks	Placebo 3x per day x 12 weeks, cross over to 200 mg zinc x 3/day x 12 weeks	24 weeks (cross over at 12 weeks)	Comparison 10 zinc vs. 8 placebo treatments Complete healing Zinc = 2/10 Placebo 1/8 Mean reduction in ulcer volume Zinc = 10.1 mL (SD, 9.0) Placebo = 6 mL (SD, 17.5)
Brewer et al., 1967 (138)	6 vs. 7 spinal cord injury inpatients				200 mg x 3 daily	Placebo x 3 daily	2–3 months	Healed ulcers Zinc 1/6 Placebo 2/7

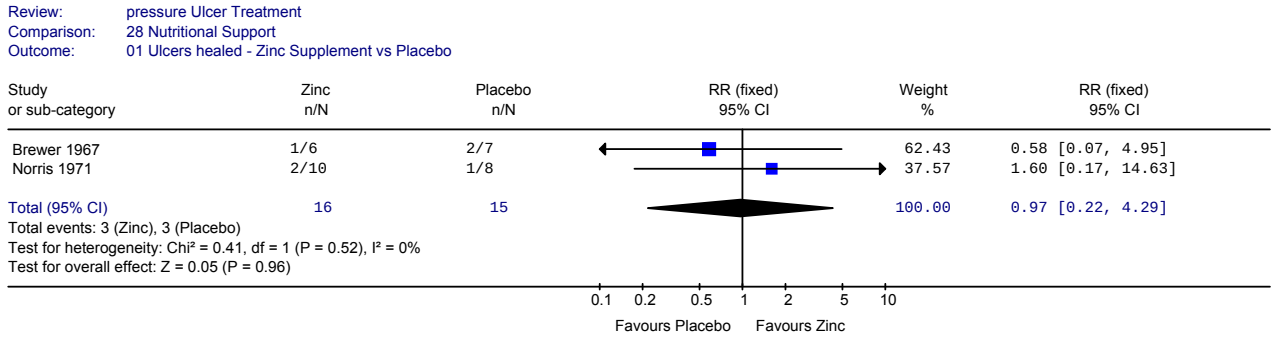
*NR indicates not reported; SD, standard deviation.

In a randomized, double-blind crossover study, Norris et al. randomized 14 patients with pressure ulcers to receive either 200 mg zinc sulphate or placebo 3 times daily placebo for 24 weeks. Volume of the ulcers was measured every 4 weeks and after 12 weeks the groups switched therapy. Only 3 patients completed the study. The mean net change in the volume of pressure ulcers was 10 mL (SD 9 mL) in the zinc sulphate treated group compared with a net change of 6.0 mL (SD 17.5 mL). The difference between the groups was not statistically significant (WMD 4.1 mL; 95% CI, –8.10 to 16.30, $P = .5$)

Brewer et al. (1967) reported no significant difference in the rate of pressure ulcer healing in spinal cord injury patients treated with 220 mg of zinc sulphate 3 times daily for 2 to 3 months (1/6 with healed pressure ulcer) compared with patients receiving a placebo (2/7 patients healed).

A pooled analysis of the studies was performed. The Forest plot of ulcers healed showed no significant difference in the proportion of ulcers healed between patients who received zinc supplement and patients who received a placebo [RR 0.97, (95% CI, 0.22–4.29), $P = .96$] (Figure 71). The test for heterogeneity was not significant. There is a possibility of type 2 error since both studies were very small.

Figure 71: Forest Plot of Ulcers Healed – Zinc Supplement Versus Placebo*



*CI indicates confidence interval; RR, relative risk.

Houston et al. compared the adverse effects of 26 older institutionalized patients that received 440 mg zinc sulphate daily for the treatment of pressure ulcers with 44 patients with pressure ulcers that received similar care without zinc sulphate supplementation. After 30 days of treatment, the beneficial effects of zinc sulphate on healing were not obvious. The only significant difference in healing between the groups over the 30 days was greater improvement in ulcer volume in patients with stage III or IV ulcer ($P < .05$), but not in stage II. However, zinc sulphate supplementation was associated with a higher incidence of adverse events. The odds of an infection requiring antibiotic therapy were 7.8 times greater in patients receiving zinc sulphate ($P < .009$). In addition, subjects with zinc sulphate were 12.5 times more likely to experience nausea/vomiting than were comparison subjects receiving similar care without zinc sulphate ($P < .02$). Adverse effects could not be explained by the presence of diabetes mellitus or differences in energy intake. (Houston, Haggard et al., 2001, Journal of American Geriatric Society 49 (8):1130)

Ascorbic Acid Supplementation

Ascorbic acid is the enolic form of vitamin C. In addition to its antioxidative effects, vitamin C also plays an important role in tissue repair and regeneration within the body. It acts as a cofactor for enzymes involved in the synthesis of connective tissues, in particular collagen, an important process in wound healing. Vitamin C deficiency has been associated with risk of pressure ulcer (Gray 2003 Journal of wound ostomy continence nursing). Elderly subjects admitted for femoral bone fracture that developed pressure ulcers were found to have leukocyte vitamin C levels about 50% lower than those in similar patients that remained ulcer free (Selvaag 2002).

The previous systematic reviews included two studies on vitamin C supplementation on the healing of pressure ulcers, which yielded conflicting results as summarized in Table 81 (the current review did not identify any new studies on this treatment). Tayor et al. (139) compared 10 surgical patients with an existing pressure ulcer who received 500 mg of ascorbic acid twice daily with 10 patients who received a placebo twice daily. Both groups received similar wound care. After 1 month, 6 of the patients in the ascorbic acid group had complete ulcer closure compared with 3 patients in the placebo group. This difference was not statistically significant; however, patients in the ascorbic acid group showed significantly greater reduction in the mean ulcer area compared with the placebo group (84% vs. 42.7%, $P < .005$).

Table 81: Randomized Controlled Trials on the Effect of Vitamin C Supplementation on the Healing of Pressure Ulcers*

Study	Sample Size	Patient	Mean Age	Ulcer Stage	Comparison	Study Duration	Outcome Measures
Taylor et al., 1974 (139)	N = 20 Double-blind RCT	Surgical patients with a pressure ulcer	74.5 (range 54–88		500 mg ascorbic acid BID vs Placebo	1 month	Healed 6/10 vs3/10 <down> in ulcer area 84% (SD, 7.6) vs. 42.7% (SD, 7.41) (P < .005)
ter Riet., 1995 (140)	N = 88 42 vs. 45 Multicentre blinded RCT	Nursing home residents with pressure ulcer		II or worse	500 mg ascorbic acid BID vs 10 mg ascorbic acid 2x daily	12 weeks	No significant difference in absolute or relative rate of <down> in surface area or volume % area reduction 13.88 % vs. 22.85% (NS)

*BID indicates twice daily; NS, not statistically significant; RCT, randomized controlled trial; SD, standard deviation.

In a more recent RCT, ter Riet et al. (140) compared 42 nursing home patients with a pressure ulcer (grade 2 or worse) that received 500 mg ascorbic acid twice daily with 45 residents that received 10 mg ascorbic acid twice daily. Patients in each group were also randomized to receive either ultrasound therapy or sham ultrasound therapy. After 12 weeks, there were no significant differences in the rate of absolute or relative reduction in surface area or volume of the ulcers between the groups. Ter Riet et al. (140) pointed out that there were differences between the studies such as age, setting, mean size of ulcers at baseline, and the amount of ascorbic acid received by the controls (none vs. 20 mg daily). For this reason, it is not appropriate to pool the two studies.

Multinutrient Supplement

The use of multinutrient (mixed nutrient) liquid nutritional supplements is a common practice to provide additional protein, energy, vitamins, and minerals to people requiring additional nutrition support. The supplement can be taken orally or administered in the form of tube feedings. The 2005 systematic reviews (Stratton and RCN) together included three RCTs that examined the effect of multinutrient nutritional supplements on the healing of pressure ulcers.(Ek 1991, (141) Chernoff 1999 (142), Benati 2001 (143)) One new study was found in the course of the MAS literature search (144); the four studies are summarized in Table 82.

With the exception of the study by Ek et al. (141) (501 patients followed for 26 weeks), the studies were generally small (N ranged from 12–16) with short durations (2–8 weeks). Most of the study subjects were elderly and institutionalized. Pooling of the results was not possible since these studies used different outcome measures (percentage of ulcers healed, reduction in surface area, change in PSST score, and change in PUSH scores).

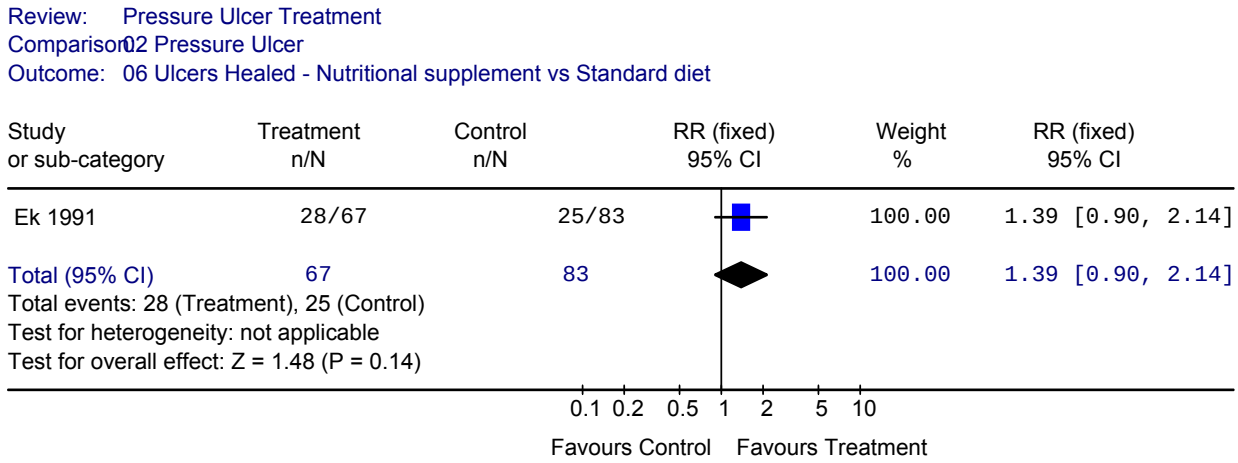
Ek et al. (141) studied the effect of a high protein, high calorie, vitamin and mineral-enriched liquid supplement on the development and healing of pressure ulcers. At the end of 26 weeks, 28 of the 67 (41.8%) pressure ulcers in the supplement group had healed compared with 25 of 83 (30.3%) pressure ulcers in the group that only received a standard diet. Although the nutritional supplement group had a higher incidence of healed ulcers compared with the control group (RR 1.39), this difference did not reach statistical significance (95% CI, 0.90–2.14, P = .14) (Figure 72).

Table 82: Randomized Controlled Trials – Added Multinutrient Enteral Supplement Versus Standard Diet*

Study	No. of Pressure Ulcers	Patient Population	Ulcer Stage	Mean Baseline Ulcer Size, Treatment vs. Control (cm^2)	Type of Nutritional Therapy	Comparator	Study Duration (weeks)	Results
Ek et al., 1991 (141)	150	Long-term care inpatient	NR	NR	Standard hospital diet plus liquid supplement containing 16 g protein, 1600 kJ, vitamins and minerals	Standard hospital diet	26	Healed ulcers Supplement group 28/67 Control 25/63
Chernoff et al., 1990 (142)	12	Institutionalized tube feeding patients with pressure ulcers	NR	NR	Very high protein tube feeding (25% of energy)	High protein tube feeding (16% of energy)	8	Ulcers healed 4/6 vs. 0/6 Very high protein tube feeding group had greater <down> in surface are of ulcer (73% vs. 42%).
Benati et al., 2001 (143)	15	Hospitalized patients with severe cognitive impairment and pressure ulcers	NR	No numerical mean values reported	Normal hospital diet plus protein calorie supplement al feeding enriched with arginine, zinc, vitamins A, C, and E	Normal hospital diet Normal hospital diet +protein calorie supplementary feeding	2	Group that received protein supplement with arginine, zinc, and antioxidants appear to have the greatest improvement in ulcer status.
Desneves et al., 2005 (144)	16	Inpatient, geriatric or spinal cord injury	II, III, or IV	PUSH score A = 8.7 (SD, 1.0) B = 8.0 (SD, 0.5) C = 9.4 (SD, 1.2)	C. Standard diet plus high protein high energy supplement with vitamin C, arginine, and zinc	A. standard hospital diet B. Stand diet + high protein-high energy supplement	3	The group receiving supplement enriched with arginine, zinc, and vitamin C had 2.5-fold greater improvement in PUSH score than the other 2 groups ($P < .05$)

*NR indicates not reported; PUSH, Pressure Ulcer Scale for Healing; SD, standard deviation.

Figure 72: Forest Plot of Ulcers Healed – Multinutrient Supplement Versus Standard Diet*



*CI indicates confidence interval; RR, relative risk.

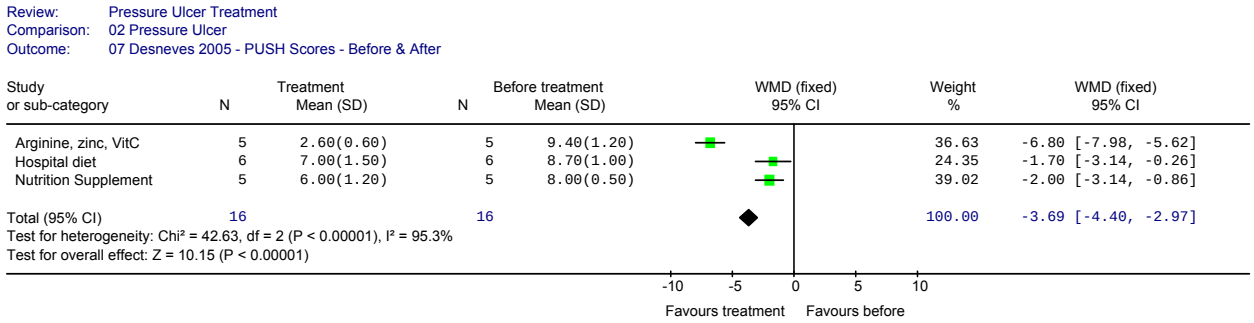
Chernoff et al. (142) reported in an RCT that 4 out of 6 institutionalized tube-fed patients that received a very high protein (25% of energy) enteral tube feeding had healed ulcers whereas none of the patients receiving a standard high protein (16% of energy) formula had healing of their pressure ulcers. The group receiving a very high protein formula also had a 73% reduction in the surface area of the pressure ulcers compared with a 42% reduction in the control group. The differences in the rate of healing and surface reduction of the pressure ulcers did not reach statistical significance.

Benati et al. (143) reported on the results of 16 hospitalized patients with severe cognitive impairment that were randomized into 3 arms. The study compared the effect of a high protein, high calorie supplement enriched with arginine, zinc, and antioxidants (vitamins A, C, and E) with a group receiving a similar supplement without the enrichment and a control group receiving a standard hospital diet. Benati et al. reported that patients treated with the supplement enriched with arginine, zinc, and antioxidants seemed to have the lowest pressure sore status tool score (best healing) and more rapid improvement. No numerical data was provided, however, and the statistical significance cannot be assessed.

Desneves et al. (144) conducted a similar study to explore the effect of a high protein, high energy supplement enriched with arginine, zinc, and vitamin C. This treatment was compared with treatment with the same high protein, high energy supplement without enrichment and to the standard hospital diet. At the end of 3 weeks, patients that received supplementary arginine, zinc, and vitamin C had significantly better PUSH scores ($P < .05$) and had approximately 2.5-fold greater improvement in PUSH score compared with the other 2 groups, even though there were no significant differences in the patients' intake of protein and energy among the 3 groups.

Figure 73 shows that the decrease in PUSH scores (improvement in pressure ulcer healing) was –6.8 for the arginine-zinc-vitamin C enrichment group compared with –2.0 for the standard supplement group and –1.7 for the hospital diet group. However, there is insufficient data to determine whether the differences in improvements among the groups are statistically significant.

Figure 73: Forest Plot of Weighted Mean Difference of Change in PUSH Scores Before and After Treatment for Each of the Study Arms*



*CI indicates confidence interval; PUSH, Pressure Ulcer Scale for Healing, SD, standard deviation; WMD, weighted mean difference.

Summary of Analysis – Nutrition Therapy

Table 83: Impact of Nutritional Support on Complete Healing and Area Reduction of Pressure Ulcers*

Comparison	No. of Studies	No. of Ulcers	Ulcer Stage	Complete Healing Relative Risk (95% CI)	Reduction in Area of Ulcer	Quality
Protein supplement (15 g 3 times daily) vs. placebo (8 weeks)	1	89	II–IV	Not reported	2-fold increase in rate of healing Reduction in PUSH score: 5.56 vs. 2.85 (Significant)	NE
Zinc supplement vs. placebo (200 mg x 3/day)	2	31	NR	0.97 (0.22, 4.29)	NR	Low
Ascorbic acid (500 mg BID) vs. no ascorbic acid supplement (4 weeks)	1	20	NR	2.0 (0.68, 5.85) NS	84% vs. 42.7% ($P < .005$)	Moderate
Ascorbic acid (500 mg BID) vs. ascorbic acid (10 mg BID) (12 weeks)	1	88	II–IV	Closure rate HR 0.21 (0.44, 1.39) NS	13.88% vs. 22.85% (NS)	Moderate
Tube feeding with 25% of energy as protein vs. tube feeding with 16% of energy as protein in institutionalized tube-fed patients	1	12	II–IV	9.0 (0.59, 137.66)	73% vs. 43%	Moderate
Multi-nutrient supplement (1600 kJ, 16g protein, vitamins/mineral supplement) vs. standard diet alone (26 weeks)	1	150	NR	1.39 (0.90, 2.14) NS	NR	Moderate
Multi-nutrient supplement (500–2100 kJ, 37g protein, vitamin C, zinc, and arginine) vs. standard diet or standard supplement (2–8 weeks)	2	31	II–IV	NR	Greater decrease in area of ulcer with supplement; significant improvement in ulcer score	Moderate to low

*BID indicates twice daily; CI, confidence interval; HR, hazard ratio; kJ, kilojoule; NR, not reported; NS, not statistically significant; PUSH, Pressure Ulcer Scale for Healing, NE= not evaluated

Summary Statements – Nutrition Therapy

- Supplementation with 15 grams of hydrolyzed protein 3 times daily did not affect complete healing but resulted in a 2-fold improvement in PUSH score compared with a placebo.
- Supplementation with 200 mg of zinc 3 times daily did not have any significant impact on the healing of pressure ulcers compared with a placebo.
- Supplementation of 500 mg ascorbic acid twice daily was associated with a significantly greater decrease in the size of the ulcer compared with a placebo but did not have any significant impact on healing when compared with supplementation of 10 mg ascorbic acid 3 times daily.
- A very high protein tube feeding (25% of energy as protein) resulted in a greater reduction in ulcer area in institutionalized tube-fed patients compared with a high protein tube feeding (16% of energy as protein).
- Multinutrient supplements that contained zinc, arginine, and vitamin C were associated with a greater reduction in the area of the ulcers compared with standard hospital diet or to a standard supplement without zinc, arginine, or vitamin C.

It should be noted, however, that firm conclusions cannot be drawn because of methodological flaws and the small sample size.

Multidisciplinary Wound Care Teams

In addition to treatment modalities used to aid healing of pressure ulcers, much attention is being focused on the approach to delivering wound care to people with pressure ulcers in the different health care settings. One of the most common forms of structured wound care delivery is the establishment of a multidisciplinary wound care team that includes wound care specialists, nurses, pharmacists, dietitians, physiotherapists, and discharge planners.

Although there are many reports describing the organization and operation of multidisciplinary wound care teams, most teams reported their impact on the incidence of new pressure ulcers. Only 2 studies reported on the impact of multidisciplinary teams on the healing of pressure ulcers. These 2 studies are summarized in Table 84.

Table 84: Studies Comparing Multidisciplinary Pressure Ulcer Care With Standard Care*

Study	Design	Sample Size	Patient Mean Age Treatment vs. Control, Years (SD)	Ulcer Stage	Multidisciplinary Arm	Maximum Treatment Duration	Findings Treatment vs. Control
Alvarez et al., 1993 (145) (Abstract)	RCT Acute care	66 pts	NR	NR	4 RNs 1 MD RD PT Discharge planner	8 weeks	LOS 32.6 days vs. 59.5 days ($P < .005$) Healed ulcers 52% vs. 14% Improved 45% vs. 23% Unchanged 3% vs. 22% Deteriorated 0% vs. 36% Average cost per patient = $29,902 vs. $40,340
Vu et al., 2007 (10)	Pseudo-RCT	Total wounds 180/162 Pressure ulcers 140/121	83.0 (9.1) vs. 83.7 (8.9)	NR Severe wounds 15% vs. 11.8%	Nurse and pharmacist trained in wound care Standard protocol Weekly meeting and telephone discussion	6 months	Healed ulcers 80/140 vs. 58/117 (NS) Mean time to heal: 82 days vs. 101.1 days ($P = .095$) Multivariate analysis: Intervention group more likely to heal RR = 1.73 (95% CI, 1.2–2.5) ($P = .003$) Pain relief: 49% vs. 29% ($P = .017$)

*CI indicates confidence interval; LOS, length of stay; MD, medical doctor; NR, not reported; NS, not statistically significant; PT, physical therapist; RCT, randomized controlled trial; RD, registered dietician; RN, registered nurse, RR, relative risk; SD, standard deviation.

In a presentation to an international conference in 1993, Alvarez et al. (145) reported on a randomized study involving 66 patients in an urban acute care setting. Patients were randomized into 2 treatment groups. One group was managed by a trained team consisting of 4 full-time registered nurses, a full-time physician, a registered dietitian, a physiotherapist, and a discharge planner. The control group was managed as per the physician according to the standards of the facility. Patients were followed until the pressure ulcer healed, up to a maximum of 8 weeks. At the end of the 8-week period, patients managed by the multidisciplinary team had significantly more pressure ulcers healed (58% vs. 14%, *P* value not reported) and improved ulcers (45% vs. 28%, *P* value not reported), shorter length of stay (32.6 days vs. 59.5 days, $P < .005$), and lower average cost ($29,902 vs. $40, 340 US) compared with patients in the control group. However, since only an abstract of this study is available, the exact number of patients allocated to each group was not available and the RR of ulcer healing could not be estimated.

Because of the paucity of studies on this subject, a pseudo-randomized trial is also included in this review. Vu et al. (10) reported on a pseudo-randomized pragmatic cluster trial in which 342 uncomplicated leg and pressure ulcers in 176 nursing home residents were allocated to 2 treatment groups based on by nursing home and region. Approximately 75% of the wounds were pressure ulcers. Wounds in the experimental group were managed by a team consisting of a pharmacist and a nurse trained in wound management using a standard treatment protocol based on an assessment of the wound. The team held weekly discussion of wounds and also telephone discussion regarding treatment. Ulcers in the control group received usual wound care from nurses with no wound care training according to the Commonwealth manual. Residents in the intervention arm were more likely to be underweight or overweight ($P = .000$) and less likely to have a history of leg or pressure ulcers ($P = .011$) compared with control residents. Wounds in the intervention arm were more likely to be severe with greater mean width and higher proportion with moderate or profuse exudates. Patients were followed until their wound(s) healed to a maximum of 6 months. At the end of the study period, 59.7% (80/134) of the pressure ulcers in the team-managed group had completely healed compared with 49% (58/117) in the control group. This result favours team management, but the difference did not reach statistical significance [RR 1.20 (95% CI, 0.96–1.52), $P = .11$] There were no statistically significant differences in the mean time to achieve complete healing between the 2 groups (82 days vs. 101 days, $P = .095$). When all wounds were considered, patients managed by the team had greater pain relief compared with the controlled arm (38.6% vs. 24.4%, $P = .017$). Mean treatment cost per patient including training was lower for the team-managed group compared with the control group ($575.6 vs. $1,005, Australian currency). (10)

Both studies reported improved healing of pressure ulcers in patients managed by a multidisciplinary team compared with the standard approach – management directed by a physician; however, the improvement in healing was significant only in the RCT. It should be noted that in the pragmatic study by Vu et al., (10) the team only consisted of a nurse and a pharmacist, whereas in the RCT by Alvarez et al., (145) the team included more disciplines. The follow-up period was also much longer in the study by Vu et. al. (10) (6 months vs. 8 weeks) compared with the study by Alvarez et al. (145)

Summary of Analysis – Multidisciplinary Wound Care Teams

The only RCT in this area suggests that multidisciplinary wound care team may significantly improve healing in the acute care setting in 8 weeks and may significantly shorten the length of hospitalization. However, since only an abstract is available, study biases cannot be assessed and no conclusion can be drawn on the quality of this evidence.

Conclusions

Based on analyses of the evidence, the following conclusion can be drawn:

- Evidence is generally based on small RCTs with methodological flaws.
- The type of nonsurgical debridement used did not appear to have a significant impact on the complete healing of ulcers.
- No significant differences in debridement abilities were detected among nonsurgical debridement agents with the following exceptions:
  - Papain urea results in better debridement than collagenase.
  - Calcium alginate resulted in better debridement than dextranomer.
  - The addition of streptokinase/streptodornase improved the debridement ability of hydrogel.
- There were no significant differences among modern dressings in influencing complete healing of pressure ulcers except:
  - Hydrocolloid dressing was associated with significantly more complete healing than saline gauze (5–12 weeks).
  - Hydrogel or hydropolymer was associated with more complete healing compared with hydrocolloid dressing.
- There is evidence that polyurethane foam dressing and hydrocellular dressing have better absorbency and less difficult removal compared with hydrocolloid dressings.
- Efficacy of topical growth factors in treating pressure ulcer has not been established. The use of PDGF has been associated with higher mortality from cancers.
- There were no significant differences in complete healing between specialized beds and mattresses except:
  - An AP bed with a heel guard improved healing of heel ulcers compared with alternating bed without a heel guard.
  - Profiling beds were superior to flat-based beds.
  - Air-fluidized beds were associated with significantly more improved ulcers compared with other low pressure beds or mattresses.
- Supplementation of standard hospital diet with protein, ascorbic acid (500 mg twice daily), or multinutrient supplements was associated with a significantly greater or faster reduction in the size of pressure ulcers, but did not result in a significant increase in the proportion of healed pressure ulcers.
- There is evidence that suggests electrotherapy may improve healing of pressure ulcers; however, no firm conclusion can be drawn. There is no evidence at this time that other adjunctive physical therapies (electromagnetic therapy, ultrasound therapy, ultrasound therapy in conjunction with ultraviolet C light, LLL therapy, and NPWT) would improve the healing of pressure ulcers.
- There is preliminary evidence that suggests multidisciplinary wound care teams may have an impact on the healing of pressure ulcers and length of hospitalization in the acute care setting; however, no firm conclusion can be drawn at this time.

Glossary

Alginate	A salt of alginic acid, a colloidal substance from brown seaweed; used, in the form of calcium, sodium, or ammonium alginate, as foam, clot, or gauze for absorbable surgical dressings.
Angiogenesis	The formation of new blood vessels.
Antimicrobial	An agent that kills bacteria or suppresses their multiplication or growth, including antibiotics and synthetic agents.
Ascorbic Acid	The chemical name for vitamin C.
Autolysis	The term used for the natural, spontaneous process of devitalized tissue being separated from viable tissue.
Braden Scale	A tool for assessing a person's risk for developing pressure ulcers.
Cadexomer iodine	An antiseptic that consists of spherical hydrophilic microbeads of modified starch, which contain iodine, is highly absorbent, and releases iodine slowly in the wound area.
Calcium Alginate	Calcium alginate is the calcium salt of alginic acid.
Chemotaxis	The phenomenon in which bodily cells, bacteria, and other single-cell or multicellular organisms direct their movements according to certain chemicals in their environment. For example, neutrophils migrating towards bacteria based on recognition of chemicals produced by the bacteria.
Collagen	The principal protein of the skin, tendons, cartilage, bone, and connective tissue.
Collagenase	An enzyme formed when the skin is irritated or inflamed. Collagenase breaks down the collagen fibers in the dermis.
Debridement	The removal of necrotic or infected tissues and excess moisture from a wound that may impair proper wound healing
Dextranomer	A sterile, insoluble powder in the form of circular beads, that are highly hydrophilic, drawing moisture away from the wound surface by capillary action, and is also capable of drawing nonviable debris from the wound bed.
Electromagnetic Stimulation	The use of pulsed electromagnetic fields in the radiofrequency band without thermal effects. It does not involve the use of current, leads, or electrodes.
Endothelial Cells	Highly specialized cells that line the endothelium. They are polygonal in shape and joined together by tight junctions. The tight junctions allow for variable permeability to specific macromolecules that are transported across the endothelial layer.
Epithelialization	The final stage of the proliferative phase of healing where skin forms over a wound.
Eschcar	A thick, coagulated crust or slough which develops following a thermal burn or chemical or physical cauterization of the skin.
Exudate	A fluid with a high content of protein and cellular debris which has escaped from blood vessels and has been deposited in tissues or on tissue surfaces, usually as a result of inflammation.

Fibroblast	Common cell type, found in connective tissue, that secretes an extracellular matrix rich in collagen and other macromolecules. Migrates and proliferates readily in wound repair and in tissue culture.
Growth Factors	Are cytokines (chemical signals) that control cell growth, cell migration, matrix production, enzyme expression, and differentiation. They play fundamental roles in the wound repair process
Granulation	That part of the healing process in which rough, pink tissue containing new connective tissue and capillaries forms around the edges of a wound. Granulation of a wound is normal and desirable.
Hydrocolloid	A waterproof, occlusive dressing that consists of a mixture of pectins, gelatins, sodium carboxymethylcellulose, and elastomers. Hydrocolloids create an environment that encourages autolysis to debride wounds that are sloughy or necrotic.
Hydrogel	A colloid in which the particles are in the external or dispersion phase and water us in the internal or dispersed phase. Gels have a high water content, which aids the rehydration of hard eschar and promotes autolysis in necrotic wounds.
Hydrolyzed	To undergo hydrolysis which is a chemical reaction or process in which a chemical compound reacts with water. This type of reaction is used to break down polymers.
Hydropolymer Dressing	Highly absorbent polyurethane dressing consisting of a vapour-permeable foam matrix.
Hydrotherapy	Is the use of water in any of its 3 forms (solid, liquid, or gas), internally or externally, for the treatment of disease and trauma or for cleansing purposes.
Hypergranulation	Granulation tissue that is raised above the periwound area.
Keratinocyte	Stratified, squamous, epithelial cells which comprise skin and mucosa; provide a barrier between the host and the environment; prevent the entry of toxic substances from the environment and the loss of important constituents from the host; differentiate as they progress from the basal layer to the skin surface.
Maceration	A softening or sogginess of the tissue due to retention of excessive moisture which presents as moist, red/white, and wrinkled.
Macrophages	A type of white blood cell that engulfs and destroys foreign materials. They are the key players in the immune response to foreign invaders such as infectious microorganisms.
Matrix Metalloproteases	A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e., extracellular matrix proteins). Because these enzymes need zinc or calcium atoms to work properly, they are called metalloproteinases. Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumor cell metastasis.
Necrotic	The local death of tissue. This tissue is often black/brown in colour and leathery in texture.

Nerve Growth Factor	A polypeptide that has been shown to promote the regeneration of injured cells that express nerve growth factor receptors in the peripheral and central nervous systems.
Neutrophil	A white blood cell that plays a central role in defence of a host against infection. Neutrophils engulf and kill foreign microorganisms.
Nitrofurazone	A pale yellow crystalline compound used externally as a bacteriostatic or bactericidal dressing for wounds and infections.
Normothermic	A condition of normal body temperature.
Periwound	The area immediately around the wound.
Phenytoin	Is an antiepileptic agent that when used topically has shown to accelerate the healing process in ulcers of various etiology.
Platelet-Derived Growth Factor (PDGF)	A mitogenic growth factor that is found especially in platelets, consists of 2 polypeptide chains linked by bonds containing 2 sulfur atoms each, stimulates cell proliferation (as in connective tissue, smooth muscle, and glia), and plays a role in wound healing
Polyurethane	A synthetic resin in which the polymer units are linked by urethane groups, used chiefly as constituents of paints, varnishes, adhesives, and foams.
Pressure Sore Status Tool (PSST)	A tool used to quantify the wound healing process. This tool assesses a pressure ulcer condition based on 13 parameters each measured on a Likert scale of 1 to 5. The total score ranges from 13 to 65 with the score of 13 indicating a healed ulcer.
Pressure Ulcer	A localized injury to the skin and/or underlying tissue usually over a bony prominence, as a result of pressure, or pressure in combination with shear and/or friction.
Pressure Ulcer Scale for Healing (PUSH)	Scores a pressure ulcer based on its surface area, amount of exudates, and the type of tissue present (e.g., granulation). The total score ranges from 0 (healed ulcer) to 17 (>24 cm^2 with heavy exudates and necrosis).
Proliferation	When new granulation tissue is formed to replace lost volume. Epithelial cells grow around the wound, or in islets, to form a new protective covering.
Slough	A term for the viscous yellow layer which often covers the wound and is strongly adherent to it. Its presence can be related to the end of the inflammatory stage of healing when dead cells have accumulated in the exudate.
Streptodornase	Liquefies the vicious nucleoprotein of dead cells or pus.
Streptokinase	A clot-dissolving medication.
Wound	A break in the integrity of the skin; an injury to the body which causes a disruption of the normal continuity of the body structures.

Appendices

Appendix 1: U.S. National Pressure Ulcer Advisory Panel Staging System (1)

Stage	Definition	Further description
Suspected Deep Tissue Injury	Purple or maroon localized area of discolored intact skin or blood-filled blister due to damage of underlying soft tissue from pressure and/or shear. The area may be preceded by tissue that is painful, firm, mushy, boggy, warmer or cooler as compared with adjacent tissue.	Deep tissue injury may be difficult to detect in individuals with dark skin tones. Evolution may include a thin blister over a dark wound bed. The wound may further evolve and become covered by thin eschar. Evolution may be rapid exposing additional layers of tissue even with optimal treatment.
Stage I	Intact skin with nonblanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area.	The area may be painful, firm, soft, warmer or cooler as compared with adjacent tissue. Stage I may be difficult to detect in individuals with dark skin tones. May indicate "at risk" persons (a heralding sign of risk)
Stage II	Partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled blister.	Presents as a shiny or dry shallow ulcer without slough or bruising.* This stage should not be used to describe skin tears, tape burns, perineal dermatitis, maceration or excoriation.
Stage III	Full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle are not exposed. Slough may be present but does not obscure the depth of tissue loss. May include undermining and tunneling.	The depth of a stage III pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and stage III ulcers can be shallow. In contrast, areas of significant adiposity can develop extremely deep stage III pressure ulcers. Bone/tendon is not visible or directly palpable.
Stage IV	Full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling.	The depth of a stage IV pressure ulcer varies by anatomical location. The bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue and these ulcers can be shallow. Stage IV ulcers can extend into muscle and/or supporting structures (e.g., fascia, tendon or joint capsule) making osteomyelitis possible. Exposed bone/tendon is visible or directly palpable.
Unstageable	Full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed.	Until enough slough and/or eschar is removed to expose the base of the wound, the true depth, and therefore stage, cannot be determined. Stable (dry, adherent, intact without erythema or fluctuance) eschar on the heels serves as "the body's natural (biological) cover" and should not be removed.

*Bruising indicates suspected deep tissue injury

Appendix 2: Summary of Studies on Factors That Predict Healing of Pressure Ulcers*

	Jones 2007	Bergstrom 2005	Kramer 2000	Berlowitz 1997
Design	Multicentre retrospective cohort study	Multicentre retrospective cohort study	Single centre retrospective cohort study	Multicentre retrospective cohort study
Setting	Pressure ulcer care in hospitals, clinics, nursing homes and home care in 3 geographical areas	95 Long-term care facilities	Chronic unit of one long-term care facility	Long-term care facilities in the United States
Sample size	82	882	106	819
Study period	6 months	12 weeks	4 weeks	6 months
Mean age, years	78.0	Stage II Stage III/IV 79.8 76.0 (P < .002)	66.8	70.4
Caucasian, %	59.3	NR	65	NR
Ulcer, %	Stage II 76.5 Stage III 33.3 Stage IV 13.3	Stage II 68 Stage III/IV 32	Stage II 21 Stage III 14 Stage IV 65	Stage II NR Stage III NR Stage IV 22.3
Source of data	Review of medical records Structured form	Review of medical records, Medical Data Set, and other records	Medical records	Veterans Affairs Assessment File
Statistical analysis	-Chi square, F-tests -Student *t* test -Variance analysis -Forward and backward conditional multiple regression modelling	2 multiple regression models: One for stage II ulcers and 1 for stage II/III ulcers	-Correlation analysis -Forward multiple regression modelling	Bivariate analysis Multiple logistic regression modelling
Measure of healing	Complete healing, % 3 mos 6 mos Stage II 27.3 76.5 Stage III 10.2 33.3 Stage IV 2.6 13.3	Complete healing, % 12 weeks Stage II 37 Stage III/IV 5	Decrease in surface area of ulcer, % Mean = 35.6	Complete healing, % Overall 54 Stage II 72 Stage III 45.2 Stage IV 30.6 Between stages (P < .001)
Performance of multivariate regression model	Backward conditional model Significant (P < .001) Explained 75.8 of the variance of healing Predicted correctly 91.5% of cases	Model for stage II ulcers Explained little of the variance (R^2 = 0.13)	3 predictors explained 25% of the variability in healing	

	Jones 2007	Bergstrom 2005	Kramer 2000	Berlowitz 1997
Factors associated with ↑ odds of healing	Use of exudate management dressing with no exudate	Associated with greatest ↓ in area of ulcer **Stage II ulcers** -Dementia and agitation without hallucination -↑ in interval of assessment -Very large ulcers -Moist dressing **Stage III/IV ulcers** -Dementia -Very large pressure ulcers ≥ 12 cm -Receiving sufficient enteral feeding >30kcal/kg (except high acuity patients) -Moist dressing	-Lower pressure ulcer stage -Higher patient weight -Lower mean body temperature Together predictors explained 25% of the variability in healing In a regression analysis of treatment variables, only shorter time on a pressure ulcer-relieving bed predicted healing	-Age ≥75 years (OR, 1.5 [95% CI, 1.1–2.0]) -Stage II ulcer vs stage IV (OR, 5.2 [95% CI, 3.5]) -Rehabilitation services (per number received) (OR, 1.3 [95% CI, 1.1–1.6])
Factors associated with ↓ odds of healing	-Medicaid (OR, 0.18, *P* = .087) -Comorbid CVD (OR, 0.14, *P* = .063) -Dressing type change (OR = 0.50, *P* = .015) -Topical antiseptics -Antibiotic administration -Pressure relief devices -No exudate management dressing for moderate or large amount of exudate -No debridement of wounds with yellow slough	**Stage II ulcers** Cleaning with saline or soap **Stage III/IV** Receiving debridement	-High pressure ulcer stage -Low patient weight -High patient temperature	-Incontinence (OR, 0.7 [95% CI, 0.4–1.0]) -Immobility (OR, 0.3 [95% CI, 0.1–0.5])

*CI, confidence interval; NR, not reported; OR, odds ratio.

Appendix 3: Search Strategies

Pressure Sores Treatment – Final Search

Search date: August 6, 2007
Databases searched: OVID MEDLINE, MEDLINE In-Process & Other Non-Indexed Citations, CINAHL, EMBASE, Cochrane Library, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to July Week 4 2007>
Search Strategy:

1	exp Pressure Ulcer/dh, dt, rt, rh, su, th [Diet Therapy, Drug Therapy, Radiotherapy, Rehabilitation, Surgery, Therapy] (905)
2	exp Pressure Ulcer/ or exp Skin Ulcer/ or (decubitus or bedsore$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (12589)
3	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6443)
4	2 or 3 (13597)
5	exp Nutritional Support/ or exp Dietary Supplements/ or exp Nutrition/ (26310)
6	Debridement/ or exp Irrigation/ or exp Suction/ or exp Bandages/ or exp Beds/ or exp pressure/ or exp Larva/ (55505)
7	(Platelet releasate or CT-102).mp. (48)
8	exp Stem Cells/ (70804)
9	exp Therapeutics/ (908746)
10	exp Surgery/ (8437)
11	exp Skin Transplantation/ or exp Skin, Artificial/ (6047)
12	exp Treatment Outcome/ (275526)
13	exp Treatment Failure/ (13032)
14	exp Hydrotherapy/ or exp Ultrasonic Therapy/ or exp Ultraviolet Therapy/ or exp Electric Stimulation Therapy/ or exp Electromagnetics/ (23802)
15	wound bed prep$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (66)
16	exp Transforming Growth Factor beta/ or exp Growth Substances/ or exp Fibroblast Growth Factors/ or exp Platelet-Derived Growth Factor/ or exp Epidermal Growth Factor/ or exp Colony-Stimulating Factors/ (248588)
17	((wound$ or ulcer$) adj3 (modulat$ or growth factor$ or stimulating factor$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (603)
18	or/5-17 (1388534)
19	4 and 18 (6644)
20	1 or 19 (6987)
21	limit 20 to (humans and english language and yr="1996 - 2007") (5718)
22	limit 21 to (controlled clinical trial or meta analysis or randomized controlled trial) (555)
23	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (53354)
24	exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (319845)
25	exp Double-Blind Method/ or exp Control Groups/ or exp placebos/ or RCT$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (55363)
26	exp Economics/ (172912)

27 (cost$ or economic$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (190006)
28 or/22-27 (614901)
29 21 and 28 (1377)
30 exp Diabetes Mellitus/ (95945)
31 exp Burns/ (10893)
32 exp Varicose Ulcer/ (1188)
33 exp Diabetic Angiopathies/ (12924)
34 or/30-33 (107894)
35 29 not 34 (875)

Database: EMBASE <1980 to 2007 Week 30>
Search Strategy:
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1 exp Decubitus/rt, dm, rh, dt, su, th [Radiotherapy, Disease Management, Rehabilitation, Drug Therapy, Surgery, Therapy] (1088)
2 exp skin ulcer/ or exp decubitus/ (16832)
3 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (8942)
4 (decubitus or bedsore$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (4887)
5 or/2-4 (19305)
6 exp nutrition/ or exp diet therapy/ or exp nutritional support/ (779276)
7 exp diet supplementation/ (25678)
8 exp LAVAGE/ (26658)
9 exp SUCTION/ (1566)
10 exp Bandage/ (1531)
11 exp "BANDAGES AND DRESSINGS"/ (9345)
12 exp bed/ (2384)
13 exp PRESSURE/ (24926)
14 wound care/ or debridement/ or maggot therapy/ or wound drainage/ or wound dressing/ or wound irrigation/ (17158)
15 exp Stem Cell/ (41237)
16 exp Therapy/ (2500403)
17 exp surgery/ (1328439)
18 exp Skin Transplantation/ (20591)
19 exp Artificial Skin/ (405)
20 exp Treatment Outcome/ (389424)
21 exp Treatment Failure/ (34266)
22 exp hydrotherapy/ or exp electrostimulation therapy/ or exp ultrasound therapy/ (78822)
23 exp phototherapy/ (20784)
24 exp Electromagnetic Field/ (5101)
25 exp Patient Positioning/ (6574)
26 exp Growth Factor/ (180173)
27 ((wound$ or ulcer$) adj3 (modulat$ or growth factor$ or stimulating factor$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1883)
28 (Platelet releasate or CT-102).mp. (58)
29 wound bed prep$.mp. [mp=title, abstract, subject headings, heading word, drug trade name,

original title, device manufacturer, drug manufacturer name] (56)
30 or/6-29 (3941237)
31 5 and 30 (13134)
32 1 or 31 (13288)
33 limit 32 to (human and english language and yr="1996 - 2007") (7329)
34 Randomized Controlled Trial/ (121547)
35 exp Randomization/ (23112)
36 exp RANDOM SAMPLE/ (692)
37 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).ti,mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (74484)
38 Double Blind Procedure/ (64908)
39 exp Triple Blind Procedure/ (7)
40 exp Control Group/ (902)
41 exp PLACEBO/ (101571)
42 exp ECONOMICS/ (12565)
43 (cost$ or economic$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (324903)
44 or/34-43 (599075)
45 33 and 44 (1289)
46 exp Diabetes Mellitus/ (206434)
47 exp Burn/ (21386)
48 exp Varicosis/ (15726)
49 or/46-48 (243034)
50 45 not 49 (732)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to July Week 4 2007>
Search Strategy:
---
1 exp Pressure Ulcer/dh, dt, rh, su, th [Diet Therapy, Drug Therapy, Rehabilitation, Surgery, Therapy] (1098)
2 exp skin ulcer/ or exp pressure ulcer/ or (decubitus or bedsore$).mp. [mp=title, subject heading word, abstract, instrumentation] (9542)
3 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6067)
4 exp NUTRITION/ (31831)
5 exp Nutritional Support/ (12258)
6 exp Dietary Supplements/ (1721)
7 exp Debridement/ (1363)
8 exp Irrigation/ (1560)
9 exp SUCTION/ (1152)
10 exp "Bandages and Dressings"/ (4922)
11 exp "Beds and Mattresses"/ (1763)
12 exp Pressure/ (1842)
13 exp Patient Positioning/ (3886)
14 exp Stem Cells/ (1757)
15 exp Therapeutics/ (346621)
16 exp Surgery, Operative/ (87954)
17 exp Skin, Artificial/ (309)

18 exp Skin Transplantation/ (825)
19 exp Treatment Outcomes/ (38071)
20 exp Treatment Failure/ (2064)
21 electrotherapy/ or hydrotherapy/ or ultrasonic therapy/ or ultraviolet therapy/ (1483)
22 exp Electromagnetics/ or exp Magnet Therapy/ (1015)
23 exp Growth Substances/ (5215)
24 ((wound$ or ulcer$) adj3 (modulat$ or growth factor$ or stimulating factor$)).mp. [mp=title, subject heading word, abstract, instrumentation] (172)
25 (Platelet releasate or CT-102).mp. (5)
26 wound bed prep$.mp. [mp=title, subject heading word, abstract, instrumentation] (78)
27 2 or 3 (10021)
28 or/4-26 (440839)
29 27 and 28 (6279)
30 1 or 29 (6500)
31 limit 30 to (english and yr="1996 - 2007") (5101)
32 exp Diabetes Mellitus/ (26976)
33 exp BURNS/ (5684)
34 exp Venous Ulcer/ (788)
35 or/32-34 (33319)
36 31 not 35 (3103)
37 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (58616)
38 RCT.mp. (680)
39 exp Meta Analysis/ (5479)
40 exp "Systematic Review"/ (3217)
41 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (19079)
42 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (11176)
43 exp PLACEBOS/ (3668)
44 exp Economics/ (215909)
45 (economic$ or cost$).mp. [mp=title, subject heading word, abstract, instrumentation] (54062)
46 or/37-45 (280064)
47 36 and 46 (885)

Final Search Strategy – Pressure Sores 2008 - Cleaning

Search date: March 19, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (3492)
2 exp Wound Healing/ or exp Wound Infection/ (34059)
3 exp Skin Ulcer/ (12547)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5 (bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)

6 or/1-5 (45415)
7 exp Irrigation/ (6280)
8 exp Hydrotherapy/ (418)
9 exp Solutions/ (33578)
10 exp Water/ (65110)
11 exp Sodium Chloride/ (15190)
12 exp Anti-Infective Agents, Local/ (52642)
13 exp acetic acids/ or acetic acid/ (32800)
14 exp Disinfection/ (3099)
15 exp Potassium Permanganate/ or exp Gentian Violet/ (943)
16 exp Surface-Active Agents/ (28536)
17 exp Castor Oil/ (293)
18 (detergent$ or whirlpool$ or saline or povidone or iodine or disinfect$ or bath$ or water or hydrotherap$ or hydro-therap$ or lavage or irrigat$ or wash$ or cleans$ or clean$ or aloe vera or gentian violet or eusol or potassium permanganate or benzoyl peroxide or hyrogen peroxide or betadine or silver chloride or vulnopur or decyl glucoside).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346012)
19 or/7-18 (460724)
20 6 and 19 (4023)
21 limit 20 to (english language and humans and yr="2003 - 2008") (1178)
22 limit 21 to (controlled clinical trial or meta analysis or randomized controlled trial) (219)
23 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
24 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
25 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346069)
26 exp Double-Blind Method/ (50381)
27 exp Control Groups/ (533)
28 exp Placebos/ (8753)
29 RCT.mp. (2244)
30 or/22-29 (414777)
31 21 and 30 (321)
32 exp *Burns/ (9607)
33 *Diabetic Foot/ (2580)
34 *Ischemia/ (8409)
35 *Surgical Wound Infection/ (4370)
36 *Postoperative Complications/ (37461)
37 *Varicose Ulcer/ (1075)
38 or/32-37 (62828)
39 31 not 38 (182)

Database: EMBASE <1980 to 2008 Week 11>
Search Strategy:
---
1 exp Decubitus/ (3882)
2 exp Skin Ulcer/ (17884)
3 exp Wound Healing/ or exp Wound Infection/ (50625)
4 exp Chronic Wound/ (227)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject

headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9428)
6 bedsore$.mp. (154)
7 or/1-6 (67100)
8 exp WOUND IRRIGATION/ (605)
9 exp HYDROTHERAPY/ (1143)
10 exp "Solution and Solubility"/ (66832)
11 exp WATER/ (110563)
12 exp Sodium Chloride/ (52921)
13 exp Hydrogen Peroxide/ (27914)
14 exp Topical Antiinfective Agent/ (104248)
15 exp Acetic Acid/ (16793)
16 exp DISINFECTION/ (8510)
17 exp Permanganate Potassium/ (1258)
18 exp Surfactant/ (79380)
19 exp Castor Oil/ (1021)
20 (detergent$ or whirlpool$ or saline or povidone or iodine or disinfect$ or bath$ or water or hydrotherap$ or hydro-therap$ or lavage or irrigat$ or wash$ or cleans$ or clean$ or aloe vera or gentian violet or eusol or potassium permanganate or benzoyl peroxide or hyrogen peroxide or betadine or silver chloride or vulnopur or decyl glucoside).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (612905)
21 or/8-20 (807447)
22 7 and 21 (6982)
23 limit 22 to (human and english language and yr="2003 - 2008") (1703)
24 Randomized Controlled Trial/ (155511)
25 exp Randomization/ (25203)
26 exp RANDOM SAMPLE/ (1011)
27 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (280926)
28 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56808)
29 Double Blind Procedure/ (68576)
30 exp Triple Blind Procedure/ (8)
31 exp Control Group/ (1516)
32 exp PLACEBO/ (111054)
33 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (402720)
34 or/24-33 (612781)
35 23 and 34 (312)
36 *Burns/ (12425)
37 *Diabetic Foot/ (1980)
38 *Varicosis/ (3636)
39 *MICROVASCULAR ISCHEMIA/ (47)
40 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10581)
41 or/36-40 (28645)
42 35 not 41 (256)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 2 2008>
Search Strategy:

1	exp Pressure Ulcer/ (5153)
2	exp Wound Healing/ or exp Wound Infection/ (9484)
3	exp Skin Ulcer/ (10197)
4	exp Wounds, Chronic/ (826)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6554)
6	bedsore$.mp. (75)
7	or/1-6 (18277)
8	exp IRRIGATION/ (1765)
9	exp HYDROTHERAPY/ (878)
10	exp SOLUTIONS/ (3029)
11	exp WATER/ (1697)
12	exp Sodium Chloride/ (1161)
13	exp Hydrogen Peroxide/ (290)
14	exp ANTIINFECTIVE AGENTS, LOCAL/ (2858)
15	exp Acetic Acid/ (205)
16	exp "Sterilization and Disinfection"/ (3167)
17	exp Surface-Active Agents/ (563)
18	(detergent$ or whirlpool$ or saline or povidone or iodine or disinfect$ or bath$ or water or hydrotherap$ or hydro-therap$ or lavage or irrigat$ or wash$ or cleans$ or clean$ or aloe vera or gentian violet or eusol or potassium permanganate or benzoyl peroxide or hyrogen peroxide or betadine or silver chloride or vulnopur or decyl glucoside).mp. [mp=title, subject heading word, abstract, instrumentation] (31568)
19	exp Castor Oil/ (26)
20	or/8-19 (36072)
21	7 and 20 (1331)
22	limit 21 to (english and yr="2003 - 2008") (598)
23	random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69213)
24	RCT.mp. (872)
25	exp Meta Analysis/ (6294)
26	exp "Systematic Review"/ (3554)
27	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22852)
28	exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13890)
29	exp PLACEBOS/ (4185)
30	or/23-29 (90540)
31	22 and 30 (130)

Final Search – Pressure Sores 2008 - Debridement

Search date: March 22, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (3492)
2 exp Skin Ulcer/ (12547)
3 exp Wound Healing/ or exp Wound Infection/ (34059)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5 (bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)
6 or/1-5 (45415)
7 exp Debridement/ (4526)
8 debrid$.mp. (8618)
9 exp Larva/ (14177)
10 exp Streptokinase/ (1402)
11 exp Iodine Compounds/ or exp Hydrogel/ (4077)
12 (trypsin or varidase or enzym$ or chemical$ or autolytic or collagenase or streptokinase or dextranoma or streptodornase or papain-urea or cadexomer iodine or larva$ or maggot$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (668012)
13 (polysaccharide$ or dextranomer$ or xerogel).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (20260)
14 (biosurger$ or bio-surg$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (39)
15 (hydrocolloid* or granuflex or tegasorb or aquacel or hydrocoll or combiderm or duoderm).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (634)
16 (fibrinolytic$ or proteolytic or hypochlorite or dakin or iodoflex or iodosorb or debrisan or eusol).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (35932)
17 (malic acid or benzoid acid or salicylic acid or propylene glycol).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (5193)
18 (hydrogel$ or intrasite gel$ or intrasitgel$ or sterigel or granugel or nugel or purilon or vigilon).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (4770)
19 or/7-18 (722998)
20 6 and 19 (5341)
21 limit 20 to (english language and humans and yr="2003 - 2008") (1823)
22 limit 21 to (controlled clinical trial or meta analysis or randomized controlled trial) (169)
23 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
24 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
25 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346069)
26 exp Double-Blind Method/ (50381)
27 exp Control Groups/ (533)

28 exp Placebos/ (8753)
29 RCT.mp. (2244)
30 or/22-29 (414778)
31 21 and 30 (262)
32 *Diabetic Foot/ (2580)
33 *Burns/ (7235)
34 *Ischemia/ (8409)
35 *Surgical Wound Infection/ (4370)
36 *Postoperative Complications/ (37461)
37 *Varicose Ulcer/ (1075)
38 or/32-37 (60476)
39 31 not 38 (163)
40 limit 39 to (case reports or comment or letter) (6)
41 39 not 40 (157)

Database: EMBASE <1980 to 2008 Week 12>
Search Strategy:
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1 exp Decubitus/ (3887)
2 exp Skin Ulcer/ (17909)
3 exp Wound Healing/ or exp Wound Infection/ (50688)
4 exp Chronic Wound/ (229)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9444)
6 bedsore$.mp. (155)
7 or/1-6 (67188)
8 exp WOUND IRRIGATION/ (606)
9 exp HYDROTHERAPY/ (1144)
10 exp "Solution and Solubility"/ (66942)
11 exp WATER/ (110696)
12 exp Sodium Chloride/ (53001)
13 exp Hydrogen Peroxide/ (27975)
14 exp Topical Antiinfective Agent/ (104398)
15 exp Acetic Acid/ (16817)
16 exp DISINFECTION/ (8516)
17 exp Permanganate Potassium/ (1260)
18 exp Surfactant/ (79483)
19 exp Castor Oil/ (1022)
20 (detergent$ or whirlpool$ or saline or povidone or iodine or disinfect$ or bath$ or water or hydrotherap$ or hydro-therap$ or lavage or irrigat$ or wash$ or cleans$ or clean$ or aloe vera or gentian violet or eusol or potassium permanganate or benzoyl peroxide or hyrogen peroxide or betadine or silver chloride or vulnopur or decyl glucoside).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (613582)
21 or/8-20 (808382)
22 7 and 21 (6992)
23 limit 22 to (human and english language and yr="2003 - 2008") (1708)
24 Randomized Controlled Trial/ (155780)
25 exp Randomization/ (25236)

26 exp RANDOM SAMPLE/ (1022)
27 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281365)
28 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56961)
29 Double Blind Procedure/ (68653)
30 exp Triple Blind Procedure/ (8)
31 exp Control Group/ (1545)
32 exp PLACEBO/ (111315)
33 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403354)
34 or/24-33 (613798)
35 23 and 34 (312)
36 *Burns/ (12430)
37 *Diabetic Foot/ (1981)
38 *Varicosis/ (3637)
39 *MICROVASCULAR ISCHEMIA/ (47)
40 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10590)
41 or/36-40 (28661)
42 35 not 41 (256)
43 limit 42 to (editorial or letter or note) (13)
44 Case Report/ (983221)
45 42 not (43 or 44) (235)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 2 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (5153)
2 exp Skin Ulcer/ (10197)
3 exp Wounds, Chronic/ (826)
4 exp Wound Healing/ or exp Wound Infection/ (9484)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6554)
6 bedsore$.mp. (75)
7 or/1-6 (18277)
8 exp DEBRIDEMENT/ (1619)
9 exp Streptokinase/ (249)
10 exp Larval Therapy/ (180)
11 exp Iodine Compounds/ (139)
12 exp HYDROGEL DRESSINGS/ (269)
13 debrid$.mp. (2318)
14 (trypsin or varidase or enzym$ or chemical$ or autolytic or collagenase or streptokinase or dextranoma or streptodornase or papain-urea or cadexomer iodine or larva$ or maggot$).mp. [mp=title, subject heading word, abstract, instrumentation] (20077)
15 (polysaccharide$ or dextranomer$ or xerogel).mp. [mp=title, subject heading word, abstract, instrumentation] (632)
16 (hydrocolloid* or granuflex or tegasorb or aquacel or hydrocoll or combiderm or duoderm).mp. [mp=title, subject heading word, abstract, instrumentation] (461)
17 (biosurger$ or bio-surg$).mp. [mp=title, subject heading word, abstract, instrumentation] (10)

18 (fibrinolytic$ or proteolytic or hypochlorite or dakin or iodoflex or iodosorb or debrisan or eusol).mp. [mp=title, subject heading word, abstract, instrumentation] (2030)
19 (malic acid or benzoid acid or salicylic acid or propylene glycol).mp. [mp=title, subject heading word, abstract, instrumentation] (65)
20 (hydrogel$ or intrasite gel$ or intrasitgel$ or sterigel or granugel or nugel or purilon or vigilon).mp. [mp=title, subject heading word, abstract, instrumentation] (389)
21 or/8-20 (25090)
22 7 and 21 (1766)
23 limit 22 to (english and yr="2003 - 2008") (840)
24 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69213)
25 RCT.mp. (872)
26 exp Meta Analysis/ (6294)
27 exp "Systematic Review"/ (3554)
28 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22852)
29 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13890)
30 exp PLACEBOS/ (4185)
31 or/24-30 (90540)
32 23 and 31 (100)
33 *Burns/ (4636)
34 *Diabetic Foot/ (1954)
35 *Surgical Wound/ or exp Postoperative Complications/ (17091)
36 *Ischemia/ (645)
37 *Venous Ulcer/ (625)
38 or/33-37 (24822)
39 32 not 38 (53)

Final Search – Pressure Sores – Dressings

Search date: March 16, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 1 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (3480)
2 exp Wound Healing/ or exp Wound Infection/ (33963)
3 exp Skin Ulcer/ (12499)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6897)
5 (bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1422)
6 or/1-5 (45284)
7 exp Bandages/ (6673)
8 ((gauze$ or dressing$ or bandage$) adj4 (biological or collagen or growth factor$ or hyaluronic acid$ or interleukin$ or stimulat$ factor$ or hydrocolloid$ or hydrogel$ or carboxymethylcellulose or hydropolymer or hydrocellular or alginate or normothermic or film$ or foam$ or antimicrobial$ or silver$ or honey or iodine or chorhexidine or polyurethane or

fabric$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1377)
9 7 or 8 (6880)
10 6 and 9 (3093)
11 limit 10 to (english language and humans and yr="2003 - 2008") (1180)
12 limit 11 to (controlled clinical trial or meta analysis or randomized controlled trial) (191)
13 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31320)
14 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59263)
15 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (345174)
16 exp Double-Blind Method/ (50275)
17 exp Control Groups/ (532)
18 exp Placebos/ (8713)
19 RCT.mp. (2232)
20 or/12-19 (413674)
21 11 and 20 (333)
22 *Burns/ (7225)
23 *Diabetic Foot/ (2565)
24 *Varicose Ulcer/ (1073)
25 *Ischemia/ (8391)
26 *Postoperative Complications/ or *Surgical Wound Infection/ (41550)
27 or/22-26 (60362)
28 21 not 27 (205)
29 limit 28 to (case reports or comment or editorial or letter) (24)
30 28 not 29 (181)

Database: EMBASE <1980 to 2008 Week 11>
Search Strategy:
---
1 exp Decubitus/ (3882)
2 exp Skin Ulcer/ (17884)
3 exp Wound Healing/ or exp Wound Infection/ (50625)
4 exp Chronic Wound/ (227)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9428)
6 bedsore$.mp. (154)
7 or/1-6 (67100)
8 exp "bandages and dressings"/ (9947)
9 ((gauze$ or dressing$ or bandage$) adj4 (biological or collagen or growth factor$ or hyaluronic acid$ or interleukin$ or stimulat$ factor$ or hydrocolloid$ or hydrogel$ or carboxymethylcellulose or hydropolymer or hydrocellular or alginate or normothermic or film$ or foam$ or antimicrobial$ or silver$ or honey or iodine or chorhexidine or polyurethane or fabric$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1422)
10 8 or 9 (10334)
11 7 and 10 (3144)
12 limit 11 to (human and english language and yr="2003 - 2008") (1072)

13 Randomized Controlled Trial/ (155511)
14 exp Randomization/ (25203)
15 exp RANDOM SAMPLE/ (1011)
16 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (280926)
17 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56808)
18 Double Blind Procedure/ (68576)
19 exp Triple Blind Procedure/ (8)
20 exp Control Group/ (1516)
21 exp PLACEBO/ (111054)
22 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (402720)
23 or/13-22 (612781)
24 12 and 23 (247)
25 *Burn/ (12425)
26 *Diabetic Foot/ (1980)
27 *Varicosis/ (3636)
28 *MICROVASCULAR ISCHEMIA/ (47)
29 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10581)
30 or/25-29 (28645)
31 24 not 30 (178)
32 limit 31 to (editorial or letter or note) (16)
33 Case Report/ (982316)
34 31 not (32 or 33) (158)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 1 2008>
Search Strategy:
---
1 exp Pressure Ulcer/ (5128)
2 exp Skin Ulcer/ (10126)
3 exp Wounds, Chronic/ (817)
4 exp Wound Healing/ or exp Wound Infection/ (9366)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6512)
6 bedsore$.mp. (74)
7 or/1-6 (18089)
8 exp "Bandages and Dressings"/ (5335)
9 ((gauze$ or dressing$ or bandage$) adj4 (biological or collagen or growth factor$ or hyaluronic acid$ or interleukin$ or stimulat$ factor$ or hydrocolloid$ or hydrogel$ or carboxymethylcellulose or hydropolymer or hydrocellular or alginate or normothermic or film$ or foam$ or antimicrobial$ or silver$ or honey or iodine or chorhexidine or polyurethane or fabric$)).mp. [mp=title, subject heading word, abstract, instrumentation] (1568)
10 8 or 9 (5419)
11 7 and 10 (2689)
12 limit 11 to (english and yr="2003 - 2008") (1124)
13 *Burns/ (4584)
14 *Diabetic Foot/ (1931)
15 *Surgical Wound/ or exp Postoperative Complications/ (16692)

16 *Ischemia/ (618)
17 *Venous Ulcer/ (619)
18 or/13-17 (24318)
19 12 not 18 (748)
20 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (67992)
21 RCT.mp. (858)
22 exp Meta Analysis/ (6223)
23 exp "Systematic Review"/ (3535)
24 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22492)
25 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13554)
26 exp PLACEBOS/ (4145)
27 or/20-26 (88939)
28 19 and 27 (67)

Final Search Strategy – Pressure Sores 2008 - Growth Factors

Search date: March 19, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 1 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (3480)
2 exp Wound Healing/ or exp Wound Infection/ (33963)
3 exp Skin Ulcer/ (12499)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6897)
5 (bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1422)
6 or/1-5 (45284)
7 exp "Intercellular Signaling Peptides and Proteins"/ (343648)
8 exp Growth Substances/ (192006)
9 ((growth or stimulat$) adj2 (substance$ or factor$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (169667)
10 interleukin$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (110693)
11 or/7-10 (555006)
12 6 and 11 (5613)
13 limit 12 to (english language and humans and yr="2003 - 2008") (1628)
14 limit 13 to (controlled clinical trial or meta analysis or randomized controlled trial) (74)
15 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31320)
16 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59263)
17 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (345174)
18 exp Double-Blind Method/ (50275)
19 exp Control Groups/ (532)

20 exp Placebos/ (8713)
21 RCT.mp. (2232)
22 or/14-21 (413657)
23 13 and 22 (153)
24 *Burns/ (7225)
25 *Diabetic Foot/ (2565)
26 *Varicose Ulcer/ (1073)
27 *Ischemia/ (8391)
28 *Postoperative Complications/ (37401)
29 *Surgical Wound Infection/ (4359)
30 or/24-29 (60362)
31 23 not 30 (107)
32 limit 31 to (case reports or comment or editorial or letter) (12)
33 31 not 32 (95)

Search Strategy:

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1 exp Decubitus/ (3882)
2 exp Skin Ulcer/ (17884)
3 exp Wound Healing/ or exp Wound Infection/ (50625)
4 exp Chronic Wound/ (227)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9428)
6 bedsore$.mp. (154)
7 or/1-6 (67100)
8 exp Growth Factor/ (192755)
9 exp Cytokine/ (469215)
10 ((growth or stimulat$) adj2 (substance$ or factor$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (254180)
11 or/8-10 (599116)
12 7 and 11 (8126)
13 limit 12 to (human and english language and yr="2003 - 2008") (2520)
14 Randomized Controlled Trial/ (155511)
15 exp Randomization/ (25203)
16 exp RANDOM SAMPLE/ (1011)
17 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (280926)
18 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56808)
19 Double Blind Procedure/ (68576)
20 exp Triple Blind Procedure/ (8)
21 exp Control Group/ (1516)
22 exp PLACEBO/ (111054)
23 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (402720)
24 or/14-23 (612781)
25 13 and 24 (397)
26 *Burn/ (12425)

27 *Diabetic Foot/ (1980)
28 *Varicosis/ (3636)
29 *MICROVASCULAR ISCHEMIA/ (47)
30 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10581)
31 or/26-30 (28645)
32 25 not 31 (357)
33 limit 32 to (editorial or letter or note) (22)
34 Case Report/ (982316)
35 32 not (33 or 34) (331)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 2 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (5153)
2 exp Skin Ulcer/ (10197)
3 exp Wounds, Chronic/ (826)
4 exp Wound Healing/ or exp Wound Infection/ (9484)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6554)
6 bedsore$.mp. (75)
7 or/1-6 (18277)
8 exp Cytokines/ (10979)
9 ((growth or stimulat$) adj2 (substance$ or factor$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6293)
10 interleukin$.mp. (3631)
11 or/8-10 (14530)
12 7 and 11 (760)
13 limit 12 to (english and yr="2003 - 2008") (404)
14 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69213)
15 RCT.mp. (872)
16 exp Meta Analysis/ (6294)
17 exp "Systematic Review"/ (3554)
18 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22852)
19 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13890)
20 exp PLACEBOS/ (4185)
21 or/14-20 (90540)
22 13 and 21 (45)
23 *Burns/ (4636)
24 *Daibetic Foot/ (0)
25 *Surgical Wound/ or *Postoperative Complications/ (4754)
26 *Ischemia/ (645)
27 *Venous Ulcer/ (625)
28 or/23-27 (10639)
29 22 not 28 (39)

Final Search – Press Sores 2008 – Support Surfaces

March 30, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 3 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (3494)
2 exp Skin Ulcer/ (12566)
3 exp Wound Healing/ or exp Wound Infection/ (34138)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6933)
5 bedsore$.mp. (97)
6 or/1-5 (45241)
7 Beds/ (1275)
8 exp "Bedding and Linens"/ (1335)
9 (pressure adj2 (relief or reliev$ or reduc$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6386)
10 (sheep?skin$ or sheep skin$ or mattress$ or pillow$ or cushion$ or (support$ adj2 surface) or (support$ adj2 air) or beds or bed or bedding or bolster$ or (foam adj2 wedge$) or (foam adj2 block$) or gelpad$ or gel pad$ or gel-pad$ or gell pad$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (36817)
11 ((pressure or bedsore$ or wound$ or ulcer$ or sore$) adj2 overlay$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (15)
12 (pressure-relief or pressure-reduc$ or pressure-reliev$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (2164)
13 or/7-12 (42829)
14 6 and 13 (2009)
15 limit 14 to (english language and humans and yr="2003 - 2008") (745)
16 limit 15 to (controlled clinical trial or meta analysis or randomized controlled trial) (81)
17 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31521)
18 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59631)
19 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346865)
20 exp Double-Blind Method/ (50479)
21 exp Control Groups/ (535)
22 exp Placebos/ (8762)
23 RCT.mp. (2250)
24 or/16-23 (415760)
25 15 and 24 (157)
26 limit 25 to (case reports or comment or editorial or letter) (4)
27 25 not 26 (153)
28 *Burns/ (7238)
29 *Diabetic Foot/ (2585)
30 *Varicose Ulcer/ (1076)
31 *Ischemia/ (8422)

32 *Postoperative Complications/ or *Surgical Wound Infection/ (41682)
33 or/28-32 (60558)
34 27 not 33 (125)

Database: EMBASE <1980 to 2008 Week 13>
Search Strategy:
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1 exp Decubitus/ (3890)
2 exp Skin Ulcer/ (17918)
3 exp Chronic Wound/ (231)
4 exp Wound Healing/ or exp Wound Infection/ (50734)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9451)
6 bedsore$.mp. (155)
7 or/1-6 (67244)
8 exp position/ (39965)
9 exp bed/ (2558)
10 exp Protective Equipment/ (11689)
11 (pressure adj2 (relief or reliev$ or reduc$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (12215)
12 (pressure-relief or pressure-reduc$ or pressure-reliev$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3964)
13 (sheep?skin$ or sheep skin$ or mattress$ or pillow$ or cushion$ or (support$ adj2 surface) or (support$ adj2 air) or beds or bed or bedding or bolster$ or (foam adj2 wedge$) or (foam adj2 block$) or gelpad$ or gel pad$ or gel-pad$ or gell pad$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (57391)
14 ((pressure or bedsore$ or wound$ or ulcer$ or sore$) adj2 overlay$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (11)
15 or/8-14 (118266)
16 7 and 15 (2582)
17 limit 16 to (human and english language and yr="2003 - 2008") (793)
18 Randomized Controlled Trial/ (155932)
19 exp Randomization/ (25259)
20 exp RANDOM SAMPLE/ (1028)
21 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281603)
22 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (57049)
23 Double Blind Procedure/ (68699)
24 exp Triple Blind Procedure/ (8)
25 exp Control Group/ (1558)
26 exp PLACEBO/ (111476)
27 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403730)
28 or/18-27 (614387)
29 17 and 28 (159)

30 limit 29 to (editorial or letter or note) (5)
31 Case Report/ (983732)
32 29 not (30 or 31) (152)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 3 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (5163)
2 exp Skin Ulcer/ (10218)
3 exp Wound Healing/ or exp Wound Infection/ (9511)
4 exp Wounds, Chronic/ (832)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6566)
6 bedsore$.mp. (75)
7 or/1-6 (18318)
8 exp Patient Positioning/ (4200)
9 exp "bedding and linens"/ or exp "beds and mattresses"/ (2265)
10 (pressure adj2 (relief or reliev$ or reduc$)).mp. [mp=title, subject heading word, abstract, instrumentation] (1462)
11 (pressure-relief or pressure-reduc$ or pressure-reliev$).mp. [mp=title, subject heading word, abstract, instrumentation] (791)
12 (sheep?skin$ or sheep skin$ or mattress$ or pillow$ or cushion$ or (support$ adj2 surface) or (support$ adj2 air) or beds or bed or bedding or bolster$ or (foam adj2 wedge$) or (foam adj2 block$) or gelpad$ or gel pad$ or gel-pad$ or gell pad$).mp. [mp=title, subject heading word, abstract, instrumentation] (10655)
13 ((pressure or bedsore$ or wound$ or ulcer$ or sore$) adj2 overlay$).mp. [mp=title, subject heading word, abstract, instrumentation] (16)
14 or/8-13 (15368)
15 7 and 14 (1908)
16 limit 15 to (english and yr="2003 - 2008") (669)
17 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69457)
18 RCT.mp. (874)
19 exp Meta Analysis/ (6315)
20 exp "Systematic Review"/ (3577)
21 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22933)
22 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13946)
23 exp PLACEBOS/ (4198)
24 or/17-23 (90860)
25 16 and 24 (88)
26 *BURNS/ (4653)
27 *Diabetic Foot/ (1957)
28 *Venous Ulcer/ (628)
29 *Ischemia/ (647)
30 *Surgical Wound/ (145)
31 *Surgical Wound Infection/ (1459)
32 *Postoperative Complications/ (4629)
33 or/26-32 (13984)
34 25 not 33 (72)

Final Search Pressure Sores 2008 – Electrical Stimulation

Search date: March 24, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>

Search Strategy:
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1 exp Pressure Ulcer/ (3492)
2 exp Skin Ulcer/ (12547)
3 exp Wound Healing/ or exp Wound Infection/ (34059)
4 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5 (bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)
6 or/1-5 (45415)
7 exp Electric Stimulation Therapy/ (13139)
8 (electrostimul$ or electro-stimul$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (833)
9 tens.mp. (2597)
10 (electro-therap$ or electrotherap$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (217)
11 ((electrical or stimulat$ or current or pulse$) adj4 (wound$ or ulcer$ or pressure sore$ or bedsore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (931)
12 or/7-10 (16001)
13 6 and 12 (184)
14 ((electrical or stimulation) adj4 (wound$ or ulcer$ or pressure sore$ or bedsore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (158)
15 13 or 14 (315)
16 limit 15 to (english language and humans and yr="2003 - 2008") (105)
17 limit 16 to (controlled clinical trial or meta analysis or randomized controlled trial) (11)
18 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
19 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
20 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346069)
21 exp Double-Blind Method/ (50381)
22 exp Control Groups/ (533)
23 exp Placebos/ (8753)
24 RCT.mp. (2244)
25 or/17-24 (414757)
26 16 and 25 (22)
27 *Burns/ (7235)
28 *Ischemia/ (8409)
29 *Varicose Ulcer/ (1075)
30 *Diabetic Foot/ (2580)
31 *Postoperative Complications/ or *Surgical Wound Infection/ (41621)

32 or/27-31 (60476)
33 26 not 32 (16)

Database: EMBASE <1980 to 2008 Week 12>
Search Strategy:
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1 exp DECUBITUS/ (3887)
2 exp Skin Ulcer/ (17909)
3 exp Wound Healing/ or exp Wound Infection/ (50688)
4 exp Chronic Wound/ (229)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9444)
6 bedsore$.mp. (155)
7 or/1-6 (67188)
8 exp Transcutaneous Nerve Stimulation/ (2628)
9 exp Electrostimulation/ (27469)
10 exp Electrostimulation Therapy/ (75561)
11 (electrostimul$ or electro-stimul$ or tens).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (34248)
12 (electro-therap$ or electrotherap$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (586)
13 or/8-12 (101146)
14 7 and 13 (535)
15 ((electrical or stimulat$ or current or pulse$) adj4 (wound$ or ulcer$ or pressure sore$ or bedsore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1666)
16 14 or 15 (2117)
17 limit 16 to (human and english language and yr="2003 - 2008") (559)
18 Randomized Controlled Trial/ (155780)
19 exp Randomization/ (25236)
20 exp RANDOM SAMPLE/ (1022)
21 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281365)
22 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56961)
23 Double Blind Procedure/ (68653)
24 exp Triple Blind Procedure/ (8)
25 exp Control Group/ (1545)
26 exp PLACEBO/ (111315)
27 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403354)
28 or/18-27 (613798)
29 17 and 28 (105)
30 *Burns/ (12430)
31 *Diabetic Foot/ (1981)
32 *Varicosis/ (3637)
33 *MICROVASCULAR ISCHEMIA/ (47)
34 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10590)
35 or/30-34 (28661)

36 29 not 35 (91)
37 limit 36 to (editorial or letter or note) (5)
38 Case Report/ (983221)
39 36 not (37 or 38) (85)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 2 2008>
Search Strategy:
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1 exp Pressure Ulcer/ (5153)
2 exp Wounds, Chronic/ (826)
3 exp Skin Ulcer/ (330)
4 exp Wound Healing/ or exp Wound Infection/ (9484)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6554)
6 bedsore*.mp. (75)
7 or/1-6 (15200)
8 exp Electrotherapy/ (4396)
9 (electrostimul$ or electro-stimul$ or tens).mp. [mp=title, subject heading word, abstract, instrumentation] (504)
10 (electro-therap$ or electrotherap$).mp. [mp=title, subject heading word, abstract, instrumentation] (540)
11 8 or 9 or 10 (4588)
12 7 and 11 (185)
13 ((electrical or stimulat$ or current or pulse$) adj4 (wound$ or ulcer$ or pressure sore$ or bedsore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (502)
14 12 or 13 (547)
15 limit 14 to (english and yr="2003 - 2008") (236)
16 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69213)
17 RCT.mp. (872)
18 exp Meta Analysis/ (6294)
19 exp "Systematic Review"/ (3554)
20 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22852)
21 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13890)
22 exp PLACEBOS/ (4185)
23 or/16-22 (90540)
24 15 and 23 (32)
25 *Burns/ (4636)
26 *Diabetic Foot/ (1954)
27 *Surgical Wound/ or exp Postoperative Complications/ (17091)
28 *Ischemia/ (645)
29 *Venous Ulcer/ (625)
30 or/25-29 (24822)
31 24 not 30 (18)

Final Search – Pressure Sores - Electromagnetics

Search date: March 24, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>

Search Strategy:

1	exp Pressure Ulcer/ (3492)
2	exp Skin Ulcer/ (12547)
3	exp Wound Healing/ or exp Wound Infection/ (34059)
4	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5	(bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)
6	or/1-5 (45415)
7	exp Electromagnetics/ (7920)
8	(electromagnet$ or electro-magnet$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (10398)
9	7 or 8 (10398)
10	6 and 9 (105)
11	limit 10 to (english language and humans and yr="2003 - 2008") (25)

Database: EMBASE <1980 to 2008 Week 12>

Search Strategy:

1	exp Decubitus/ (3887)
2	exp Skin Ulcer/ (17909)
3	exp Wound Healing/ or exp Wound Infection/ (50688)
4	exp Chronic Wound/ (229)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9444)
6	bedsore$.mp. (155)
7	or/1-6 (67188)
8	exp Electromagnetic Field/ (5464)
9	(electromagnet$ or electro-magnet$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (11265)
10	8 or 9 (11265)
11	7 and 10 (93)
12	limit 11 to (human and english language and yr="2003 - 2008") (20)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 2 2008>

Search Strategy:

1	exp Pressure Ulcer/ (5153)
2	exp Skin Ulcer/ (10197)
3	exp Wounds, Chronic/ (826)
4	exp Wound Healing/ or exp Wound Infection/ (9484)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6554)
6	bedsore$.mp. (75)
7	or/1-6 (18277)
8	exp Electromagnetics/ (798)
9	(electro-magnet$ or electromagnet$).mp. [mp=title, subject heading word, abstract, instrumentation] (1089)
10	8 or 9 (1089)
11	7 and 10 (46)
12	limit 11 to (english and yr="2003 - 2008") (11)

Final Search – Pressure Sores 2008 – Laser Therapy

Search date: March 24, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>

Search Strategy:

1	exp Pressure Ulcer/ (3492)
2	exp Skin Ulcer/ (12547)
3	exp Wound Healing/ or exp Wound Infection/ (34059)
4	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5	(bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)
6	or/1-5 (45415)
7	exp Laser Therapy/ (20540)
8	(laser$ or lllt or biostimulat$ or bio-stimulat$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (72144)
9	7 or 8 (72742)
10	6 and 9 (1637)
11	limit 10 to (english language and humans and yr="2003 - 2008") (393)
12	limit 11 to (controlled clinical trial or meta analysis or randomized controlled trial) (65)
13	exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
14	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
15	exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance

word, subject heading word] (346069)
16 exp Double-Blind Method/ (50381)
17 exp Control Groups/ (533)
18 exp Placebos/ (8753)
19 RCT.mp. (2244)
20 or/12-19 (414769)
21 11 and 20 (86)
22 *corneal surgery, laser/ or *keratectomy, subepithelial, laser-assisted/ (153)
23 *Burns/ (7235)
24 *Varicose Ulcer/ (1075)
25 *Diabetic Foot/ (2580)
26 *Ischemia/ (8409)
27 *Postoperative Complications/ or *Surgical Wound Infection/ (41621)
28 or/22-27 (60612)
29 21 not 28 (67)

Database: EMBASE <1980 to 2008 Week 12>

Search Strategy:
---
1 exp Decubitus/ (3887)
2 exp Skin Ulcer/ (17909)
3 exp Chronic Wound/ (229)
4 exp Wound Healing/ or exp Wound Infection/ (50688)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9444)
6 bedsore$.mp. (155)
7 or/1-6 (67188)
8 exp Low Level Laser Therapy/ (3056)
9 exp Laser/ (36300)
10 (laser$ or lllt or biostim$ or bio-stim$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (102471)
11 or/8-10 (102471)
12 7 and 11 (3025)
13 limit 12 to (human and english language and yr="2003 - 2008") (816)
14 Randomized Controlled Trial/ (155780)
15 exp Randomization/ (25236)
16 exp RANDOM SAMPLE/ (1022)
17 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281365)
18 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56961)
19 Double Blind Procedure/ (68653)
20 exp Triple Blind Procedure/ (8)
21 exp Control Group/ (1545)
22 exp PLACEBO/ (111315)
23 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403354)
24 or/14-23 (613798)

25 13 and 24 (131)
26 *keratomileusis/ or *laser epithelial keratomileusis/ or *laser prostatectomy/ or *photorefractive keratectomy/ (2493)
27 *Burns/ (12430)
28 *Varicosis/ (3637)
29 *MICROVASCULAR ISCHEMIA/ (47)
30 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10590)
31 *Diabetic Foot/ (1981)
32 or/26-31 (31113)
33 25 not 32 (110)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 3 2008>

Search Strategy:
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1 exp Pressure Ulcer/ (5163)
2 exp Skin Ulcer/ (10218)
3 exp Wounds, Chronic/ (832)
4 exp Wound Healing/ or exp Wound Infection/ (9511)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6566)
6 bedsore$.mp. (75)
7 exp Lasers/ (1449)
8 (laser$ or lllt or biostimulat$ or bio-stimulat$).mp. [mp=title, subject heading word, abstract, instrumentation] (4819)
9 or/1-6 (18318)
10 7 or 8 (4907)
11 9 and 10 (223)
12 limit 11 to (english and yr="2003 - 2008") (124)
13 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69457)
14 RCT.mp. (874)
15 exp Meta Analysis/ (6315)
16 exp "Systematic Review"/ (3577)
17 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22933)
18 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13946)
19 exp PLACEBOS/ (4198)
20 or/13-19 (90860)
21 12 and 20 (26)

Final Search - Pressure Sores 2008 –Ultrasound Therapy

Search date: March 25, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>

Search Strategy:

1	exp Pressure Ulcer/ (3492)
2	exp Skin Ulcer/ (12547)
3	exp Wound Healing/ or exp Wound Infection/ (34059)
4	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
5	(bedsore$ or (chronic adj2 wound$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (1425)
6	or/1-5 (45415)
7	exp Ultrasonic Therapy/ (2477)
8	exp ultrasonography/ (88850)
9	ultraso$.mp. (111180)
10	or/7-9 (148047)
11	6 and 10 (884)
12	limit 11 to (english language and humans and yr="2003 - 2008") (286)
13	limit 12 to (controlled clinical trial or meta analysis or randomized controlled trial) (47)
14	exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
15	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
16	exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346069)
17	exp Double-Blind Method/ (50381)
18	exp Control Groups/ (533)
19	exp Placebos/ (8753)
20	RCT.mp. (2244)
21	or/13-20 (414764)
22	12 and 21 (59)
23	*Burns/ (7235)
24	*Varicose Ulcer/ (1075)
25	*Diabetic Foot/ (2580)
26	*Ischemia/ (8409)
27	*Postoperative Complications/ or *Surgical Wound Infection/ (41621)
28	or/23-27 (60476)
29	22 not 28 (37)
30	limit 29 to (case reports or comment or editorial or letter) (2)
31	29 not 30 (35)

Database: EMBASE <1980 to 2008 Week 12>

Search Strategy:

1	exp Decubitus/ (3887)
2	exp Skin Ulcer/ (17909)
3	exp Wound Healing/ (37834)
4	exp Wound Infection/ (14264)
5	exp Chronic Wound/ (229)
6	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (9444)
7	bedsore*.mp. (155)
8	or/1-7 (67188)
9	exp Ultrasound Therapy/ (7582)
10	exp ULTRASOUND/ (36147)
11	ultraso$.mp. (159081)
12	or/9-11 (163633)
13	8 and 12 (1064)
14	limit 13 to (human and english language and yr="2003 - 2008") (430)
15	Randomized Controlled Trial/ (155780)
16	exp Randomization/ (25236)
17	exp RANDOM SAMPLE/ (1022)
18	exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281365)
19	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56961)
20	Double Blind Procedure/ (68653)
21	exp Triple Blind Procedure/ (8)
22	exp Control Group/ (1545)
23	exp PLACEBO/ (111315)
24	(random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403354)
25	or/15-24 (613798)
26	14 and 25 (73)
27	*Burns/ (12430)
28	*Diabetic Foot/ (1981)
29	*Varicosis/ (3637)
30	*MICROVASCULAR ISCHEMIA/ (47)
31	*Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10590)
32	or/27-31 (28661)
33	26 not 32 (70)
34	limit 33 to (editorial or letter or note) (1)
35	Case Report/ (983221)
36	33 not (34 or 35) (68)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 3 2008>

Search Strategy:

1	exp Pressure Ulcer/ (5163)
2	exp Skin Ulcer/ (10218)
3	exp Wounds, Chronic/ (832)
4	exp Wound Healing/ or exp Wound Infection/ (9511)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6566)
6	bedsore$.mp. (75)
7	or/1-6 (18318)
8	exp Ultrasonic Therapy/ (690)
9	exp Ultrasonography/ (11547)
10	ultraso$.mp. (11565)
11	or/8-10 (16647)
12	7 and 11 (255)
13	limit 12 to (english and yr="2003 - 2008") (139)
14	random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69457)
15	RCT.mp. (874)
16	exp Meta Analysis/ (6315)
17	exp "Systematic Review"/ (3577)
18	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22933)
19	exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13946)
20	exp PLACEBOS/ (4198)
21	or/14-20 (90860)
22	13 and 21 (29

Final Search – Pressure Sores 2008 – Nutrition

Search date: March 26, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1996 to March Week 2 2008>

Search Strategy:

1	exp Pressure Ulcer/ (3492)
2	exp Skin Ulcer/ (12547)
3	bedsore$.mp. (97)
4	exp Wound Healing/ or exp Wound Infection/ (34059)
5	((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (6921)
6	or/1-5 (45146)
7	exp Nutrition Therapy/ or exp Nutrition Phenomena/ or exp Diet/ or exp Food/ or exp Nutrition Assessment/ (365004)
8	exp Dietary Supplements/ or exp Minerals/ or exp Antioxidants/ (174383)
9	exp Micronutrients/ (141278)

10 exp Arginine/ (22951)
11 (nutrient$ or nutrition$ or enteral or parenteral or vitamin$ or diet$ or zinc or arginine).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (331182)
12 or/7-11 (654297)
13 6 and 12 (2974)
14 exp Skin Ulcer/dh [Diet Therapy] (27)
15 exp Pressure Ulcer/dh [Diet Therapy] (16)
16 13 or 14 or 15 (2977)
17 limit 16 to (english language and humans and yr="2003 - 2008") (899)
18 limit 17 to (controlled clinical trial or meta analysis or randomized controlled trial) (105)
19 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (31410)
20 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (59462)
21 exp Random Allocation/ or random$.mp. [mp=title, original title, abstract, name of substance word, subject heading word] (346069)
22 exp Double-Blind Method/ (50381)
23 exp Control Groups/ (533)
24 exp Placebos/ (8753)
25 RCT.mp. (2244)
26 or/18-25 (414768)
27 17 and 26 (179)
28 *Burns/ (7235)
29 *Venous Ulcer/ (1075)
30 *Diabetic Foot/ (2580)
31 *Ischemia/ (8409)
32 *Postoperative Complications/ or *Surgical Wound Infection/ (41621)
33 or/28-32 (60476)
34 27 not 33 (128)

Database: EMBASE <1980 to 2008 Week 12>

Search Strategy:

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1 exp DECUBITUS/ (3887)
2 exp Skin Ulcer/ (17909)
3 exp Chronic Wound/ (229)
4 exp Wound Healing/ or exp Wound Infection/ (50688)
5 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3776)
6 bedsore*.mp. (155)
7 or/1-6 (66870)
8 exp nutrition/ (824071)
9 exp Antioxidant/ (40665)
10 exp Arginine/ (29469)
11 (nutrient$ or nutrition$ or enteral or parenteral or vitamin$ or diet$ or zinc or arginine).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (588013)
12 or/8-11 (1068613)
13 7 and 12 (5795)

14 limit 13 to (human and english language and yr="2003 - 2008") (2120)
15 Randomized Controlled Trial/ (155780)
16 exp Randomization/ (25236)
17 exp RANDOM SAMPLE/ (1022)
18 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (281365)
19 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56961)
20 Double Blind Procedure/ (68653)
21 exp Triple Blind Procedure/ (8)
22 exp Control Group/ (1545)
23 exp PLACEBO/ (111315)
24 (random$ or RCT).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (403354)
25 or/15-24 (613798)
26 14 and 25 (480)
27 *burns/ (12430)
28 *Diabetic Foot/ (1981)
29 *Varicosis/ (3637)
30 *MICROVASCULAR ISCHEMIA/ (47)
31 *keratomileusis/ or *laser epithelial keratomileusis/ or *laser prostatectomy/ or *photorefractive keratectomy/ (2493)
32 *Postoperative Complication/ or *Surgical Wound/ or *Surgical Infection/ (10590)
33 or/27-32 (31113)
34 26 not 33 (432)

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Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to March Week 3 2008>

Search Strategy:
---
1 exp Pressure Ulcer/ (5163)
2 exp Skin Ulcer/ (10218)
3 exp Wounds, Chronic/ (832)
4 exp Wound Healing/ or exp Wound Infection/ (9511)
5 ((pressure or bed or skin or decubitus) adj2 (ulcer$ or sore$)).mp. [mp=title, subject heading word, abstract, instrumentation] (6566)
6 bedsore$.mp. (75)
7 or/1-6 (18318)
8 exp Diet Therapy/ (7022)
9 exp NUTRITION/ (35506)
10 exp Nutritional Support/ (13136)
11 exp "food and beverages"/ (34182)
12 exp Nutritional Assessment/ (5654)
13 exp Arginine/ (572)
14 (nutrient$ or nutrition$ or enteral or parenteral or vitamin$ or diet$ or zinc or protein$ or arginine).mp. [mp=title, subject heading word, abstract, instrumentation] (92476)
15 or/8-14 (110901)

16 7 and 15 (1604)
17 exp Pressure Ulcer/dh [Diet Therapy] (52)
18 16 or 17 (1615)
19 limit 18 to (english and yr="2003 - 2008") (754)
20 random$.mp. or exp RANDOM ASSIGNMENT/ or exp RANDOM SAMPLE/ (69457)
21 RCT.mp. (874)
22 exp Meta Analysis/ (6315)
23 exp "Systematic Review"/ (3577)
24 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22933)
25 exp double-blind studies/ or exp single-blind studies/ or exp triple-blind studies/ (13946)
26 exp PLACEBOS/ (4198)
27 or/20-26 (90860)
28 19 and 27 (95)
29 *burns/ (4653)
30 *Diabetic Foot/ (1957)
31 *Varicose Ulcer/ (628)
32 *ISCHEMIA/ (647)
33 *Surgical Wound Infection/ (1459)
34 *Postoperative Complications/ (4629)
35 *Surgical Wound/ (145)
36 *Keratectomy, Laser/ (3)
37 or/29-36 (13987)
38 28 not 37 (66)

Final Search – Pressure Ulcers – Patient Care Teams

Search date: March 10, 2008
Databases searched: OVID MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, EMBASE, Cochrane Library, CINAHL, INAHTA/CRD

Database: Ovid MEDLINE(R) <1950 to February Week 4 2008>

Search Strategy:
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1 exp Pressure Ulcer/ (7365)
2 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (9219)
3 bedsore$.mp. (275)
4 or/1-3 (9287)
5 exp Patient Care Team/ or exp Combined Modality Therapy/ (179245)
6 exp Delivery of Health Care, Integrated/ or exp "Continuity of Patient Care"/ (14412)
7 exp Interdisciplinary Communication/ (3093)
8 exp Interprofessional Relations/ (37746)
9 (team$ or multi-facet$ or multifacet$ or multifactor$ or multidisciplin$ or multicomponent$ or multi-factor$ or multi-disciplin$ or multi-component$ or interdisciplin$ or inter-disciplin$ or collaborat$ or cooperat$ or co-operat$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (265601)
10 ((wound$ or pressure sore$ or pressure ulcer$ or bedsore$ or bed sore$) adj3 (centre$ or team$ or program$ or clinic or clinics)).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (335)

11 exp Cooperative Behavior/ (12997)
12 or/5-11 (436527)
13 4 and 12 (690)
14 limit 13 to (english language and humans) (561)
15 exp Technology Assessment, Biomedical/ or exp Evidence-based Medicine/ (34815)
16 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$)).mp. or (published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ab. (68160)
17 14 and (15 or 16) (32)
18 14 (561)
19 limit 18 to (case reports or comment or editorial or letter or "review") (190)
20 18 not 19 (371)
21 17 or 20 (384)

Database: EMBASE <1980 to 2008 Week 09>

Search Strategy:
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1 exp Decubitus/ (3874)
2 ((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (3767)
3 exp Decubitus/ (3874)
4 or/1-3 (5279)
5 exp Integrated Health Care System/ (189)
6 exp Interdisciplinary Communication/ (755)
7 exp Cooperation/ or exp Teamwork/ (12687)
8 (team$ or multi-facet$ or multifacet$ or multifactor$ or multidisciplin$ or multicomponent$ or multi-factor$ or multi-disciplin$ or multi-component$ or interdisciplin$ or inter-disciplin$ or collaborat$ or cooperat$ or co-operat$).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (176388)
9 ((wound$ or pressure sore$ or pressure ulcer$ or bedsore$ or bed sore$) adj3 (centre$ or team$ or program$ or clinic or clinics)).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (214)
10 or/5-9 (176649)
11 4 and 10 (300)
12 limit 11 to (human and english language) (205)
13 exp Biomedical Technology Assessment/ or exp Evidence Based Medicine/ (280024)
14 (meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or published literature or medline or embase or data synthesis or data extraction or cochrane).ti,ab. (56485)
15 12 and (13 or 14) (27)
16 12 (205)
17 limit 16 to (editorial or letter or note or "review") (70)
18 16 not 17 (135)
19 15 or 18 (145)

Database: CINAHL - Cumulative Index to Nursing & Allied Health Literature <1982 to February Week 5 2008>

Search Strategy:

1	exp Pressure Ulcer/ (5100)
2	((bed or pressure or decubit$ or isch?emic) adj2 (sore$ or ulcer$)).mp. [mp=title, subject heading word, abstract, instrumentation] (5799)
3	bedsore$.mp. (74)
4	or/1-3 (5814)
5	exp Multidisciplinary Care Team/ (11467)
6	exp Combined Modality Therapy/ (6430)
7	exp Health Care Delivery, Integrated/ (1644)
8	exp "Continuity of Patient Care"/ (5258)
9	exp Interprofessional Relations/ (8875)
10	exp Cooperative Behavior/ (1027)
11	exp TEAMWORK/ (3186)
12	(team$ or multi-facet$ or multifacet$ or multifactor$ or multidisciplin$ or multicomponent$ or multi-factor$ or multi-disciplin$ or multi-component$ or interdisciplin$ or inter-disciplin$ or collaborat$ or cooperat$ or co-operat$).mp. [mp=title, subject heading word, abstract, instrumentation] (61923)
13	((wound$ or pressure sore$ or pressure ulcer$ or bedsore$ or bed sore$) adj3 (centre$ or team$ or program$ or clinic or clinics)).mp. [mp=title, subject heading word, abstract, instrumentation] (1178)
14	or/5-13 (79579)
15	4 and 14 (691)
16	limit 15 to english (663)
17	exp Meta Analysis/ (6147)
18	exp "Systematic Review"/ (3512)
19	(meta analy$ or metaanaly$ or pooled analysis or (systematic$ adj2 review$) or published studies or medline or embase or data synthesis or data extraction or cochrane).mp. (22063)
20	or/17-19 (22063)
21	16 and 20 (12)
22	16 (663)
23	limit 22 to (editorial or letter or "review") (56)
24	22 not 23 (607)
25	21 or 24 (607)

Appendix 4: Quality Assessment of Individual Studies

Debridement

Study	Randomization method stated	Concealment of allocation stated	Inclusion/ exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Lee and Ambus, 1975 (24)	×	×	√	×	√	×	√	×
Parish and Collins, 1979 (25)	×	×	√	×	√	×	No withdrawal	NA
Burgos et al., 2000 (small sample) (26)	√	×	√	×	√	√	√ (High)	√
Muller et al., 2001 (small sample) (27)	×	×	×	√	Only stage	×	√	×
Pullen et al, 2002 (28)	×	×	√	√	√	√	√	√
Alvarez et al., 2002 (small sample) (22)	√	×	√	×	√	×	√	√
Agren and Stromberg, 1985 (29)	×	×	√ (Inclusion)	×	√	√	√	√
Martin et al, 1996	√ *	×	√	×	×	×	×	×
Nasar and Morley, 1982 (30)	×	×	√	×	×	√	√	×
Ljungberg 1998 (31)	×	No	√	×	√	×	√	NA
Colin et al., 1996 (32)	×	×	×	×	√	×	√	√
Thomas et al., 1993 (33)	√ †	×	√	×	√	×	√	×
Sayag et al., 1996 (34)	√	√	√	√	√	√	√ (High)	√
Moberg et al., 1983 (35)	×	×	√	×	√	×	√	×
Sherman 2002 (36)	× (Non-random)	×	√	×	√	×	×	×

* Computer-generated † sealed envelopes ‡ Table of random numbers §Opaque envelops

Dressings

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Xakellis, 1992 (54)	×	×	√	×	√	×	√	×
Alm 1989, (53)	×	×	×	×	√	√	√	×
Colwell et al., 1993 (55)	×	×	√	× (No description of statistical analysis	√	×	√	×
Matzen, 1998 (56)	×	×	√	×	√	×	√	√
Hollisaz et al., 2004 (41)	√	√	√	√	√	√	√	√
Barrois, 1992 (61)	×	×	√	×	√ (Limited)	×	√	×
Kim et al., 1996 (59)	×	×	×	×	√	×	√	×
Kaya et al., 2005 (63)	×	×	×	×	√	×	None reported	×
Mulder et al., 1993 (57)	√	×	√	×	√	×	×	×
Bale, 1997 (66)	√	×	√	×	√	×	√ (High)	×
Banks, 1994a (67)	×	×	√	×	√	×	√	×
Banks, 1994b(68)	√	×	√	×	√	×	√	×
Thomas, 1997 (44)	√	√	√	×	√	×	×	×
Honde, 1994 (69)	√	×	√	×	√	×	√	√
Banks, 1996 (77)	×	×	√	×	√	×	√	×
Seeley et al., 1999 (70)	√	×	√	×	√	×	√	√
Belmin, 2002(72)	×	×	√	√	√	√		√
Meaume et al., 2005 (49)	√	×	√	×	√	×		√
Munter et al., 2006 (50)	√	√	√	√	√	×		√
Kloth et al., 2002 (73)	√	×	√	×	√	×	√	√
Price et al., 2000 (75)	√	√	√	×	√ (Stage)	√	√	√
Thomas et al., 2005 (52)	√	√	√	×	√	×	√	×
Banks, 1997 (43)	√ (Computer)	×	√	×	√	×	√	×

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Gunes et al., 2007 (51)	√	×	√	×	√	×	×	×
Graumlich, 2003 (11)	√	√	√	√	√	√	√	√
Subbanna et al., 2007 (40)	√	×	√	×	√	×	√	×

Support Surfaces

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported and reason provided	ITT reported
Devine et al., 1995 (94)	√	×	Exclusion criteria not reported	× (Post hoc)	√	√	√	√
Evans, 2000 (95)	√†	√†	√	×	√	√	√	√
Russell, 2000a (96)	×	×	√	√	√	√	√	×
Russell, 2003 (97)	√*	√†	√	√	√	√	√	?
Nixon et al., 2006 (91)	√	√	√	√	√	×	√	√
Allman et al.,1987(98)	√‡	√†	√	√	√	√		
Strauss, 1991 (100)	√*	×	√	×	Inadequate	√	√ (High deaths and dropout)	×
Ferrell and Christenson, 1993 (101)	×† (Blocks of 10)	√†	√	√	√	×	√	
Mulder et al., 1994 (102)	×	×	√	×	No demographic info or baseline ulcer data	×	× (Overall, not by study groups)	×
Day et al., 1993 (103)	√†	√†	√	×	√	×	√	×
Groen et al., 1999 (104)	×	×	√	√	√	×	√	×
Keogh et al., 2001 (105)	√*	√§	√	Stated but not described	√	× (Patient and researcher)	√	√
Rosenthal et al., 2003 (92)	√§	√§	√	√	√	×	√	×
Clark et al., 1999 (106)	×	√§ (Central)	√	√	√	×	√	×
Ochs et al., 2005 (93)	× (Retrospective)	×	×	×	√	×	NA	NA

* Computer-generated † sealed envelopes ‡ Table of random numbers § Opaque envelops

Adjunctive Physical Therapy

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Electrical								
Adunsky et al., 2005 (112)	×	×	√	×	√	√	√	√
Griffin et al., 1991 (110)	×	√†	√	√	√	×	√	×
Wood et al., 1993 (111)	×	√†	√	×	√	√	√	×
Electromagnetic								
Comorosan, 1993 (115)								
Salsberg, 1995 (116)	×	√	√	×	√	√	√	×
Ritz et al., 2002 (117)	×	×	√	×	√	√	×	×
Burke et al., 1998 (20)	×	√	√	×	×	√	√	×
Laser Therapy								
Nussbaum et al., 1994 (123)	×	×	×	×	√	√	√	×
Lucas et al., 2000 (119)	×	×	√	×	√	√	√	×
Lucas et al., 2003 (125)	√	×	√	√	√	√	√	√
Taly et al., 2004 (121)	√	×	√	×	√	√	√	√
Schubert et al., 2001 (124)	×	×	Minimal	×	I√ (Inadequate)	×	√	×
Ultrasound Therapy								
McDiarmid, 1985 (127)	×	×	√	×	×	√	√	×
ter Riet et al., 1995) (128)	√*	√	√	√	√	√	√	√
Nussbaum et al., 1994 (123)	×	×	×	×	√	√	√	×

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Multidisciplinary teams								
Vu et al., 2007 (10)	Inadequate†	×	√	√	√	×	√	√

* By random permuted blocks of 6 prepared in advance using a computer program (Stratified by nursing home, vitamin C supplementation, and grade IV ulcers)
† Cluster, not truly randomized

Growth Factors

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Mustoe, 1994(78)	×	×	√	√	√	√	√	×
Rees, 1999 (79)	×	×	√	×	√	×	×	√
Robson, 2000 (80)	×	×	√	×	√	√	√	√
Landi, 2003 (82)	√	×	√	×	√	√	√	×

Nutrition Therapy

Study	Randomization method stated	Concealment of allocation stated	Inclusion/exclusion criteria stated	A priori power calculation reported	Baseline characteristics reported	Blinded outcome assessment stated	Attrition reported	ITT reported
Chernoff, 1990 (142)	×	×	√	×	√ (Inadequate)	×	×	×
Norris et al., 1971 (137)	×	√	√	×	√ (Inadequate)	×	√	×
Taylor et al., 1974 (139)	√	×	×	×	√ (Inadequate)	×	×	×
Ek et al., 1991 (141)	×	×	×	×	√	×	√	×
Benati et al, 2001 (143)	×	×	×	×	×	×	×	×
Desneves et al., 2005 (144)	√	×	√	×	√	√	√	√
Lee et al., 2006 (24)	√	√	√	×	√	√	√	×
ter Riet, 1995 (140)	√	×	√	×	√	√	×	×

Appendix 5: Assessment of Quality of Evidence (GRADE)

Quality of Evidence on Debridement

GRADE Quality Assessment*					
There was no evidence that debridement using collagenase, dextranomer, or cadexomer iodine significantly improved complete healing compared with placebo.					
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Outcome**
15 studies	RCT	Many limitations†	No limitations	None	Important
	High	Low	Low	Low	Low

*RCT, randomized controlled trial.
†Most were small and did not have a priori power calculation, intention-to-treat, or concealment of allocation. <50% gave method of randomization or reported blinded assessment.

GRADE Quality Assessment*					
Papain urea resulted in better debridement than collagenase. Adding streptokinase/streptodornase to hydrogel resulted in faster debridement.					
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Outcome**
Alvarez, 2002 Martin, 1996	RCT	Many limitations†	No limitations	None	Important
	High	Low	Low	Low	Low

*RCT, randomized controlled trial.
†No concealment of allocation, no a priori power calculation, no blinded outcome assessment, no intention-to-treat in one of the studies.

GRADE Quality Assessment*					
Calcium alginate resulted in a greater reduction in ulcer size compared with dextranomer. Weighted mean difference in ulcer reduction −2.12 (95% CI, −3.50 to −0.74) (cm^2/week)					
Studies	**Design**	**Quality of Study**	**Directness**	**Modifying Factors**	**Outcome**
Sayag 1996	RCT	limitation†	No limitations	None	Important
	High	Moderate	Moderate	Moderate	Moderate

*CI, confidence interval; RCT, randomized controlled trial. Consistency is Not applicable with only 1 study
†High attrition.

GRADE Quality Assessment*					
Maggot debridement resulted in more complete debridement than conventional treatment. Complete debridement at 5 weeks = 80% vs. 52%, *P* = .021.					
Studies	**Design**	**Quality of Study**	**Directness**	**Modifying Factors**	**Outcome**
Sherman, 2002	Non-randomized Clinical controlled trial	Some limitations†	No limitations	None	Important
	Low	Very low	Very low	Very low	Very low

* Consistency is not applicable with only 1 study
†Nonrandomized controlled study, no randomization, no concealment, no blinded outcome assessment, and no intention-to-treat.

Quality of Evidence on Dressings

GRADE Quality Assessment*						
Ulcer (≥Stage II) treated with hydrocolloid dressing for 5–12 weeks had a higher proportion of complete healing compared with those treated with saline gauze dressing (RR, 2.91 [95% CI, 1.52–5.57]).						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Alm, 1989 Colwell, 1993 Matzen, 1999 Hollisaz, 2004	RCTs	Many limitations†	No	No limitation	RR > 2	Important
N = 127 vs. 119	High	Low	Low	Low	Moderate	Moderate

*CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small sample; no a priori sample calculation; method of randomization not stated; and no blinded outcome assessment.

GRADE Quality Assessment*						
Ulcers (Stage II–III) treated with hydrogel dressing had a higher proportion of complete healing compared with those treated with hydrocolloid dressing (RR, 1.71 [95% CI,1.05–2.79])						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Darkovich, 1990 Motta, 1999	RCTs	Many limitations†	No limitation	No limitation	None	Important
N = 67 vs. 72	High	Low	Low	Low	Low	Low

*CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small samples, no a priori sample calculation, method of randomization not stated, concealment of allocation not stated, attrition not reported, no blinded outcome assessment, and no intention-to-treat analysis.

GRADE Quality Assessment*						
Ulcers (Stage II–III) treated with hydropolymer dressing had a higher proportion of complete healing compared with those treated with hydrocolloid dressing (RR, 1.53 [95% CI, 1.05–2.22]).						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Thomas, 1997 Honde, 1994	RCTs	Many limitations†	No limitation	No limitation	None	Important
N = 129 vs 138	High	Low	Low	Low	Low	Low

*CI, confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small samples, no a priori sample calculation, method of randomization not stated, concealment of allocation not stated, attrition not reported, no blinded outcome assessment, and no intention-to-treat analysis

GRADE Quality Assessment*						
There were no significant differences in complete healing of ulcers (Stage III–IV) treated with normothermic or radiant heat dressing compared with those treated with other advanced dressings.						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Price, 2000 Whitney, 2001 Kloth, 2002 Thomas, 2005	RCTs	Some limitations	No limitation	No limitation	None	Important
N = 75 vs. 77	High	Moderate	Moderate	Moderate	Moderate	Moderate

*RCT, randomized controlled trial.

Quality of Evidence on Growth Factors

GRADE Quality Assessment*						
No significant difference in complete healing in pressure ulcers treated with platelet derived growth factor, fibroblast growth factors, or granulocyte macrophage colony-stimulating factor compared with pressure ulcers treated with placebo.						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Mustoe, 1994 Rees, 1999 Payne, 2001 Landi, 2003	RCTs	Some limitations†	Some limitations‡	No limitation	None	Important
N = 75 vs. 77	High	Moderate	Low	Low	Low	Low

*RCT, randomized controlled trial.
†Small sample, method of randomization not stated, and no priori sample size calculation. Uncertainty due to small study size and methodological flaws.
‡One study showed a different trend in complete healing compared with the other 3 studies.

Quality of Evidence on Electrotherapy

GRADE Quality Assessment*						
The adjunct use of electrotherapy significantly improved complete healing compared with sham therapy when a fixed effects model was used but there was significant heterogeneity (RR, 4.48 [95% CI, 1.91–10.51], P = .0006, I^2 = 70.1%). The RR became insignificant when a random effects model was used. There was no significant difference when a random effects model was used (RR, 3.08 [95% CI, 0.58–16.41], P = .19, I^2 = 70.1%)						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Griffin, 1991 Wood, 1993 Adunsky, 2005	RCTs	Some limitations†	Some inconsistency	No limitation	None	Important
N = 86 vs. 68	High	Moderate	Low	Low	Low	Low

*CI refers to confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small sample size, no method of randomization, no concealment of allocation, and no a priori power calculation.

GRADE Quality Assessment*						
The adjunct use of electrotherapy was associated with significantly greater reduction in the size of pressure ulcers.						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Gentzkow, 1991 Griffin, 1991 Wood, 1993	RCTs	Many limitations†	No inconsistency	No limitation	None	Important
N = 41 vs. 28	High	Moderate	Moderate	Moderate	Moderate	Moderate

*RCT refers to randomized controlled trial.
†Small sample size, no method of randomization, no concealment of allocation, and no a priori power calculation.

Quality of Evidence on Electromagnetic Therapy

GRADE Quality Assessment*						
The adjunct use of electromagnetic therapy did not significantly improve complete healing compared with sham therapy (RR, 3.43 [95% CI, 0.35–33.61], *P* = .29).						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Comorosan, 1993 Salsberg, 1995 Ritz, 2002	RCTs	Many limitations†	No inconsistency	No limitation	None	Important
N = 41 vs. 28	High	Low	Low	Low	Low	Low

*CI refers to confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small samples, no method of randomization, no concealment of allocation, no a priori power calculation, and no intention-to-treat analysis. One study did not provide patient or ulcer characteristics and had imbalanced sample sizes.

Quality of Evidence on Low-Level Laser Therapy

GRADE Quality Assessment*						
The adjunct use of low level laser therapy did not significantly improve the complete healing of pressure ulcers compared with standard therapy or sham therapy (RR, 1.17 [95% CI, 0.85–1.63], *P* = .33).						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Nussbaum, 1994 Lucas, 2000 Lucas, 2003 Taly, 2004	RCTs	Some limitations†	Some inconsistency‡	No limitation	None	Important
N = 85 vs. 86	High	moderate	Low	Low	Low	Low

*CI refers to confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small sample, no concealment of allocation, and no a priori power calculation.
‡One study had a different trend.

Quality of Evidence on Ultrasound Therapy

GRADE Quality Assessment*						
The adjunct use of ultrasound therapy did not significantly improve complete healing of pressure ulcers compared with sham therapy (RR, 0.97 [95% CI, 0.65–1.45], *P* = .89)						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
McDiarmid, 1985† ter Riet, 1995	RCTs	Some limitations†	No inconsistency	No limitation	None	Important
N = 66 vs. 62	High	Moderate	Moderate	Moderate	Moderate	Moderate

*CI refers to confidence interval; RCT, randomized controlled trial; RR, relative risk.
†Small samples. One study had no description of method of randomization, no concealment of allocation, and no a priori sample calculation.

GRADE Quality Assessment*					
The adjunct use of ultrasound therapy in conjunction with ultraviolet therapy did not significantly improve complete healing compared with standard therapy or low-level laser therapy.					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
Nussbaum, 1994	RCT	Many limitations†	No limitation	None	Important
N = 6 vs. 6	High	Low	Low	Low	Low

*RCT refers to randomized controlled trial; Consistency is not applicable with 1 study
†No method of randomization or concealment, no inclusion/exclusion criteria, no a priori power calculation, and no intention-to-treat.

Quality of Evidence on Negative Pressure Therapy

GRADE Quality Assessment*					
The adjunct use of negative pressure therapy did not significantly improve complete healing compared with standard therapy including a debridement gel.					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
Ford, 2002	RCT	Many limitations†	No limitation	None	Important
N = 20 vs. 15	High	Low	Low	Low	Low

*RCT refers to randomized controlled trial; Consistency is not applicable with 1 study
†Very small sample, no method of randomization, no concealment of allocation, no inclusion/exclusion criteria, and no apriori power calculation.

Quality of Evidence on Nutrition Support Therapy

GRADE Quality Assessment*					
Supplementation with 15 grams of hydrolyzed protein 3 times daily did not improve complete healing of pressure ulcers but was associated with a 2-fold improvement in PUSH score compared with placebo.					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
Lee, 2006	RCTs	Some limitations†	No limitation	None	Important
N = 89	High	Moderate	Low	Low	Low

*RCT refers to randomized controlled trial; PUSH, pressure ulcer scale for healing; Consistency is not applicable with 1 study

GRADE Quality Assessment*					
Supplementation with 500 mg ascorbic acid twice daily for 1 month was associated with significantly greater reduction in the size of ulcers compared with placebo.					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
Taylor, 1974	RCT	Many limitations†	No limitation	None	Important
N = 20	High	Low	Low	Low	Low

*RCT refers to randomized controlled trial; Consistency is not applicable with 1 study
†No concealment of allocation, no inclusion/exclusion criteria, no a priori power calculation, inadequate baseline information, no report on attrition, and no intention-to-treat.

GRADE Quality Assessment*						
Supplementation with 200 mg Zinc (as zinc sulphate) did not significantly improve the healing of pressure ulcers compared with placebo.						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Norris 1971 Brewer 1967	RCT	Some limitations†	Some inconsistency	No limitation	None	Important
N = 31	High	Moderate	Low	Low	Low	Low

*RCT refers to randomized controlled trial.
†No method of randomization, a priori power calculation, inadequate baseline information, no blinded assessment, no intention-to-treat.

GRADE Quality Assessment*					
Supplementation with 500 mg ascorbic acid twice daily for 12 weeks did not significantly improve the absolute or relative reduction in the surface area or volume of ulcers compared with supplementation with 10 mg ascorbic acid twice daily.					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
ter Riet, 1995	RCT	Some limitations	No limitation	None	Important
N = 88	High	Moderate	Low	Low	Low

*RCT refers to randomized controlled trial; consistency not applicable with 1 study

GRADE Quality Assessment*					
A very high protein feeding (25% of energy as protein) resulted in a greater reduction in the area of ulcers in institutionalized tube-fed patients compared with a lower protein feeding (16% of the energy as protein).					
Studies	**Design**	**Quality of Studies**	**Directness**	**Modifying Factors**	**Outcome**
Chernoff, 1990	RCT	Many limitations†	No limitation	None	Important
N = 12	High	Low	Low	Low	Low

*RCT, randomized controlled trial; Consistency is not applicable with only 1 study
†No method of randomization, concealment of allocation, a priori power calculation, inadequate baseline information, no blinded outcome assessment, no report on attrition, and no intention-to-treat.

GRADE Quality Assessment*					
A multinutrient supplemental feeding containing 1600 kJ, 16 g protein, and vitamins and minerals did not significantly improve the complete healing of pressure ulcers compared with standard diet alone.					
Studies	**Design**	**Quality of studies**	**Directness**	**Modifying Factors**	**Outcome**
Ek, 1991	RCTs	Many limitations†	No limitation	None	Important
N = 150	High	Low	Low	Low	Low

*RCT, randomized controlled trial; Consistency is not applicable with only 1 study.
†No method of randomization, concealment of allocation, no inclusion/exclusion criteria, no a priori power calculation, no blinded outcome assessment, and no intention-to-treat.

GRADE Quality Assessment*						
A high protein high energy multinutrient supplemental feeding with added arginine, zinc, and vitamins was associated with a greater decrease in the size of the ulcer and improvement in ulcer scores compared with a similar feeding without added arginine, zinc and vitamin C or compared with a standard diet alone.						
Studies	**Design**	**Quality of Studies**	**Consistency**	**Directness**	**Modifying Factors**	**Outcome**
Benati, 2001 Desneves, 2005	RCTs	Many limitations†	No inconsistency	No limitation	None	Important
N = 31	High	Low	Low	Low	Low	Low

*RCT, randomized controlled trial.
†One study had better quality than the other did. No method of randomization in one study, no blinded outcome assessment in one study, and no intention-to-treat in one study. No method of concealment of allocation no a priori power calculation in either study,.

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