

Volume 22 Number 8
August 2016

Review

Comparing the efficacies of alginate, foam, hydrocolloid, hydrofiber, and hydrogel dressings in the management of diabetic foot ulcers and venous leg ulcers: a systematic review and meta-analysis examining how to dress for success

Michael Saco MD¹, Nicole Howe MD¹, Rajiv Nathoo MD² Basil Cherpelis MD¹

Dermatology Online Journal 22 (8): 1

¹**Department of Dermatology & Cutaneous Surgery, University of South Florida, Tampa**

²**Department of Dermatology, University of Florida, Gainesville**

Correspondence:

Michael Saco MD
University of South Florida, Department of Dermatology & Cutaneous Surgery
13330 USF Laurel Drive, Tampa, FL 33612
Tel. (813) 974-4744 Fax. (813) 974-2132
Email: ms20142018@aol.com

Abstract

Diabetic foot ulcers and venous leg ulcers are chronic wounds frequently encountered by dermatologists. Choosing appropriate wound dressings can effectively promote wound healing and potentially reduce morbidity and financial burden experienced by patients. The objective of our systematic review and meta-analysis was to evaluate wound healing efficacies of synthetic active dressings in diabetic foot ulcer and venous leg ulcer management. For data collection, PubMed, Embase, Cochrane Library, CINAHL, and clinicaltrials.gov online databases were searched from database inception to 10 May 2015. Fixed and random effects modeling were used to calculate pooled risk ratios for complete ulcer healing from pairwise dressing comparisons. The results of our review showed moderate-quality level evidence that hydrogels were more effective in healing diabetic foot ulcers than basic wound contact dressings (RR 1.80 [95% CI, 1.27-2.56]). The other dressing comparisons showed no statistically significant differences between the interventions examined in terms of achieving complete diabetic foot ulcer healing. Non-adherent dressings were more cost-effective than hydrofiber dressings for diabetic foot ulcers in terms of mean total cost per patient of the dressings themselves. All venous leg ulcer pairwise dressing comparisons showed equivalent dressing efficacies in terms of promoting complete ulcer healing. Overall, most synthetic active dressings and traditional wound dressings are equally efficacious in treating diabetic foot ulcers and venous leg ulcers. For treating diabetic foot ulcers, hydrogels are more efficacious than basic wound contact dressings, and non-adherent dressings are more cost-effective than hydrofiber dressings. Ultimately, dressing choice should be tailored to the wound and the patient.

Keywords: alginate, foam, hydrocolloid, hydrofiber, hydrogel, diabetic foot ulcer, venous leg ulcer, systematic review, meta-analysis

Introduction

Diabetic foot ulcers and venous leg ulcers are both common types of chronic wounds with potentially serious consequences that are often difficult to treat. Diabetic foot ulcers affect approximately 15-20% of diabetics in the United States and result in over 85,000 lower extremity amputations and billions of dollars in expenses yearly [1, 2]. Venous leg ulcers affect roughly 1% of Americans and result in a financial burden of nearly \$2 billion annually in the United States [3]. Both diabetic foot ulcers and venous leg ulcers are primarily treated in outpatient settings and are often managed by dermatologists, primary care physicians, and vascular surgeons [4]. Early intervention is paramount in order to promote ulcer healing and prevent recurrence [2]. Choosing the appropriate dressing can assist in wound healing [5] and can therefore potentially obviate the need for inpatient management or surgery, thus reducing patient morbidity and associated costs.

The ideal dressing should be cost-effective, provide a moist environment, absorb excess exudate from the wound bed, help with autolytic debridement, speed up granulation, and help protect wounds from fluid loss and infection [6]. Furthermore, it should not cause trauma upon removal, leave debris in the wound bed, damage the ulcer edges, cause discomfort with use, or induce an allergic reaction [7-11]. Synthetic active dressings, such as acrylic, alginate, film, foam, hydrocolloid, hydrofiber, and hydrogel dressings, have purportedly improved outcomes in many situations and have been slowly replacing gauze and other traditional dressings. Although synthetic active dressings are advertised to make gauze and other traditional dressings appear antiquated by comparison, their supposed superiority remains questionable in the context of diabetic foot ulcer and venous leg ulcer treatment [12-19]. The purpose of our systematic review and meta-analysis is to critically assess the efficacies of alginate, foam, hydrocolloid, hydrofiber, and hydrogel dressings in diabetic foot ulcer and venous leg ulcer healing and then make clinical practice recommendations based on our findings.

Methods

A systematic literature search was conducted using the PubMed, Embase, Cochrane Library, CINAHL, and clinicaltrials.gov online medical databases from database inception to 10 May 2015. Figure 1 demonstrates the process through which the articles included in our systematic review and meta-analysis were chosen out of all of the articles examined during our literature search. For all five database queries, the following search expression in which terms and phrases were combined through the Boolean connectors AND and OR was entered: ((diabetic foot ulcer OR diabetic foot ulcers) OR (venous leg ulcer OR venous leg ulcers)) AND (((((((((((fiber OR fibrous OR hydrofiber OR hydrofibre OR fibre OR fibers OR fibres OR hydrofibers OR hydrofibres) OR (alginate OR alginates) OR (foam OR foams) OR (hydrocolloid OR hydrocolloids OR colloid OR colloids) OR (hydrogel OR hydrogels OR gel OR gels) OR (amorphous) OR (film OR films) OR (membrane OR membranes) OR (acrylic OR acrylics) OR (dressing OR dressings)))))))))). Search results from PubMed were limited to randomized-controlled trials (RCTs), systematic reviews, meta-analyses, reviews, clinical trials, comparative studies, controlled clinical trials, and multicenter studies. No filters were applied to the Embase, Cochrane Library, CINAHL, and clinicaltrials.gov searches. For all five databases, we conducted our searches without any language restrictions and assessed both published and unpublished reports of data for eligibility.

Three of the authors (M.S., N.H., and R.N.) independently reviewed the 2284 titles and abstracts identified during our literature searches and narrowed them down to 630 full-text articles on the basis of our predefined inclusion criteria.

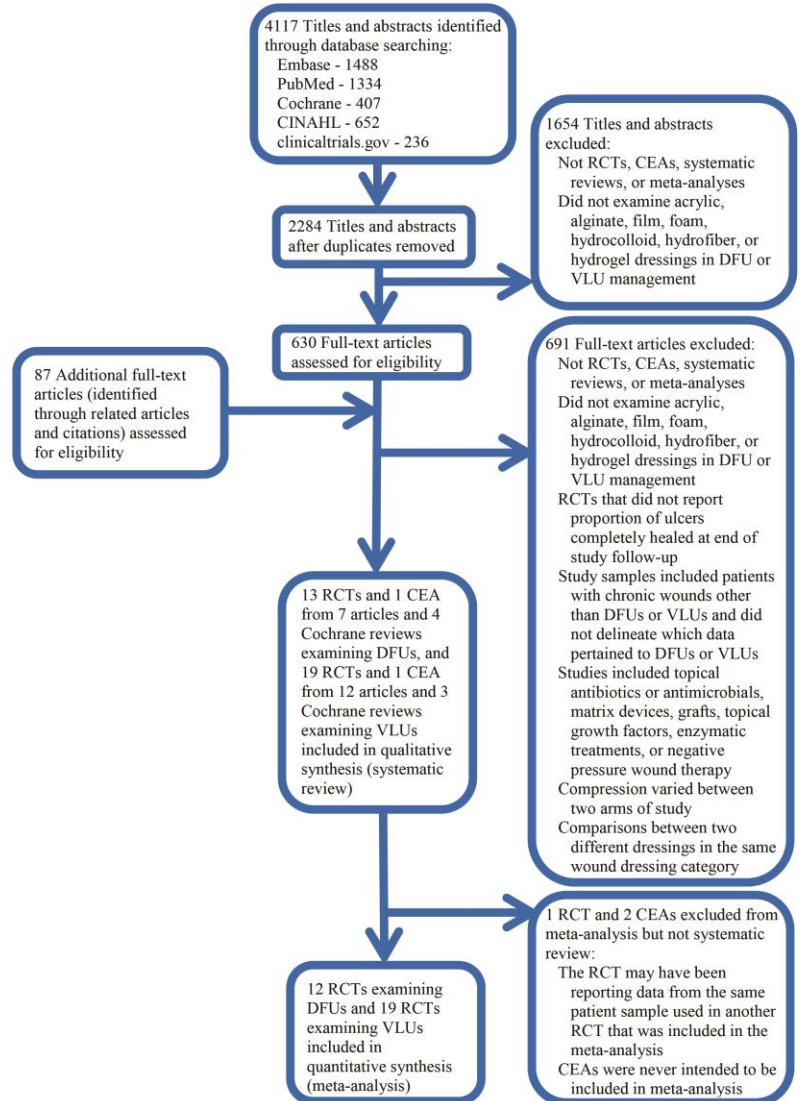


Figure 1. Flowchart demonstrating selection of studies for systematic review and meta-analysis. CEA, cost-effectiveness analysis; DFU, diabetic foot ulcer; VLU, venous leg ulcer; RCT, randomized-controlled trial.

Eighty-seven additional full-text articles were identified through related articles and citations. These 717 articles were subsequently evaluated by the same three authors using our predefined inclusion and exclusion criteria to determine which articles were eligible for our systematic review and meta-analysis. At least two of the three authors needed to agree that an article met our inclusion and exclusion criteria in order for it to be eligible. Of the 717 full-text articles assessed, 32 RCTs and two cost-effectiveness analyses from 19 articles and seven Cochrane reviews were selected for our systematic review. One of these 32 RCTs [20] was excluded from our meta-analysis in order to limit potential multiple publication bias based on our suspicion that it was reporting different outcome data for the same patient sample used in another RCT [21] that we chose to include in our meta-analysis. Cost-effectiveness analyses were never intended to be included in the meta-analysis.

Inclusion criteria for our review included cost-effectiveness analyses, RCTs, systematic reviews, and meta-analyses examining the efficacies of alginate, foam, hydrocolloid, hydrofiber, hydrogel, film, and acrylic dressings in the setting of either diabetic foot ulcers or venous leg ulcers. Although dressing efficacy can be assessed through multiple different variables, we chose to measure dressing efficacy specifically as the proportion of ulcers completely healed at the end of study follow-up for each dressing in order to analyze a relatively objective variable that would likely maintain consistency across studies in terms of definition of outcome measurement. A general overview of the characteristics of these seven dressings can be found in Table 1.

Table 1. Synthetic active dressings

Dressing	Composition/Mechanism	Advantages/Indications	Disadvantages/Contraindications
Acrylic	Clear film Permeable to water vapor [33]	Reserve for dry wounds or minimally exudative wounds [33]	Little absorbency Can be difficult to remove Do not use on infected or heavily exudative wounds [33]
Alginate	Sodium/calcium salts of alginic acid (brown algae derivative) Loose framework Gel forms on wound and provides moist milieu conducive to healing Highly absorbent Promotes hemostasis through calcium release [7, 11]	Low allergenicity Painless and injury-free dressing changes Reduces pain at wound site Can mold to fit wounds and pack cavities Can use for bleeding wounds Used for minimally, moderately, and heavily exudative wounds, deep chronic wounds, and inflamed wounds with bacterial contamination [7, 11, 34]	Often requires secondary dressings for protection Gel can appear similar to pus in wound and thus may be mistaken for infection [5] Fibrous debris left in wound may cause foreign body-type reaction [11] Do not use on dry wounds or wounds with necrotic tissue (exudates are needed for gel formation) Caution advised when used on deep wounds since alginates can overstimulate fibroblasts and consequently inhibit wound healing [7]
Film	Semipermeable adhesive sheets Transparent Allows water vapor and oxygen exchange between wound bed and environment Non-absorbent [11, 33]	Retains moisture Transparency allows visualization of wound without necessitating dressing removal Protects wound from contamination (impermeable to liquid and bacteria from outside environment) Reserve for dry wounds or minimally exudative wounds [11, 33]	May strip skin upon removal Do not use on infected or heavily exudative wounds (films can trap fluid and cause maceration) [11, 33]
Foam	Often composed of polyurethane Hydrophilic foam with porous architecture Moderately absorbent, semi-occlusive Permeable to water and gas (allows effective absorption of wound exudate) [7]	Nontraumatic dressing changes [11] Can use in minimally, moderately, or heavily exudative wounds and surface epithelial wounds with sensitive skin [33] Can use in combination with compression therapy for venous ulcers [7]	Non-adherent, requires secondary dressings for protection Opaque, so difficult to visualize wound without removing dressing [5] Can produce malodorous discharge that may be mistaken for infection [11] Do not use polyurethane foam on dry wounds covered by necrotic debris (could stimulate overgranulation) [5, 7]

Hydrocolloid	Carboxymethylcellulose, gelatin, and pectins that absorb wound exudate to form hydrophilic gel Retains moisture [7, 35] Absorbent [35]	Painless and injury-free dressing changes External layer of dressing forms barrier to water (allows patients to shower and protects wound from environment) Powder and paste forms of hydrocolloid dressings can treat deeper wounds Used for dry wounds and minimally to moderately exudative wounds [7, 34, 35]	Can cause skin maceration around wounds secondary to excessive moisture since they are occlusive dressings; accordingly, limited utility in highly exudative wounds Opaque, so difficult to visualize wound without removing dressing [11] Can produce malodorous discharge that may be mistaken for infection [5] Do not use on infected, necrotic, or very highly exudative wounds [7]
Hydrogel	Insoluble methylacrylate polymers with hydrophilic components [7, 36] Hydrophilic gel structure dissolves necrotic tissue and promotes autolytic debridement in wound [37] Retains moisture [11]	Painless and injury-free dressing changes [11] Cooling effect decreases wound-associated pain [5] Elasticity allows use on joints Gel can be directly applied to wounds Surgical debridement unnecessary prior to application on necrotic wounds [7, 38] Can treat deep wounds Used for dry wounds, including those covered with fibrin and necrotic devitalized tissue [7, 36], and minimally exudative wounds [11]	Non-adherent, requires secondary dressings for protection Functions poorly as antimicrobial barrier May overhydrate wound Do not use on heavily exudative wounds (can cause maceration of integument bordering wound) [7, 11, 38] Caution in wounds that are infected [33]
Hydrofiber	Carboxymethylcellulose fibers [11] Exudate absorbed inside hydrofibers, gel forms and fills wound bed Microbes/exudates trapped inside gel, wound kept moist, fibrinolysis activated [7, 39]	High degree of exudate absorption and retention [11] Painless and injury-free dressing changes Can treat deep wounds Ideal for wounds infected by bacteria and moderately to heavily exudative wounds [7, 39]	Non-adherent, requires secondary dressings for protection [5] Do not use on dry wounds or minimally exudative wounds [7]

Exclusion criteria included RCTs that did not report the proportion of ulcers completely healed at the end of study follow-up for each dressing or provide enough data for this variable to be calculated. Additionally, RCTs with study samples that included patients with chronic wounds other than diabetic foot ulcers or venous leg ulcers were excluded if they did not analyze the data for diabetic foot ulcers or venous leg ulcers separately. Studies of wound dressings impregnated with topical antibiotics or antimicrobials, such as silver, iodine, zinc, and honey, were excluded because the wound dressings in and of themselves alone were the intervention being examined in our review. Based on the same reasoning, devices other than wound dressings, such as matrix devices and grafts; topical growth factors, such as platelet-derived growth factor; enzymatic treatments, such as collagenase and protease; and negative pressure wound therapy were also excluded from our review. Studies in which the amount of compression applied or the methods used to apply compression to venous leg ulcers varied between the two arms of the study, including studies that compared dressings against compression alone, were excluded since the difference in compression prevented an evaluation of the efficacy of the dressing itself on ulcer healing. Comparisons between two different dressings in the same wound dressing category (e.g., hydrocellular foam vs. polyurethane foam) were excluded as well since the focus of our review was to compare dressings in different categories.

Three of the authors (M.S., N.H., and R.N.) independently extracted data and performed a systematic review. For each RCT, the three authors recorded interventions; sample sizes; length of follow-up; proportion of ulcers completely healed at the end of study follow-up with the associated risk ratio (RR), 95% confidence interval, and *p*-value; overall risk of bias and potential sources; authors' conclusions; and data from cost-effectiveness analyses if available. Overall risk of bias for each study was classified as low, unclear, or high based on three key domains: randomization through random sequence generation, allocation concealment, and blinding of outcome assessment. Studies at low risk of bias for all three key domains were determined to have low overall risk of bias, whereas studies at high risk of bias for any one of the three key domains were rated as having high overall risk of bias.

Studies that did not meet the aforementioned criteria for either low overall risk of bias or high overall risk of bias were categorized as having unclear overall risk of bias. This method for assessing risk of bias was based on the system used by a Cochrane review from Dumville et al. [15]. The same three authors (M.S., N.H., and R.N.) independently assessed the quality of evidence for each RCT and subsequently graded the strength of their clinical recommendations based on available data pertaining to risks, benefits, costs, and biases. Determinations of quality of evidence (A, B, C) and grade of recommendation (1, 2A, 2B) were based on the stratification systems published in the *Archives of Dermatology* by Robinson et al. [22]. Quality of evidence was categorized as A (systematic reviews or meta-analyses, RCTs with consistent findings, and all-or-none observational studies), B (systematic reviews or meta-analyses of lower-quality RCTs/clinical trials or studies with limitations and inconsistent findings, lower quality RCTs/clinical trials, cohort studies, and case control studies), and C (case series, usual practice, consensus guidelines, and expert opinions). RCTs at low overall risk of bias were ranked as having level A quality of evidence, whereas RCTs classified as having unclear or high overall risk of bias were categorized as having level B quality of evidence. The three authors (M.S., N.H., and R.N.) independently rated each RCT as having high-, moderate-, or low-quality evidence based on the aforementioned classification system for evidence quality A, B, or C, respectively. Grade 1 recommendations were reserved for strong recommendations based on high-quality patient-oriented evidence. In contrast, grade 2A and 2B recommendations were assigned to weak recommendations based on moderate/limited-quality patient-oriented evidence and low-quality evidence, respectively [22]. Final determinations of quality of evidence and grade of recommendation were based on consensus amongst the three authors.

For our statistical analyses, a p -value <0.05 was considered statistically significant. We utilized the Mantel-Haenszel method to calculate the pooled RR for each set of pairwise comparisons of complete ulcer healing incidences among dressings used to treat diabetic foot ulcers and venous leg ulcers via the fixed effects model under the assumption that results were pooled from RCTs with low statistical heterogeneity and lack of apparent clinical heterogeneity. Clinical heterogeneity was evaluated based on our assessment of the study populations, interventions, and outcomes measured for each RCT. Statistical heterogeneity was assessed using the Chi^2 test in conjunction with the I^2 statistic. An I^2 statistic $\leq 40\%$ implied low statistical heterogeneity and supported the use of a fixed effects model to calculate pooled RR. Either a significance level of $p < 0.10$ with the Chi^2 test or an I^2 statistic $> 40\%$ was considered to indicate statistical heterogeneity and thus warrant determination of the pooled RR under the random effects model as well. In cases where the pooled RR was calculated using the fixed effects model and the random effects model, both values for the pooled RR were reported. We planned to avoid pooling data in cases where statistical heterogeneity was very high (i.e., an I^2 statistic $\geq 75\%$) and/or clinical heterogeneity was present. Our approach for assessing and dealing with heterogeneity was based on the system used by a Cochrane review from O'Meara and Martyn-St James [18]. All statistical analyses were conducted using commercial software (Review Manager, version 5.2; The Cochrane Collaboration).

Results

Despite our intent, we did not find any RCTs assessing efficacies of acrylic or film dressings for diabetic foot ulcers or venous leg ulcers, hydrocolloids for diabetic foot ulcers, or hydrogels for venous leg ulcers that met our eligibility criteria. Table 2 presents an overview of the 13 RCTs examining dressing efficacies in diabetic foot ulcers that were included in our systematic review. The quantitative results of the fixed effects meta-analysis assessing the data from 12 of these 13 RCTs are shown in Figure 2. For the foam vs. basic wound contact dressing comparison, Blackman et al.'s 1994 RCT [20] and Mazzone and Blackman's 1993 RCT [21] both appeared to have a similar study design with a similar number of participants comparing the same two interventions and were both funded by the same company. Moreover, Blackman and Mazzone were listed as authors on both RCTs. However, the outcome data reported varied between these two RCTs. Given our suspicion that these two RCTs were reporting different outcome data from the same patient sample, we decided to include both RCTs in our systematic review but only include Mazzone and Blackman's 1993 RCT in our meta-analysis since it had a narrower confidence interval than Blackman et al.'s 1994 RCT. For the pairwise comparisons of alginate vs. basic wound contact dressings, alginate vs. foam, foam vs. basic wound contact dressings, and hydrofiber vs. basic wound contact dressings, the pooled RRs did not show statistically significant differences between the two interventions in terms of experiencing complete diabetic foot ulcer healing. The pooled RR of the hydrogel vs. basic wound contact dressing comparison (RR 1.80 [95% CI, 1.27 to 2.56], $p=0.001$) indicated that hydrogel dressings were more efficacious than basic wound contact dressings in terms of achieving complete diabetic foot ulcer healing. Statistical heterogeneity was present in the alginate vs. foam comparison ($I^2=45\%$) and the hydrofiber vs. basic wound contact dressing comparison ($I^2=54\%$). Although the pooled RRs calculated using the random effects model for the alginate vs. foam comparison (RR 0.66 [95% CI, 0.33 to 1.29], $p=0.22$) and the hydrofiber vs. basic wound contact dressing comparison (RR 1.01 [95% CI, 0.74 to 1.38], $p=0.94$) were different from the pooled RRs calculated via the fixed effects model for these two comparisons, the pooled RRs from both models indicated that there was no statistically significant difference between alginate and foam dressings or between hydrofiber and basic wound contact dressings in terms of promoting complete diabetic foot ulcer healing.

An RCT by Jeffcoate et al. comparing hydrofiber and non-adherent dressings for diabetic foot ulcer management also included a detailed cost-effectiveness analysis. There was no statistically significant difference between non-adherent dressings and hydrofiber dressings in terms of cost of staff time associated with changing dressings, mean ulcer healing time, and the number of dressings used per patient. However, the mean total cost per patient of the dressings themselves was less for non-adherent dressings (£14.85 [95% CI, £12.10 to £17.61]) than for hydrofiber dressings (£43.60 [95% CI, £35.04 to £52.16]) [23].

Table 2. Randomized-controlled trials examining comparative efficacies of wound dressings in diabetic foot ulcer healing

Source, Year	Interventions (n=sample size) and Length of Follow-Up	Proportions of Ulcers Completely Healed at End of Follow-Up†	Risk of Bias (Low, Unclear, or High)‡	Authors' Conclusions and Quality of Evidence (QOE)
Ahroni et al., 1993 [13]	Calcium alginate: 20 Dry gauze: 19 Total sample: 39 Follow-up: 4 weeks	Calcium alginate: 5/20 (25%) Dry gauze: 7/19 (37%) Difference not statistically significant; RR 0.68 [0.26 to 1.77], $p=0.43$	ORB: High RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: High (outcome assessors not blinded) FUN: Commercial organization	Calcium alginate and dry gauze are equally efficacious QOE: B
Donaghue et al., 1998 [13, 40]	Collagen alginate: 50 Saline-moistened gauze: 25 Total sample: 75 Follow-up: 8 weeks	Collagen alginate: 24/50 (48%) Saline-moistened gauze: 9/25 (36%) Difference not statistically significant; RR 1.33 [0.73 to 2.42], $p=0.34$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (unclear whether outcome assessment was blinded) FUN: Commercial organization	Collagen alginate and saline-moistened gauze are equally efficacious QOE: B
Baker and Creevy, 1993 [13]	Calcium alginate: 10 Foam: 10 Total sample: 20 Follow-up: 12 weeks	Calcium alginate: 4/10 (40%) Foam: 9/10 (90%) Difference statistically significant; RR 0.44 [0.20 to 0.98], $p=0.04$	ORB: Unclear RSG: Low (method adequate) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Not reported	Foam is more efficacious than alginate QOE: B
Foster et al., 1994 [13]	Calcium alginate: 15 Foam: 15 Total sample: 30 Follow-up: 8 weeks	Calcium alginate: 8/15 (53%) Foam: 9/15 (60%) Difference not statistically significant; RR 0.89 [0.47 to 1.67], $p=0.71$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Not reported	Foam and alginates are equally efficacious QOE: B
Blackman et al., 1994 [14, 20]	Foam: 11 Wet-to-dry saline gauze: 7 Total sample: 18 Follow-up: 8 weeks	Foam: 3/11 (27%) Wet-to-dry saline gauze: 0/7 (0%) Difference not statistically significant; RR 4.67 [0.28 to 78.68], $p=0.29$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Foam and wet-to-dry saline gauze are equally efficacious QOE: B
Mazzone and Blackman, 1993 [14, 21]	Foam: 11 Wet-to-dry saline gauze: 8 Total sample: 19 Follow-up: 8 weeks	Foam: 7/11 (64%) Wet-to-dry saline gauze: 2/8 (25%) Difference not statistically significant; RR 2.55 [0.71 to 9.16], $p=0.15$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Foam and wet-to-dry saline gauze are equally efficacious QOE: B
Roberts et al., 2001 [14]	Foam: 14 Saline-soaked low-adherent dressings: 16 Total sample: 30 Follow-up: 13 weeks	Foam: 6/14 (43%) Saline-soaked low adherent dressings: 4/16 (25%) Difference not statistically significant; RR 1.71 [0.60 to 4.86], $p=0.31$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Foam and saline-soaked low-adherent dressings are equally efficacious QOE: B
Zhang and Xing, 2014 [41]	Foam: 24 Vaseline gauze: 26 Total sample: 50 Follow-up: 12 weeks	Foam: 18/24 (75%) Vaseline gauze: 16/26 (62%) Difference not statistically significant; RR 1.22 [0.83 to 1.79], $p=0.31$	ORB: High RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: High (outcome assessors not blinded) FUN: Not reported	Foam and vaseline gauze are equally efficacious QOE: B

Jeffcoate et al., 2009 [15, 23]	Hydrofiber: 103 Non-adherent, knitted, viscose filament gauze: 106 Total sample: 209 Follow-up: 24 weeks	Hydrofiber: 46/103 (45%) Non-adherent dressings: 41/106 (39%) Difference not statistically significant; RR 1.15 [0.84 to 1.59], $p=0.38$	ORB: Low RSG: Low (method adequate) ALC: Low (central allocation via telephone) BOA: Low (outcome assessors were blinded) FUN: Non-commercial organization	Hydrofiber and non-adherent dressings are equally efficacious; non-adherent dressings are more cost-effective than hydrofiber QOE: A
Piaggese et al., 2001 [15, 42]	Hydrofiber: 10 Saline-moistened gauze: 10 Total sample: 20 Follow-up: Not reported, maximum follow-up recorded was 350 days	Hydrofiber: 9/10 (90%) Saline-moistened gauze: 10/10 (100%) Difference not statistically significant; RR 0.90 [0.69 to 1.18], $p=0.46$	ORB: Unclear RSG: Low (method adequate) ALC: Unclear (not reported) BOA: Unclear (unclear whether outcome assessment was blinded) FUN: Non-commercial organization	Hydrofiber and saline-moistened gauze are equally efficacious QOE: B
D'Hemecourt et al., 1998 [16]	Hydrogel: 70 Wet-to-moist saline dressing: 68 Total sample: 138 Follow-up: 20 weeks	Hydrogel: 25/70 (36%) Wet-to-moist saline dressing: 15/68 (22%) Difference not statistically significant; RR 1.62 [0.94 to 2.80], $p=0.08$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Low (outcome assessors were blinded) FUN: Not reported	Hydrogel and wet-to-moist saline dressings are equally efficacious QOE: B
Jensen et al., 1998 [16, 43]	Hydrogel: 14 Saline-soaked gauze: 17 Total sample: 31 Follow-up: 16 weeks	Hydrogel: 11/14 (79%) Saline-soaked gauze: 6/17 (35%) Difference statistically significant; RR 2.23 [1.11 to 4.48], $p=0.02$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Hydrogel is more efficacious than saline-soaked gauze QOE: B
Vandeputte and Gryson, 1997 [16]	Hydrogel: 14 Dry gauze: 15 Total sample: 29 Follow-up: 12 weeks	Hydrogel: 14/15 (93%) Dry gauze: 7/14 (50%) Difference statistically significant; RR 1.87 [1.09 to 3.21], $p=0.02$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (not clear who assessed wounds for healing) FUN: Not reported	Hydrogel is more efficacious than dry gauze QOE: B

†RR, risk ratio followed by 95% confidence interval in brackets and p -value.

‡Overall risk of bias (ORB) determined by risk of bias in three key domains: randomization through random sequence generation (RSG), allocation concealment (ALC), and blinding of outcome assessment (BOA). Study at low ORB if at low risk of bias for all three key domains (RSG, ALC, and BOA). Study at high ORB if at high risk of bias for any one of the three key domains. Study at unclear ORB if it did not meet criteria for low ORB or high ORB. FUN, funding source.

Table 3 gives an overview of the 19 RCTs examining dressing efficacies in venous leg ulcers that were analyzed in our systematic review and meta-analysis. The quantitative results of the fixed effects meta-analysis assessing the data from these 19 RCTs are shown in Figure 3. For the pairwise comparisons of alginate vs. low-adherent dressings, alginate vs. hydrocolloid, alginate vs. hydrofiber, foam vs. low-adherent dressings, foam vs. hydrocolloid, and hydrocolloid vs. low-adherent dressings, the pooled RRs did not show statistically significant differences between the two interventions in terms of achieving complete venous leg ulcer healing. Statistical heterogeneity was present in the alginate vs. hydrofiber comparison ($I^2=55%$) and in the hydrocolloid vs. low-adherent dressing comparison ($p=0.03$ for Chi² test and $I^2=55%$). Even though the pooled RRs calculated via the random effects model for the alginate vs. hydrofiber comparison (RR 0.68 [95% CI, 0.22 to 2.09], $p=0.50$) and the hydrocolloid vs. low-adherent dressing comparison (RR 1.15 [95% CI, 0.93-1.43], $p=0.21$) varied from the pooled RRs calculated using the fixed effects model for these two comparisons, the pooled RRs from both models indicated that there was no statistically significant difference between alginate and hydrofiber dressings or between hydrocolloid and low-adherent dressings in terms of promoting complete venous leg ulcer healing.

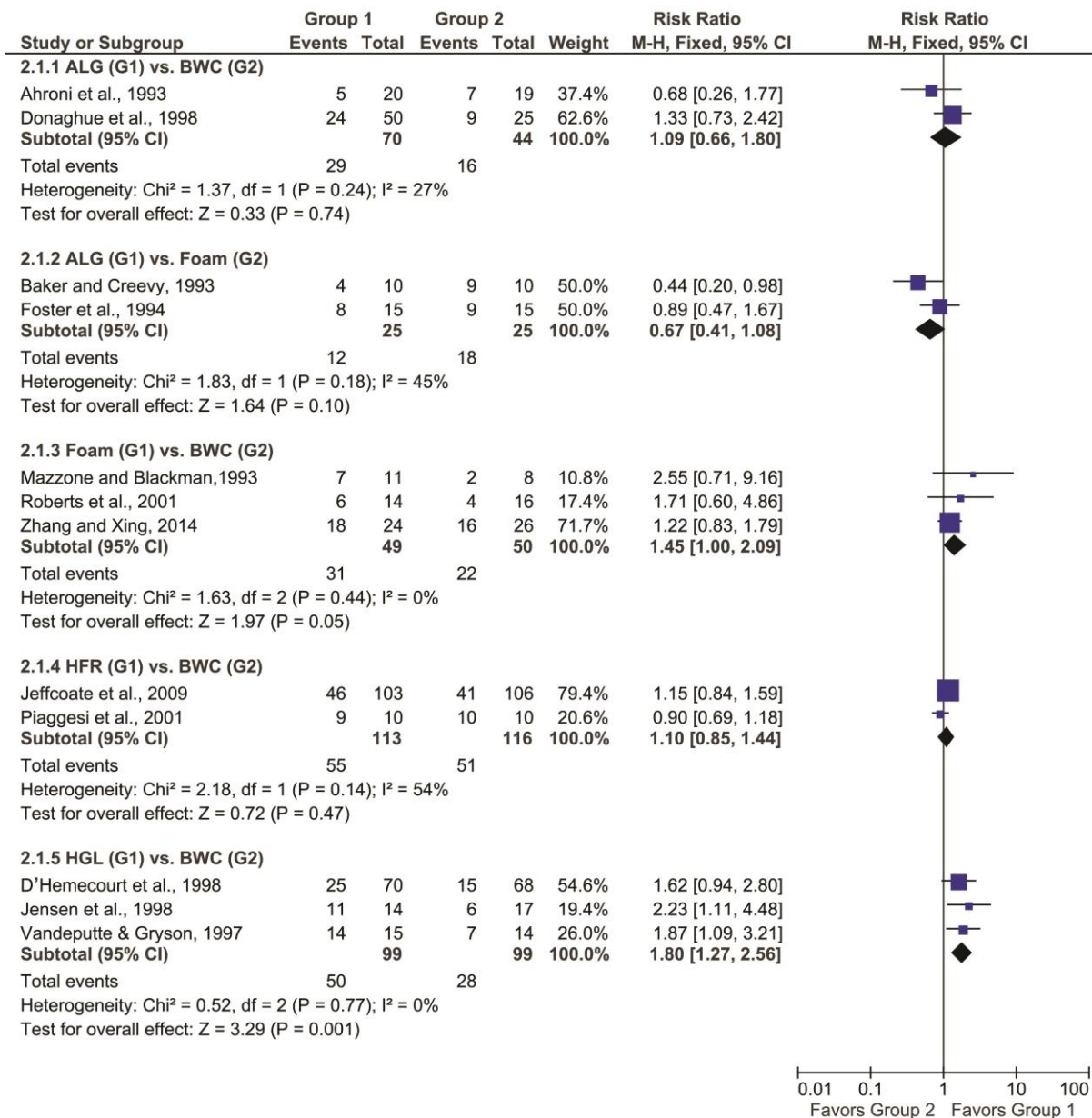


Figure 2. Diabetic foot ulcer fixed effects meta-analysis with pairwise dressing comparisons examining complete ulcer healing incidents. RR >1 favors dressing in group 1, whereas RR <1 favors dressing in group 2. ALG, alginate; BWC, basic wound contact dressing; G1, group 1; G2, group 2; HFR, hydrofiber; HGL, hydrogel; M-H, Mantel-Haenszel; middle vertical line, line of no difference; squares with horizontal lines, risk ratios with 95% CIs; diamond, pooled analysis of overall 95% CI of effect estimate of two different dressings on complete ulcer healing incidence.

Table 3. Randomized-controlled trials examining comparative efficacies of wound dressings in venous leg ulcer healing

Source, Year	Interventions* (n=sample size) and Length of Follow-Up	Proportion of Ulcers Completely Healed at End of Follow-Up†	Risk of Bias (Low, Unclear, or High)‡	Authors' Conclusions and Quality of Evidence (QOE)
Moffatt et al., 1992a [17]	Alginate: 30 Plain non-adherent dressings: 30 Total sample: 60 Follow-up: 12 weeks	Alginate: 26/30 (87%) Plain non-adherent dressings: 24/30 (80%) Difference not statistically significant; RR 1.08 [0.86 to 1.36], p=0.49	ORB: High RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: High (outcome assessment not blinded) FUN: Commercial organization	Alginate and plain non-adherent dressings are equally efficacious QOE: B
Smith, 1994 [17, 44]	Alginate: 18 Hydrocolloid: 22 Total sample: 40 Follow-up: 6 weeks	Alginate: 2/18 (11%) Hydrocolloid: 4/22 (18%) Difference not statistically significant; RR 0.61 [0.13 to 2.96], p=0.54	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned)	Alginate and hydrocolloid are equally efficacious QOE: B

			FUN: Commercial organization	
Armstrong and Ruckley, 1997 [17, 45]	Alginate: 23 Hydrofiber: 21 Total sample: 44 Follow-up: 6 weeks	Alginate: 2/23 (9%) Hydrofiber: 6/21 (29%) Difference not statistically significant; RR 0.30 [0.07 to 1.35], $p=0.12$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (intervention allocated via sealed envelopes opened in numerical order, whether envelopes were opaque was not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Alginate and hydrofiber are equally efficacious QOE: B
Harding et al., 2001 [17, 46]	Alginate: 65 Hydrofiber: 66 Total sample: 131 Follow-up: 12 weeks	Alginate: 17/65 (26%) Hydrofiber: 17/66 (26%) Difference not statistically significant; RR 1.02 [0.57 to 1.81], $p=0.96$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (intervention allocated via sealed envelopes, whether envelopes were opaque and numbered sequentially was not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Alginate and hydrofiber are equally efficacious QOE: B
Banerjee et al., 1990 [18]	Foam: 36 Paraffin gauze: 35 Total sample: 71 Follow-up: 17 weeks	Foam: 11/36 (31%) Paraffin gauze: 8/35 (23%) Difference not statistically significant; RR 1.34 [0.61 to 2.92], $p=0.46$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Not reported	Foam and paraffin gauze are equally efficacious QOE: B
Callam et al., 1992 [18]	Foam: 66 Non-adherent dressings: 66 Total sample: 132 Follow-up: 12 weeks	Foam: 31/66 (47%) Non-adherent dressings: 23/66 (35%) Difference not statistically significant; RR 1.35 [0.89 to 2.05], $p=0.16$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Non-commercial organization, but commercial organization provided bandages and dressings	Foam and non-adherent dressings are equally efficacious QOE: B
Bowszyc et al., 1995 [18, 47]	Polyurethane foam: 41 Hydrocolloid: 41 Total sample: 82 Follow-up: 16 weeks	Polyurethane foam: 24/41 (59%) Hydrocolloid: 24/41 (59%) Difference not statistically significant; RR 1.00 [0.51 to 1.95], $p=1.00$	ORB: Unclear RSG: Unclear (insufficient detail to determine whether method was adequate) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Polyurethane foam and hydrocolloid are equally efficacious QOE: B
Charles et al., 2002 [18, 48]	Polyurethane foam: 31 Hydrocolloid: 60 Total sample: 91 Follow-up: 12 weeks	Polyurethane foam: 18/31 (58%) Hydrocolloid: 34/60 (57%) Difference not statistically significant; RR 1.02 [0.71 to 1.49], $p=0.90$	ORB: Unclear RSG: Low (method adequate) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Polyurethane foam and hydrocolloid are equally efficacious QOE: B
Thomas et al., 1997 [18, 49]	Polyurethane foam: 50 Hydrocolloid: 50 Total sample: 100 Follow-up: 13 weeks	Polyurethane foam: 17/50 (34%) Hydrocolloid: 19/50 (38%) Difference not statistically significant; RR 0.89 [0.53 to 1.51], $p=0.68$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (intervention allocated via sealed envelopes, whether envelopes were opaque and numbered sequentially was not reported) BOA: Unclear (unclear whether outcome assessors were blinded) FUN: Not reported	Polyurethane foam and hydrocolloid are equally efficacious QOE: B

Vanscheidt et. al, 2004 [18, 50]	Hydrocellular foam: 52 Hydrocolloid: 55 Total sample: 107 Follow-up: 12 weeks	Hydrocellular foam: 20/52 (38%) Hydrocolloid: 20/55 (36%) Difference not statistically significant; RR 1.06 [0.65 to 1.73], $p=0.82$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Hydrocellular foam and hydrocolloid are equally efficacious QOE: B
Zuccarelli, 1992 [18]	Hydrocellular foam: 19 Hydrocolloid: 19 Total sample: 38 Follow-up: 12 weeks	Hydrocellular foam: 9/19 (47%) Hydrocolloid: 9/19 (47%) Difference not statistically significant; RR 1.00 [0.51 to 1.95], $p=1.00$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Hydrocellular foam and hydrocolloid are equally efficacious QOE: B
Backhouse et al., 1987 [19, 51]	Hydrocolloid: 28 Non-adherent dressings: 28 Total: 56 Follow-up: 12 weeks	Hydrocolloid: 21/28 (75%) Non-adherent dressings: 22/28 (79%) Difference not statistically significant; RR 0.95 [0.72 to 1.27], $p=0.75$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Not reported	Hydrocolloid and non-adherent dressings are equally efficacious QOE: B
Blair et al., 1988 [19]	Hydrocolloid: 30 Non-adherent dressings: 30 Total sample: 60 Follow-up: 12 weeks	Hydrocolloid: 22/30 (73%) Non-adherent dressings: 23/30 (77%) Difference not statistically significant; RR [0.71 to 1.28], $p=0.77$	ORB: Unclear RSG: Low (method adequate) ALC: Unclear (intervention allocated via sealed envelopes, whether envelopes were opaque and numbered sequentially was not reported) BOA: Unclear (blinding not mentioned) FUN: Not reported	Hydrocolloid and non-adherent dressings are equally efficacious QOE: B
Hansson et al., 1998 [19, 25]	Hydrocolloid: 48 Paraffin gauze: 49 Total sample: 97 Follow-up: 12 weeks	Hydrocolloid: 5/48 (10%) Paraffin gauze: 7/49 (14%) Difference not statistically significant; RR 0.73 [0.25 to 2.14], $p=0.57$	ORB: Unclear RSG: Unclear (method not reported) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Hydrocolloid and paraffin gauze are equally efficacious QOE: B
Meredith and Gray, 1988 [19]	Hydrocolloid: 25 Paraffin gauze: 24 Total sample: 49 Follow-up: 6 weeks	Hydrocolloid: 19/25 (76%) Paraffin gauze: 6/24 (25%) Difference statistically significant; RR 3.04 [1.47 to 6.29], $p=0.003$	ORB: High RSG: Low (method adequate) ALC: Unclear (not reported) BOA: High (outcome assessment not blinded) FUN: Not reported	Hydrocolloid is more efficacious than paraffin gauze QOE: B
Moffatt et al., 1992b [19]	Hydrocolloid: 30 Non-adherent dressings: 30 Total sample: 60 Follow-up: 12 weeks	Hydrocolloid: 13/30 (43%) Non-adherent dressings: 7/30 (23%) Difference not statistically significant; RR 1.86 [0.86 to 4.00], $p=0.11$	ORB: Unclear RSG: Low (method adequate) ALC: Unclear (not reported) BOA: Unclear (blinding not mentioned) FUN: Commercial organization	Hydrocolloid and non-adherent dressings are equally efficacious QOE: B
Nelson et al., 1995 [19]	Hydrocolloid: 102 Non-adherent dressings: 98 Total sample: 200 Follow-up: 24 weeks	Hydrocolloid: 49/102 (48%) Non-adherent dressings: 44/98 (45%) Difference not statistically significant; RR 1.07 [0.79 to 1.44], $p=0.66$	ORB: High RSG: Low (method adequate) ALC: Low (method adequate, sealed opaque envelopes that were sequentially numbered) BOA: High (outcome assessment not blinded) FUN: Commercial organization	Hydrocolloid and non-adherent dressings are equally efficacious QOE: B
Nelson et al., 2007 [52]	Hydrocolloid: 64 Knitted viscose (non-adherent) dressing: 60 Total sample: 124	Hydrocolloid: 33/64 (52%) Knitted viscose dressing: 33/60 (55%) Difference not statistically	ORB: High RSG: Low (method adequate) ALC: Low (method adequate, sealed opaque envelopes that were	Hydrocolloid and knitted viscose dressings are equally efficacious

	Follow-up: 24 weeks	significant; RR 0.94 [0.67 to 1.30], $p=0.70$	sequentially numbered) BOA: High (outcome assessment not blinded) FUN: Commercial organization	QOE: B
Srivastava et al., 2001 [53]	Hydrocolloid: 50 Paraffin gauze: 50 Total sample: 100 Follow-up: Not reported	Hydrocolloid: 33/50 (66%) Paraffin gauze: 23/50 (46%) Difference statistically significant; RR 1.43 [1.00 to 2.06], $p= 0.0495$	ORB: High RSG: Low (method adequate) ALC: Low (method adequate, sealed opaque envelopes containing computer-generated random numbers) BOA: High (outcome assessment not blinded) FUN: Commercial organization	Hydrocolloid is more efficacious than paraffin gauze QOE: B

*With two exceptions, all of the interventions listed in Table 3 were administered with concomitant compression. Banerjee et al. and Srivastava et al. did not report whether the interventions in their studies were administered with concomitant compression.

†RR, risk ratio followed by 95% confidence interval in brackets and p -value.

‡Overall risk of bias (ORB) determined by risk of bias in three key domains: randomization through random sequence generation (RSG), allocation concealment (ALC), and blinding of outcome assessment (BOA). Study at low ORB if at low risk of bias for all three key domains (RSG, ALC, and BOA). Study at high ORB if at high risk of bias for any one of the three key domains. Study at unclear ORB if it did not meet criteria for low ORB or high ORB. FUN, funding source.

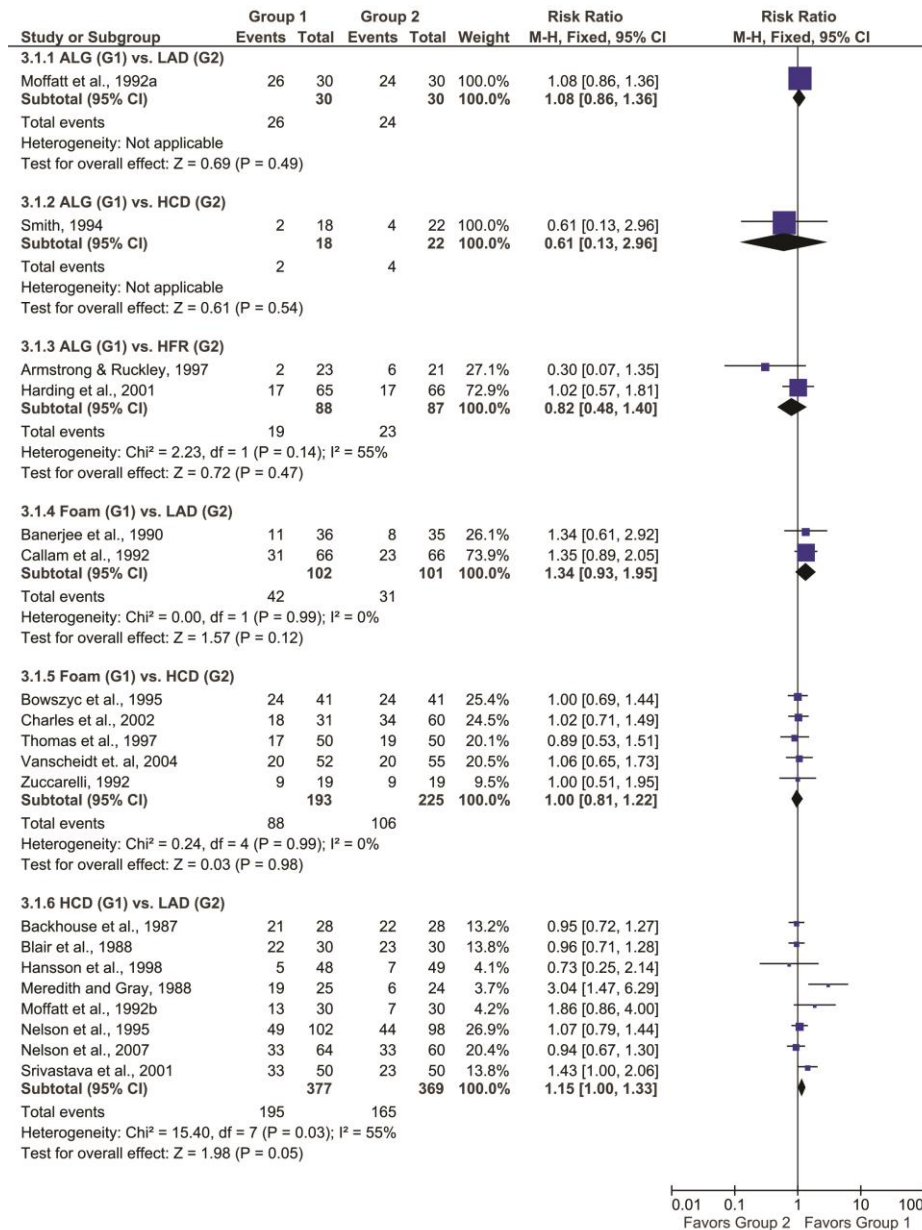


Figure 3. Venous leg ulcer fixed effects meta-analysis with pairwise dressing comparisons examining complete ulcer healing incidences. RR >1 favors dressing in group 1, whereas RR <1 favors dressing in group 2. ALG, alginate; G1, group 1; G2, group 2; HCD, hydrocolloid; HFR, hydrofiber; LAD, low-adherent dressing; M-H, Mantel-Haenszel; middle vertical line, line of no difference; squares with horizontal lines, risk ratios with 95% CIs; diamond, pooled analysis of overall 95% CI of effect estimate of two different dressings on complete ulcer healing incidence.

A cost-effectiveness modeling study from Guest et al. estimated that the total United States healthcare costs per patient after 18 weeks of starting venous leg ulcer treatment with hydrofiber dressings and gauze dressings under compression were \$3797 and \$5288, respectively. Their model was based on what they claimed to be a systematic review of the literature supplemented by utilization estimates from a panel of clinicians and considered costs of dressings, time to complete ulcer healing, frequency of dressing changes, and associated nursing and physician costs in their calculations. However, they did not mention whether they assessed the studies they included for bias, and they did not report their search strategy. Furthermore, upon reviewing the RCTs cited by Guest et al., we determined that the RCTs that we had also included in our systematic review and meta-analysis did not actually compare hydrofiber dressings directly against gauze, and the other RCTs cited by Guest et al. were ones that we had excluded from our review because they did not meet our inclusion and exclusion criteria. In fact, we did not find any RCTs comparing hydrofiber vs. low-adherent dressings for treating venous leg ulcers that met our eligibility criteria during our literature search. Additionally, we classified the utilization estimates from the panel of clinicians interviewed that were included in the authors' calculations to be expert opinion at best. Moreover, we were unable to determine the degree to which the utilization estimates influenced the calculations in this study. Finally, this study was sponsored by a commercial organization, but the authors reported no conflicts of interest directly relevant to their manuscript. However, they did not report whether anyone on the panel of clinicians that they interviewed to obtain their utilization estimates had relevant conflicts of interest [24].

Discussion

Diabetic foot ulcers and venous leg ulcers contribute significantly to morbidity, healthcare costs, and overall quality of life. Appropriate and diligent wound care is paramount for patients to achieve better outcomes related to these ulcers. Therefore, the main goal of our systematic review and meta-analysis was to determine which wound dressings are most efficacious for treating diabetic foot ulcers and venous leg ulcers.

Of the five sets of diabetic foot ulcer pairwise dressing comparisons examined in our systematic review and meta-analysis, only hydrogel dressings demonstrated superiority over basic wound contact dressings in promoting complete ulcer healing to a degree that was statistically significant. Accordingly, based on moderate-quality level B evidence from our meta-analysis of three RCTs at unclear risk of bias, we give a weak grade 2A recommendation to use hydrogel dressings instead of basic wound contact dressings in diabetic foot ulcer management. The pairwise comparisons of alginate vs. basic wound contact dressings, alginate vs. foam, and foam vs. basic wound contact dressings included in our meta-analysis provided moderate-quality level B evidence that there were no statistically significant differences in diabetic foot ulcer healing efficacies between the two interventions examined in each comparison. As a result, we were unable to provide recommendations pertaining to which dressing is superior for treating diabetic foot ulcers in the context of these pairwise comparisons.

The hydrofiber vs. basic wound contact dressing comparison included in our meta-analysis for diabetic foot ulcers showed no statistically significant difference in complete wound healing efficacy between these two dressings, and was based on high-quality level A evidence from Jeffcoate et al.'s RCT at low risk of bias and moderate-quality level B evidence from Piaggese et al.'s RCT at unclear risk of bias. Furthermore, the cost-effectiveness analysis included in Jeffcoate et al.'s RCT showed that the average total cost of dressings per patient was less for non-adherent dressings than for hydrofiber dressings when treating diabetic foot ulcers [23]. Therefore, based on high-quality level A evidence showing no statistically significant difference in wound-healing efficacy between hydrofiber and non-adherent dressings and a statistically significant decrease in cost of dressings per patient observed with non-adherent dressings relative to hydrofiber dressings, we give a strong grade 1 recommendation to use non-adherent dressings instead of hydrofiber dressings to treat diabetic foot ulcers.

The venous leg ulcer pairwise comparisons of alginate vs. low-adherent dressings, alginate vs. hydrocolloid, alginate vs. hydrofiber, foam vs. low-adherent dressings, foam vs. hydrocolloid, and hydrocolloid vs. low-adherent dressings included in our meta-analysis revealed moderate-quality level B evidence that there were no statistically significant differences in ulcer healing efficacies between the two interventions examined in each comparison. Therefore, we were unable to provide recommendations pertaining to which dressing is superior for treating venous leg ulcers in the context of these pairwise comparisons. Of note, although the meta-analyses of the venous leg ulcer pairwise comparisons of foam vs. hydrocolloid and hydrocolloid vs. low-adherent dressings were each based on large pooled data samples from several RCTs, we still assigned moderate-quality level B

evidence to these meta-analyses based on risk of bias in these RCTs. All five RCTs assessed in the foam vs. hydrocolloid comparison and four out of the eight RCTs analyzed in the hydrocolloid vs. low-adherent dressing comparison were at unclear risk of bias. More importantly, the other four RCTs in the hydrocolloid vs. low-adherent dressing comparison, which collectively comprised more than half of the entire pooled patient sample from all eight RCTs in this comparison, were at high risk of bias because the outcome assessments were not blinded in any of these four RCTs.

Cost plays a vital role in choosing between wound dressings, especially considering the lack of evidence of superiority of most synthetic active dressings over basic wound contact or low-adherent dressings for diabetic foot ulcer and venous leg ulcer management. Accordingly, cost-effectiveness analyses can provide data that can greatly influence dressing choice. However, many of the cost-effectiveness analyses published do not provide enough detail regarding how they were performed, fail to include the statistical significance of the differences in cost between dressings that they report, or neglect to examine several variables that are crucial in order to accurately assess cost-effectiveness [25, 26, 27, 28, 29, 30]. Cost-effectiveness is related not only to costs of the dressings themselves, but also to average wound healing times since wounds taking longer to heal can increase costs of staff time associated with dressing changes and the number of dressings used [23, 24]. Even though Guest et al.'s cost-effectiveness analysis comparing hydrofiber and gauze dressings under compression in venous leg ulcer management included these important variables, in light of all of the threats to validity present in the study methods, we could not accurately determine this study's quality of evidence or use this study to make clinical recommendations [24]. With respect to all of the available dressings, future studies should focus on performing more rigorous and extensive cost-effectiveness analyses without commercial organization sponsorship, especially in the United States, where there are severe deficiencies in data pertaining to this critical variable.

Our review had several strengths. For our literature search, we used five online medical databases to review both published and unpublished reports of data from database inception to 10 May 2015, reviewing decades of literature in the process. Furthermore, three authors independently isolated articles for systematic review and meta-analysis based on predefined inclusion and exclusion criteria, extracted data from and assigned quality of evidence to the included RCTs, performed meta-analyses of these RCTs, and wrote graded recommendations based on their findings. Subsequently, the three authors compared their notes and made final determinations for these variables based on group consensus.

In order to minimize language bias in our systematic review, we conducted our literature searches without any language restrictions. Although we were only able to include studies not published in English if the abstracts were written in English or if a systematic review written in English listed the data from the study, we did not come across any instances where we were unable to assess non-English sources for eligibility or include pertinent data from non-English sources in our systematic review and meta-analysis if warranted.

Admittedly, our study also had several limitations. However, most of the major limitations of our review were related to the quality of the studies available. Relatively few studies, most of which had small study populations, were available for the different dressing comparisons. Out of the 11 pairwise dressing comparisons included in our meta-analysis, only 4 contained data pooled from three or more RCTs, none of which contained data from studies at overall low risk of bias. Moreover, assessing overall risk of bias for each RCT proved difficult due to poor reporting, especially related to descriptions of randomization methods, allocation concealment, and blinding of outcome assessments. Only one RCT had low overall risk of bias, while 24 RCTs had unclear overall risk of bias and seven RCTs had high overall risk of bias. All seven RCTs at high overall risk of bias were at high risk of detection bias due to nonblinded outcome assessments, though three of these seven RCTs were at low risk of selection bias based on adequate randomization methods and allocation concealment. Given the fact that only two of the RCTs examined in our review were sponsored solely by non-commercial organizations, with the rest of the RCTs either receiving funding from commercial organizations or not reporting their funding source, our review was likely subject to publication bias in spite of our meticulous database searches. The presence of publication bias may be further suggested by the dearth of RCTs in the literature reporting data indicative of superiority of traditional wound dressings over synthetic active dressings.

For our systematic review and meta-analysis, we only included RCTs that reported the proportion of ulcers completely healed at the end of study follow-up. This was done in order to base our clinical practice recommendations on a presumably objective variable that would be more likely to maintain uniformity between studies in terms of definition of outcome measured relative to other variables that could be used to evaluate dressing efficacy. However, in the process, we did not assess other important variables that could be used to choose between different dressings, such as rates of ulcer recurrence, adverse events, allergic reactions, percentage of wound area healed, time to ulcer healing, ulcer healing rates, number of dressings used, and pain relief. Moreover, we evaluated efficacies of dressings in different categories and did not attempt to compare efficacies of dressings in the same category, limiting our ability to generalize our clinical practice recommendations to all dressings in the same category. Since our review only examined dressings in the context of diabetic foot ulcers or venous leg ulcers, our findings cannot be applied to

other types of chronic wounds, such as pressure ulcers or arterial ulcers. Also, even though an attempt was made to examine the cost-effectiveness of the dressings in our study, insufficient reliable data was available to compare the overall cost-effectiveness of the different dressings. Out of all of the cost-effectiveness analyses examined during our literature search, only two met our eligibility criteria, with one of these cost-effectiveness analyses producing questionable results that could not be used to make any clinical recommendations.

In every pairwise comparison examined in our meta-analysis, there was no uniformity in length of study follow-up between the RCTs pooled for each comparison. Moreover, the follow-up times for the majority of the RCTs were 8 or 12 weeks. Diabetic foot ulcers and venous leg ulcers are chronic wounds that usually take longer than two-three months to heal [31, 32], so RCTs with short follow-up times in which complete ulcer healing is assessed will have low event rates and consequently low power [19]. Therefore, pooling data from RCTs with different follow-up times may have increased clinical heterogeneity and consequently reduced the validity of our results. However, since our goal was to compare the proportion of ulcers completely healed at the end of study follow-up for each dressing, and because the two arms of each study were assessed for the same amount of time, we felt that the RCTs pooled together still lacked enough clinical heterogeneity to allow comparisons to be made between RCTs examining the same interventions in similar study populations.

Conclusion

In summary, although a variety of synthetic active dressings and traditional wound dressings are available to treat diabetic foot ulcers and venous leg ulcers, most of the different options have similar efficacies in terms of achieving complete ulcer healing. Accordingly, we are only able to make two clinical practice recommendations based on our systematic review and meta-analysis. For diabetic foot ulcer management, we give a strong recommendation to use non-adherent dressings instead of the equally efficacious but less cost-effective hydrofiber dressings, and a weak recommendation to use hydrogel dressings instead of the less efficacious basic wound contact dressings. Overall, deciding which dressing is appropriate for each patient should depend on healing benefit, exudate management, allergen exposure, local costs of available dressings, and physician and patient preference. Future studies examining cost-effectiveness of the different wound dressings are in dire need, as data examining this critical variable are currently lacking.

References

1. Kantor J, Margolis DJ. Treatment options for diabetic neuropathic foot ulcers: a cost-effectiveness analysis. *Dermatol Surg.* 2001 Apr;27(4):347-51. [PMID:11298704]
2. Frykberg RG. Diabetic foot ulcers: pathogenesis and management. *Am Fam Physician.* 2002 Nov 1;66(9):1655-62. [PMID:12449264]
3. Collins L, Seraj S. Diagnosis and treatment of venous ulcers. *Am Fam Physician.* 2010 Apr 15;81(8):989-96. [PMID:20387775]
4. Margolis DJ, Berlin JA, Strom BL. Risk factors associated with the failure of a venous leg ulcer to heal. *Arch Dermatol.* 1999 Aug;135(8):920-6. [PMID:10456340]
5. Okan D, Woo K, Ayello EA, Sibbald G. The role of moisture balance in wound healing. *Adv Skin Wound Care.* 2007 Jan;20(1):39-53; quiz 53-5. [PMID:17195786]
6. Limova M. Active wound coverings: bioengineered skin and dermal substitutes. *Surg Clin North Am.* 2010 Dec;90(6):1237-55. [PMID:21074039]
7. Skorkowska-Telichowska K, Czemplik M, Kulma A, Szopa J. The local treatment and available dressings designed for chronic wounds. *J Am Acad Dermatol.* 2013 Apr;68(4):e117-26. [PMID:21982060]
8. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. *Physiol Rev.* 2003 Jul;83(3):835-70. [PMID:12843410]
9. Singer AJ, Clark RA. Cutaneous wound healing. *N Engl J Med.* 1999 Sep 2;341(10):738-46. [PMID:10471461]
10. Renner R, Simon JC, Treudler R. Contact sensitization to modern wound dressings in 70 patients with chronic leg ulcers. *Dermatitis.* 2013 Mar;24(2):60-3. [PMID:23474445]
11. Fonder MA, Lazarus GS, Cowan DA, Aronson-Cook B, Kohli AR, Mamelak AJ. Treating the chronic wound: A practical approach to the care of nonhealing wounds and wound care dressings. *J Am Acad Dermatol.* 2008 Feb;58(2):185-206. [PMID:18222318]
12. Valle MF, Maruthur NM, Wilson LM, Malas M, Qazi U, Haberl E, Bass EB, Zenilman J, Lazarus G. Comparative effectiveness of advanced wound dressings for patients with chronic venous leg ulcers: A systematic review. *Wound Repair Regen.* 2014 Mar;22(2):193-204. [PMID:24635169]

13. Dumville JC, O'Meara S, Deshpande S, Speak K. Alginate dressings for healing diabetic foot ulcers. *Cochrane Database Syst Rev.* 2013 Jun 25;6:CD009110. [PMID:23799857]
14. Dumville JC, Deshpande S, O'Meara S, Speak K. Foam dressings for healing diabetic foot ulcers. *Cochrane Database Syst Rev.* 2013 Jun 6;6:CD009111. [PMID:23740766]
15. Dumville JC, Deshpande S, O'Meara S, Speak K. Hydrocolloid dressings for healing diabetic foot ulcers. *Cochrane Database Syst Rev.* 2013;8:CD009099. [PMID:23922167]
16. Dumville JC, O'Meara S, Deshpande S, Speak K. Hydrogel dressings for healing diabetic foot ulcers. *Cochrane Database Syst Rev.* 2013;7:CD009101. [PMID:23846869]
17. O'Meara S, Martyn-St James M. Alginate dressings for venous leg ulcers. *Cochrane Database Syst Rev.* 2013;4:CD010182. [PMID:23633381]
18. O'Meara S, Martyn-St James M. Foam dressings for venous leg ulcers. *Cochrane Database Syst Rev.* 2013;5:CD009907. [PMID:23728697]
19. Palfreyman SJ, Nelson EA, Lochiel R, Michaels JA. Dressings for healing venous leg ulcers. *Cochrane Database Syst Rev.* 2006;3:CD001103. [PMID:16855958]
20. Blackman JD, Senseng D, Quinn L, Mazzone T. Clinical evaluation of a semipermeable polymeric membrane dressing for the treatment of chronic diabetic foot ulcers. *Diabetes Care.* 1994 Apr;17(4):322-5. [PMID:8026290]
21. First Joint Meeting of The Wound Healing Society and the European Tissue Repair Society. RAI Congress Centre, Amsterdam, The Netherlands, August 22-25, 1993. *Wound Repair Regen.* 1993 Mar-Apr;1(2):84. [PMID:17134387]
22. Robinson JK, Dellavalle RP, Bigby M, Callen JP. Systematic reviews: grading recommendations and evidence quality. *Arch Dermatol.* 2008 Jan;144(1):97-9. [PMID:18209174]
23. Jeffcoate WJ, Price PE, Phillips CJ, Game FL, Mudge E, Davies S, Amery CM, Edmonds ME, Gibby OM, Johnson AB, Jones GR, Masson E, Patmore JE, Price D, Rayman G, Harding KG. Randomised controlled trial of the use of three dressing preparations in the management of chronic ulceration of the foot in diabetes. *Health Technol Assess.* 2009 Nov;13(54):1-86, iii-iv. [PMID:19922726]
24. Guest JF, Ruiz FJ, Mihai A, Lehman A. Cost effectiveness of using carboxymethylcellulose dressing compared with gauze in the management of exuding venous leg ulcers in Germany and the USA. *Curr Med Res Opin.* 2005 Jan;21(1):81-92. [PMID:15881478]
25. Hansson C. The effects of cadexomer iodine paste in the treatment of venous leg ulcers compared with hydrocolloid dressing and paraffin gauze dressing. Cadexomer Iodine Study Group. *Int J Dermatol.* 1998 May;37(5):390-6. [PMID:9620490]
26. Harding K, Cutting K, Price P. The cost-effectiveness of wound management protocols of care. *Br J Nurs.* 2000 Oct;9(19 Suppl):S6, S8, S10 passim. [PMID:12271239]
27. Meaume S, Gemmen E. Cost-effectiveness of wound management in France: pressure ulcers and venous leg ulcers. *J Wound Care.* 2002 Jun;11(6):219-24. [PMID:12096580]
28. Kerstein MD, Gemmen E, van Rijswijk L, Lyder CH, Phillips T, Xakellis G, Golden K, Harrington C. Cost and cost effectiveness of venous and pressure ulcer protocols of care. *Dis Manage Health Outcomes.* 2001;9(11):651-63
29. Langer A, Rogowski W. Systematic review of economic evaluations of human cell-derived wound care products for the treatment of venous leg and diabetic foot ulcers. *BMC Health Serv Res.* 2009;9:115. [PMID:19591680]
30. Yan S, Colin X, Coudray-Omnes C, Guido-Morin P, Kommala DR. A budget impact analysis comparing a Hydrofiber(R) dressing to an alginate dressing in managing exuding venous leg ulcers in France. *Int Wound J.* 2012 Oct 1. [PMID:23020759]
31. Alavi A, Sibbald RG, Mayer D, Goodman L, Botros M, Armstrong DG, Woo K, Boeni T, Ayello EA, Kirsner RS. Diabetic foot ulcers: Part I. Pathophysiology and prevention. *J Am Acad Dermatol.* 2014 Jan;70(1):1 e1-18; quiz 19-20. [PMID:24355275]
32. Iglesias C, Nelson EA, Cullum NA, Torgerson DJ, Ven UST. VenUS I: a randomised controlled trial of two types of bandage for treating venous leg ulcers. *Health Technol Assess.* 2004 Jul;8(29):iii, 1-105. [PMID:15248939]
33. Alavi A, Sibbald RG, Mayer D, Goodman L, Botros M, Armstrong DG, Woo K, Boeni T, Ayello EA, Kirsner RS. Diabetic foot ulcers: Part II. Management. *J Am Acad Dermatol.* 2014 Jan;70(1):21 e1-24; quiz 45-6. [PMID:24355276]
34. Carville K. Which dressing should I use? It all depends on the 'TIMEING'. *Aust Fam Physician.* 2006;35(7):486-89
35. Hollisaz MT, Khedmat H, Yari F. A randomized clinical trial comparing hydrocolloid, phenytoin and simple dressings for the treatment of pressure ulcers [ISRCTN33429693]. *BMC Dermatol.* 2004;4(1):18. [PMID:15601464]
36. Bruggisser R. Bacterial and fungal absorption properties of a hydrogel dressing with a superabsorbent polymer core. *J Wound Care.* 2005 Oct;14(9):438-42. [PMID:16240626]
37. Lay-Flurrie K. The properties of hydrogel dressings and their impact on wound healing. *Prof Nurse.* 2004 Jan;19(5):269-73. [PMID:14737800]
38. Jones V, Milton T. When and how to use hydrogels. *Nurs Times.* 2000 Jun 8;96(23 Suppl):3-4. [PMID:11963421]
39. Robinson BJ. The use of a hydrofibre dressing in wound management. *J Wound Care.* 2000 Jan;9(1):32-4. [PMID:10827666]

40. Donaghue VM, Chrzan JS, Rosenblum BI, Giurini JM, Habershaw GM, Veves A. Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers. *Adv Wound Care*. 1998 May-Jun;11(3):114-9. [PMID:9729942]
41. Zhang Y, Xing SZ. Treatment of diabetic foot ulcers using Mepilex Lite Dressings: a pilot study. *Exp Clin Endocrinol Diabetes*. 2014 Apr;122(4):227-30. [PMID:24623502]
42. Piaggese A, Baccetti F, Rizzo L, Romanelli M, Navalesi R, Benzi L. Sodium carboxyl-methyl-cellulose dressings in the management of deep ulcerations of diabetic foot. *Diabet Med*. 2001 Apr;18(4):320-4. [PMID:11437864]
43. Jensen JL, Seeley J, Gillin B. Diabetic foot ulcerations. A controlled, randomized comparison of two moist wound healing protocols: Carrasyn Hydrogel Wound dressing and wet-to-moist saline gauze. *Adv Wound Care*. 1998 Nov-Dec;11(7 Suppl):1-4. [PMID:10326334]
44. Smith BA. The dressing makes the difference. Trial of two modern dressings on venous ulcers. *Prof Nurse*. 1994 Feb;9(5):348, 50-2. [PMID:8140111]
45. Armstrong SH, Ruckley CV. Use of a fibrous dressing in exuding leg ulcers. *J Wound Care*. 1997 Jul;6(7):322-4. [PMID:9325826]
46. Harding KG, Price P, Robinson B, Thomas S, Hofman D. Cost and dressing evaluation of hydrofiber and alginate dressings in the management of community-based patients with chronic leg ulceration. *Wounds: A Compendium of Clinical Research & Practice*. 2001;13(6):229-36
47. Bowszyc J, Bowszyc-Dmochowska M, Kazmierowski M, Ben-Amer HM, Garbowska T, Harding E. Comparison of two dressings in the treatment of venous leg ulcers. *J Wound Care*. 1995 Mar;4(3):106-10. [PMID:7600346]
48. Charles H, Callicot C, Mathurin D, Ballard K, Hart J. Randomised, comparative study of three primary dressings for the treatment of venous ulcers. *Br J Community Nurs*. 2002 Jun;7(6 Suppl):48-54. [PMID:12066081]
49. Thomas S, Banks V, Bale S, Fear-Price M, Hagelstein S, Harding KG, Orpin J, Thomas N. A comparison of two dressings in the management of chronic wounds. *J Wound Care*. 1997 Sep;6(8):383-6. [PMID:9341430]
50. Vanscheidt W, Sibbald RG, Eager CA. Comparing a foam composite to a hydrocellular foam dressing in the management of venous leg ulcers: a controlled clinical study. *Ostomy Wound Manage*. 2004 Nov;50(11):42-55. [PMID:15545697]
51. Backhouse CM, Blair SD, Savage AP, Walton J, McCollum CN. Controlled trial of occlusive dressings in healing chronic venous ulcers. *Br J Surg*. 1987 Jul;74(7):626-7. [PMID:3304523]
52. Nelson EA, Prescott RJ, Harper DR, Gibson B, Brown D, Ruckley CV. A factorial, randomized trial of pentoxifylline or placebo, four-layer or single-layer compression, and knitted viscose or hydrocolloid dressings for venous ulcers. *J Vasc Surg*. 2007 Jan;45(1):134-41. [PMID:17210398]
53. Singh A, Halder S, Menon GR, Chumber S, Misra MC, Sharma LK, Srivastava A. Meta-analysis of randomized controlled trials on hydrocolloid occlusive dressing versus conventional gauze dressing in the healing of chronic wounds. *Asian J Surg*. 2004 Oct;27(4):326-32. [PMID:15564189]