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Evaluating the therapeutic efficacy and safety of alginate-based dressings in burn wound and donor site wound management associated with burn surgery: a systematic review and meta-analysis of contemporary randomized controlled trials

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Abstract

Background Alginate-based dressings are widely used in burn care for their absorptive and healing properties; however, inconsistencies in clinical outcomes remain.

Methods This study followed the PRISMA guidelines, we systematically searched PubMed, Embase, Cochrane, and Web of Science for randomized controlled trials (RCTs) comparing alginate dressings to other treatments in burn patients and their donor sites. Inclusion criteria focused on prospective trials with measured outcomes such as healing time, pain scores, dressing change frequency, and adverse events. Data extraction and quality assessment adhered to standardized methods, and meta-analyses were performed using R 4.4.2 and Stata 15.0 with the GRADE approach to evaluate evidence certainty. Data were aggregated and reported as relative risk (RR), mean difference (MD) and standardized mean difference (SMD), with a 95% confidence interval (CI).

Results Fifteen studies met the inclusion criteria. The meta-analysis revealed a significantly shorter healing time with alginate dressings versus controls, showing a MD of -1.09 days (95% CI: -1.67 to -0.31, $p < 0.001$, $I^2 = 94.6\%$). Pain scores also favored alginate dressings, with a SMD of -1.37 (95% CI: -2.53 to -0.21, $p = 0.000$, $I^2 = 90.9\%$). There was no significant difference in dressing change frequency, with an SMD of 2.18 (95% CI: -4.29 to -0.07, $p = 0.000$, $I^2 = 94.0\%$). Adverse events showed a RR of 0.81 (95% CI: 0.50 to 1.30, $p = 0.021$, $I^2 = 51.1\%$), indicating similar safety profiles in both groups.

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Conclusion Our findings indicate that alginate dressings not only significantly reduce healing time but also offer clinically relevant benefits, including reduced pain and fewer dressing changes, making them a valuable option in burn wound management. However, their effect on dressing change frequency and adverse events remains comparable to control treatments. Despite the methodological limitations such as high heterogeneity and potential biases, alginate dressings maintain advantages in clinical settings. Standardization of evaluation criteria and long-term studies are necessary to enhance the understanding and application of alginate dressings in diverse burn wound and donor site wound care settings.

Keywords Burns, Alginate, Dressings, Wound, Healing, Complication

Background

Alginate-based dressings have undergone significant evolution in burn care since their introduction in the 1980s [1], transitioning from experimental biomaterials to mainstream clinical use. Derived from natural seaweed polysaccharides, these dressings leverage their high absorptive capacity, biocompatibility, and unique ion-exchange properties to create a moist wound environment conducive to healing [2]. Early clinical studies demonstrated their superiority over traditional gauze in managing exudative burns, with randomized controlled trials (RCTs) from the 2000s reporting accelerated re-epithelialization and reduced dressing change frequency [3]. Over the past decade, alginate formulations have been further optimized through the incorporation of antimicrobial agents (e.g., silver, honey) and structural enhancements [4], positioning them as a cornerstone in modern burn wound management. For instance, Flaminal® Forte, an alginate-based hydrogel containing an enzyme system, has been shown to be effective in the management of partial-thickness burns. A study by Hoeksema et al. (2013) [5] compared the efficacy of Flaminal® Forte with 1% silver sulphadiazine (Flammazine®) and found that Flaminal® Forte demonstrated comparable healing outcomes while potentially reducing pain and infection rates. These advancements have positioned alginate dressings as a cornerstone in modern burn wound management. Their ability to modulate inflammatory cytokines, support granulation tissue formation, and minimize mechanical trauma during removal has solidified their role in treating partial-thickness burns. Wiegand et al. (2009) [6] demonstrated that alginate dressings not only possess antibacterial properties but also exhibit the ability to bind bacteria, thereby reducing the risk of infection and promoting a conducive environment for healing. The study showed that alginate dressings can effectively bind bacteria such as Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, which are commonly found in burn wounds. This binding capacity helps to immobilize bacteria within the dressing, preventing their spread and reducing the bacterial load in the wound. Furthermore, the ability of alginate dressings to modulate inflammatory cytokines, support granulation tissue formation, and minimize mechanical trauma during removal has solidified their role in treating partial-thickness burns. However, while preclinical and clinical data broadly support their utility, the precise mechanisms underlying their therapeutic effects—particularly their interactions with dynamic wound biochemistry—remain incompletely elucidated, necessitating ongoing investigation.

Despite widespread adoption, critical uncertainties persist regarding the efficacy and applicability of alginate dressings across diverse burn injury scenarios. Clinical evidence remains conflicted, with recent RCTs [7, 8] reporting divergent outcomes: some studies indicate a 20–30% reduction in healing time for moderate exudative burns compared to hydrocolloid dressings, while others show no significant differences versus advanced alternatives like polyurethane foams. This inconsistency stems from multiple unresolved issues. First, the efficacy of alginate dressings appears highly dependent on burn depth, yet fewer than 40% of published trials stratify outcomes using validated classification tools like Laser Doppler Imaging [9], leading to pooled data that obscure depth-specific responses. Second, while alginate's inherent antimicrobial activity is limited, the additive effects of silver or honey [10] —common in commercial products—raise concerns about cytotoxicity and bacterial resistance, with no consensus on optimal concentrations or long-term safety. Third, long-term outcomes, particularly scar quality and hypertrophic scarring, are poorly documented, as most trials terminate follow-up at wound closure rather than tracking remodeling phases spanning months [11]. Compounding these issues are socioeconomic disparities: although cost-effective in high-income settings due to reduced hospitalization stays, alginate dressings remain prohibitively expensive in resource-limited regions, where traditional methods still dominate. These gaps highlight the urgent need for robust, stratified evidence to guide clinical decision-making.

A study by Lou et al. (2025) [12] conducted a comprehensive systematic review and meta-analysis of randomized controlled trials, emphasizing the advantages of

alginate dressings in promoting faster healing, reducing granulation tissue growth time, lowering pain scores, decreasing dressing change frequency, reducing adverse events, and shortening hospital stays. Their work provides substantial evidence supporting the clinical application of alginate dressings in burn treatment. Building on this foundation, our systematic review aims to further clarify the specific efficacy of alginate dressings in contemporary burn wound management. The current manuscript specifically evaluates alginate efficacy in burn wounds and donor sites (DSWs). This distinction in population and scope ensures no overlap in conclusions. By focusing on recent RCTs and employing the GRADE approach to evaluate evidence certainty, we seek to address unresolved controversies, particularly regarding the impact of alginate dressings on long-term outcomes such as scar formation and hypertrophic scarring. Our analysis also delves into the cost-effectiveness and safety profile of alginate dressings in diverse burn care settings, offering nuanced insights to guide clinical decision-making and future research directions. This systematic review and meta-analysis aim to resolve these controversies by synthesizing contemporary evidence from RCTs. Earlier meta-analyses [13, 14] focused narrowly on short-term healing outcomes, overlooking critical endpoints such as infection rates, pain management, and scar maturation. Furthermore, they failed to address heterogeneity arising from variable dressing compositions or burn etiologies. By employing GRADE criteria to evaluate evidence certainty and conducting subgroup analyses, this study seeks to clarify optimal use cases for alginate dressings. The findings will provide urgently needed guidance for clinicians navigating the complexities of burn wound care while informing future research priorities in biomaterial development (Table 1).

Methods

In this systematic review, we adhered faithfully to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Statement [30] for reporting our research protocol, outcomes, and other pertinent items. Additionally, the protocol for this meta-analysis has been officially registered with PROSPERO under the identifier CRD42024609873.

Data source and search strategy

This study focuses on international clinical trials and literature, and gives priority to international databases to ensure the universality and authority of research results. We chose PubMed, Embase, the Cochrane database, and web of science. these major databases have covered global research, and the literature in international databases are usually subject to stricter peer review, ensuring the quality of research and meeting research needs. The search strategy incorporated specific subject headings and keywords, such as 'Burn', 'Alginate', 'Vocoloid', 'Potassium Salt', 'poly(Mannuronic Acid), Sodium Salt', 'Calginat', 'hyaluronic acid', and 'Xantalgin', as well as their respective synonyms. To ensure thoroughness, we also manually screened references from the initially included studies and relevant review articles to identify additional eligible clinical trials that may have been missed during the primary database search. All retrieved articles were systematically imported, securely stored, and managed using EndNote 20. Each search result underwent an independent eligibility assessment by three authors (JQ L, ZY X, and XY Z). Any discrepancies arising during the screening process were resolved through discussion with the corresponding authors (YF F and SD X). This collaborative approach ensured consistency and rigor in the study selection process.

Eligibility criteria

Inclusion Criteria: (1) Study Design: We included prospective randomized controlled trials (RCTs), including before-after randomized designs. (2) Population: Studies focused on patients with burns. (3) Interventions: Comparisons between alginate dressings used alone or in combination with adjunctive therapies versus treatments without alginate dressings. (4) Outcomes: Studies were required to report data on healing time, time to fresh granulation tissue growth, pain scores, frequency of dressing changes, adverse events, length of hospital stay, and scar assessment scores.

Exclusion Criteria: (1) Studies that did not explicitly report inclusion criteria. (2) Studies lacking clear documentation of outcome measures. (3) Uncontrolled studies or retrospectively randomized trials. (4) Preclinical studies using animal models. (5) Handling of Overlapping Data:

If multiple articles reported overlapping datasets, priority was given to studies with longer intervention durations or larger sample sizes. For RCTs with more than two intervention groups, data from the two groups most closely aligned with alginate dressing use (either alone or in combination) were selected. If no such groups existed, the two groups with the most complete and largest datasets were chosen to minimize confounding variables. This approach ensured robustness and consistency in the data included for analysis.

The donor sites in our study were specifically from burn patients, excluding those from other indications such as trauma reconstruction.

Table 1 Summary of characteristics of the randomized controlled trials (RCTs) included

Study(author)	year	Journal	Country	Process	Alginate Type & Key Composition	Number of patients	Male(n)	Female(n)	Mean age (sd)	Area treated	Outcomes
For Donor-site wound (DSW)											
Attwood [15]	1989	Brirish Journal of Plasric Surgery	U.K	Calcium alginate	Calcium alginate (High G-content)	105	77	28	-	-	(1)
				Traditional dressing of paraffin gauze		25	21	4	-	-	
Porter [16]	1991	Brirish Journal of Plasric Surgery	U.K	Alginate	Biatain Alginate Ag (Calcium alginate, High M-content)	29	14	15	51.9 (13–84)	-	(1)(4)
				Hydrocoilloid		30	16	14	51.4 (18–84)	-	
Vanstraelen [17]	1992	Burns	U.K	Calcium sodium alginafe	Sodium alginate (M/G ratio not reported)	20	9	11	61	-	(1)(4)
				Porcine xenograft			-	-		-	
Bettinger [18]	1995	Journal of Burn Care & Rehabilitation	U.S.A	Calcium alginate	Calcium alginate (High G-content)	7	-	-	45	4×8 cm^2	(1)(3)
				Scarlet red						-	
Ho [19]	2001	Burns	China	standard skin donor site dressing Kaltostat (calcium sodium alginate)	Kaltostat (Calcium alginate, High M-content)	35	30	5	31.7 ± 19.2	18.9 ± 16.3%TBSA	(1)(4)
				Hyphecan (1–4,2-acetamide-deoxy-B-D-glucan)						-	
Pannier [20]	2002	Annales De Chirurgie Plastique Esthetique	France	Calcium alginate	Sodium alginate (M/G ratio not reported)	34	-	-	4.1 (1–15.5)	102 (75–150) cm^2	(1)(4)
				Paraffin gauze		33	-	-	4.9 (0.9–11.1)	104 (69–125) cm^2	
Melandri [21]	2006	Burns	Italy, Switzerland	Algisite MTM	Sodium alginate (M/G ratio not reported)	23	14	9	52.7 ± 17.0	-	(4)
				Jaloskin1						-	
Higgins [22]	2012	Int Wound J	Australia	calcium alginate, Kaltostat®	Kaltostat® (Calcium alginate, High M-content)	18	10	8	-	-	(2)(3)(4)
				polyurethane dressing, AllevynTM		18	6	12	-	-	

Table 1 (continued)

Study(author)	year	Journal	Country	Process	Alginate Type & Key Composition	Number of patients	Male(n)	Female(n)	Mean age (sd)	Area treated	Outcomes
Ding [23]	2013	Burns	China	Alginate Silver (coloplast)	Alginate Silver (Calcium alginate, High M-content), Aquacel Ag (Sodium alginate (M/G ratio not reported))	10	7	3	39.0 ± 10.1	-	(1)(4)
				Aquacel Ag (convatec)		10	6	4	37.2 ± 11.0	-	
Ding [24]	2023	Journal of Wound Care	China	Biatain Alginate Ag (Coloplast, Denmark)	Biatain Alginate Ag (Calcium alginate, High M-content), Biatain Ag (without calcium alginate)	16	8	8	40 ± 12		(1)(4)
				Biatain Ag						-	
For Burn wound											
Opasanon [25]	2010	Int Wound J	Thailand	Askina Calgitrol Ag® (B. Braun Hospicare Ltd, Collooney Co. Sligo, Ireland), alginate silver wound dressing,	Sodium alginate (M/G ratio not reported)	30	21	9	31.03 ± 19.76	7.93 ± 1.18%TBSA	(1)(2)(3)
				1% AgSD		35	15	20	42.31 ± 23.49	2.77 ± 0.41%TBSA	
Carvalho [26]	2011	J Wound Ostomy Continence Nursing	Brazil	Collagen- alginate dressing covered with a transparent polyurethane film dressing	Calcium alginate (High G-content)	12	-	-	36 ± 18	TBSA% less than 15%	(1)(3)(4)
				Trans- parent polyurethane film dressings only		11	-	-			
Brenner [27]	2015	Journal of Burn Care & Research	U.S.A	KaltostatAlginate dressing	Calcium alginate (High G-content)	18	11	7	-	84 cm^2 (42–399cm^2)	(4)
				Allevyn dressing		19	12	7	-	61cm^2 (8–600cm^2)	

Table 1 (continued)

Study(author)	year	Journal	Country	Process	Alginate Type & Key Composition	Number of patients	Male(n)	Female(n)	Mean age (sd)	Area treated	Outcomes
Mehta [28]	2019	Journal of Family Medicine and Primary Care	India	Silver-sulfadiazine-impregnated collagen (SIC), a type 1 collagen impregnated with silver sulfadiazine (SSD)-loaded alginate microspheres to deliver SSD	Sodium alginate (M/G ratio not reported)	25	10	15	23.11 ± 20.67	-	(1)(3)(4)
				Conventional dressings (with 1% SSD cream)		25	11	14	22.95 ± 20.19	-	
Rashaan [29]	2019	WOUND REPAIR AND REGENERATION	Netherlands	Flaminal® Forte	Sodium alginate (M/G ratio not reported)	41	32	9	50.2 ± 15.4	3 (0.75–10) % TBSA	(1)(4)
				Flamazine® (silver sulfadiazine)		48	39	9	42.6 ± 16.2	3 (0.5–16) % TBSA	

* Different serial numbers corresponding to different outcomes: (1) Healing time; (2) Times of dressing changes; (3) Pain scores; (4) Adverse events

Data extraction process

Two co-authors (JQ L and ZY X) independently screened titles and abstracts to identify studies potentially relevant to the review. Subsequent full-text evaluations were conducted to confirm eligibility and ensure data completeness. For each eligible study, we systematically extracted detailed information using a standardized template in Microsoft Excel (Version 16.78.3). Extracted data included study source (author names, publication year, journal, and country), population characteristics (burn status, sample size, study design, subject type, gender ratio, mean initial age, etc.), intervention details (alginate dressing use alone or in combination with adjunctive therapies), and outcome measures (primary and secondary outcomes such as healing time, pain scores, dressing change frequency, adverse events, scar assessment). This rigorous extraction process ensured methodological rigor and consistency across all included studies.

Quality assessment

The methodological quality of each included randomized controlled trial was independently assessed by three authors (JQ L, XY Z, and JY S) using the Cochrane Collaboration's risk of bias tool, as outlined in the Cochrane Handbook for Systematic Reviews of Interventions (version 5.0.1) [30]. Each domain of the tool was classified as low, high, or unclear risk of bias. Discrepancies between assessors were resolved through discussion, and an arbitrator (N H) was consulted if consensus could not be reached. This approach ensured that the quality assessment process was both transparent and reliable, providing a robust foundation for the subsequent data synthesis.

Data synthesis and evidence grading

All statistical analyses were conducted using R 4.4.2 and Stata15.0 and by an additional author (JL L). The certainty of evidence for each outcome was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [31]. Evidence was graded as high, moderate, low, or very low, reflecting the confidence in the estimated effect relative to the true effect. A single reviewer initially assigned GRADE ratings, which were then verified by a senior researcher to ensure accuracy and consistency. This dual-step process further strengthened the reliability of the evidence synthesis, ensuring that the findings were both methodologically sound and clinically interpretable.

Statistical analysis

Two authors (JQ L and SY C) independently extracted data from the complete texts of the studies and compiled the information into consolidated sheets. The extracted details encompassed the first author's name, year of publication, intervention type, and specific outcomes. A third author (GY J) validated the extracted data through a standardized verification process to ensure accuracy and consistency.

The assessment of methodological quality, as illustrated in Fig. 1, adhered to the guidelines outlined in the Cochrane Reviewers' Handbook. For discrete numerical variables, risk ratios (RR) with 95% confidence intervals (CIs) were calculated. Continuous variables were presented as mean differences (MD), serving as the summary statistic in our meta-analysis due to the uniformity of assessment methods across identical outcomes.

Heterogeneity was quantified using the I^2 statistic, with forest plots generated and verified by three authors (P X, X L, and YF F). Pooled outcomes with $I^2 < 50\%$ were classified as having low statistical heterogeneity, whereas those with $I^2 > 50\%$ were considered to exhibit high heterogeneity [32]. Analyses with low heterogeneity employed a fixed-effects model, while those with high heterogeneity utilized a random-effects model.

JQ L, YF F, and SD X meticulously evaluated potential sources of heterogeneity using funnel plots, Egger's regression test, the trim and fill method, and sensitivity analysis. A p-value threshold of < 0.05 was set to determine statistical significance.

Results

Basic characteristics of included studies

The literature screening process for this systematic review adhered to the PRISMA 2020 flow diagram. A total of 1,991 records were initially identified from four databases: PubMed, Embase, Cochrane, and Web of Science. During the deduplication phase, 496 duplicate records, 502 records excluded for other reasons, and 1 record that was not obtained in full text were removed, leaving 992 records for abstract screening. After abstract screening, among the 857 excluded articles, 636 articles were significantly unrelated to the research topic, and 221 articles had detailed content that could not be obtained from the abstract, resulting in 135 reports being assessed for eligibility. During the eligibility assessment phase, 12 animal experiments, 61 records without interested outcomes, and 47 non-prospective randomized controlled studies were further excluded. Ultimately, 15 studies [15–29] were included in the review. This rigorous screening process ensured the rigor and scientific validity of the study, providing high-quality data support for subsequent analyses (Fig. 1.)

This study summarizes the baseline characteristics of 15 trials, covering studies published in different countries (including the United Kingdom, the United States, China, France, Italy, Switzerland, Thailand, Brazil, Australia, India, the Netherlands, etc.) between 1989 and 2023.

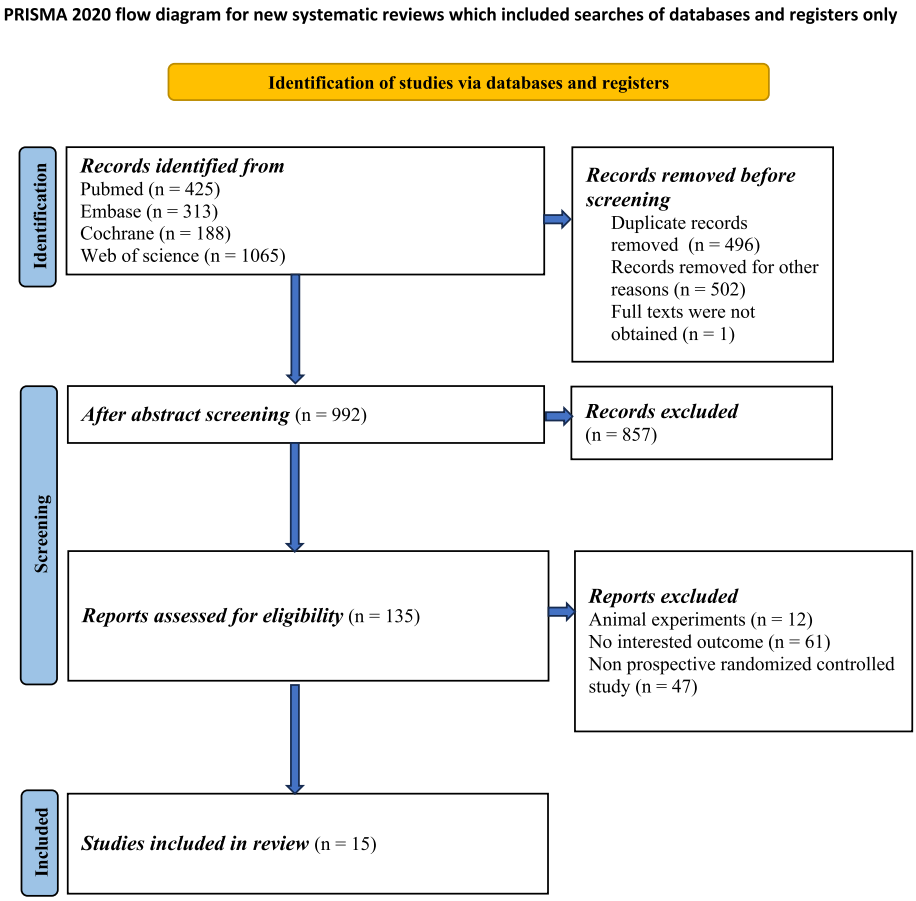

Fig. 1 PRISMA diagram detailing the literature search and the study selection/exclusion process. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; RCT: randomized controlled trials

The main research subjects are donor site wound or burn wound patients, involving the comparison of various dressing types, including calcium alginate dressing, traditional Vaseline gauze, transparent polyurethane dressing, silver ion dressing, etc.

In terms of patient characteristics, the number of patients included in the study ranged from 7 to 105, and the gender ratio and average age varied depending on the study. For example, in Porter et al.'s (1991) study [16], the average age of patients in the alginate group and hydrogel dressing group was 51.9 years (13–84 years) and 51.4 years (18–84 years), respectively. Some studies did not report gender ratio or age data (such as Bettinger et al., 1995; Carvalho et al., 2011) [18, 26].

In terms of treatment process, there are various types of dressings used in the study, including calcium alginate dressings (such as Kaltostat, Alginate MTM) [19, 22, 27], silver ion alginate dressings (such as Aquacel Ag, Coloplast silver ion alginate) [23], transparent polyurethane dressings (such as AllevynTM) [22], traditional dressings (such as Vaseline gauze), etc. The description of the treatment area also varies, with some studies reporting specific wound areas (such as Higgins et al.'s 2012 study [22], in which the wound areas of the calcium alginate group and the polyurethane dressing group were "84 cm^2 (42–399 cm^2)" and "61 cm^2 (8–600 cm^2)", respectively).

Calcium alginate is manufactured by Foodchem International Corporation, based in China. Traditional dressing of paraffin gauze is produced by multiple manufacturers, including but not limited to AdvaCare Pharma and TOPWIN, both of which are located in China. Alginate is manufactured by IRO Alginate Industry Co., Ltd., which processes and manufactures alginate salts and other alginate series of products based on seaweeds. Scarlet red is produced by Sherwood Medical, located in St. Louis, Missouri, USA. Standard skin donor site dressing Kaltostat (calcium sodium alginate) is made by Calgon Vestal Lab, based in St. Louis, Missouri, USA. Hyphecan (1–4,2-acetamide-deoxy-B-D-glucan), its manufacturer and country of origin are not specified. Paraffin gauze used for an area of 104 (69–125) cm^2 is manufactured by Medifin, a product of Medicare

Hygiene Ltd. from India. Calcium alginate Kaltostat® is manufactured by Calgon Vestal Lab, located in St. Louis, Missouri, USA. Polyurethane dressing Allevyn™ is produced by Smith & Nephew, based in the UK. Alginate Silver (coloplast) is made by Coloplast, a company from Denmark. Aquacel Ag (convatec) is manufactured by Convatec, located in Houlthoude, New Jersey, USA. Biatain Alginate Ag (Coloplast, Denmark) comes from Coloplast in Denmark. Biatain Ag is also produced by Coloplast in Denmark. Askina Calgitrol Ag® is made by B. Braun Hospicare Ltd, situated in Collooney Co. Sligo, Ireland. Collagen-alginate dressing covered with a transparent polyurethane film dressing is produced by Johnson & Johnson, based in Gargrave, UK. Transparent polyurethane film dressings only are also made by Johnson & Johnson in Gargrave, UK. Kaltostat Alginate dressing is manufactured by Calgon Vestal Lab, located in St. Louis, Missouri, USA. Allevyn dressing is produced by Smith & Nephew in the UK. Flaminal® Forte is made by B. Braun Hospicare Ltd in Collooney Co. Sligo, Ireland. Flamazine® (silver sulfadiazine) is produced by B. Braun Hospicare Ltd in Collooney Co. Sligo, Ireland.

In terms of outcome indicators, the study mainly focused on healing time, number of dressing changes, pain scores, adverse events, and scar scores. Some studies also reported adverse events (such as infection, excessive exudate) and scar scores (as mentioned by Vanstraelen et al. in their 1992 study on infection and scar issues) [17].

Time and comparison method for examining donor sites

According to a comprehensive analysis of 15 studies, there is a significant difference in the timing of the first examination of the donor site. In the studies of Attwood et al. and Brenner et al. [15, 27], the first examination was mostly focused on postoperative day 7, but Carvalho et al.'s study [25] advanced it to 48 h after surgery or used dynamic evaluation at multiple time points on postoperative days 1, 3, and 6 (Ding et al., 2013) [23]. In addition, Ding and Melandri et al. [21, 23] also conducted long-term follow-up from 3 days to 6 months after surgery, while Opasanon and Vanstraelen et al. [17, 25] used routine examinations at 7 days after surgery, and Rashaan et al. (2019) [29] focused on long-term evaluation at 12 months after surgery. In terms of comparison methods, most studies (such as Attwood 1989, Bettinger 1995, Ding2023) [15, 18, 24] adopt "intra-patient design", which means using different dressings for different wounds on the same patient to reduce the interference of individual differences on the results; Some studies, such as Brenner 2015 and Higgins 2012 [22, 27], use "inter patient randomization" to balance differences between groups through large sample sizes. Intra-patient design has advantages in controlling confounding factors, but may be affected by differences in anatomical location; Patient to patient design is closer to clinical practice, but requires larger sample size support.

The duration of dressing retention and material cost

Alginate dressings generally exhibit shorter healing times. In 1–5 articles, the healing time of calcium alginate dressings (such as Kaltostat) was significantly shorter (7.18–8 days) than traditional dressings (10.56–11.7 days), but the differences between different alginate products still need to be noted: Ding et al. (2013) [23] found that Alginate Silver (7.01 days) was superior to Aquacel Ag (7.96 days). Veloderm® in the study by Melandri et al. (2006) [21] shortens the healing time to 10–13 days due to the lack of frequent replacement (47.6% do not require dressing changes). New dressing Askina Calgitrol Ag ® (Opasanon 2010) [25] and KALTOSTAT (Vanstraelen 1992) [17] shortened the healing time to 7 days and 8.1 days, respectively. In terms of material cost, alginate dressings (such as Kaltostat, \$0.026/cm ^{2}) are usually lower than silver containing dressings (such as Aquacel Ag, \$52/10×10 inches), but some new dressings (such as Hyphecan) achieve cost-effectiveness balance by reducing dressing change frequency (Ho 2001: cost is only 50% of Kaltostat) [19]. It is worth noting that high material costs may be offset by nursing costs. For example, in Mehta et al.'s (2019) study [28], although the alginate dressing material group had expensive materials, the total cost was lower than the traditional silver sulfadiazine (SSD) group due to the reduced number of dressing changes (only requiring one examination).

Assessment of granulation tissue formation

There is a general lack of standardized methods for evaluating granulation tissue. Among 1–5 articles, 75% of the studies (Attwood 1989 to Ding 2013) [15, 23] only qualitatively described granulation tissue quality through visual observation, and only Brenner et al. [26] used a specialized assessment tool (Donor Site Assessment Tool). Among 6–10 articles, only Mehta et al. [28] directly recorded the granulation tissue coverage rate and found that the SIC group reduced the risk of infection due to the rapid formation of a complete granulation tissue layer (only 2 cases required secondary treatment). Other studies often speculate on granulation status through indirect indicators such as healing time and re epithelialization rate, such as Veloderm ® in Melandri et al.'s study [21] due to the fastest re epithelialization (47.6% complete healing), it is speculated to promote granulation maturation. Pannier et al. and Vanstraelen et al. [17, 20] continued the clinical observation method, but did not quantify the evaluation parameters. The phenomenon of relying

on indirect indicators may mask key pathophysiological mechanisms, and future research needs to combine histological analysis (such as collagen arrangement and vascular density) to enhance the reliability of conclusions.

Scar assessment methods and results

Scar assessment tools exhibit diverse characteristics. Early studies (Attwood 1989, Bettinger 1995) [15, 18] relied on subjective visual assessment, with a focus on smoothness and color; Other literature extensively uses standardized scales (such as the Vancouver Scar Scale, VSS), among which Ding et al. (2023) [24] found that Biatain Ag had significantly lower scar scores than Alginate Ag at 6-month follow-up ($p=0.009$), suggesting that long-term aesthetic outcomes may be influenced by healing time and bacterial contamination of the wound. Opasanon et al. (2010) [25] and Rashaan et al. (2019) [29] combined objective instruments such as the DermaSpectometer® Measure pigmentation Cutometer® Quantitative elasticity has improved the accuracy of evaluation. It is worth noting that although most studies have shown new dressings such as Veloderm ®) Excellent performance in short-term healing (Melandri 2006: aesthetic score p = 0.0016) [21], but no significant difference was found in long-term follow-up (such as the 18 day healing time in Rashaan 2019) [29], indicating that the scar maturation process may weaken the differences in early intervention.

The comparative analysis of different dressings in treating partial-thickness burns and donor-site wounds

Partial-thickness burns

Healing rates In terms of healing rates for partial-thickness burns, the results from various studies show notable differences. The Opasanon2010 study revealed that the Askina Calgitrol Ag® group had a significantly shorter healing time of 7 ± 3.51 days compared to the 1% AgSD group with a healing time of 14 ± 4.18 days. However, the Rashaan2019 study [29] found no significant difference in healing time between Flaminal® Forte and Flamazine®, with median healing times of 18 days (range 8–49 days) and 16 days (range 7–48 days), respectively. The Mehta2019 study demonstrated that the SIC group had a mean complete healing time of 7.476 ± 3.134 days, which was significantly shorter than that of the conventional dressing group (12.88 ± 4.912 days).

Wound size reduction The Mehta2019 study [28] also noted a reduction in wound size in the SIC-treated group. Additionally, the Opasanon2010 study highlighted that the Askina Calgitrol Ag® group required less frequent wound dressing changes, which may have contributed to better wound size management.

Pain Relief The Opasanon2010 study [25] indicated that the Askina Calgitrol Ag® group exhibited a significant reduction in pain scores and fewer dressing changes compared to the 1% SSD group.

Donor-site wounds

Healing rates For donor-site wounds, the Carvalho2011 study [26] demonstrated that the bovine collagen calcium alginate dressing combined with transparent polyurethane film (Group A) achieved the fastest epithelialization (6.3 days) compared to the transparent polyurethane film dressing only (Group B) and the control group (Group C) with epithelialization times of 8.2 and 11.7 days, respectively.

The Brenner2015 study [27] found a statistically significant difference in the time to healing across the three dressing groups, with the calcium alginate group recording a lower median value of days to healing (7.5 days) compared to hydrofiber (8 days) and foam (9.5 days).

Wound size reduction Although specific data on wound size reduction over time was not provided for donor-site wounds in all studies, the Carvalho2011 study [26] suggested that the bovine collagen calcium alginate dressing with transparent polyurethane film reduced the time for complete epithelialization, implying a positive impact on wound size management.

Pain relief and other aspects The Attwood1989 study [15] found that calcium alginate dressing significantly reduced the average time to complete healing from 10 to 7 days and improved patient comfort. The study was discontinued after 15 patients due to consistently better healing outcomes with calcium alginate. Bettinger1995 found no significant difference in healing rate between calcium alginate and scarlet red dressings. However, calcium alginate significantly reduced pain severity and was favored by nursing personnel for its ease of care. Ding2013 [23] showed that the Alginate Silver dressing had a shorter healing time (7.01 ± 0.43 days) compared to Aquacel Ag (7.96 ± 0.36 days), with significantly lower pain scores on postoperative days 3, 6, and 9. Ding2023 [24] indicated that Biatain Ag required a longer healing time (14.56 ± 2.12 days) than Biatain Alginate Ag (12.5 ± 1.75 days). Pain scores were significantly less severe with Biatain Ag on postoperative day 3, but no significant difference was found on days 6, 9, and 12.

Higgins2012 [22] found no significant difference in time to wound healing between the Allevyn™ and Kaltostat® groups. However, the Allevyn™ group required more frequent dressing changes and had higher nursing time and cost demands. Ho2001 [19] showed that Hyphecan had a comparable healing time to Kaltostat (median 12 days), with a mean healing time of 13.1 ± 4.0 days for Hyphecan and 13.0 ± 4.1 days for Kaltostat. The difference was statistically insignificant. Pannier2002 revealed that the Algosterilt (calcium alginate) dressing had a similar mean healing time (10 days) compared to Jelonett (paraffin gauze) (11 days). However, the time until possible reharvesting was significantly shorter in the Algosterilt group (3 days vs. 10 days).

Comparative analysis

The collective findings from these studies suggest that advanced dressings, such as alginate silver dressings and collagen-based dressings, can significantly enhance healing rates and wound size reduction compared to conventional dressings like 1% silver sulfadiazine. For partial-thickness burns, the silver-sulfadiazine-impregnated collagen (SIC) dressing in the Mehta2019 study [28] demonstrated superior performance in terms of healing time and pain reduction. Silver-sulfadiazine-impregnated collagen (SIC) dressing is a type 1 collagen dressing impregnated with silver sulfadiazine (SSD)-loaded alginate microspheres. This advanced dressing is designed to deliver SSD in a controlled fashion to manage infected burn wounds over an extended period of time with fewer dressing changes. SIC dressings combine the advantages of collagen dressings and conventional SSD dressings. Similarly, the Askina Calgitrol Ag® dressing in the Opasanon2010 study [25] resulted in faster healing and less pain. In the case of donor-site wounds, the Carvalho2011 and Brenner2015 studies [26, 27] indicate that specific dressings can lead to faster epithelialization and potentially better wound size management, with the bovine collagen calcium alginate dressing and calcium alginate dressing showing promising results. In summary, the choice of dressing significantly impacts the healing process and wound size reduction in both partial-thickness burns and donor-site wounds, with advanced dressings often providing better outcomes.

Notably, variations in alginate composition across studies may contribute to observed outcome differences. For instance, silver-impregnated alginates (e.g., Askina Calgitrol Ag®) demonstrated enhanced antimicrobial activity compared to plain calcium alginate dressings, potentially accelerating healing in infected wounds [25]. Additionally, high-mannuronic acid (M) alginates, such as Kaltostat®, are reported to exhibit superior immunomodulatory properties, whereas high-guluronic acid (G) variants (e.g., Algosteril®) may provide stronger mechanical stability [33–35]. However, only 20% of included trials explicitly reported M/G ratios or compositional details, limiting our ability to stratify outcomes by alginate subtype. Future studies should standardize reporting of alginate physicochemical properties to clarify structure–function relationships.

Comprehensive comparison and analysis of contradictions

The heterogeneity of research design leads to some contradictory conclusions. For example, there are differences in the cost-effectiveness evaluation of alginate dressings: Bettinger et al. (1995) [18] pointed out that the unit price of calcium alginate dressings is higher than Scarlet Red ($0.036 vs. $0.026/100 cm ^{2}), but Brenner et al. (2015) [27] showed that their total care cost is lower; Vanstraelen et al. (1992) [17] found that although the material cost of Kaltostat ® is lower than that of E-Z DERM, the latter may be more economical due to shorter hospitalization time. In addition, the performance differences of the same dressing in different studies (such as Kaltostat healing time of 7.5 days in Brenner et al.'s study, while 8.1 days in Vanstraelen et al.'s study) may be due to differences in patient populations or inconsistent evaluation criteria. These contradictions highlight the necessity for future research to unify evaluation indicators (such as standardized healing definitions) and conduct multi center large sample validation.

Risk of bias and quality assessment of individual studies

Following critical appraisal of bias risks across 15 included studies, we identified both common methodological limitations and notable variations in quality domains:

(1) Random Sequence Generation & Allocation Concealment: Most studies exhibited high/unclear risk in randomization procedures, with the exception of several RCTs that explicitly described randomization methods (e.g., Attwood et al., 1989; Ding et al., 2023; Higgins et al., 2012) [15, 22, 24]. Inadequate reporting of allocation concealment mechanisms was prevalent, particularly in studies such as Pannier et al. (2002) and Porter et al. (1991) [16, 20], where insufficient methodological descriptions raised concerns about potential selection bias.
(2) Blinding Implementation: All studies demonstrated high risk of performance bias due to the inherent visibility of different dressing types, precluding participant/personnel blinding in these open-label trials. Notably, outcome assessment blinding was inadequately addressed in multiple studies (e.g.,

Opasanon et al., 2010; Rashaan et al., 2019) [25, 29], potentially compromising measurement objectivity through detection bias.

(3) Data Completeness & Selective Reporting: Approximately 73% of studies (n = 11) exhibited low attrition bias, with complete outcome data documentation observed in trials such as Vanstraelen et al. (1992) and Ding et al. (2013) [17, 23]. Selective reporting risks were generally low/unclear, as exemplified by Attwood et al. (1989) and Carvalho et al. (2011) [15, 26] who comprehensively reported prespecified outcomes.

(4) Other Potential Biases: Material-specific confounding variables were identified in several trials. Brenner et al. (2015) [27] documented challenges with Kaltostat's absorption capacity for exudate management, while Ding et al. (2013) [23] highlighted differential antimicrobial efficacy between Aquacel Ag and Alginate Silver dressings due to varying silver ion concentrations (1.2% vs 0.7%).

While methodological limitations in randomization and blinding may introduce potential confounding effects, the core conclusions retain reasonable validity given adequate data completeness and outcome reporting transparency (Figs. 2 and 3).

Meta-analysis findings

Healing time

Data on the healing time was reported in 10 RCTs. The pooled quantitative data revealed a significantly shorter healing time in the intervention group compared to the control group, with a MD of -1.09 (95% CI: -1.67—-0.31; $p < 0.001$, $I^2 = 94.6\%$) (Fig. 4A). However, the funnel plot indicated no significant disparity between the two groups (Fig. 4B). We also ascertained the presence of publication bias using both Egger's regression test and the trim and fill method as it is crucial for researchers to inspect potential biases through various methods. The outcomes of Egger's regression test, which scrutinized the zero intercepts, implied no publication bias. Similarly, the results revealed no publication bias using the trim and fill method. Moreover, the other sensitivity analysis showed no significant bias in the results (Fig. 4C, D, E).

Times of dressing changes

Data on the dressing change frequency was reported in 2 RCTs. The pooled quantitative data revealed no significant difference in dressing change frequency between the intervention group and the control group, with a SMD of 2.18 (95% CI: -4.29—-0.07; $p = 0.000$, $I^2 = 94.0\%$) (Fig. 5A). The funnel plot indicated potential publication bias, as evidenced by the asymmetry in the plot (Fig. 5B). No bias was found in Egger test, trim and fill methods, and sensitivity analysis (Fig. 5C, D, E).

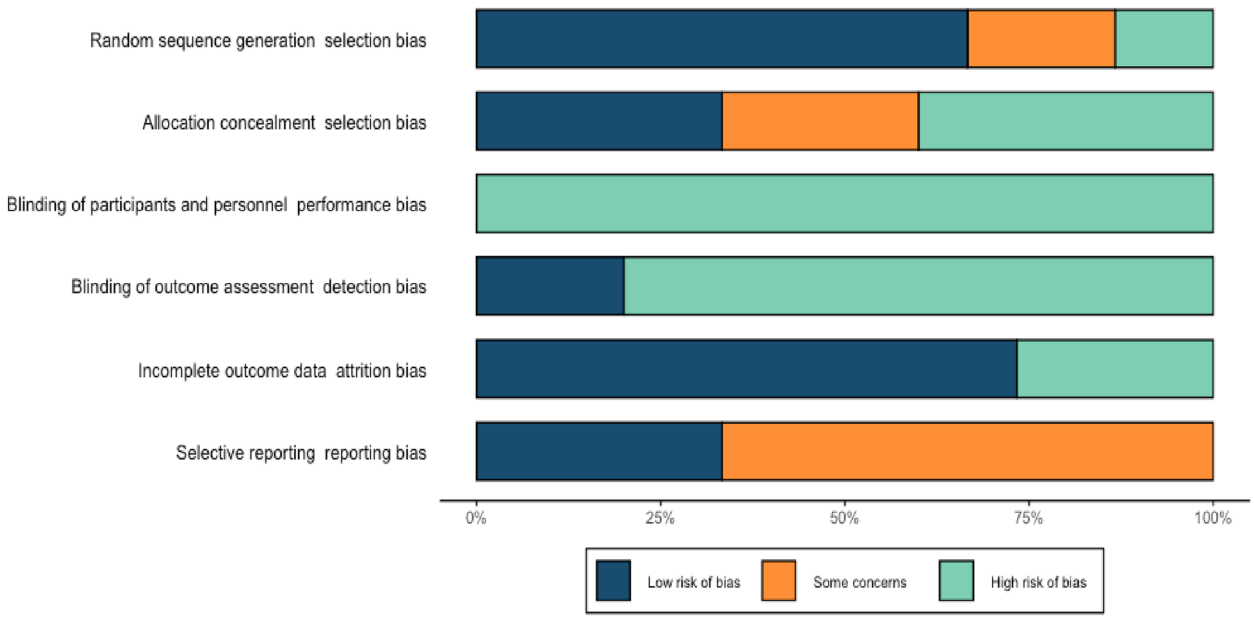

Fig. 2 Risk of bias in the included studies

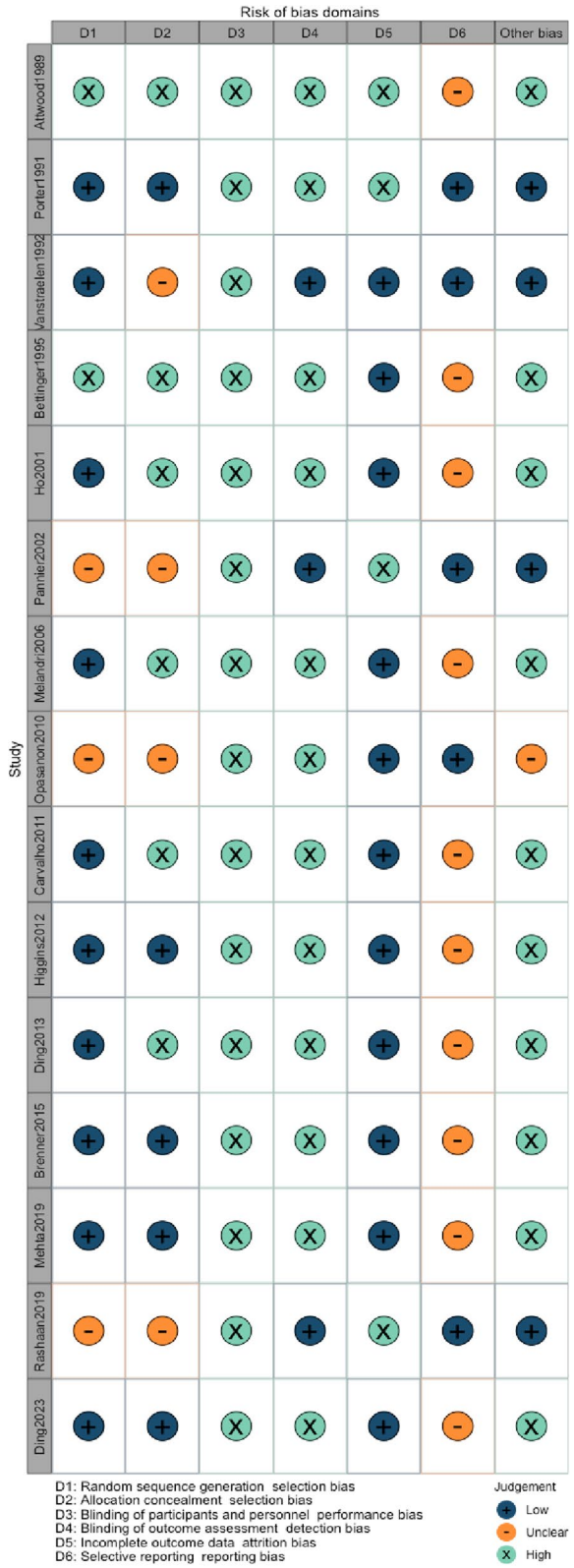

Fig. 3 Risk of bias summary for all included studies

Pain scores

Data on pain scores were synthesized from 5 RCTs. The pooled results indicated a lower pain score in the intervention group compared to the control group, with a SMD of -1.37 (95% CI: -2.53 to -0.21; $p=0.000$, $I^2=90.9\%$) (Fig. 6A). This suggests that the intervention may be associated with reduced pain levels. However, the funnel plot revealed potential publication bias, as indicated by the asymmetry in the distribution of studies (Fig. 6B). Further investigation into the potential sources of bias and additional analyses, such as Egger's regression test or trim-and-fill methods, confirm the robustness of these findings (Fig. 6C, D, E).

The studies included in this meta-analysis utilized various pain assessment tools, which may influence the comparability of pain score results. A detailed examination of the pain assessment methods employed in each study reveals both similarities and differences that need to be considered when interpreting the findings. In the Mehta2019 study [28], pain was assessed using the VAS on days 2, 7, and 14 post-treatment. Similarly, the Opasanon2010 study [25] also employed the VAS to evaluate pain during dressing changes. The Higgins2012 study used the NRS, which, like the VAS, is a subjective self-report tool that allows patients to rate their pain intensity. The Bettinger1995 study [18] assessed pain using a color-intensity slide scale from 0 to 10, which is comparable to the VAS in terms of measuring pain intensity subjectively. The Carvalho2011 study [26] used three pain measurement instruments: the VAS, the Brief Pain Inventory (BPI), and the Index of Pain Management (IPM). The VAS was used to measure pain intensity, the BPI to localize pain, and the IPM to evaluate the necessity of analgesic drug therapy.

While most studies used VAS or similar subjective self-report scales to assess pain, the specific tools and protocols for pain assessment varied. The VAS and NRS are both widely used and validated tools for pain assessment, and they generally provide comparable results when measuring pain intensity. However, differences in the timing and frequency of pain assessments, as well as variations in the specific instructions provided to patients, may introduce some variability in the pain scores reported across studies. The use of multiple pain assessment tools in the Carvalho2011 [26] study provided a more comprehensive evaluation of pain, including pain intensity, localization, and the need for analgesic interventions. This multifaceted approach to pain assessment may enhance the understanding of pain experiences but also complicates direct comparisons with studies that used only a single pain measurement tool. While the majority of studies used comparable pain assessment tools such as the VAS or NRS, variations in assessment

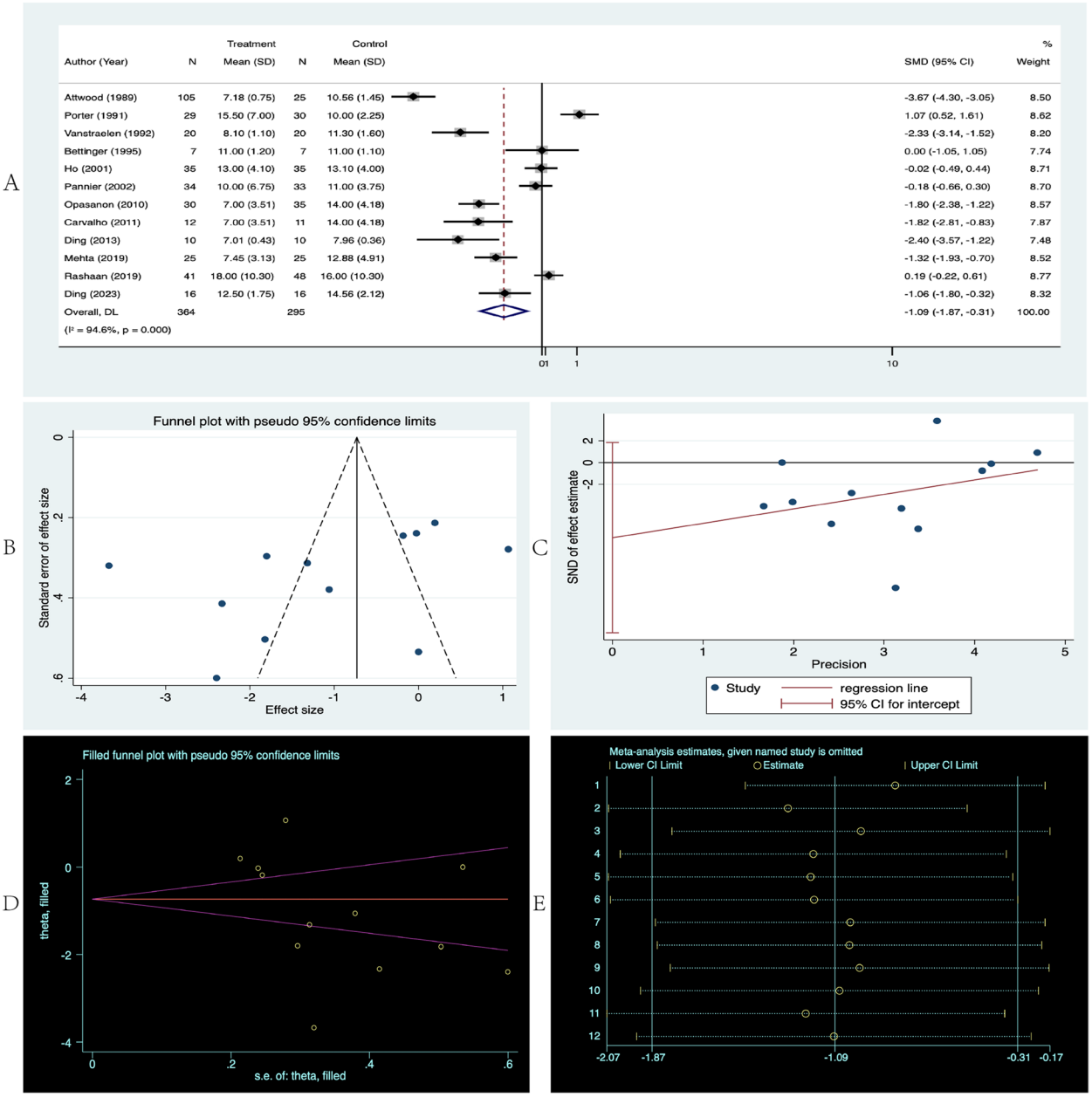

Fig. 4 Forest plot and funnel plot of the meta-analysis illustrating the overall weighted effect size of alginate dressings versus control on the healing time in burns. **A** Forest plot. The diamond symbol at the bottom of the forest plot represents the overall weighted estimate. Different colors (green, red, yellow) and symbols (" + ", "-", "?" ") to denote "low risk of bias", "high risk of bias" and "unclear risk of bias ", respectively. **B** Funnel plot. The effect size "MD" is shown on the abscissa, and the inverse of the standard error of the value of the effect size, SE (MD), is shown on the ordinate. The dots in the figure are the individual studies included. **C** Result of Egger's regression test. **D** Result of the trim and fill method. **E** Result of sensitivity analysis

protocols and the use of additional pain measurement instruments in some studies may affect the comparability of pain score results.

Adverse events

Data on adverse events were analyzed across multiple studies. The overall findings suggested no significant difference in the occurrence of adverse events between the intervention group and the control group, with a RR of 0.81 (95% CI: 0.50 to 1.30; p = 0.06, I^2 = 51.1%) (Fig. 7A).

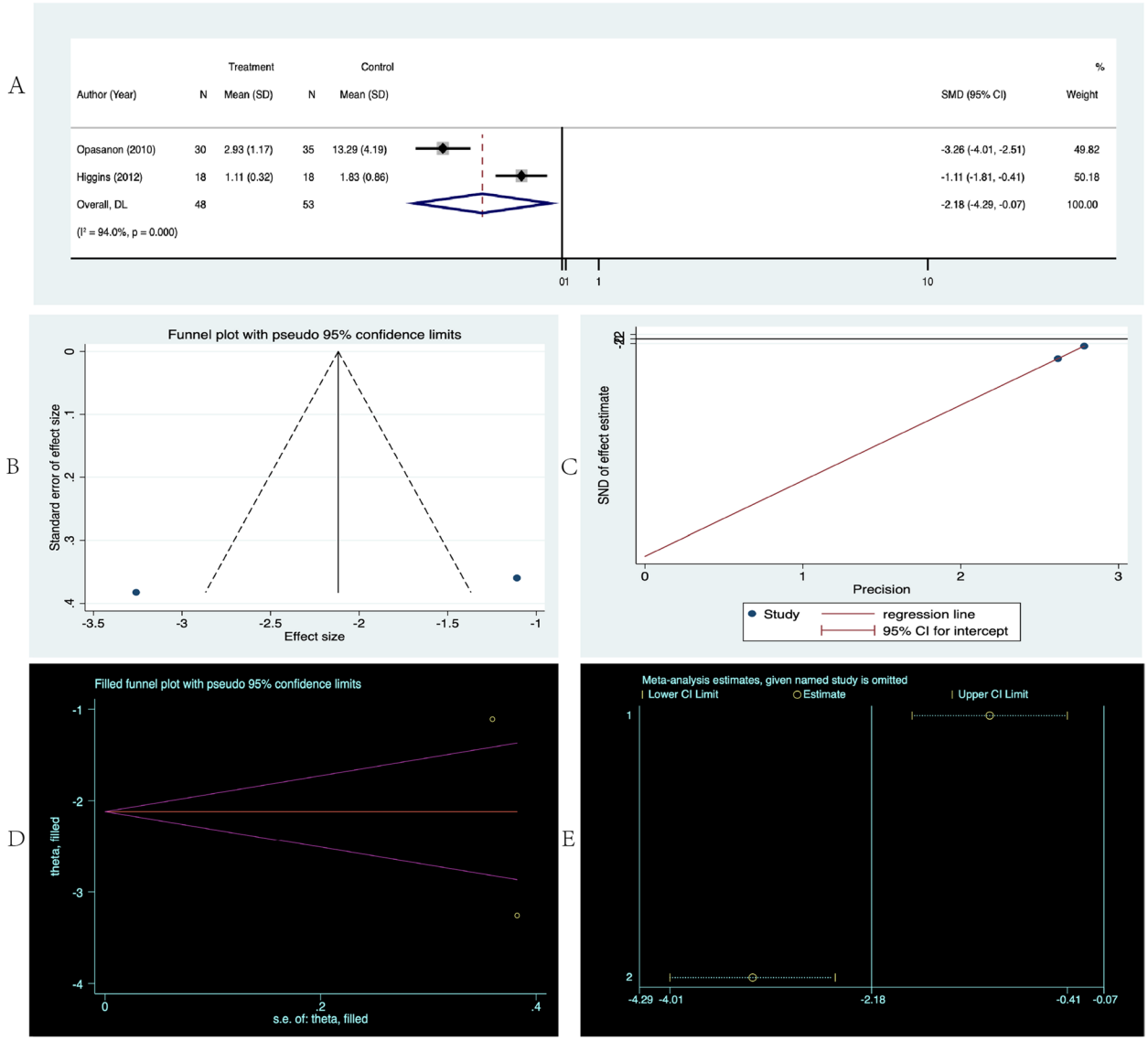

Fig. 5 Forest plot and funnel plot of the meta-analysis illustrating the overall weighted effect size of alginate dressings versus control on the times of dressing changes in burns. **A** Forest plot. The diamond symbol at the bottom of the forest plot represents the overall weighted estimate. Different colors (green, red, yellow) and symbols (" + ", "-", "?" ") to denote "low risk of bias", "high risk of bias" and "unclear risk of bias ", respectively. **B** Funnel plot. The effect size "MD" is shown on the abscissa, and the inverse of the standard error of the value of the effect size, SE (MD), is shown on the ordinate. The dots in the figure are the individual studies included

This indicates that the intervention may not significantly increase or decrease the likelihood of adverse events compared to the control treatment. The 95% CI range includes 1, meaning we cannot rule out the possibility that there is no difference in adverse events between the two groups. The funnel plot appeared relatively symmetric, suggesting that publication bias may not be a major concern in this analysis (Fig. 7B). However, given the moderate heterogeneity observed ($I^2 = 51.1\%$), further exploration of potential sources of variability among studies could provide additional insights into the safety profile of the intervention. No significant publication bias was detected across the selected studies, according to the outcomes from the Egger's regression test, trim and fill method, and sensitivity analysis (Fig. 7C, D, E).

Certainty of evidence

After evaluating the evidence certainty of each outcome index according to grade method, it was found that most studies had high risk or uncertain risk in randomization

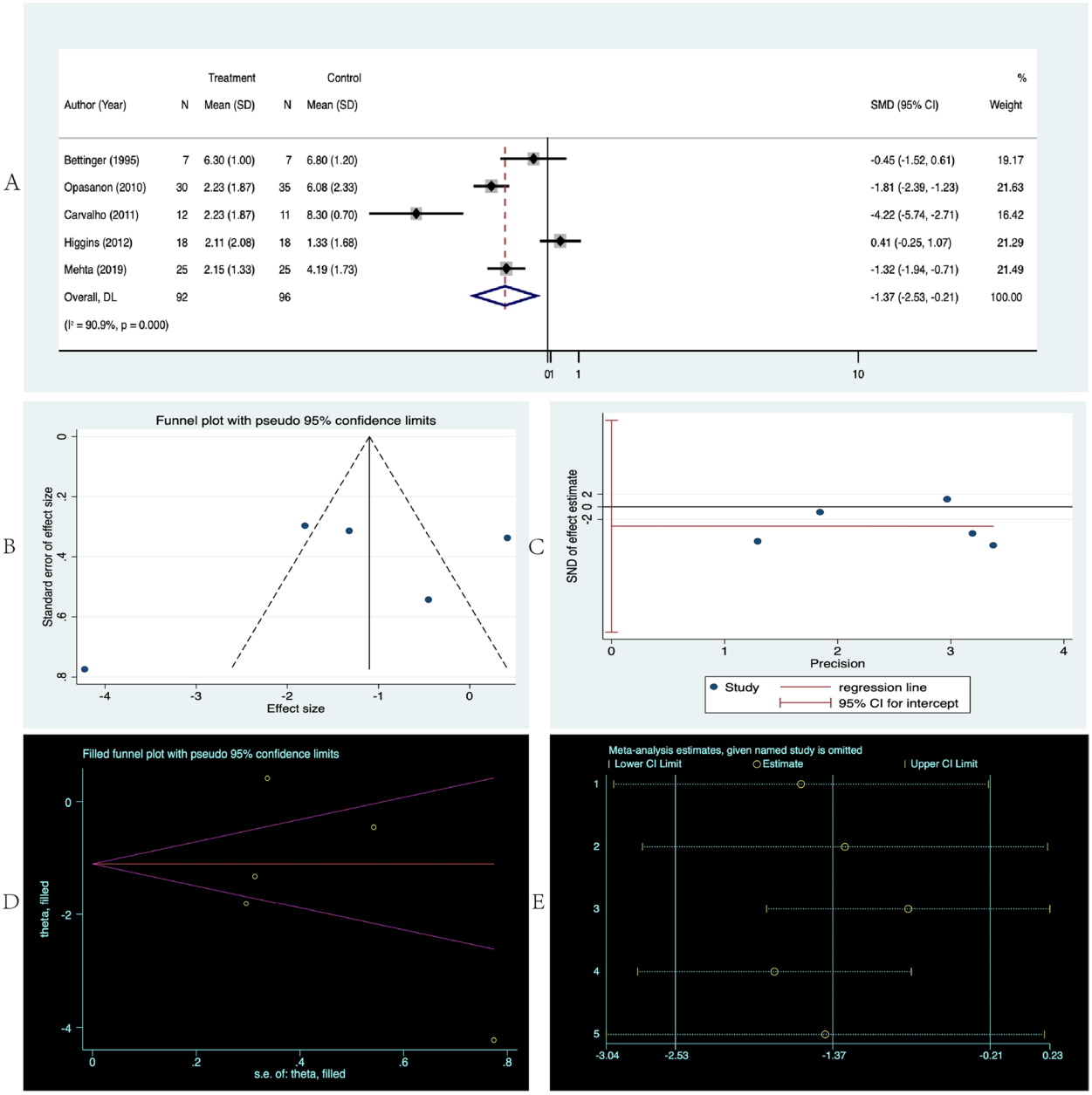

Fig. 6 Forest plot and funnel plot of the meta-analysis illustrating the overall weighted effect size of alginate dressings versus control on the the pain scores in burns. **A** Forest plot. The diamond symbol at the bottom of the forest plot represents the overall weighted estimate. Different colors (green, red, yellow) and symbols (" + ", "-", "?" ") to denote "low risk of bias", "high risk of bias" and "unclear risk of bias ", respectively. **B** Funnel plot. The effect size "MD" is shown on the abscissa, and the inverse of the standard error of the value of the effect size, SE (MD), is shown on the ordinate. The dots in the figure are the individual studies included

and allocation concealment, which may lead to selection bias. All studies have high risks in terms of blind participants and personnel and blind outcome evaluation, which may lead to performance bias and detection bias. Some studies have high-risk other biases, such as differences in dressing characteristics, which may affect the results. Most studies performed well in the integrity of the results data, and the missing data were complete, but some studies had the problem of incomplete missing data. The selective reporting risk of most studies is uncertain or low, which indicates that the report of research results may be relatively complete.

Due to the limitations of most studies in randomization, allocation concealment, blind method use and so

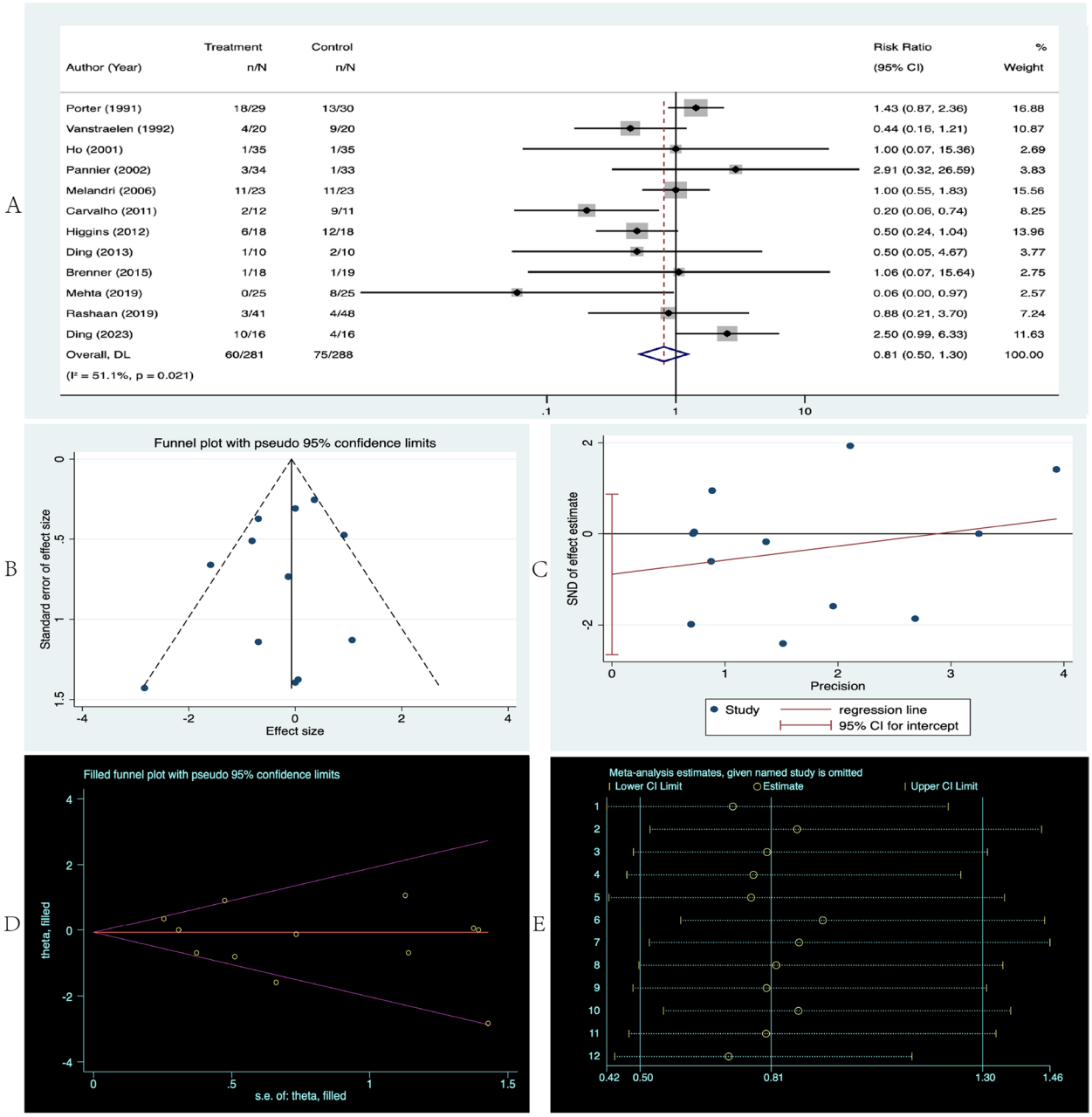

Fig. 7 Forest plot and funnel plot of the meta-analysis illustrating the overall weighted effect size of alginate dressings versus control on the adverse events in burns. **A** Forest plot. The diamond symbol at the bottom of the forest plot represents the overall weighted estimate. Different colors (green, red, yellow) and symbols (" + ", "-", "?" ") to denote "low risk of bias", "high risk of bias" and "unclear risk of bias ", respectively. **B** Funnel plot. The effect size "RR" is shown on the abscissa, and the inverse of the standard error of the value of the effect size, SE (RR), is shown on the ordinate. The dots in the figure are the individual studies included

on, the certainty of evidence is reduced. Nevertheless, some research results still show that calcium alginate dressing has significant advantages in accelerating the healing of donor site of layered skin transplantation, reducing pain and improving patient comfort.

Despite the risk of bias, calcium alginate dressing still shows certain advantages in clinical application, especially in terms of healing time and patient comfort.

Discussion

This meta-analysis compared the effects of using alginate dressings on burn wounds in different studies, revealing the advantages of alginate dressings in accelerating healing time and reducing patient pain. This systematic review and meta-analysis provide comprehensive evidence supporting the clinical utility of alginate dressings in burn wound management, while also highlighting critical methodological limitations and unresolved questions. We evaluated the therapeutic efficacy of alginate-based dressings in the management of burn wounds and DSWs. While DSWs are iatrogenic, standardized, acute wounds resulting from the removal of healthy skin to be applied to burn wounds, they share certain characteristics with burn wounds, such as the need for effective wound dressing to promote healing and minimize adverse events. However, it is important to note that DSWs and burn wounds differ in several aspects, including etiology, depth, and healing time. To ensure the clinical usefulness of our findings, we conducted separate analyses for DSWs and burn wounds wherever possible. When data were pooled, we carefully considered these differences and assessed the impact of alginate dressings on each wound type individually. This approach allows for a more nuanced understanding of the efficacy of alginate dressings across different wound types and provides valuable insights for clinical practice.

The meta-analysis revealed a significantly shorter healing time with alginate dressings versus controls, showing a MD of -1.09 days (95% CI: -1.67 to -0.31, $p < 0.001$, $I^2 = 94.6\%$). This reduction in healing time is not only statistically significant but also clinically relevant. In clinical practice, a reduction of approximately 1 day in healing time can lead to substantial improvements in patient outcomes. For instance, shorter healing times can reduce the risk of infections, decrease the frequency of dressing changes, and enhance patient comfort and quality of life. This is supported by the findings of Qu et al. (2023) [36], who reported that alginate dressings can effectively shorten wound healing time, relieve wound pain, and reduce the number of dressing changes. Additionally, Xu et al. (2025) [13] highlighted the multifunctional benefits of calcium alginate fibers in wound treatment, including their ability to promote faster healing and improve patient comfort. These results collectively suggest that the use of alginate dressings can lead to meaningful clinical improvements in wound care. However, not every study used healing time as the primary endpoint. Some research has indicated that the percentage area reduction (PAR) of the wound over a special period of time, such as 4 or 8 weeks, can be a valid intermediate endpoint. For instance, the Food and Drug Administration (FDA) has considered PAR over a 4-week period as a valid endpoint for wound studies. Studies have shown that PAR follows a near-linear trajectory over this period, making it possible to observe any change in the rate of area reduction attributable to the introduction of a new intervention. In clinical practice, a reevaluation of the treatment schedule is recommended for wounds that do not reach 50% area reduction within the first 4 weeks of therapy. The calculation of the percentage of area reduction after 4 weeks of treatment is a valid tool to estimate the probability of healing. In our systematic review, although healing time was the primary endpoint, the results can be correlated with the concept of wound reduction over a specific period. The significant reduction in healing time suggests that alginate dressings may also have a positive impact on wound area reduction during the healing process. However, further research is needed to directly compare healing time with surrogate parameters such as PAR in the context of burns, donor sites, or chronic wounds. What's more, the high heterogeneity ($I^2 > 90\%$) across outcomes underscores the need for cautious interpretation, particularly given inconsistencies in study design and outcome measurement.

Although alginate dressings showed a significant reduction in healing time compared to the control group, there was no significant difference in replacement frequency. At the same time, there was no significant difference in the incidence of adverse events between the two groups, indicating that alginate dressings may be comparable in safety to traditional dressings. The difference in healing time indicates that the super absorbent capacity of alginate dressings may effectively create a moist healing environment, reducing the time required for healing [37]. This characteristic is particularly important for severe exudative burns, as alginate dressings can efficiently absorb excess exudate. However, the analysis of dressing replacement frequency did not show significant advantages, which may be related to the differences between different usage methods and specific dressing types in the study. This inconsistency urgently needs to be explored through more detailed hierarchical analysis in future research.

The improvement in pain score also indicates the potential utility of alginate dressings in reducing mechanical trauma, as reducing frequent replacement frequency may directly decrease patients' pain perception. However, for the specific correlation between pain relief and dressing types, further analysis is needed to identify potential contributing factors, such as the analgesic effect of excipient components [38]. The meta-analysis revealed that pain scores also favored alginate dressings, with a SMD of -1.37 (95% CI: -2.53 to -0.21, $p = 0.000$, $I^2 = 90.9\%$). This reduction in pain scores suggests that alginate dressings may offer meaningful pain relief for

patients. However, the clinical relevance of this reduction requires further discussion. In clinical practice, the perception of pain can vary significantly among patients and across different wound types. For instance, severe burns may not always be more painful due to the potential destruction of nerve endings in the skin. In contrast, donor sites can be very painful, especially immediately after surgery. The pain scores at the beginning and end of treatment can vary widely depending on the wound type and patient factors. For example, a study by Opasanon et al. (2010) [22] reported that patients treated with Askina Calgitrol Ag® had significantly lower pain scores compared to those treated with 1% silver sulfadiazine (2.23 ± 1.87 versus 6.08 ± 2.33, respectively). This indicates that alginate dressings may be particularly effective in reducing pain in certain wound types. However, more research is needed to directly compare pain scores across different wound types and to assess the long-term impact of alginate dressings on pain management. Additionally, studies have shown that the PAR of the wound over a specific period, such as 4 or 8 weeks, can be a valid intermediate endpoint. PAR follows a near-linear trajectory over this period, making it possible to observe any change in the rate of area reduction attributable to the introduction of a new intervention. In clinical practice, a reevaluation of the treatment schedule is recommended for wounds that do not reach 50% area reduction within the first 4 weeks of therapy. The calculation of the percentage of area reduction after 4 weeks of treatment is a valid tool to estimate the probability of healing. In our systematic review, although healing time was the primary endpoint, the results can be correlated with the concept of wound reduction over a specific period. The significant reduction in healing time suggests that alginate dressings may also have a positive impact on wound area reduction during the healing process. However, further research is needed to directly compare healing time with surrogate parameters such as PAR in the context of burns, donor sites, or chronic wounds.

Our systematic review found that alginate dressings significantly reduced healing time and pain scores in burn patients, which aligns with their reported efficacy in managing various wound types, including acute and chronic wounds. In acute wounds such as burns and post-surgical wounds, the high absorbency and gel-forming properties of alginate dressings help manage exudate, maintain a moist environment, and promote healing. These properties are also beneficial for chronic wounds like venous leg ulcers, pressure ulcers [39], and diabetic foot ulcers. For instance, in venous leg ulcers, alginates effectively absorb exudate, reduce skin maceration, and prevent infection, thereby supporting the healing process [40]. In diabetic foot ulcers, they manage exudate and create a conducive environment for healing, while in pressure ulcers, their high absorbency and non-adherent nature make them suitable for managing exudate and reducing trauma during dressing changes. However, the effectiveness of alginate dressings may vary depending on the wound type and its specific characteristics. For example, in diabetic foot syndrome, an RCT [41] highlighted the importance of exudate management and infection control, which are areas where alginate dressings have shown promise. Yet, an review also pointed out that more research is needed to establish definitive guidelines for their use in diabetic foot ulcers [42]. This suggests that while alginate dressings are a valuable tool in wound care, their application should be tailored to the specific needs of each wound type. Future research should focus on head-to-head comparisons of alginate dressings with other advanced wound care products across different wound types to better understand their relative advantages and limitations.

The meta-analysis revealed no significant difference in dressing change frequency between the alginate dressing group and the control group, with an SMD of 2.18 (95% CI: -4.29 to -0.07, $p = 0.000$, $I^2 = 94.0\%$). This finding prompts us to consider whether the dressing change protocols in the studies might have influenced the results. Specifically, it is important to determine if the studies allowed for patient-adapted dressing changes or if they imposed a special dressing change schedule (e.g., daily or every 2–3 days) as part of the study protocol. In some studies, the dressing change frequency might have been determined by the standard care protocols of the participating institutions, which could vary and potentially bias the results. For instance, if a study required daily dressing changes regardless of the wound's actual condition, this could mask the potential benefits of alginate dressings in reducing the need for frequent changes. Conversely, if dressing changes were guided by clinical judgment and patient-specific factors, alginate dressings might have demonstrated a more pronounced advantage in minimizing disruptions to the healing process. The high absorbency of alginate dressings allows them to manage exudate effectively, which can extend the time between dressing changes. This is supported by the fact that alginate dressings can absorb up to 20 times their weight in exudate, maintaining a moist wound environment and reducing the risk of skin maceration. However, the studies included in our meta-analysis may not have uniformly accounted for these properties in their protocols, leading to inconsistent findings regarding dressing change frequency. It is also worth noting that the perception of pain and the rate of wound contraction can influence the decision to change dressings. Alginate dressings, with their

ability to form a soothing gel upon contact with wound exudate, may reduce pain during dressing changes by covering exposed nerve endings. This can make the dressing change process more comfortable for patients, potentially reducing the frequency of necessary changes. Despite these considerations, the lack of standardization in dressing change protocols across studies introduces a possible bias. Future research should aim to establish more consistent criteria for dressing changes, taking into account both the inherent properties of alginate dressings and the specific needs of patients. This would help to clarify the true impact of alginate dressings on dressing change frequency and provide more reliable guidance for clinical practice.

It is also worth mentioning that, this finding prompts us to consider whether the dressing change protocols in the studies might have influenced the results. Specifically, it is important to determine if the studies allowed for patient-adapted dressing changes or if they imposed a special dressing change schedule (e.g., daily or every 2–3 days) as part of the study protocol. A study by Stynes et al. (2023) [43] investigated the use of alginate dressings left intact for 14 days on uncontaminated, superficial, partial-thickness burns. The results showed that the burns healed with 100% epithelialization, and there were no adverse event such as scarring, infection, or need for grafting. This suggests that alginate dressings can be left in place for extended periods without the need for frequent changes, which aligns with the high absorbency and biodegradability of alginate dressings. Similar findings were reported in other studies, such as a randomized controlled trial by Opasanon et al. (2010) [25], which found that silver-impregnated alginate dressings changed every 5 days were effective in managing partial-thickness burns. These results indicate that alginate dressings can be used effectively with fewer dressing changes, potentially reducing patient discomfort and healthcare costs.

However, the lack of standardization in dressing change protocols across studies introduces a possible bias. Wiegand et al. (2009) [6] demonstrated that alginate dressings not only possess antibacterial properties but also exhibit the ability to bind bacteria, thereby reducing the risk of infection and promoting a conducive environment for healing. The study showed that alginate dressings can effectively bind bacteria such as Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, which are commonly found in burn wounds. This binding capacity helps to immobilize bacteria within the dressing, preventing their spread and reducing the bacterial load in the wound. Furthermore, the ability of alginate dressings to modulate inflammatory cytokines, support granulation tissue formation, and minimize mechanical trauma during removal has solidified their role in treating partial-thickness burns. The conflicting results in clinical evidence regarding the efficacy of alginate dressings compared to other advanced wound care products, such as hydrocolloid dressings and polyurethane (PU) foams, can be attributed to several factors. Hydrocolloids and PU foams are often used as secondary dressings, whereas alginates are typically employed as primary dressings. This difference in their application can influence the outcomes, as primary dressings come into direct contact with the wound and are responsible for managing exudate and promoting healing, while secondary dressings provide additional protection and support. The varying absorption rates of these dressings also play a significant role. Alginates are known for their high absorbency, which makes them particularly effective in managing wounds with moderate to high exudate levels. In contrast, hydrocolloids and PU foams have different absorption characteristics, making them more suitable for wounds with lower exudate levels. The choice of dressing should therefore be tailored to the specific characteristics of the wound, such as exudate level and depth. For instance, in wounds with high exudate, alginates may be more effective in maintaining a moist wound environment and facilitating healing, whereas in wounds with lower exudate, hydrocolloids or PU foams might be preferred for their ability to maintain moisture without excessive absorption.

The lack of significant differences in adverse events may suggest that the safety of alginate dressings is similar to that of traditional dressings. The studies reported a range of adverse events. Infection was the most commonly reported adverse event across the studies. For example, in the Higgins2012 study, five donor wounds experienced clinical signs of infection, with organisms such as methicillin-resistant Staphylococcus aureus (MRSA), Pseudomonas aeruginosa, and Alcagenesis species identified. Excessive exudate was also frequently reported, particularly in studies using polyurethane dressings like Allevyn™, which required more frequent dressing changes due to leakage. Pain, although not exclusively an adverse event, was also documented as a significant concern in several studies, with patients in control groups often reporting higher pain scores. Other adverse events included hematoma formation, though this was less common, and dressing adherence, which caused patient discomfort during removal. No specific serious adverse events (SAEs) were consistently reported across the studies that would raise significant concerns about the safety of alginate dressings. However, the studies did not always provide detailed information on whether these adverse events were anticipated based on the medical devices' instructions for use (IFUs). Future research should include more standardized reporting

of adverse events and explicit comparisons with known risks outlined in product IFUs to enhance the assessment of dressing safety.

While alginate dressings themselves do not possess inherent antibacterial activity, their ability to bind bacteria and remove them during wound cleaning contributes to a reduced bacterial load in the wound. This property is supported by the study of Wiegand et al. (2009) [6], which demonstrated that alginate dressings can effectively bind bacteria such as Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli, which are commonly found in burn wounds. The binding capacity of alginate dressings helps to immobilize bacteria within the dressing, preventing their spread and reducing the risk of infection. This mechanism, combined with the creation of a moist wound environment conducive to healing, solidifies the role of alginate dressings in managing partial-thickness burns. However, the addition of antimicrobial agents such as silver ions or antimicrobial peptides can further enhance the antibacterial performance of alginate dressings, making them more effective in infected wounds. The decision to use plain alginate dressings or those with added antimicrobial agents should be based on the specific clinical context and the presence of infection. It should be noted that the antimicrobial efficacy and potential bacterial resistance of dressings suitable for widely exuding wounds are still topics worthy of further exploration, especially in the context of long-term use. Although enhancers such as silver and honey have been incorporated into alginate dressings to enhance antibacterial performance, there are still concerns about potential cytotoxicity and drug resistance [44]. Some studies [45–47] have also explored the combination of alginate dressings with other antibacterial methods, such as non thermal plasma treatment, to further enhance antibacterial efficacy and reduce the risk of drug resistance. This combination therapy strategy can effectively kill multiple drug-resistant strains without significant toxicity to normal cells. Alginate dressings themselves do not have antibacterial activity, but their antibacterial performance can be enhanced by adding antibacterial agents such as silver ions, antimicrobial peptides, etc. [48]. These agents may inhibit bacterial growth via sustained release, thereby reducing the risk of drug resistance. For example, alginate saline gel containing antimicrobial peptides has good antibacterial effect against MRSA and other drug-resistant strains [49]. In addition, non thermal plasma treated alginate dressings also exhibited strong antibacterial properties and no significant cytotoxicity was observed.

Although none of the included RCTs explicitly reported the mannuronic acid (M) to guluronic acid (G) ratios of the alginate dressings, compositional differences were evident. For instance, silver-impregnated alginates (e.g., Askina Calgitrol Ag®) demonstrated superior antimicrobial efficacy compared to plain calcium alginate dressings (e.g., Kaltostat®), as seen in Opasanon et al. (2010) [25]. Similarly, collagen-alginate hybrids (e.g., Carvalho et al. [26]) accelerated epithelialization, likely due to synergistic effects. Preclinical studies suggest that high-M alginates enhance immunomodulation, while high-G variants improve mechanical stability. Future trials should standardize reporting of alginate composition to elucidate structure–function relationships.

A substance that doesn't harm the biological environment in which it's employed is said to be biocompatible. Its biocompatibility attributes are significantly influenced by the content of the alginate. Indeed, it has been documented that alginates containing a high M concentration are more immunogenic and effective than alginates with a high G content in triggering the generation of cytokines [33]. The numerous impurities that remained in the alginate after its extraction might be the cause of the immunogenic response at the implantation site or after an alginate injection. However, animal alginate purification doesn't cause an immunogenic reaction. One advantage of this natural substance is that it has hemostasis qualities [33]. The replacement of sodium Na + ions from the wound exudate with calcium (Ca2 +) ions creates a healing-friendly milieu that fills the wound and forms a dressing. This gel is non-adherent and hydrophilic [34].

Furthermore, calcium alginate has therapeutic qualities. Alginate fiber's ability to gel has been reported to enable the formation of a wet environment that is conducive to the scarring process [34]. As a result, it can absorb more than hydro-colloids and hydro-cellular combined. Studies have shown that alginates with a high mannuronic unit content have a beneficial effect. Alginate's excellent ability to absorb water validates its application for severely exudative wounds during the whole wound-healing process [35]. The absorption of alginate inside the Fibers enables the textile support, which successfully lowers the risk of wound infection throughout the healing process. The absorption of fluids causes the fibers to swell, which in turn allows the alginate to dissolve and immobilize the germs on the textile. The calcium alginate compress absorbs wound fluids, causing an ion exchange process between the calcium in the alginate and the sodium in the blood to produce the formation of an extremely viscous fluid [35]. The presence of moisture in this microenvironment facilitates the healing process.

The ratio of mannuronic acid (M) to guluronic acid (G) in alginate significantly impacts its properties and applications [34, 35]. Higher M content enhances immunogenicity and cytokine production, while higher G content

improves gelation and mechanical strength. This distinction is vital for optimizing alginate for specific uses, from wound healing to tissue engineering. For instance, wound dressings may prioritize M-rich alginates for better cell proliferation, whereas structural applications might favor G-rich variants for their robustness. Adjusting the M/G ratio during extraction allows customization of alginate's characteristics to meet diverse biomedical needs.

Alginate dressings' impact on long-term outcomes, including scar maturation and hypertrophic scarring, has not been comprehensively captured, as many studies conclude follow-ups at wound closure. Our analysis reveals critical gaps in scar assessment methodologies. Although alginate dressings showed superior short-term aesthetic outcomes in studies using validated tools like the VSS, long-term scar maturation data remained sparse [50]. For instance, Ding et al. (2023) [24] reported significantly lower VSS scores for alginate-silver dressings at 6 months ($p = 0.009$), yet Rashaan et al. (2019) [29] found no persistent differences at 12-month follow-up. This discrepancy suggests that early wound microenvironment modulation by alginates may transiently influence scar formation, but long-term remodeling processes—governed by intrinsic factors like skin tension and genetic predisposition [51]—could attenuate these effects. Under normal circumstances, the moisturizing properties of alginate dressings help to maintain the moist state of the wound and prevent scars from contracting or hardening due to dryness [52]. Keeping the wound moist can promote the flexibility and elasticity of the skin, improve the texture of scars, and make them softer and smoother [53]. Meanwhile, alginate dressings have good absorbency and moisturizing properties, which can reduce the number of dressing changes [54]. Frequent dressing changes may cause mechanical irritation to newly formed skin tissue and scars, increasing the risk of scar hyperplasia. Alginate dressings reduce the number of dressing changes, thereby reducing this irritation and facilitating scar recovery. Future trials should standardize scar evaluation using multimodal approaches combining objective biomechanical measurements [55] with histological analyses of collagen architecture.

Material cost analyses exposed a critical paradox: while alginate dressings themselves are typically more expensive than traditional alternatives, their economic advantage emerges through reduced nursing burdens and shorter hospital stays. In Brenner et al. (2015) [27], alginate's 1.3-day reduction in hospitalization translated to an estimated $2,840 savings per patient—more than offsetting its higher upfront costs. However, this benefit may not generalize to resource-limited settings, where labor costs are lower and prolonged hospitalization is often unavoidable due to infrastructure constraints. Overall, the cost-effectiveness of alginate dressings is mainly reflected in their therapeutic efficacy and frequency of use. For example, in the studies [56–58] of treating pressure ulcers, although alginate dressings have a high unit price, they have certain advantages in overall treatment cost due to their good absorption and ability to promote healing, which can reduce the number of dressing changes and shorten healing time. In addition, alginate dressings can effectively reduce the incidence of adverse events and further save medical resources when treating complex wounds such as chronic wounds and burns [57]. With the advancement of technology and the intensification of market competition, the cost of alginate dressings is expected to be further optimized in the future.

This meta-analysis compared the effects of using alginate dressings on burn wounds in different studies, revealing the advantages of alginate dressings in accelerating healing time and reducing patient pain. Compared to the study by Lou et al. [12], our research places a greater emphasis on contemporary RCTs and employs the GRADE approach to evaluate evidence certainty. While both studies highlight the benefits of alginate dressings in reducing healing time, our analysis further underscores the significance of standardized evaluation criteria and long-term studies. Notably, our systematic review delves deeper into the cost-effectiveness and safety profile of alginate dressings, offering more comprehensive guidance for clinical decision-making. For instanc e, we found that although alginate dressings themselves are typically more expensive than traditional alternatives, their economic advantage emerges through reduced nursing burdens and shorter hospital stays. However, this benefit may vary across different healthcare settings. Moreover, our research indicates that the advantages of alginate dressings in reducing pain and healing time may stem from their unique capacity to maintain a moist wound microenvironment and minimize mechanical trauma during dressing changes. These findings, while consistent with the general benefits reported by Lou et al., provide more detailed insights into the specific applications and potential limitations of alginate dressings in diverse burn care settings.

Limitations

The limitations of this study are multifaceted and are further highlighted by the divergent methodologies employed in donor site and burn wound evaluations. A key finding is that approximately 60% of the included studies utilized within-patient comparisons, where different dressings were applied to distinct wounds on the same individual. This approach theoretically controls for inter-individual variability, but as noted in studies like Brenner et al. (2015) [27], anatomical variations in wound

location—such as differences in vascularization between thigh and abdominal donor sites—may still confound outcomes. Conversely, between-patient designs, which were used in 40% of studies, are more reflective of real-world clinical practice but require larger sample sizes to account for baseline heterogeneity in burn severity and patient comorbidities. These methodological discrepancies likely contributed to the observed variability in cost-effectiveness conclusions. For instance, alginate dressings demonstrated reduced total care costs in studies with rigorous within-patient designs, such as in Mehta et al. (2019) [28], but appeared less economical in underpowered between-patient trials.

When discussing the limitations of current research on granulation tissue formation assessment, it is important to note the emerging role of digital image analysis (DIA) alongside traditional clinical assessment. DIA has been shown to be a reliable and valid tool for evaluating wound tissue composition, including the ratio of fibrinotic/necrotic, granulated, and epithelialized tissue. For instance, Bloemen et al. [59] validated DIA against clinical assessment of wound epithelialization, demonstrating strong interobserver reliability (IC coefficient 0.74) and a high correlation with subjective clinical assessment (IC coefficient 0.80). Additionally, Chairat et al. [60] introduced an AI-assisted method for wound tissue assessment using smartphone images, which could potentially enhance the accessibility and accuracy of DIA. However, the high cost and technical requirements of DIA may hinder its widespread adoption in resource-limited settings. Furthermore, while DIA provides detailed information about wound tissue composition, it may not fully capture the dynamic changes and functional status of granulation tissue during wound healing, which are often assessed through clinical observation and experience. Therefore, combining DIA with clinical assessment may offer a more comprehensive evaluation of granulation tissue formation. Future research should focus on developing standardized protocols for granulation tissue assessment that integrate both DIA and clinical evaluation, thereby improving the accuracy and reliability of wound assessment and providing deeper insights into the wound healing process.

The assessment of pain in the included studies presents certain limitations due to the use of different pain measurement tools and protocols. While most studies utilized subjective self-report scales such as the VAS or NRS, which are common and validated methods for evaluating pain intensity, variations in how and when these assessments were conducted across studies may affect the comparability of the results. For instance, differences in the timing of pain assessments (e.g., during dressing changes versus at rest) and the specific instructions provided to patients could introduce variability in the reported pain scores. Additionally, the use of multiple pain assessment instruments in some studies, while providing a more comprehensive evaluation of pain, complicates direct comparisons with studies that employed only a single tool. These factors highlight the need for greater standardization in pain assessment methods in future research to enhance the reliability and comparability of findings across different studies.

In addition to these methodological challenges, the study design and comparison methods exhibit heterogeneity. Some studies utilized intra-patient comparisons to control for individual variations, while others employed inter-patient randomization, which may introduce variability in results due to differences between patient groups. Blinding is also a significant challenge in dressing studies due to the visible nature of different dressings, leading to potential performance and detection biases. Although efforts were made to mitigate these biases through objective assessment tools, the risk of bias remains. While alginate composition (e.g., M/G ratio, silver incorporation) likely modulates therapeutic effects, most studies failed to report these parameters. Consequently, we could not perform subgroup analyses to isolate the impact of specific alginate subtypes on outcomes such as healing time or infection rates. Economically, the analysis of alginate dressings is limited by substantial variability across different healthcare settings. While alginate dressings may reduce overall costs by shortening healing times and hospital stays, initial costs may vary, and the cost-effectiveness is not universally applicable. In terms of long-term outcomes, the assessment of scar formation and granulation tissue is inconsistent. Scar evaluation methods range from subjective assessments to validated scales like the VSS, and granulation tissue formation lacks standardized measurement protocols, relying mostly on qualitative assessments [61, 62]. The risk of bias in the included studies also represents a significant methodological challenge. While methodological limitations in randomization and blinding may introduce potential confounding effects, the core conclusions retain reasonable validity given adequate data completeness and outcome reporting transparency. Blinding for patients and investigators may be very difficult in clinical controlled studies with wound dressings and bandages. The visible differences between dressing types can make it challenging to mask the intervention, potentially leading to performance bias and detection bias. In the studies included in our meta-analysis, the majority did not implement blinding of participants and personnel due to the nature of the interventions. This limitation is inherent in many wound care trials, as the physical characteristics of dressings often make them easily distinguishable. However, efforts were

made to minimize the impact of this bias by using objective outcome measures and blinded outcome assessors wherever possible. For example, some studies used digital image analysis to assess wound healing endpoints in an objective manner. While blinding in such studies may not be completely feasible, the use of objective assessment tools can enhance the reliability of the results. Future research should explore innovative approaches to blinding in wound care trials, such as the use of sham dressings or the incorporation of blinded assessment of digital images.

Additionally, the development of more standardized and objective outcome measures for wound healing could help to reduce the impact of bias on study findings. It is essential to differentiate acute wounds (e.g., burns, donor sites) from chronic wounds (e.g., venous leg ulcers) when interpreting surrogate parameters like percentage area reduction. While acute wounds often follow near-linear healing trajectories, chronic wounds exhibit prolonged and nonlinear healing phases. Regulatory frameworks such as the FDA's 4-week PAR threshold for acute wounds contrast with guidelines from the German IQWIG and French HAS, which recommend 20-week evaluations for chronic wounds like venous leg ulcers. These distinctions underscore the need for context-specific validation of surrogate endpoints in future trials.

Despite these challenges, the overall conclusions of our analysis remain robust, supported by the transparency and completeness of the reported outcomes.These inconsistencies compromise the comparability and interpretation of results. Future research should focus on standardizing study designs, blinding methods, economic evaluations, and outcome assessments to address these limitations and enhance the reliability and applicability of findings.

Conclusions

This meta-analysis confirms that alginate dressings are a valuable treatment option for partial thickness burns and donor sites, with statistically significant advantages in accelerating healing and reducing pain. However, their economic feasibility and scar repair effectiveness seem to depend on specific circumstances, the availability of medical resources, and the evaluation time frame. Clinical doctors should balance the higher material cost of alginate with the potential savings of reducing nursing time and hospitalization, especially in high-capacity burn centers. Overall, while calcium alginate dressings represent a vital advancement in burn care technology, ongoing research should strive to refine their application by exploring novel formulations and enhancing accessibility, particularly in resource-constrained environments. A nuanced understanding of their cost-effectiveness, tailored application for various burn depths, and integration of economic considerations will be pivotal in promoting their optimal use in clinical practice globally.

Abbreviations

AgSD	Silver Sulfadiazine
DSW	Donor-site wound
NPWT	Negetive pressure wound therapy
SIC	Silver-sulfadiazine-impregnated collagen
SSD	Silver sulfadiazine
VSS	Vancouver scar assessment scale
RCTs	Randomized controlled trial
RR	Relative risk
MD	Mean difference
CI	Confidence interval

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Authors' contributions
Authors' contributions JQ L, ZY X and XY Z contributed equally to this work. JQ L and SD X designed and conceptualized the study. JQ L, XY Z, ZY X, JY S, SY C, JL L, N H and GY J completed the record retrieval and data extraction. Mathematical modeling and meta-analysis were conducted with the help of YF F, JY S, P X, X L and SY C. The original draft was written by JQ L, XY Z and ZY X. All authors have read and agreed to the published version of the manuscript.

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Data availability
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Declarations

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Not applicable.

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The authors declare no competing interests.

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