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Review Article

The effect of various interventions on the prevention of radiation dermatitis: a network meta-analysis

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Abstract: Objective: High doses of radiation, while effective at destroying tumor tissues, also result in radiation dermatitis (RD) at irradiated sites, which is one of the most common complications in cancer radiotherapy. Currently, no standardized protocols for the prevention and treatment of RD have been established in clinical practices, and severe RD can compromise treatment efficacy and reduce patients' quality of life. This systematic review and network meta-analysis (NMA) aims to compare the effectiveness of various interventions in preventing RD in patients. Methods: As of June 2023, four databases, including PubMed, Embase, Web of Science, and the Cochrane Library, were searched, with a total of 19 interventions obtained for comparative analysis of their effectiveness in preventing RD. The Cochrane risk-of-bias tool was employed to screen literature, extract data, and appraise the quality of the studies by two researchers. Bayesian network meta-analysis (NMA) was conducted utilizing StataSE 15 and R 4.2.3. Results: A total of 33 studies involving 4307 patients were included in this analysis. From the 33 studies, 19 interventions, encompassing Barrier Films and Dressings (BFD), Boron_Gel, Best supportive care, Corticosteroids_cream, Doxepin_cream, Eau Thermale Avèn_gel, Epidermal Growth Factor_cream, Hyaluronan_cream, Medicinal_Plants, Mineral_Oil, Olive oil and calcium hydroxide (OOCH), Photobiomodulation therapy, Recove_cream, Silicone_gel, Silver sulfadiazine (SSD), Timolol_Gel, Trolamine, VitD_Gel, and VitE_Gel, were retrieved and compared. The NMA results indicated that Hyaluronan_cream (SUCRA: 94.9%) was highly effective in preventing Grade 0/1 RD. Meanwhile, OOCH (SUCRA: 95.7%) demonstrated the most prominent effect in preventing ≥ Grade 2 RD. Conclusion: The study reveals that Hyaluronan_cream and OOCH are two promising treatments for the prevention of RD in patients undergoing radiotherapy. Future research might focus on validating the efficacy of these two therapies with large sample sizes and on identifying an optimal intervention strategy.

Keywords: Radiation dermatitis, network meta-analysis, radiotherapy, topical interventions, clinical efficacy

Introduction

Radiotherapy has now become an extensively employed treatment for cancer patients, with nearly 50% of cancer patients undergoing it at some point during their illness. However, radiotherapy can give rise to specific side effects, one of the most common being radiation dermatitis (RD), which affects up to 95% of patients [1, 2]. Typically, RD manifests within 2 to 3 weeks after the commencement of radiotherapy and persists for 4 to 5 weeks after radiotherapy [3]. RD refers to inflammatory skin and mucosal damage caused by exposure to radiation, primarily β-rays, γ-rays, and X-rays. It mainly presents with symptoms such as erythema, edema, dryness, dry desquamation, and pigmentation on the skin. In severe cases, it can escalate to moist desquamation, skin damage, hemorrhagic necrosis. This condition can cause significant physical and psychological discomfort to patients and may potentially affect the radiotherapy progress [4, 5]. The mechanism of RD involves high-energy radiation causing direct damage to the DNA of human epidermal cells, either in single or double strands, resulting in cell mutations and a series of skin reactions and injuries [6, 7]. These injuries typically

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progress from mild erythema to dry desquamation and moist desquamation. Grade 3 or higher RD is the primary cause of treatment interruption during radiotherapy [6].

Commonly prescribed treatments for RD encompass topical corticosteroids, trichloroacetic acid, aloe vera, sucralfate, and hyaluronic acid [8, 9]. However, so far there is no evidence to indicate whether these topical medications could prevent or alleviate RD. Still, a variety of topical medications have been developed to treat acute RD, which are extensively employed in clinical practice. But these medications do not always yield satisfactory clinical effects due to various confounding factors. Therefore, it becomes particularly important to choose appropriate interventions for the prevention of RD.

In this study, a network meta-analysis (NMA) was carried out to thoroughly assess the effects of various interventions in preventing RD, while simultaneously exploring their differences and feasibility as RD intervention measures. By employing this analysis, we can identify the advantages and disadvantages of different intervention measures, thereby providing more reliable evidence and guidance for clinical practice. Ultimately, this approach aims to enhance patients' treatment experience and outcomes.

Data and methods

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [10] and followed the Population, Intervention, Comparator, and Outcome (PICO) framework. The study was registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42023481643).

Literature retrieval

Two authors, Hongxin Cao and Wangbin Li, independently searched for articles in four databases, including PubMed, Embase, Web of Science, and Cochrane Library, covering the period from the earliest available records to June 7, 2023. Any disagreements regarding the search results were resolved through discussion between the two authors, or consultation from a senior author. The keywords were set as ("radiation dermatitis", "radiation-induced dermatitis", "skin toxicity", "skin reaction", "skin damage", or "cutaneous reaction") and ("prevention" or "reduction"). The search strategy is detailed in Supplementary File 1.

Inclusion and exclusion criteria

Studies were eligible if they included adult patients that had undergone radiotherapy for breast cancer, head and neck cancer, neck cancer or rectal and anal cancer undergoing radiotherapy; they designed an intervention group that had received at least one drug intervention; they encompassed a control group receiving either a placebo or standard of care; their enrolled patients in both intervention and control groups underwent the same general adjunctive treatment simultaneously, if such treatment was necessary; they reported the intervention effects on Grade 0 or Grade 1 dermatitis (F1) or ≥ Grade 2 dermatitis (F2); they were randomized controlled trials (RCT); and they were written in English.

Studies were ineligible if they were case reports, case series, cohort studies, case-control studies, non-RCTs, or self-controlled trials; their diagnostic and effect criteria were unclear; their full texts were unavailable; they were conference posters; their data were incomplete or incorrect that couldn't be pooled.

The incidence and grading of RD in the included studies were assessed using the Acute Radiation Morbidity Scoring Criteria of the Radiation Therapy Oncology Group (RTOG) [11]. This scale consists of six grades: Grade 0 indicates no change in baseline data; Grade 1 denotes for follicular, faint, or dull erythema/depilation/dry desquamation/reduced sweating; Grade 2 stands for tender or bright erythema, patchy moist desquamation/moderate edema; Grade 3 means confluent moist desquamation, except in skin folds and creases/skin wrinkling, and pitting edema; Grade 4 suggests ulceration, bleeding, necrosis; Grade 5 stands for death directly related to acute radiation reactions. An I^2 of 0%-25% signifies no heterogeneity, 25%-50% suggests mild heterogeneity, 50%-75% represents moderate hetero-

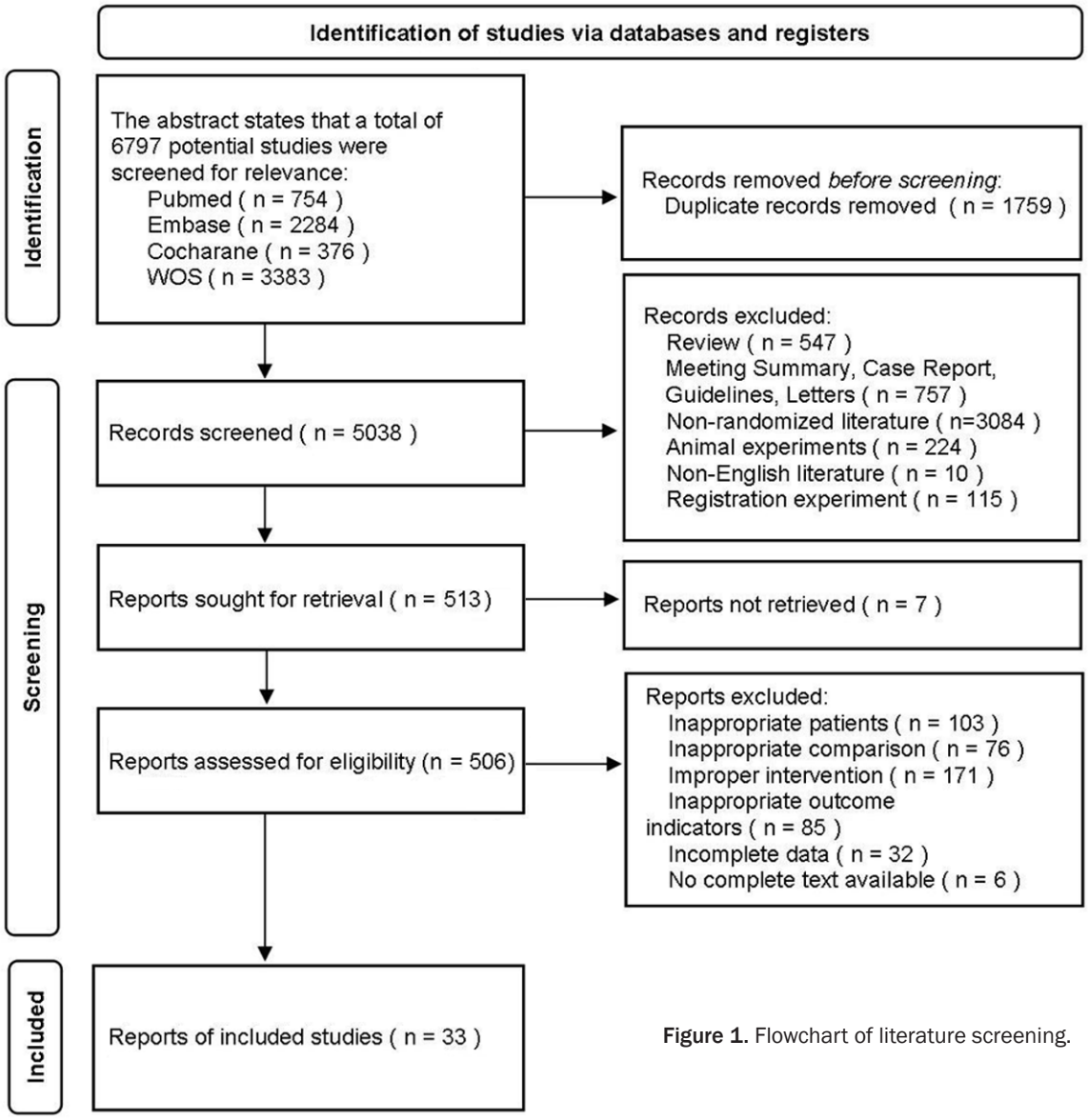


Figure 1. Flowchart of literature screening.

geneity, and 75%-100% indicates substantial heterogeneity.

Data extraction and quality assessment

Two authors, Hongxin Cao and Wangbin Li, independently extracted relevant data from the eligible studies, including the grading of RD. In cases of discrepancies, a senior author, Hongyi Cai, was consulted to resolve the issue. The extracted data were as follows: authors, publication year, country where the study was conducted, the number of patients, treatment details, cancer type, outcome measures, and radiation dose. The primary endpoint was set as the occurrence of Grade 0 or Grade 1 RD. These grades were considered equivalent because the RTOG RD grading system and the CTCAE RD grading system were similar [11]. The secondary endpoint was the occurrence of ≥ Grade 2 RD.

The quality of the included RCTs was evaluated using the risk of bias tools described in the Cochrane Handbook [12]. Two authors, Hongxin Cao and Wangbin Li, independently assessed the studies for potential biases. Any disagreements were resolved by reaching a consensus between the two. The risk of bias assessments were then visualized using the Revman 5.4.1

Table 1. Characteristics of included studies

Study	Sample size	Gender (M/F)	Mean age	Type of tumor	Intervention	Outcome	DT
Fisher [13] 2000 USA	Trolamine: 83 BSC: 89	0/172	Trolamine: 61.2 BSC: 61.8	Breast cancer	Trolamine: TID	Grade 0, 1, 2, 3	50-64 Gy
Pasalar [14] 2022 Iran	D-H (Medicinal_Plants): (n = 48) Mometasone (Corticosteroids_cream): (n = 53)	0/106	D: 46.64-10.49 M: 47.54-9.4	Breast cancer	Mometasone: 5 g QD	Grade 1, 2	About 50 Gy
Marzbali [15] 2022 Iran	Recove: 37 Petrolatum ointment (Mineral_Oil): 34	0/71	Recove: 50.68±13.4 Petrolatum ointment: 49.8±9.83	Breast cancer	Not reported	Grade 0, 1, 2, 3, 4	50 Gy
Togni [16] 2015 Italy	Boswellia (Medicinal_Plants): 55 BSC (placebo): 59	0/114	Mean: 58.2±11.1 Median: 58.5 Age range: 32-78	Breast cancer	BID	Grade 1, 2	50 Gy
Schmeel [17] 2019 Germany	Hydrofilm (BFD): 74 BSC: 74	1/79	Median: 62 Mean: 60.31 Age range: 37-84	Breast cancer	Not reported	Grade 0, 1, 2, 3	40.05 Gy
Shariati [18] 2020 Iran	Doxepin: 24 BSC (Placebo): 24	0/48	Mean: 48±10 vs. 47.8±11	Breast cancer	TID	Grade 0, 1, 2	50 Gy
Pommier [19] 2004 France	Calendula (Medicinal_Plants): 126 Trolamine: 128	0/254	M 56.5 R 28.5-74.5 VS. M 55.1 R 26.5-74.3	Breast cancer	>BID	Grade 0, 1, 2, 3	52-62 Gy
Nasser [20] 2017 Israel	VitD_Gel: 23 BSC: 23	0/23	Mean: 63 Range: 37-74	Breast cancer	QD	Grade 0, 1, 2, 3, 4	42.72-50 Gy
Karbasforooshan [21] 2019 Iran	Silymarin (Medicinal_Plants): 20 BSC (placebo): 20	0/40	S: Mean 49.5±10 P: Mean 47.30±11.46	Breast cancer	QD	Grade 0, 1, 2, 3, 4	50 Gy
Omidvari [22] 2022 Iran	Silicone_gel: 50 BSC (Control): 50	0/100	Control: 45.08±14.38 Silicone: 43.04±10.61	Breast cancer	BID	Grade 0, 1, 2, 3, 4	50 Gy
Thanthong [23] 2020 Thailand	Centella (Medicinal_Plants): 29 Thunbergia (Medicinal_Plants): 30 BSC: 27	0/90	Mean: 56.7±11.4 Mean: 56.5±10.4 Mean: 53.4±13.2	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	50-66 Gy
Meybodi [24] 2022 Iran	Timolol: 32 BSC (placebo): 32	0/64	Timolol: 53.8 (11.0) Placebo: 54.8 (12.4)	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	50-60 Gy
Liao [41] 2019 China	Mometasone (Corticosteroids): 41 BSC: 41	Not specifically reported	Mean: 53.3±12.64 Range: 19-74	Neck cancer	Not specifically reported	Grade 1, 2, 3, 4	About 60 Gy
Sharp [25] 2013 Sweden	Calendula (Medicinal_Plants): 194 Essex (BSC): 196	0/420	Calendula Mean: 58±11.1 Range: 30-79 Essex Mean: 58±10.8 Range: 29-86	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3, 4	Calendula Mean 49.3±6.4 Gy Range: 42.4-66 Gy Essex (BSC): 49.1±6.7 Gy Range: 20-66 Gy
Rahimi [26] 2020 USA	Hyaluronan_cream: 30 BSC (placebo): 30	0/30	Mean: 60 Range: 33-66	Breast cancer	TID	Grade 0, 1, 2, 3	50-60 Gy
Ribet [42] 2008 France	ETA_gel: 35 Trolamine: 34	8/61	ETA_gel: Mean 57.4±9.5 Range 36-78 Trolamine: Mean 58.4±13.1 Range 35-84	Breast cancer head and neck cancer	Not specifically reported	Grade 1, 2, 3, 4	Not specifically reported
Ulff [27] 2017 Sweden	Steroid (Corticosteroids_cream): 102 Moisturizer (BSC): 100	0/202	Steroid (Corticosteroids_cream): Mean 64 Moisturizer (BSC): Mean 62	Breast cancer	BID	Grade 0, 1, 2, 3	42.56-50 Gy

Liu [45] 2022 China	EGF: 193 BSC: 193	111/82	Mean: 54.1 Range: 16-80	Rectal and anal cancer	2000 IU BID	Grade 0, 1, 2, 3, 4	45.0-64 Gy
Hindley [28] 2014 United Kingdom	Mometasone (Corticosteroids_cream): 62 Diprobase (BSC): 58	0/120	Mometasone (Corticosteroids_cream): Mean 59±11 Diprobase (BSC): Mean 60±10	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	About 50 Gy
Chitapanarux [29] 2019 Thailand	Control (BSC): 31 Olive oil calcium hydroxide (OOCH): 31	0/62	Control (BSC): Mean 55 Range 47-62 Olive oil calcium hydroxide (OOCH): Mean 56 Range 51-61	Breast cancer	Not specifically reported	Grade 1, 2	50.39±3.39 49.76±3.38
Sahin [30] 2022 Iran	Boron_Gel: 181 Placebo (BSC): 76	0/257	Boron_Gel: Mean 50.0±12.1 Placebo (BSC): Mean 48.1±11.1	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3, 4	50 Gy
Elliott [43] 2006 Canada	Trolamine: 163 Institutional Preference (BSC): 159	264/331	Trolamine: 59.1 Preference (BSC): 58.8	Head and neck	Not specifically reported	Grade 0, 1, 2, 3, 4	About 60 Gy, Not specifically reported
Hemati [31] 2012 Iran	SSD: 51 Control (BSC): 51	0/102	SSD: 48.7±10.3 Control (BSC): 48.1±9.9	Breast cancer	TID	Grade 0, 1, 2, 3, 4	50 Gy
Kong [32] 2013 Korea	EGF: 20 BSC: 20	0/40	EGF: Mean 57.3 Range 40.2-74.0 BSC: Mean 51.8 Range 36.5-76.1	Breast cancer	TID	Grade 1, 2, 3	EGF: 56 (46-66) Gy BSC: 56 (46-60) Gy
Schmidt [33] 2022 Brazil	Vit E: 12 BSC: 14	0/26	Mean: 60 Range: 29-91	Breast cancer	TID	Grade 1, 2, 3	50-60 Gy
Fife [34] 2010 USA	Treatment (PBMT): 18 No Treatment (BSC): 15	0/33	Not specifically reported	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	45-61.2 Gy
Robijns [35] 2016 Belgium	No Treatment (BSC): 27 LT (PBMT): 30	0/57	Not specifically reported	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	Not specifically reported
Møller [36] 2018 Denmark	Mepitel film (BFD): 76 BSC: 76	0/79	Mean: 61.9	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	40-50 Gy
Schmeel [37] 2018 Germany	Hydrofilm (BFD): 62 BSC: 62	0/62	Mean: 62 Range: 36-82	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	50-66 Gy
Wooding [38] 2018 New Zealand/China	Film (BFD): 22 Sorbolene (Mineral_Oil): 22 Film (BFD): 11 Trolamine: 11	0/36	Not specifically reported	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	50-74 Gy
Zhang [44] 2018 China	Treatment (PBMT): 30 No Treatment (BSC): 30	42/18	Treatment (PBMT): 46.4±11.91 No Treatment (BSC): 45.23±12.70	Head and neck	Not specifically reported	Grade 0, 1, 2, 3	Not specifically reported
Robijns [35] 2019 Belgium	Control (BSC): 60 PBMT: 60	0/120	Control (BSC): 56.92±10.34 PBMT: 56.52±10.54	Breast cancer	Not specifically reported	Grade 1, 2, 3	40-66 Gy
Behroozian [40] 2023 USA	MF (BFD): 251 BSC: 125	0/376	MF (BFD): Mean 58.2±11.7 BSC: Mean 59.5±13.4	Breast cancer	Not specifically reported	Grade 0, 1, 2, 3	40-50 Gy

BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

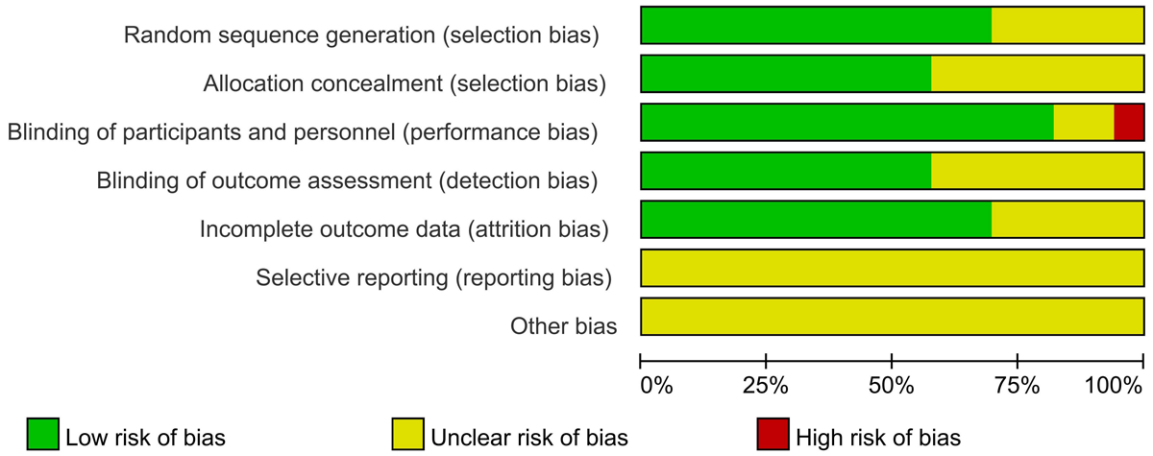


Figure 2. Risk of bias plot: in the form of a percentage of each bias risk in all included studies.

software, allowing for clear presentation and analysis of the findings.

Statistical analysis

The statistical model for this study was developed based on a Bayesian framework using the JAGS software (gem 0.8-2 and rags 4-10 packages) in R (V4.2.3) (Rstudio, Boston, MA, USA). For the analysis of categorical data, the pooled odds ratio (OR) was calculated, and the 95% confidence interval (CI) was provided. All NMAs were performed using a random-effect model to account for the clinical heterogeneity observed in the included studies. The surface under the cumulative ranking curve (SUCRA) was employed to estimate the relative effectiveness of each intervention, providing a ranking based on the probability of each intervention being the most effective option. A higher SUCRA value indicates a greater likelihood that the intervention measure is among the most effective options available. Additionally, the consistency and inconsistency models were compared utilizing the Deviance Information Criterion (DIC) to evaluate the fit of the models and assess whether direct and indirect evidence within the network were in agreement. A difference in DIC of less than 5 between two models indicates good consistency, suggesting that the consistency model should be adopted. To address potential publication bias, a comparison-adjusted funnel plot was employed. Both the network plot and the comparison-adjusted funnel plot for the NMA were generated using Stata 15.0 (StataCorp, College Station, Texas, USA).

Results

Study selection

A total of 6797 articles were initially identified from searches in PubMed, Embase, Web of Science, and Cochrane Library databases. After removing 1759 duplicates, 5038 articles remained for further review. Of these, 4949 articles were exclude through scanning the abstracts, and an additional 56 were eliminated after full-text review. In the end, 33 studies met the inclusion criteria and were included in this NMA. The literature screening process is illustrated in **Figure 1**.

Characteristics of the included studies

Characteristics of all included studies are detailed in **Table 1**. The included studies were published between the years 2000 and 2023, involving 4,307 patients, from 11 to 251 in each study. Among these, 28 studies involved breast cancer patients [13-40], 1 study focused on patients with either breast cancer or head and neck cancer [41], 3 studies encompassed patients with head and neck cancer [42-44], and 1 study involved rectal and anal cancer patients [45]. Medicinal_Plants was as an intervention in 6 studies [14, 16, 19, 21, 23, 25], Trolamine in 5 studies [13, 19, 38, 42, 43], Barrier Films and Dressings (BFD) in 5 studies [17, 36-38, 40], for Photobiomodulation thera-

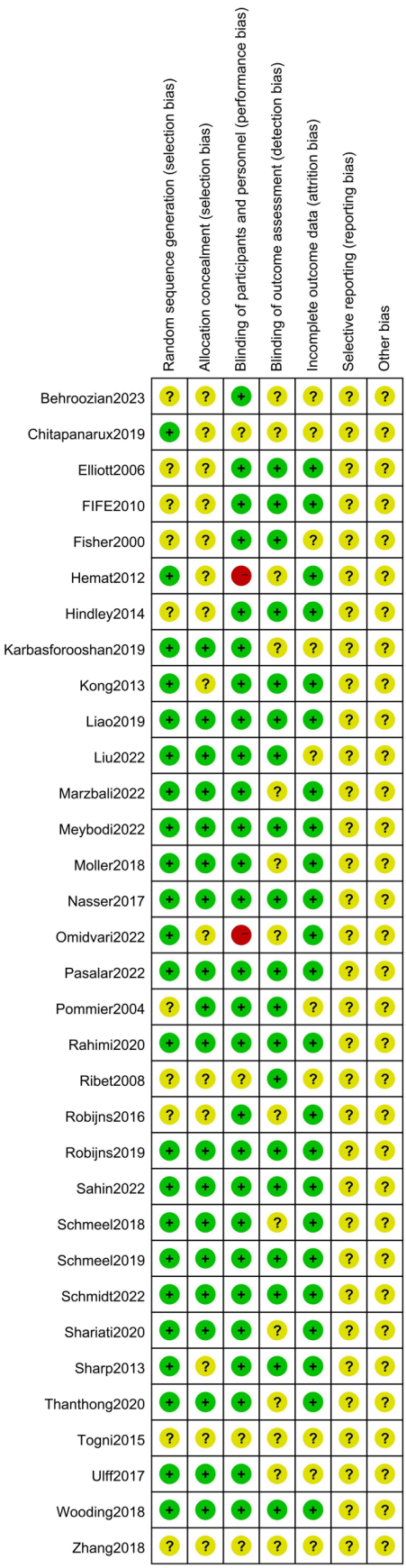


Figure 3. Each risk of bias item for the included studies.

py (PBMT) in 4 studies [32, 35, 39, 44], Corticosteroids_cream in 3 studies [14, 27, 28], Mineral_Oil in 2 studies [15, 38], and Epidermal Growth Factor (EGF) in 2 studies [32, 45]. There was only one study reported the use of Doxepin [18], VitD_Gel [20], Silicone_gel (StrataXRT) [22], Timolol [24], Corticosteroids [41], Hyaluronan_cream [26], Eau Thermale Avèn (EAT)_gel [42], Olive oil and calcium hydroxide (OOCH) [29], Boron_Gel [30], Silver sulfadiazine (SSD) [31], Vit E [33].

Risk of bias assessment

The risk of bias in the included studies is summarized in **Figures 2** and **3**. Two studies were considered to have a high risk of bias due to the lack of double-blinding. Thirty-one studies were assessed as having an unclear risk of bias because one or more domains were not clearly reported. The overall quality of the studies was considered moderate.

Network meta-analysis of Grade 0/1 radiation dermatitis

The meta-analysis involved 33 studies encompassing a total of 4307 patients. The network plot is presented in **Figures 4** and **5**. The effects of different intervention measures on RD patients are summarized in **Figure 6**. It was found that Hyaluronan_cream was superior to BFD in preventing Grade 0/1 RD (OR = 19.01, 95% CI [1.8, 598.81]), Hyaluronan_cream outperformed Boron_Gel (OR = 33.06, 95% CI [2.44, 1186.56]), Corticosteroids_cream (OR = 14.35, 95% CI [1.34, 452.9]) and Doxepin_cream (OR = 354.99, 95% CI [16.37, 20544.31]). However, the difference between BFD and Boron_Gel was not statistically significant. The results of the probability ranking for the effects of 19 intervention measures showed that, in the prevention of Grade 0/1 RD, Hyaluronan_cream had the most significant impact (SUCRA: 94.9%), as shown in **Table 2**.

Network meta-analysis of ≥ Grade 2 radiation dermatitis

The network plot showed that OOCH was superior to BFD (OR = 4047979559468390,

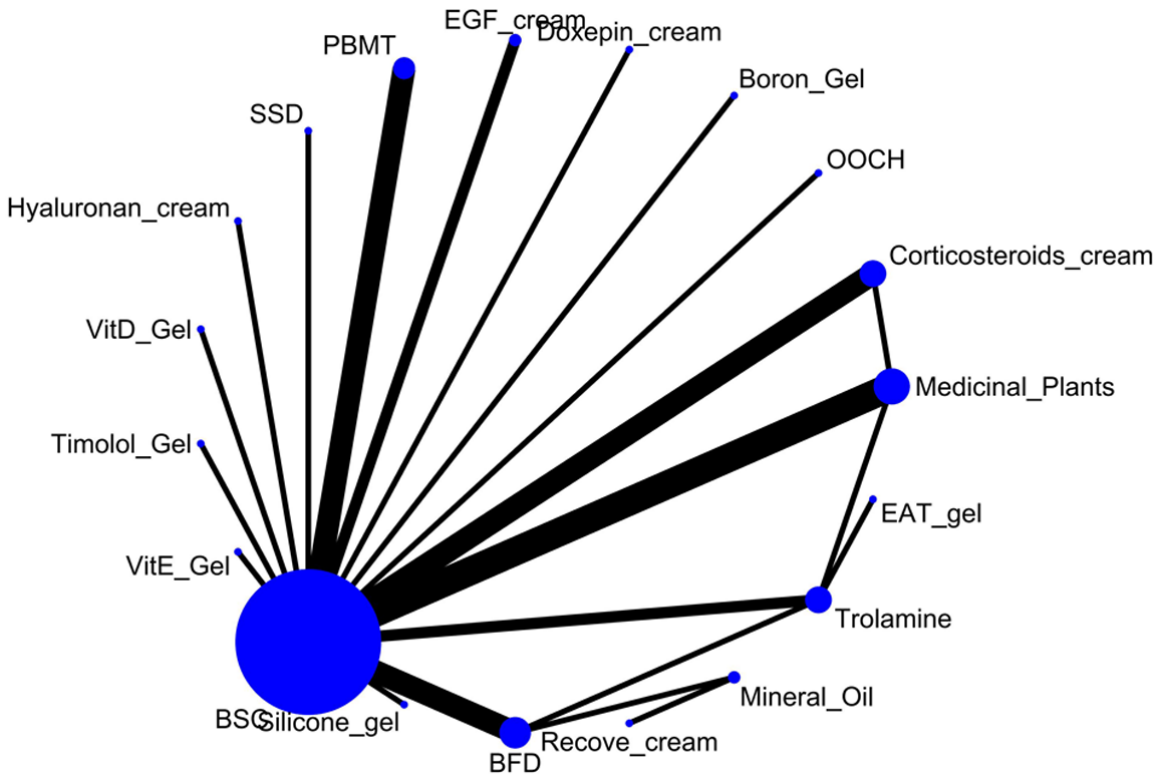


Figure 4. The network plot of included treatments in the Grade 0/1 radiation dermatitis network meta-analysis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

95% CI [1.07, 1.61748812958921e+53]), Boron_Gel (OR = 2346960783629546, 95% CI [0.59, 9.97191853181877e+52]), and BSC (OR = 18145697219621848, 95% CI [4.93, 7.70348826941922e+53]) in preventing ≥ Grade 2 RD (**Figures 7** and **8**). No statistically significant differences were found between Boron_Gel and BFD, while BFD had a better effect than BSC (OR = 0.22, 95% CI [0.15, 0.32]). Compared to BSC, Boron_Gel had a better effect (OR = 0.13, 95% CI [0.04, 0.37]), as shown in **Figure 9**. The probability ranking results for the impact of 19 intervention measures showed that OOCH was the most effective intervention for preventing Grade 2 RD (SUCRA: 95.7%), as shown in **Table 3**.

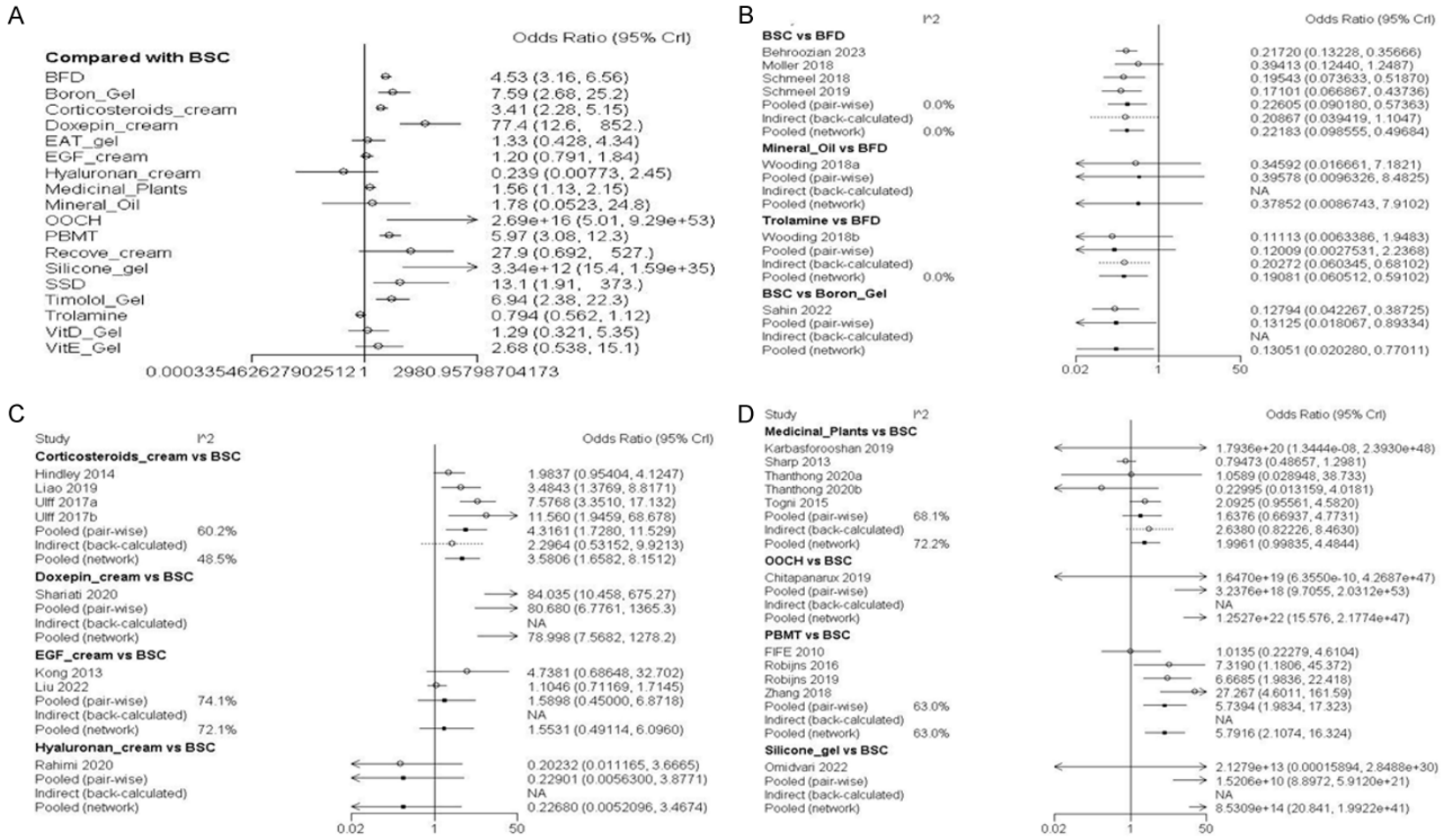
Assessment of publication bias

Publication bias was adjusted utilizing funnel plots, as shown in **Figures 10** and **11**. The funnel plots suggested that there was no evidence of publication bias in this meta-analysis, indicating a balanced distribution of studies irrespective of their results.

Discussion

We comprehensively retrieved relevant studies and compared the effects of 19 intervention measures on RD based on 33 studies. The results revealed that Hyaluronan_cream and Trolamine were the most effective interventions for preventing Grade 0/1 RD, while OOCH and Silicone gel were the optimal interventions for preventing ≥ Grade 2 RD.

Most clinical studies have adopted topical hyaluronic acid cream to inhibit skin irritation and prevent infection. Hyaluronic acid is a natural carbohydrate polymer widely distributed in connective tissues and is a critical element in the extracellular matrix of dermal cells. The meta-analysis conducted by Chieh-Jui Lee et al. showed that hyaluronic acid exhibited a remarkably lower risk ratio in comparison to phytoster-


A
Odds Ratio (95% CrI)
Compared with BSC
BFD 4.53 (3.16, 6.56)
Boron_Gel 7.59 (2.68, 25.2)
Corticosteroids_cream 3.41 (2.28, 5.15)
Doxepin_cream 77.4 (12.6, 852.)
EAT_gel 1.33 (0.428, 4.34)
EGF_cream 1.20 (0.791, 1.84)
Hyaluronan_cream 0.239 (0.00773, 2.45)
Medicinal_Plants 1.56 (1.13, 2.15)
Mineral_Oil 1.78 (0.0523, 24.8)
OOCH 2.69e+16 (5.01, 9.29e+53)
PBMT 5.97 (3.08, 12.3)
Recove_cream 27.9 (0.692, 527.)
Silicone_gel 3.34e+12 (15.4, 1.59e+35)
SSD 13.1 (1.91, 373.)
Timolol_Gel 6.94 (2.38, 22.3)
Trolamine 0.794 (0.562, 1.12)
VitD_Gel 1.29 (0.321, 5.35)
VitE_Gel 2.68 (0.538, 15.1)
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B
I^2
BSC vs BFD
Behroozian 2023 0.21720 (0.13228, 0.35666)
Moller 2018 0.39413 (0.12440, 1.2487)
Schmeel 2018 0.19543 (0.073633, 0.51870)
Schmeel 2019 0.17101 (0.066867, 0.43736)
Pooled (pair-wise) 0.0% 0.22605 (0.090180, 0.57363)
Indirect (back-calculated) 0.20867 (0.039419, 1.1047)
Pooled (network) 0.0% 0.22183 (0.098555, 0.49684)
Mineral_Oil vs BFD
Wooding 2018a 0.34592 (0.016661, 7.1821)
Pooled (pair-wise) 0.39578 (0.0096326, 8.4825)
Indirect (back-calculated) NA
Pooled (network) 0.37852 (0.0086743, 7.9102)
Trolamine vs BFD
Wooding 2018b 0.11113 (0.0063386, 1.9483)
Pooled (pair-wise) 0.12009 (0.0027531, 2.2368)
Indirect (back-calculated) 0.20272 (0.060345, 0.68102)
Pooled (network) 0.0% 0.19081 (0.060512, 0.59102)
BSC vs Boron_Gel
Sahin 2022 0.12794 (0.042267, 0.38725)
Pooled (pair-wise) 0.13125 (0.018067, 0.89334)
Indirect (back-calculated) NA
Pooled (network) 0.13051 (0.020280, 0.77011)
Odds Ratio (95% CrI)
0.02 1 50
C
Study I^2
Odds Ratio (95% CrI)
Corticosteroids_cream vs BSC
Hindley 2014 1.9837 (0.95404, 4.1247)
Liao 2019 3.4843 (1.3769, 8.8171)
Ulff 2017a 7.5768 (3.3510, 17.132)
Ulff 2017b 11.560 (1.9459, 68.678)
Pooled (pair-wise) 60.2% 4.3161 (1.7280, 11.529)
Indirect (back-calculated) 2.2964 (0.53152, 9.9213)
Pooled (network) 48.5% 3.5806 (1.6582, 8.1512)
Doxepin_cream vs BSC
Shariati 2020 84.035 (10.458, 675.27)
Pooled (pair-wise) 80.680 (6.7761, 1365.3)
Indirect (back-calculated) NA
Pooled (network) 78.998 (7.5682, 1278.2)
EGF_cream vs BSC
Kong 2013 4.7381 (0.68648, 32.702)
Liu 2022 1.1046 (0.71169, 1.7145)
Pooled (pair-wise) 74.1% 1.5898 (0.45000, 6.8718)
Indirect (back-calculated) NA
Pooled (network) 72.1% 1.5531 (0.49114, 6.0960)
Hyaluronan_cream vs BSC
Rahimi 2020 0.20232 (0.011165, 3.6665)
Pooled (pair-wise) 0.22901 (0.0056300, 3.8771)
Indirect (back-calculated) NA
Pooled (network) 0.22680 (0.0052096, 3.4674)
0.02 1 50
D
Study I^2
Odds Ratio (95% CrI)
Medicinal_Plants vs BSC
Karbasforooshan 2019 1.7936e+20 (1.3444e-08, 2.3930e+48)
Sharp 2013 0.79473 (0.48657, 1.2981)
Thanthong 2020a 1.0589 (0.028948, 38.733)
Thanthong 2020b 0.22995 (0.013159, 4.0181)
Togni 2015 2.0925 (0.95561, 4.5820)
Pooled (pair-wise) 68.1% 1.6376 (0.66937, 4.7731)
Indirect (back-calculated) 2.6380 (0.82226, 8.4630)
Pooled (network) 72.2% 1.9961 (0.99835, 4.4844)
OOCH vs BSC
Chitapanarux 2019 1.6470e+19 (6.3550e-10, 4.2687e+47)
Pooled (pair-wise) 3.2376e+18 (9.7055, 2.0312e+53)
Indirect (back-calculated) NA
Pooled (network) 1.2527e+22 (15.576, 2.1774e+47)
PBMT vs BSC
FIFE 2010 1.0135 (0.22279, 4.6104)
Robijns 2016 7.3190 (1.1806, 45.372)
Robijns 2019 6.6685 (1.9836, 22.418)
Zhang 2018 27.267 (4.6011, 161.59)
Pooled (pair-wise) 63.0% 5.7394 (1.9834, 17.323)
Indirect (back-calculated) NA
Pooled (network) 63.0% 5.7916 (2.1074, 16.324)
Silicone_gel vs BSC
Omidvari 2022 2.1279e+13 (0.00015894, 2.8488e+30)
Pooled (pair-wise) 1.5206e+10 (8.8972, 5.9120e+21)
Indirect (back-calculated) NA
Pooled (network) 8.5309e+14 (20.841, 1.9922e+41)
0.02 1 50

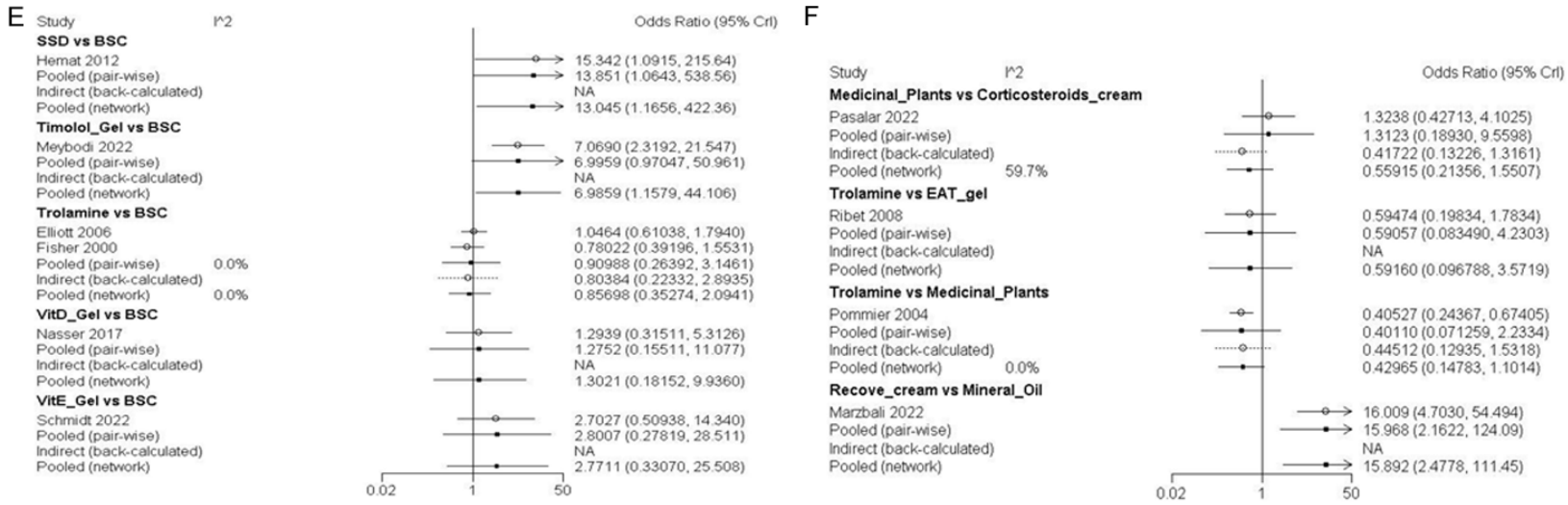


Figure 5. Forest and heterogeneity analysis plot for the network meta-analysis of Grade 0/1 radiation dermatitis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

BFD																		
0.6 (0.17, 1.8)	Boron_Gel																	
4.53 (3.16, 6.56)*	7.59 (2.68, 25.2)*	BSC																
1.33 (0.77, 2.3)	2.23 (0.73, 7.88)	0.29 (0.19, 0.44)*	Corticosteroids_cream															
0.06 (0.01, 0.37)*	0.1 (0.01, 0.87)*	0.01 (0, 0.08)*	0.04 (0, 0.28)*	Doxepin_cream														
3.41 (1, 11.22)	5.76 (1.18, 29.27)*	0.75 (0.23, 2.34)	2.56 (0.74, 8.57)	59.25 (6.62, 801.46)*	EAT_gel													
3.76 (2.16, 6.6)*	6.31 (2.04, 22.45)*	0.83 (0.54, 1.26)	2.83 (1.58, 5.11)*	64.5 (9.92, 736.98)*	1.1 (0.33, 3.87)	EGF_cream												
19.01 (1.8, 598.81)*	33.06 (2.44, 1186.56)*	4.19 (0.41, 129.33)	14.35 (1.34, 452.9)*	354.99 (16.37, 20544.31)*	5.69 (0.41, 207.8)	5.05 (0.47, 158.34)	Hyaluronan_cream											
2.9 (1.79, 4.74)*	4.88 (1.64, 16.78)*	0.64 (0.46, 0.88)*	2.19 (1.34, 3.6)*	49.77 (7.87, 561.99)*	0.85 (0.27, 2.79)	0.77 (0.45, 1.32)	0.15 (0, 1.62)	Medicinal_Plants										
2.54 (0.19, 84.67)	4.41 (0.25, 169.53)	0.56 (0.04, 19.12)	1.92 (0.13, 66.53)	47.6 (1.75, 2986.05)*	0.76 (0.04, 29.78)	0.68 (0.05, 23.65)	0.13 (0, 8.82)	0.88 (0.06, 30.09)	Mineral_Oil									
0 (0, 0.91)*	0 (0, 1.62)	0 (0, 0.2)*	0 (0, 0.69)*	0 (0, 18.08)	0 (0, 0.28)*	0 (0, 0.24)*	0 (0, 0.05)*	0 (0, 0.31)*	0 (0, 0.42)*	OOCH								
0.76 (0.34, 1.62)	1.27 (0.36, 5)	0.17 (0.08, 0.33)*	0.57 (0.25, 1.25)	12.95 (1.81, 156.27)*	0.22 (0.06, 0.86)*	0.2 (0.09, 0.44)*	0.04 (0, 0.45)*	0.26 (0.12, 0.55)*	0.29 (0.01, 4.49)	44983850128465 49 (0.81, 1.63963610639633e+53)	PBMT							
0.16 (0.01, 6.44)	0.28 (0.01, 12.79)	0.04 (0, 1.44)	0.12 (0.01, 4.95)	3 (0.09, 215.5)	0.05 (0, 2.25)	0.04 (0, 1.78)	0.01 (0, 0.65)*	0.06 (0, 2.25)	0.06 (0.02, 0.2)*	10968505361890 37 (0.15, 4.27676198437556e+52)	0.22 (0.01, 9.2)	Recove_cream						
0 (0, 0.3)	0 (0, 0.54)*	0 (0, 0.06)*	0 (0, 0.22)*	0 (0, 6.29)	0 (0, 0.09)*	0 (0, 0.08)*	0 (0, 0.02)*	0 (0, 0.1)*	0 (0, 0.14)*	3891.17 (0, 2.866338426255 75e+43)	0 (0, 0.4)*	0 (0, 2.34)	Silicone_gel					
0.35 (0.01, 2.46)	0.57 (0.02, 5.74)	0.08 (0, 0.52)*	0.26 (0.01, 1.88)	5.71 (0.14, 130.2)	0.1 (0, 1)	0.09 (0, 0.67)*	0.02 (0, 0.4)*	0.12 (0, 0.84)*	0.12 (0, 3.6)	17493600136811 87 (0.27, 6.86561186629527e+52)	0.45 (0.02, 3.65)	1.86 (0.02, 72.99)	213187429848.12 (0.8, 1.0551219401664e+34)	SSD				
0.65 (0.19, 2.03)	1.1 (0.23, 5.44)	0.14 (0.04, 0.42)*	0.49 (0.14, 1.56)	11.22 (1.28, 152.85)*	0.19 (0.04, 0.95)*	0.17 (0.05, 0.55)*	0.03 (0, 0.45)*	0.22 (0.07, 0.69)*	0.25 (0.01, 4.44)	38135689116844 64 (0.68, 1.30755410801596e+53)	0.86 (0.23, 3.15)	3.95 (0.08, 92.47)	460104795278.28 (2.07, 2.1308808869544e+34)*	1.93 (0.19, 63.64)	Timolol_Gel			
5.71 (3.49, 9.42)*	9.59 (3.2, 33.24)*	1.26 (0.89, 1.78)	4.3 (2.55, 7.29)*	97.91 (15.35, 1096.34)*	1.68 (0.57, 5.18)	1.52 (0.88, 2.62)	0.3 (0.01, 3.16)	1.96 (1.35, 2.85)*	2.23 (0.07, 31.99)	33784594217237108 (6.25, 1.16728693181646e+54)*	7.55 (3.56, 16.84)*	35.07 (0.87, 678.84)	4198755041271.29 (19.47, 1.96174332205061e+35)*	16.52 (2.32, 479.07)*	8.76 (2.84, 29.63)*	Trolamine		
3.51 (0.81, 14.84)	5.95 (1, 36.85)	0.77 (0.19, 3.12)	2.64 (0.6, 11.34)	61.2 (5.94, 933)*	1.03 (0.17, 6.36)	0.93 (0.21, 4)	0.18 (0, 2.84)	1.21 (0.28, 5.05)	1.34 (0.03, 27.4)	20903805421692528 (3.73, 7.27998654023815e+53)*	4.65 (0.96, 22.21)	21.23 (0.42, 562.25)	2509350541151.23 (11.12, 1.0940721212977e+35)*	10.57 (0.89, 374.88)	5.4 (0.9, 33.03)	0.61 (0.14, 2.59)	VitD_Gel	
1.69 (0.29, 8.8)	2.86 (0.38, 20.89)	0.37 (0.07, 1.86)	1.27 (0.21, 6.73)	29.52 (2.34, 502.58)*	0.5 (0.06, 3.61)	0.45 (0.08, 2.35)	0.09 (0, 1.53)	0.58 (0.1, 2.99)	0.64 (0.01, 14.67)	98888540829209 40 (1.7, 3.563821668375e+53)*	2.24 (0.35, 13.01)	10.06 (0.18, 298.98)	1211449015764.89 (5.13, 6.26421520216367e+34)*	5.12 (0.36, 192.78)	2.59 (0.34, 18.96)	0.3 (0.05, 1.52)	0.48 (0.05, 4.17)	VitE_Gel
* P < 0.05 OR (95%CI)																		

Figure 6. Effects of different intervention measures on patients with Grade 0/1 radiation dermatitis.

Table 2. Probability of effects of different intervention measures on patients with Grade 0/1 radiation dermatitis

Interventions	Grade 0/1 radiation dermatitis
Hyaluronan_cream	94.9%
Trolamine	89.8%
BSC	82.4%
EGF_cream	75.8%
VitD_Gel	73.8%
EAT_gel	73.3%
Medicinal_Plants	67.8%
Mineral_Oil	66.1%
VitE_Gel	56.2%
Corticosteroids_cream	51.1%
BFD	43.1%
PBMT	36.1%
Timolol_Gel	34.1%
Boron_Gel	32.2%
SSD	27.1%
Recove_cream	23.9%
Doxepin_cream	13.2%
OOCH	4.4%
Silicone_gel	4.4%

BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

ols and vitamin E. Moreover, the study demonstrated that hyaluronic acid was more effective in preventing RD in breast cancer patients and had a lower incidence of desquamation events compared to other topical medications [46]. A double-blind, randomized clinical study also indicated that the use of hyaluronic acid cream significantly reduced the incidence of high-grade RD in patients undergoing radiotherapy for head and neck cancer, breast cancer, or pelvic cancer [47]. A single-masked, randomized Phase III study indicated that the hyaluronic acid emulsion reduced the development of Grade 2 RD following adjuvant breast radiotherapy [48]. In this study, the effects of 19 different intervention measures on RD patients were evaluated. The results showed that Hyaluronan_cream was the most effective intervention in preventing the occurrence of Grade 0 or 1 RD. The possible reason for the effectiveness of Hyaluronan_cream in treating Grade 0 or 1 RD, which manifests as mild erythema and dry desquamation, is that the water content in hydrophilic creams and gels can be quickly absorbed by the skin. Hyaluronan_cream and gels like those containing hyaluronic acid not only provide water but also form a protective film over the skin. This film helps to reduce moisture loss, increase the skin's tolerance to radiation, and alleviate discomfort caused by skin dryness. Hyaluronic acid has the ability to help water penetrate into the intercellular spaces, maintaining cell moisture, and enhancing the skin's healing capabilities. Therefore, Hyaluronan_cream has shown superior preventive effects in the management of RD patients.

Trolamine has long been considered a topical skin radioprotective agent, valued for its good tolerance and effectiveness in moisturizing the skin and alleviating local discomfort. Its properties make it a popular choice for managing and preventing skin issues in association with RD. However, the results of the random-effect meta-analysis conducted by Amanda Gomes de Menêses et al. indicated that there were no significant differences in effectiveness between the trolamine group and the control group (RR = 1.02, 95% CI [0.92-1.14], I^2 = 49%). Trolamine could not effectively prevent RD in patients with breast, head, and neck cancer [49]. The results of a systematic review and meta-analysis conducted by Sakeena Fatima et al. suggested that using Trolamine alone could not significantly prevent the occurrence of RD [50]. An NMA conducted by Yung-Shuo Kao et al. found that Trolamine showed no statistical significance in alleviating RD in patients with head and neck cancer [51]. In our study, Trolamine was found to be effective in preventing Grade 0 or 1 RD, but its effect in preventing RD of ≥ Grade 2 was not satisfactory. In addition, Trolamine is not suggested as an intervention measure for the prevention of RD in a few randomized studies. The limited effectiveness could be attributed to various risk factors, including body size, comorbidities, lifestyle choices, concurrent chemotherapy, and the dose and duration of radiation. In addition, patient's sensitivity to radiation can vary significantly depending on the body part being treated. Given these complexities, more evidence is needed to conclusively determine whether Trolamine can be an effective intervention for preventing RD.

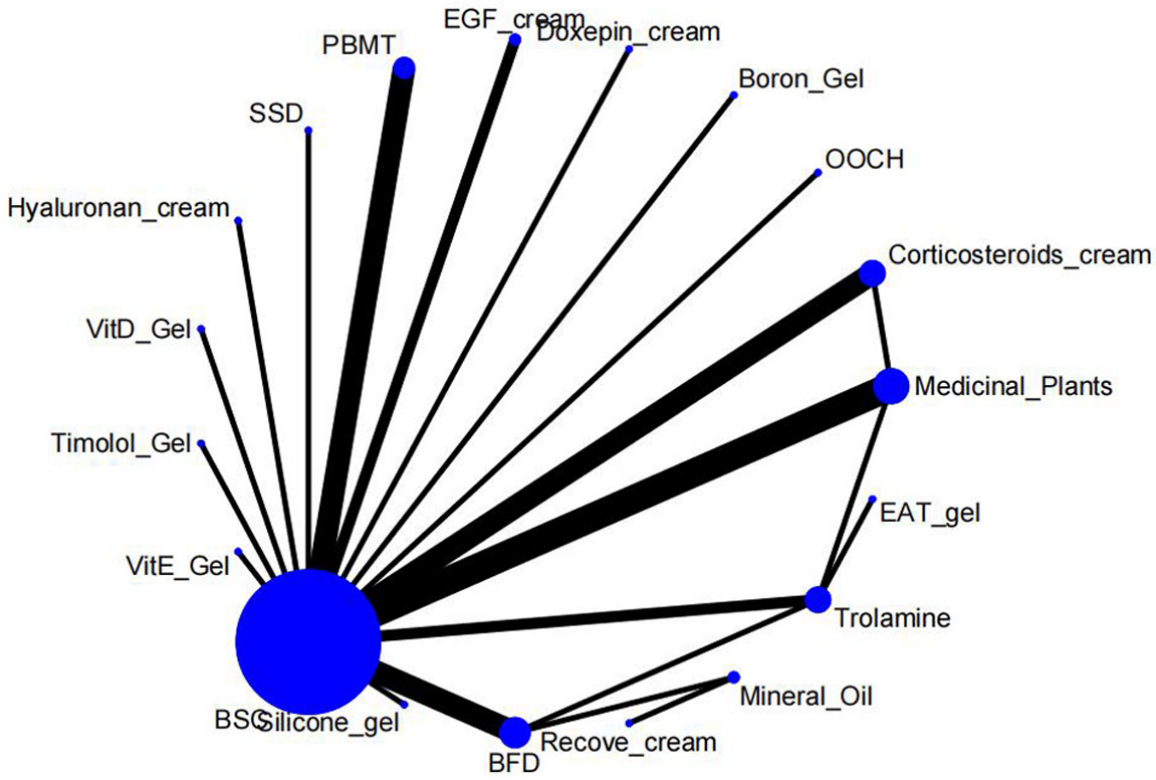
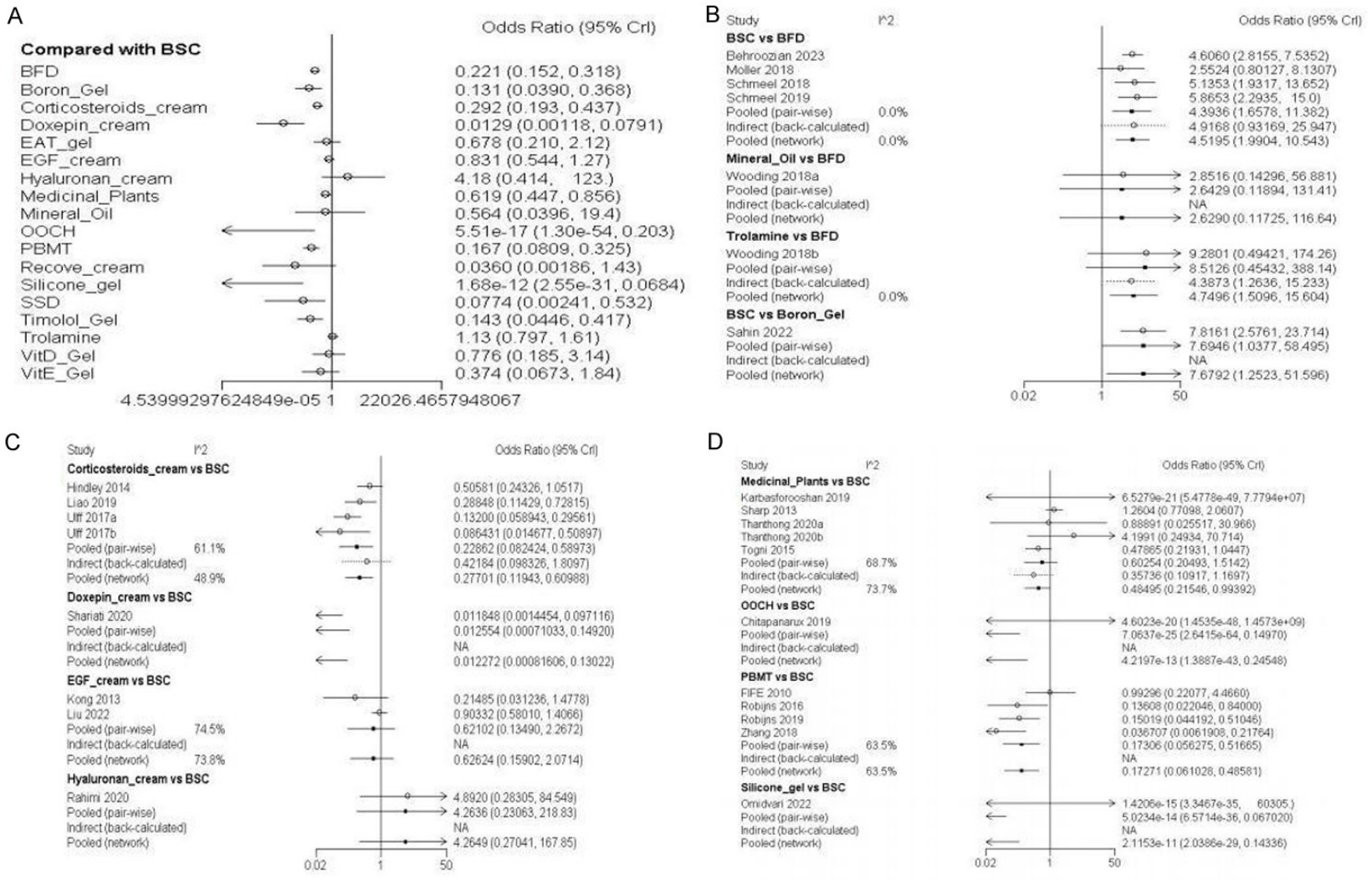


Figure 7. Network plot of included treatments for ≥ Grade 2 radiation dermatitis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

Olive oil is an extensively used treatment regimen. An NMA conducted by Yung-Shuo Kao et al. found that compared to conventional care, olive oil demonstrated better preventive capabilities for localized RD in patients with head and neck cancer (OR = 0.18, 95% CI = 0.03-0.95) [51]. An NMA conducted by Jolien Robijns et al. also found that oral olive oil (RR: 0.66, 95% CI: 0.51-0.85) significantly reduced the incidence of Grade 2 RD in individuals receiving radiotherapy [52]. Our study unveils that OOCH has a better effect in preventing ≥ Grade 2 RD. Olive oil has antioxidant components, including phenolic constituents, squalene, and oleic acid, which may hold promise for treating those suffering from seborrhoeic dermatitis, acne, psoriasis, and atopic dermatitis [53]. Therefore, OOCH may be a potential candidate for preventing RD, but more evidence is needed to prove its effectiveness.

Early evidence suggested that silicone resin film dressings can reduce the severity of radiation-induced acute skin reactions without affecting the rate of moist desquamation [54]. A systematic review and meta-analysis of a randomized, controlled study conducted by Shing Fung Lee et al. indicated that Silicone gel (StrataXRT) effectively prevented Grade 3 acute RD in patients with breast cancer undergoing radiotherapy (OR = 0.05, 95% CI [0.01-0.22]) [55]. Robijns J et al. found that the soft silicone polyurethane film dressing Mepitel Film could significantly reduce the incidence of ≥ Grade 2 acute RD in cancer patients (RR = 0.21, 95% CI [0.05, 0.89]) [56]. A single-masked, randomized study showed that Grade 2 and Grade 3 RD incidence in the StrataXRT treatment group was lower than that in the sorbolene group (80% vs. 91% and 28% vs. 45%, respectively) [57]. In another phase III randomized study with 78 patients, the use of Mepitel that started before radiotherapy and persisted for several weeks after radiotherapy [54] significantly reduced the incidence of moist desquamation compared with the control group (metal film group 0% vs. aqueous cream group 26%).


A
Odds Ratio (95% CrI)
Compared with BSC
BFD 0.221 (0.152, 0.318)
Boron_Gel 0.131 (0.0390, 0.368)
Corticosteroids_cream 0.292 (0.193, 0.437)
Doxepin_cream 0.0129 (0.00118, 0.0791)
EAT_gel 0.678 (0.210, 2.12)
EGF_cream 0.831 (0.544, 1.27)
Hyaluronan_cream 4.18 (0.414, 123.)
Medicinal_Plants 0.619 (0.447, 0.856)
Mineral_Oil 0.564 (0.0396, 19.4)
OOCH 5.51e-17 (1.30e-54, 0.203)
PBMT 0.167 (0.0809, 0.325)
Recove_cream 0.0360 (0.00186, 1.43)
Silicone_gel 1.68e-12 (2.55e-31, 0.0684)
SSD 0.0774 (0.00241, 0.532)
Timolol_Gel 0.143 (0.0446, 0.417)
Trolamine 1.13 (0.797, 1.61)
VitD_Gel 0.776 (0.185, 3.14)
VitE_Gel 0.374 (0.0673, 1.84)
4.539992976248 49e-05 1 22026.4657948067
B
Study I^2
BSC vs BFD
Behroozian 2023 4.6060 (2.8155, 7.5352)
Moller 2018 2.5524 (0.80127, 8.1307)
Schmeel 2018 5.1353 (1.9317, 13.652)
Schmeel 2019 5.8653 (2.2935, 15.0)
Pooled (pair-wise) 0.0% 4.3936 (1.6578, 11.382)
Indirect (back-calculated) 4.9168 (0.93169, 25.947)
Pooled (network) 0.0% 4.5195 (1.9904, 10.543)
Mineral_Oil vs BFD
Wooding 2018a 2.8516 (0.14296, 56.881)
Pooled (pair-wise) 2.6429 (0.11894, 131.41)
Indirect (back-calculated) NA
Pooled (network) 2.6290 (0.11725, 116.64)
Trolamine vs BFD
Wooding 2018b 9.2801 (0.49421, 174.26)
Pooled (pair-wise) 8.5126 (0.45432, 388.14)
Indirect (back-calculated) 4.3873 (1.2636, 15.233)
Pooled (network) 0.0% 4.7496 (1.5096, 15.604)
BSC vs Boron_Gel
Sahin 2022 7.8161 (2.5761, 23.714)
Pooled (pair-wise) 7.6946 (1.0377, 58.495)
Indirect (back-calculated) NA
Pooled (network) 7.6792 (1.2523, 51.596)
Odds Ratio (95% CrI)
0.02 1 50
C
Study I^2
Corticosteroids_cream vs BSC
Hindley 2014 0.50581 (0.24326, 1.0517)
Liao 2019 0.28848 (0.11429, 0.72815)
Uff 2017a 0.13200 (0.058943, 0.29561)
Uff 2017b 0.086431 (0.014677, 0.50897)
Pooled (pair-wise) 61.1% 0.22862 (0.082424, 0.58973)
Indirect (back-calculated) 0.42184 (0.098326, 1.8097)
Pooled (network) 48.9% 0.27701 (0.11943, 0.60988)
Doxepin_cream vs BSC
Shariati 2020 0.011848 (0.0014454, 0.097116)
Pooled (pair-wise) 0.012554 (0.00071033, 0.14920)
Indirect (back-calculated) NA
Pooled (network) 0.012272 (0.00081606, 0.13022)
EGF_cream vs BSC
Kong 2013 0.21485 (0.031236, 1.4778)
Liu 2022 0.90332 (0.58010, 1.4066)
Pooled (pair-wise) 74.5% 0.62102 (0.13490, 2.2672)
Indirect (back-calculated) NA
Pooled (network) 73.8% 0.62624 (0.15902, 2.0714)
Hyaluronan_cream vs BSC
Rahimi 2020 4.8920 (0.28305, 84.549)
Pooled (pair-wise) 4.2636 (0.23063, 218.83)
Indirect (back-calculated) NA
Pooled (network) 4.2649 (0.27041, 167.85)
Odds Ratio (95% CrI)
0.02 1 50
D
Study I^2
Medicinal_Plants vs BSC
Karbasforooshan 2019 6.5279e-21 (5.4778e-49, 7.7794e+07)
Sharp 2013 1.2604 (0.77098, 2.0607)
Thanthong 2020a 0.88891 (0.025517, 30.966)
Thanthong 2020b 4.1991 (0.24934, 70.714)
Togni 2015 0.47865 (0.21931, 1.0447)
Pooled (pair-wise) 68.7% 0.60254 (0.20493, 1.5142)
Indirect (back-calculated) 0.35736 (0.10917, 1.1697)
Pooled (network) 73.7% 0.48495 (0.21546, 0.99392)
OOCH vs BSC
Chitapanarux 2019 4.6023e-20 (1.4535e-48, 1.4573e+09)
Pooled (pair-wise) 7.0637e-25 (2.6415e-64, 0.14970)
Indirect (back-calculated) NA
Pooled (network) 4.2197e-13 (1.3887e-43, 0.24548)
PBMT vs BSC
FIFE 2010 0.99296 (0.22077, 4.4660)
Robijns 2016 0.13608 (0.022046, 0.84000)
Robijns 2019 0.15019 (0.044192, 0.51046)
Zhang 2018 0.036707 (0.0061908, 0.21764)
Pooled (pair-wise) 63.5% 0.17306 (0.056275, 0.51665)
Indirect (back-calculated) NA
Pooled (network) 63.5% 0.17271 (0.061028, 0.48581)
Silicone_gel vs BSC
Omidvari 2022 1.4206e-15 (3.3467e-35, 60305.)
Pooled (pair-wise) 5.0234e-14 (6.5714e-36, 0.067020)
Indirect (back-calculated) NA
Pooled (network) 2.1153e-11 (2.0386e-29, 0.14336)
Odds Ratio (95% CrI)
0.02 1 50

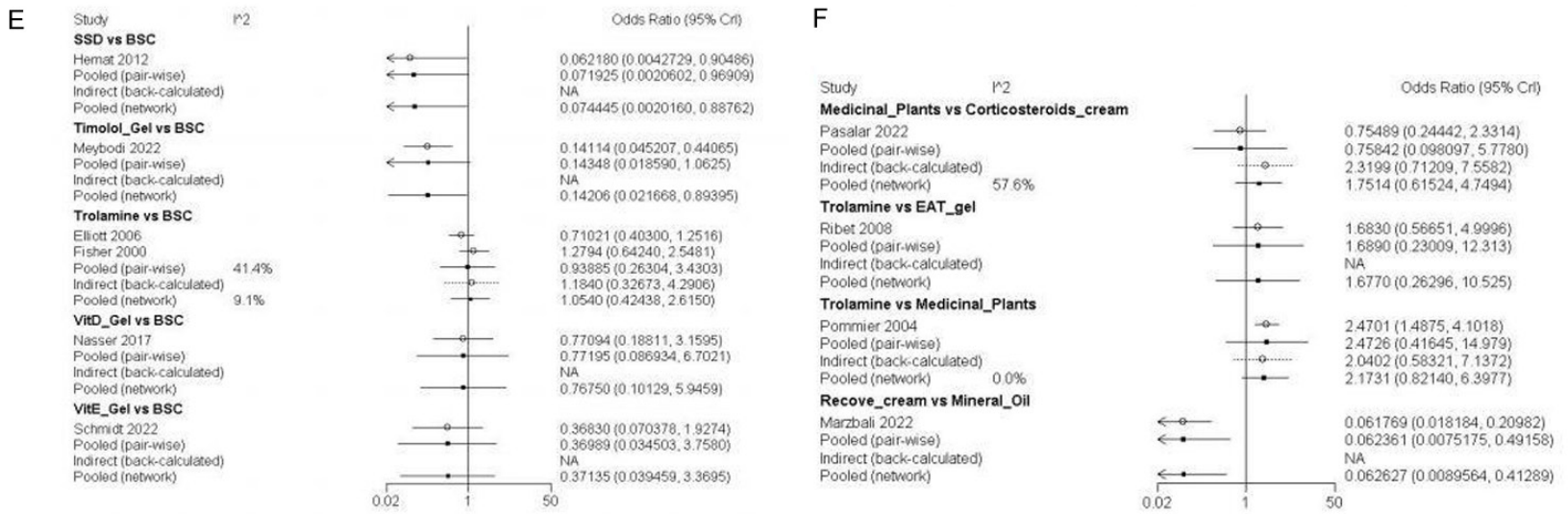


Figure 8. Forest and heterogeneity analysis plot of included treatments for ≥ Grade 2 radiation dermatitis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

BFD																		
1.69 (0.56, 5.96)	Boron_Gel																	
0.22 (0.15, 0.32)*	0.13 (0.04, 0.37)*	BSC																
0.76 (0.44, 1.31)	0.45 (0.13, 1.37)	3.42 (2.29, 5.17)*	Corticosteroids_cream															
17.19 (2.68, 193.8)*	10.15 (1.14, 139.37)*	77.64 (12.65, 849.93)*	22.72 (3.5, 257.53)*	Doxepin_cream														
0.33 (0.1, 1.11)	0.19 (0.04, 0.92)*	1.47 (0.47, 4.76)	0.43 (0.13, 1.48)	0.02 (0, 0.17)*	EAT_gel													
0.27 (0.15, 0.47)*	0.16 (0.04, 0.48)*	1.2 (0.79, 1.84)	0.35 (0.19, 0.63)*	0.02 (0, 0.1)*	0.81 (0.23, 2.76)	EGF_cream												
0.05 (0, 0.55)*	0.03 (0, 0.39)*	0.24 (0.01, 2.42)	0.07 (0, 0.73)*	0 (0, 0.06)*	0.16 (0, 2.15)	0.2 (0.01, 2.1)	Hyaluronan_cream											
0.36 (0.22, 0.58)*	0.21 (0.06, 0.62)*	1.61 (1.17, 2.24)*	0.47 (0.29, 0.77)*	0.02 (0, 0.13)*	1.1 (0.34, 3.45)	1.34 (0.79, 2.29)	6.78 (0.65, 202)	Medicinal_Plants										
0.39 (0.01, 5.39)	0.23 (0.01, 4.03)	1.77 (0.05, 25.25)	0.52 (0.01, 7.57)	0.02 (0, 0.59)*	1.18 (0.03, 21.61)	1.47 (0.04, 21.63)	7.55 (0.11, 509.28)	1.09 (0.03, 15.82)	Mineral_Oil									
4047979559468390 (1.07, 1.61748812958921e+53)*	2346960783629546 (0.59, 9.97191853181877e+52)*	18145697219621848 (4.93, 7.70348826941922e+53)*	5317392878023475 (1.42, 2.19738921487151e+53)*	2191574055557769 (0.05, 8.77333582103519e+51)	12485922318045518 (3.25, 5.42575788095402e+53)*	150061549863162 38 (4.08, 6.3362182422703e+53)*	885640741274114 24 (19.28, 4.10139727341056e+54)*	112558070552869 82 (3.06, 4.91934066487215e+53)*	118677231733522 40 (2.36, 5.07082032744016e+53)*	OOCH								
1.32 (0.61, 2.97)	0.78 (0.2, 2.77)	5.98 (3.08, 12.36)*	1.75 (0.8, 4)	0.08 (0.01, 0.54)*	4.08 (1.06, 15.65)*	4.99 (2.26, 11.49)*	25.4 (2.24, 789.36)*	3.72 (1.76, 8.16)*	3.42 (0.22, 124)	0 (0, 1.25)	PBMT							
6.15 (0.16, 115.75)	3.55 (0.08, 84.72)	27.75 (0.7, 537.91)	8.1 (0.2, 161.75)	0.33 (0, 11.91)	18.68 (0.4, 454.42)	23.08 (0.57, 461.65)	120.77 (1.56, 9660.08)*	17.15 (0.43, 339.87)	15.75 (4.93, 57.42)*	0 (0, 7.02)	4.58 (0.11, 96.91)	Recove_cream						
130145629399.1 (3.24, 8.91760857038065e+29)*	75697103086.57 (1.82, 5.07865522511 82e+29)*	595848188463.25 (14.62, 3.91788497955184e+30)*	175559791664.23 (4.2, 1.14225405179699e+30)*	74356293 23.84 (0.15, 4.72239048577 6e+28)	398106569072.34 (9.38, 2.77125555957726e+30)*	497561495395.76 (12, 3.25070746260862e+30)*	283342760462 9.11 (51.83, 2.04887203235162e+31)*	369874301658.69 (8.95, 2.43935542938562e+30)*	354856977236.59 (6.9, 3.12026177487887e+30)*	0 (0, 7.4648017056 9625e+21)	976890731 02.64 (2.37, 6.72663864422475e+29)*	225955424 33.89 (0.41, 1.93364901422 03e+29)	Silicone_gel					
2.87 (0.4, 92.36)	1.72 (0.17, 62.7)	12.92 (1.88, 415.19)*	3.79 (0.52, 123.4)	0.17 (0.01, 7.9)	9.07 (0.89, 325.41)	10.84 (1.48, 351.61)*	62.74 (2.48, 6616.98)*	8.03 (1.13, 257.46)*	8.49 (0.27, 946.97)	0 (0, 3.8)	2.18 (0.27, 72.52)	0.53 (0.01, 66.94)	0 (0, 1.48)	SSD				
1.55 (0.49, 5.26)	0.92 (0.18, 4.32)	7 (2.4, 22.44)*	2.05 (0.65, 7.04)	0.09 (0.01, 0.79)*	4.78 (0.97, 24.02)	5.83 (1.84, 20.22)*	30.17 (2.25, 1000.33)*	4.35 (1.41, 14.54)*	4.04 (0.23, 161.55)	0 (0, 1.47)	1.17 (0.32, 4.45)	0.26 (0.01, 11.91)	0 (0, 0.5)*	0.53 (0.01, 5.31)	Timolol_Gel			
0.19 (0.12, 0.32)*	0.12 (0.03, 0.34)*	0.88 (0.62, 1.25)	0.26 (0.15, 0.44)*	0.01 (0, 0.07)*	0.6 (0.2, 1.77)	0.73 (0.42, 1.27)	3.7 (0.35, 109.82)	0.55 (0.37, 0.79)*	0.5 (0.03, 17.32)	0 (0, 0.18)*	0.15 (0.07, 0.31)*	0.03 (0, 1.28)	0 (0, 0.06)*	0.07 (0, 0.49)*	0.13 (0.04, 0.39)*	Trolamine		
0.28 (0.07, 1.25)	0.17 (0.03, 0.98)*	1.29 (0.32, 5.39)	0.38 (0.09, 1.67)	0.02 (0, 0.17)*	0.87 (0.14, 5.44)	1.07 (0.25, 4.79)	5.54 (0.36, 206.1)	0.8 (0.19, 3.45)	0.74 (0.04, 31.44)	0 (0, 0.28)*	0.21 (0.04, 1.04)	0.05 (0, 2.33)	0 (0, 0.09)*	0.1 (0, 1.12)	0.18 (0.03, 1.1)	1.46 (0.35, 6.39)	VitD_Gel	
0.59 (0.11, 3.41)	0.35 (0.05, 2.58)	2.67 (0.54, 14.85)	0.78 (0.15, 4.54)	0.03 (0, 0.42)*	1.82 (0.25, 14.11)	2.22 (0.43, 12.95)	11.66 (0.66, 470.41)	1.65 (0.32, 9.48)	1.56 (0.07, 73.38)	0 (0, 0.59)*	0.45 (0.08, 2.8)	0.1 (0, 5.47)	0 (0, 0.2)*	0.2 (0, 2.77)	0.38 (0.05, 2.86)	3.03 (0.59, 17.34)	2.08 (0.24, 18.88)	VitE_Gel
* P < 0.05 OR (95%CI)																		

Figure 9. Effects of different intervention measures on ≥ Grade 2 radiation dermatitis.

Table 3. Probability of effects of different intervention measures on ≥ Grade 2 radiation dermatitis

Interventions	≥ Grade 2 radiation dermatitis
OOCH	95.7%
Silicone_gel	95.4%
Doxepin_cream	86.8%
Recove_cream	76.0%
SSD	72.7%
Boron_Gel	67.9%
Timolol_Gel	66.0%
PBMT	63.8%
BFD	56.9%
Corticosteroids_cream	48.8%
VitE_Gel	43.4%
Mineral_Oil	33.6%
Medicinal_Plants	32.4%
EAT_gel	28.6%
VitD_Gel	25.5%
EGF_cream	23.2%
BSC	16.4%
Trolamine	12.0%
Hyaluronan_cream	4.9%

BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

In this study, Silicone-based gel (StrataXRT) was found to have effectively prevented ≥ Grade 2 RD. This may be attributed to the ability of Silicone-based gel (StrataXRT) to form a protective film over the skin surface. This film creates a slightly moist environment that protects the skin, potentially reducing irritation and promoting the skin's healing process. Further research is necessary to fully assess the effect of Silicone-based gel (StrataXRT) in preventing RD.

The strengths of this study lie in its comprehensive focus on RD across a diverse range of cancer types, encompassing breast cancer, head and neck tumors, rectal cancer, and anal cancer. Furthermore, the inclusion of only high-quality randomized controlled studies strengthens the reliability of the findings. A thorough literature retrieval was also conducted, and rigorous quality assessments were performed to minimize potential biases, further enhancing the study's validity and applicability.

However, the study has its limitations. First, while the quality of all randomized controlled studies was considered reasonable, the sample sizes of some studies are small. Second, differences in tumor types and radiotherapy doses among the included studies may be a significant source of heterogeneity. Third, most comparisons in the NMA were indirect; thus, more head-to-head studies are needed to compare the effects of different treatments directly.

Conclusion

Based on the NMA results, Hyaluronan_cream is the most effective intervention for preventing Grade 0/1 RD caused by radiotherapy, and OOCH has the best effect in preventing ≥ Grade 2 RD. However, due to the limited number of included studies, multi-center randomized controlled studies with larger samples are warranted to validate this study's findings further. Simultaneously, it is essential to improve the evaluation variables to assess the effectiveness of interventions from multiple dimensions.

Disclosure of conflict of interest

None.

Abbreviations

BSC, Best supportive care; BFD, Barrier Films and Dressings; EAT, Eau Thermale Avèn; EGF, Epidermal Growth Factor; OOCH, Olive oil and calcium hydroxide; PBMT, Photobiomodulation therapy; SSD, Silver sulfadiazine.

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References

[1] Rzepecki A, Birnbaum M, Ohri N, Daily J, Fox J, Bodner W, Kabarriti R, Garg M, Mehta K, Kalnicki S and McLellan BN. Characterizing the effects of radiation dermatitis on quality of life:

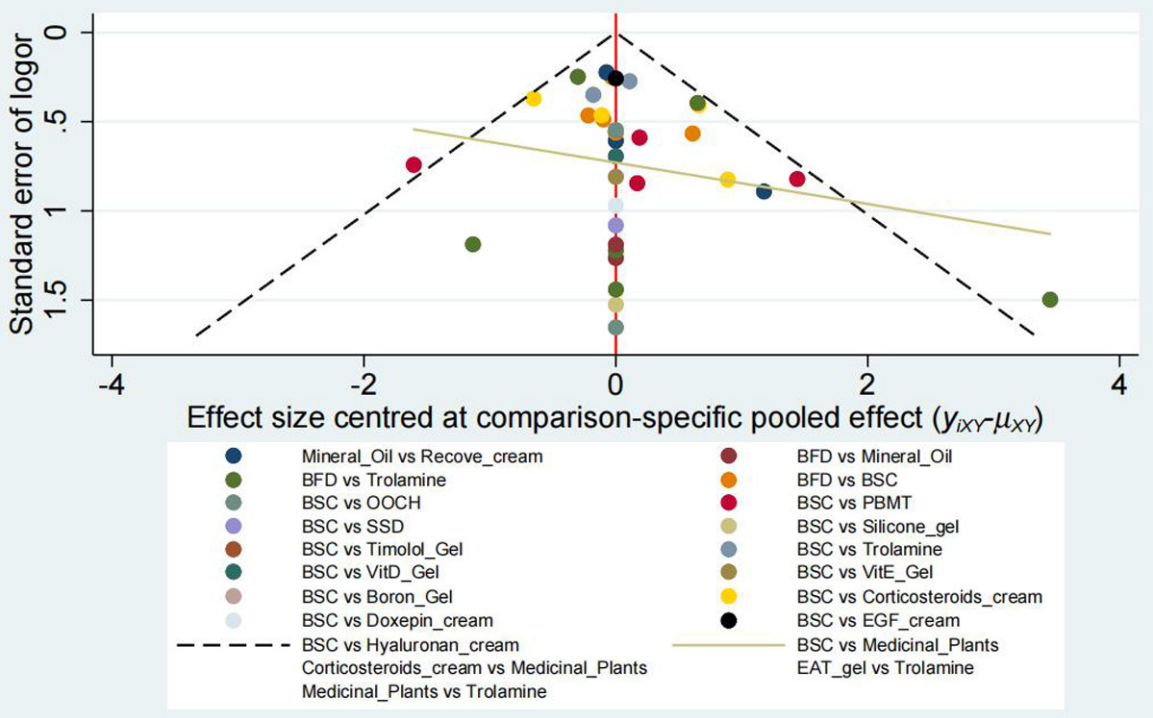

Figure 10. Funnel plot for the Grade 0/1 radiation dermatitis network meta-analysis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

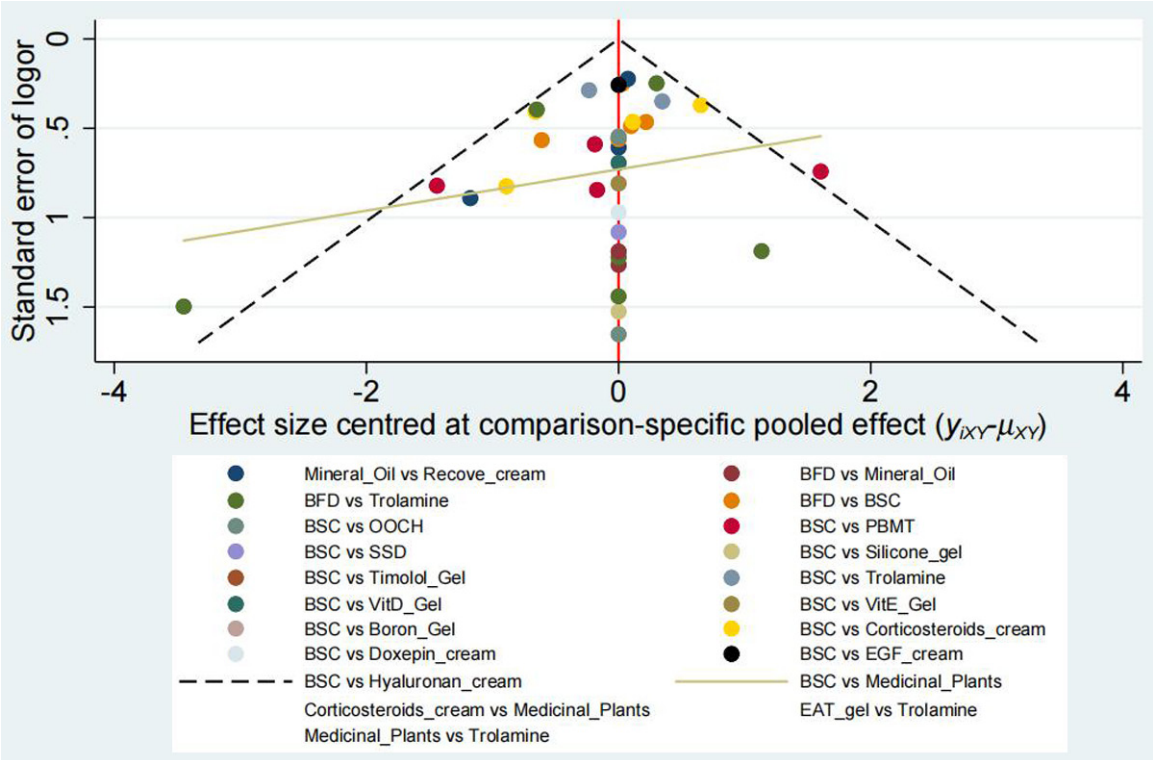

Figure 11. Funnel plot for the network meta-analysis of ≥ Grade 2 radiation dermatitis. BSC: Best supportive care; BFD: Barrier Films and Dressings; EAT: Eau Thermale Avèn; EGF: Epidermal Growth Factor; OOCH: Olive oil and calcium hydroxide; PBMT: Photobiomodulation therapy; SSD: Silver sulfadiazine.

a prospective survey-based study. J Am Acad Dermatol 2022; 86: 161-163.
[2] Ji Z, Jiang Y, Guo F, Peng R, Sun H, Wang P, Fan J and Wang J. Radiation-related adverse effects of CT-guided implantation of (125)I seeds for thoracic recurrent and/or metastatic malignancy. Sci Rep 2019; 9: 14803.
[3] Xie Y, Wang Q, Hu T, Chen R, Wang J, Chang H and Cheng J. Risk factors related to acute radiation dermatitis in breast cancer patients after radiotherapy: a systematic review and meta-analysis. Front Oncol 2021; 11: 738851.
[4] Guangmei D, Weishan H, Wenya L, Fasheng W and Jibing C. Evolution of radiation-induced dermatitis treatment. Clin Transl Oncol 2024; 3: 1-17.
[5] Wilson BN, Shah R, Menzer C, Aleisa A, Sun MD, Kwong BY, Kaffenberger BH, Seminario-Vidal L, Barker CA, Stubblefield MD, Romesser PB, Fabbrocini G, Alam M, Abdulla F, Dulmage B, Sibaud V, Anadkat M, Mazer JM, Parikh D, McLellan B, Cartier H, Pugliese S, Wolkerstorfer A, Laubach HJ, LeBoeuf N, Leventhal J, Wan DC, Choi J, Tran TN, Anderson RR, Markova A and Rossi A. Consensus on the clinical management of chronic radiation dermatitis and radiation fibrosis: a Delphi survey. Br J Dermatol 2022; 187: 1054-1056.
[6] Ma L, Chen Y, Gong Q, Cheng Z, Ran C, Liu K and Shi C. Cold atmospheric plasma alleviates radiation-induced skin injury by suppressing inflammation and promoting repair. Free Radic Biol Med 2023; 204: 184-194.
[7] Salminen A, Kaarniranta K and Kauppinen A. Photoaging: UV radiation-induced inflammation and immunosuppression accelerate the aging process in the skin. Inflamm Res 2022; 71: 817-831.
[8] de Araújo Andrade T, Heimfarth L, Dos Santos DM, Dos Santos MRV, de Albuquerque-Júnior RLC, Dos Santos-Neto AG, de Araujo GRS, Lira AAM, Matos SS, Frank LA, Rabelo TK, Quintans-Júnior LJ, de Souza Siqueira Quintans J, de Souza Araujo AA and Serafini MR. Hesperetin-based hydrogels protect the skin against UV radiation-induced damage. AAPS PharmSciTech 2022; 23: 170.
[9] Wang T, Liao J, Zheng L, Zhou Y, Jin Q and Wu Y. Aloe vera for prevention of radiation-induced dermatitis: a systematic review and cumulative analysis of randomized controlled trials. Front Pharmacol 2022; 13: 976698.
[10] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P and Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021; 88: 105906.
[11] Cox JD, Stetz J and Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys 1995; 31: 1341-1346.
[12] Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L and Sterne JA; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928.
[13] Fisher J, Scott C, Stevens R, Marconi B, Champion L, Freedman GM, Asrari F, Pilepich MV, Gagnon JD and Wong G. Randomized phase III study comparing Best Supportive Care to Biafine as a prophylactic agent for radiation-induced skin toxicity for women undergoing breast irradiation: Radiation Therapy Oncology Group (RTOG) 97-13. Int J Radiat Oncol Biol Phys 2000; 48: 1307-1310.
[14] Pasalar M, Ahadi B, Mirzaei HR, Buentzel J, Mehri Ardestani M, Kamian S and Heydarirad G. Comparing dermolina-henna cream with mometasone cream in improving radiodermatitis among patients with breast cancer: a randomized active-control double-blind clinical trial. J Integr Complement Med 2022; 28: 895-903.
[15] Abbaszade Marzbali N, Zabihi E, Vallard A, Magne N, Moslemi M and Moslemi D. Recove® burn ointment for managing acute radiodermatitis in patients with breast cancer: a double blind randomized controlled trial. Caspian J Intern Med 2022; 13: 349-355.
[16] Togni S, Maramaldi G, Bonetta A, Giacomelli L and Di Pierro F. Clinical evaluation of safety and efficacy of Boswellia-based cream for prevention of adjuvant radiotherapy skin damage in mammary carcinoma: a randomized placebo controlled trial. Eur Rev Med Pharmacol Sci 2015; 19: 1338-1344.
[17] Schmeel LC, Koch D, Schmeel FC, Bücheler B, Leitzen C, Mahlmann B, Kunze D, Heimann M, Brüser D, Abramian AV, Schoroth F, Müdder T, Röhner F, Garbe S, Baumert BG, Schild HH and Wilhelm-Buchstab TM. Hydrofilm polyurethane films reduce radiation dermatitis severity in hypofractionated whole-breast irradiation: an objective, intra-patient randomized dual-center assessment. Polymers (Basel) 2019; 11: 2112.
[18] Shariati L, Amouheidari A, Naji Esfahani H, Abed A, Haghjooy Javanmard S, Laher I, Ghasemi A and Vaseghi G. Protective effects of doxepin cream on radiation dermatitis in breast

cancer: a single arm double-blind randomized clinical trial. Br J Clin Pharmacol 2020; 86: 1875-1881.
[19] Pommier P, Gomez F, Sunyach MP, D'Hombres A, Carrie C and Montbarbon X. Phase III randomized trial of Calendula officinalis compared with trolamine for the prevention of acute dermatitis during irradiation for breast cancer. J Clin Oncol 2004; 22: 1447-1453.
[20] Nasser NJ, Fenig S, Ravid A, Nouriel A, Ozery N, Gardyn S, Koren R and Fenig E. Vitamin D ointment for prevention of radiation dermatitis in breast cancer patients. NPJ Breast Cancer 2017; 3: 10.
[21] Karbasforooshan H, Hosseini S, Elyasi S, Fani Pakdel A and Karimi G. Topical silymarin administration for prevention of acute radiodermatitis in breast cancer patients: a randomized, double-blind, placebo-controlled clinical trial. Phytother Res 2019; 33: 379-386.
[22] Omidvari S, Eskandari Z, Nasrollahi H, Ahmadloo N, Ansari M, Hamedi SH, Khanjani N, Kadkhodaei B, Mosalaei A and Mohammadianpanah M. The investigation of prophylactic effect of StrataXRT gel on radiation-induced dermatitis in breast cancer patients: a randomized clinical trial. Middle East J Cancer 2022; 13: 293-298.
[23] Thanthong S, Nanthong R, Kongwattanakul S, Laebua K, Trirussapanich P, Pitiporn S and Nantajit D. Prophylaxis of radiation-induced dermatitis in patients with breast cancer using herbal creams: a prospective randomized controlled trial. Integr Cancer Ther 2020; 19: 1534735420920714.
[24] Nabi-Meybodi M, Sahebnasagh A, Hakimi Z, Shabani M, Shakeri AA and Saghafi F. Effects of topical timolol for the prevention of radiation-induced dermatitis in breast cancer: a pilot triple-blind, placebo-controlled trial. BMC Cancer 2022; 22: 1079.
[25] Sharp L, Finnilä K, Johansson H, Abrahamsson M, Hatschek T and Bergenmar M. No differences between Calendula cream and aqueous cream in the prevention of acute radiation skin reactions--results from a randomised blinded trial. Eur J Oncol Nurs 2013; 17: 429-435.
[26] Rahimi A, Mohamad O, Albuquerque K, Kim DWN, Chen D, Thomas K, Wooldridge R, Rivers A, Leitch M, Rao R, Haley B, Ahn C, Garwood D and Spangler A. Novel hyaluronan formulation for preventing acute skin reactions in breast during radiotherapy: a randomized clinical trial. Support Care Cancer 2020; 28: 1481-1489.
[27] Ulff E, Maroti M, Serup J, Nilsson M and Falkmer U. Prophylactic treatment with a potent corticosteroid cream ameliorates radiodermatitis, independent of radiation schedule: a randomized double blinded study. Radiother Oncol 2017; 122: 50-53.
[28] Hindley A, Zain Z, Wood L, Whitehead A, Sanneh A, Barber D and Hornsby R. Mometasone furoate cream reduces acute radiation dermatitis in patients receiving breast radiation therapy: results of a randomized trial. Int J Radiat Oncol Biol Phys 2014; 90: 748-755.
[29] Chitapanarux I, Tovanabutra N, Chiewchanvit S, Sripan P, Chumachote A, Nobnop W, Tippanya D and Khamchompoo D. Emulsion of olive oil and calcium hydroxide for the prevention of radiation dermatitis in hypofractionation postmastectomy radiotherapy: a randomized controlled trial. Breast Care (Basel) 2019; 14: 394-400.
[30] Sahin F, Pirouzpanah MB, Bijanpour H, Mohammadzadeh M, Eghdam Zamiri R, Ghasemi Jangjoo A, Nasiri B, Saboori H, Doğan A, Demirci S, Ayşan E, Çağrı Büke A, Naseri AR, Shakouri SK, Aghamohammadi D, Alizade-Harakiyan M and Seyed Nejad F. The preventive effects of boron-based gel on radiation dermatitis in patients being treated for breast cancer: a phase III randomized, double-blind, placebo-controlled clinical trial. Oncol Res Treat 2022; 45: 197-204.
[31] Hemati S, Asnaashari O, Sarvizadeh M, Motlagh BN, Akbari M, Tajvidi M and Gookizadeh A. Topical silver sulfadiazine for the prevention of acute dermatitis during irradiation for breast cancer. Support Care Cancer 2012; 20: 1613-1618.
[32] Kong M and Hong SE. Topical use of recombinant human epidermal growth factor (EGF)-based cream to prevent radiation dermatitis in breast cancer patients: a single-blind randomized preliminary study. Asian Pac J Cancer Prev 2013; 14: 4859-4864.
[33] Queiroz Schmidt FM, Serna González CV, Mattar RC, Lopes LB, Santos MF and Santos VLCG. Topical application of a cream containing nanoparticles with vitamin E for radiodermatitis prevention in women with breast cancer: a randomized, triple-blind, controlled pilot trial. Eur J Oncol Nurs 2022; 61: 102230.
[34] Fife D, Rayhan DJ, Behnam S, Ortiz A, Elkeeb L, Aquino L, Eduardo Roa D, Ramsinghani N, Kuo J, Newcomb R, Zachary CB and Kelly KM. A randomized, controlled, double-blind study of light emitting diode photomodulation for the prevention of radiation dermatitis in patients with breast cancer. Dermatol Surg 2010; 36: 1921-1927.
[35] Robijns J, Censabella S, Claes S, Bussé L, Hellings N, Lambrichts I, Timmermans A, Maes A, Bulens P, Somers V and Mebis J. Photobiomodulation for the prevention of radiodermatitis: preliminary results of a randomized con-

trolled clinical trial in breast cancer patients. Ann Oncol 2016; 27: vi511.
[36] Møller PK, Olling K, Berg M, Habæk I, Haislund B, Iversen AM, Ewertz M, Lorenzen EL and Brink C. Breast cancer patients report reduced sensitivity and pain using a barrier film during radiotherapy - a Danish intra-patient randomized multicentre study. Tech Innov Patient Support Radiat Oncol 2018; 7: 20-25.
[37] Schmeel LC, Koch D, Stumpf S, Leitzen C, Simon B, Schüller H, Vornholt S, Schoroth F, Müdder T, Röhner F, Garbe S, Schmeel FC, Schild HH and Wilhelm-Buchstab TM. Prophylactically applied Hydrofilm polyurethane film dressings reduce radiation dermatitis in adjuvant radiation therapy of breast cancer patients. Acta Oncol 2018; 57: 908-915.
[38] Wooding H, Yan J, Yuan L, Chyou TY, Gao S, Ward I and Herst PM. The effect of Mepitel Film on acute radiation-induced skin reactions in head and neck cancer patients: a feasibility study. Br J Radiol 2018; 91: 20170298.
[39] Robijns J, Censabella S, Claes S, Pannekoeke L, Bussé L, Colson D, Kaminski I, Lodewijckx J, Bulens P, Maes A, Noé L, Brosens M, Timmermans A, Lambrichts I, Somers V and Mebis J. Biophysical skin measurements to evaluate the effectiveness of photobiomodulation therapy in the prevention of acute radiation dermatitis in breast cancer patients. Support Care Cancer 2019; 27: 1245-1254.
[40] Behroozian T, Milton L, Karam I, Zhang L, Ding K, Lou J, Gallant F, Rakovitch E, Tran W, Soliman H, Leung E, Vesprini D, Szumacher E, Chen H, Donovan E, Lam J, Spadafora S, Wronski M, Lavoie C, Walde N, Lam E, Wong G, McKenzie E, Ariello K, Kennedy S, Shariati S, Carothers K, Gonzales G, Kagan Y and Chow E. Mepitel Film for the prevention of acute radiation dermatitis in breast cancer: a randomized multicenter open-label phase III trial. J Clin Oncol 2023; 41: 1250-1264.
[41] Ribet V, Salas S, Levecq JM, Bastit L, Alfonsi M, De Rauglaudre G, Talon B, Allavena C, Miot C, Boisseau JM and Faure P. Interest of a sterilised anti-burning gel in radiation dermatitis: results of a comparative study. Ann Dermatol Venereol 2008; Spec No 1: 5-10.
[42] Liao Y, Feng G, Dai T, Long F, Tang J, Pu Y, Zheng X, Cao S, Xu S and Du X. Randomized, self-controlled, prospective assessment of the efficacy of mometasone furoate local application in reducing acute radiation dermatitis in patients with head and neck squamous cell carcinomas. Medicine (Baltimore) 2019; 98: e18230.
[43] Elliott EA, Wright JR, Swann RS, Nguyen-Tân F, Takita C, Bucci MK, Garden AS, Kim H, Hug EB, Ryu J, Greenberg M, Saxton JP, Ang K and Berk L; Radiation Therapy Oncology Group Trial 99-13. Phase III Trial of an emulsion containing trolamine for the prevention of radiation dermatitis in patients with advanced squamous cell carcinoma of the head and neck: results of Radiation Therapy Oncology Group Trial 99-13. J Clin Oncol 2006; 24: 2092-2097.
[44] Zhang X, Li H, Li Q, Li Y, Li C, Zhu M, Zhao B and Li G. Application of red light phototherapy in the treatment of radioactive dermatitis in patients with head and neck cancer. World J Surg Oncol 2018; 16: 222.
[45] Liu S, Wang YL, Shi ST, Zeng GD, Song YW, Zhang XD, Zheng J, Fan XJ and Liu YP. The effect of recombinant human epidermal growth factor on radiation dermatitis in rectal and anal cancer patients: a self-controlled study. BMC Cancer 2022; 22: 1140.
[46] Lee CJ, Fang HF, Wang CY, Chou KR and Huang TW. Effect of hyaluronic acid on radiodermatitis in patients with breast cancer: a meta-analysis of randomized controlled trials. Support Care Cancer 2022; 30: 3965-3975.
[47] Liguori V, Guillemin C, Pesce GF, Mirimanoff RO and Bernier J. Double-blind, randomized clinical study comparing hyaluronic acid cream to placebo in patients treated with radiotherapy. Radiother Oncol 1997; 42: 155-161.
[48] Pinnix C, Perkins GH, Strom EA, Tereffe W, Woodward W, Oh JL, Arriaga L, Munsell MF, Kelly P, Hoffman KE, Smith BD, Buchholz TA and Yu TK. Topical hyaluronic acid vs. standard of care for the prevention of radiation dermatitis after adjuvant radiotherapy for breast cancer: single-blind randomized phase III clinical trial. Int J Radiat Oncol Biol Phys 2012; 83: 1089-1094.
[49] Menêses AG, Reis PEDD, Guerra ENS, Canto GL and Ferreira EB. Use of trolamine to prevent and treat acute radiation dermatitis: a systematic review and meta-analysis. Rev Lat Am Enfermagem 2018; 26: e2929.
[50] Fatima S, Hirakawa S, Marta GN, Caini S, Beveridge M, Bonomo P, Chow E, van den Hurk C, Ryan Wolf J, Lam H and Behroozian T. Topical non-steroidal agents for the prevention of radiation dermatitis: a systematic review and meta-analysis. Support Care Cancer 2023; 31: 217.
[51] Kao YS, Ma KS, Wu MY, Wu YC, Tu YK and Hung CH. Topical prevention of radiation dermatitis in head and neck cancer patients: a network meta-analysis. In Vivo 2022; 36: 1453-1460.
[52] Robijns J, Becherini C, Caini S, Wolf JR, van den Hurk C, Beveridge M, Lam H, Bonomo P, Chow E and Behroozian T. Natural and miscellaneous agents for the prevention of acute radiation dermatitis: a systematic review and

meta-analysis. Support Care Cancer 2023; 31: 195.

[53] Panahi Y, Rastgar N, Zamani A and Sahebkar A. Comparing the therapeutic effects of aloe vera and olive oil combination cream versus topical betamethasone for atopic dermatitis: a randomized double-blind clinical trial. J Pharmacopuncture 2020; 23: 173-178.

[54] Herst PM, Bennett NC, Sutherland AE, Peszynski RI, Paterson DB and Jasperse ML. Prophylactic use of Mepitel Film prevents radiation-induced moist desquamation in an intra-patient randomised controlled clinical trial of 78 breast cancer patients. Radiother Oncol 2014; 110: 137-143.

[55] Lee SF, Shariati S, Caini S, Wong H, Chan AW, Gojsevic M, Ogita M, Ye JC, Chia D, Chao M, Sung K, Kennedy SKF, Rajeswaran T, van den Hurk C, Wolf JR, Chan RJ, Behroozian T, Bonomo P and Chow E. StrataXRT for the prevention of acute radiation dermatitis in breast cancer: a systematic review and meta-analysis of randomized controlled trials. Support Care Cancer 2023; 31: 515.

[56] Robijns J, Aquilano M, Banerjee S, Caini S, Wolf JR, van den Hurk C, Beveridge M, Lam H, Bonomo P, Chow E and Behroozian T. Barrier films and dressings for the prevention of acute radiation dermatitis: a systematic review and meta-analysis. Support Care Cancer 2023; 31: 219.

[57] Chan RJ, Blades R, Jones L, Downer TR, Peet SC, Button E, Wyld D, McPhail S, Doolan M and Yates P. A single-blind, randomised controlled trial of StrataXRT® - A silicone-based film-forming gel dressing for prophylaxis and management of radiation dermatitis in patients with head and neck cancer. Radiother Oncol 2019; 139: 72-78.

Supplementary File 1: search strategy

Cochrane Library

Search Name:

Date Run: 06/06/2023 16:11:45

Comment:

ID Search Hits

#1 (radiodermatitis):ti,ab,kw OR (Radiodermatitides):ti,ab,kw OR ("Radiation-Induced Dermatitis"):ti,ab,kw OR ("Radiation Induced Dermatitis"):ti,ab,kw OR ("Dermatitis, Radiation-Induced"):ti,ab,kw (Word variations have been searched) 434

#2 ("Dermatitides, Radiation-Induced"):ti,ab,kw OR ("Dermatitis, Radiation Induced"):ti,ab,kw OR ("Radiation-Induced Dermatitides"):ti,ab,kw OR ("Radiation Recall Dermatitis"):ti,ab,kw OR ("Dermatitides, Radiation Recal"):ti,ab,kw (Word variations have been searched) 1

#3 ("Dermatitis, Radiation Recal"):ti,ab,kw OR ("Radiation Recall Dermatitides"):ti,ab,kw OR ("Radiation Recall Reaction"):ti,ab,kw OR ("Radiation Recall Reactions"):ti,ab,kw OR ("Reaction, Radiation Recal"):ti,ab,kw (Word variations have been searched) 0

#4 ("Reactions, Radiation Recall"):ti,ab,kw OR ("Recall Reaction, Radiation"):ti,ab,kw OR ("Recall Reactions, Radiation"):ti,ab,kw (Word variations have been searched) 0

#5 #1 OR #2 OR #3 OR #4 434

#6 (prevention):ti,ab,kw OR (control):ti,ab,kw OR (preventive):ti,ab,kw OR (prophylaxis):ti,ab,kw OR (reduce):ti,ab,kw (Word variations have been searched) 1346970

#7 (precautions):ti,ab,kw OR (prophylactic):ti,ab,kw OR (preventable):ti,ab,kw OR (prevent):ti,ab,kw (Word variations have been searched) 279782

#8 #6 OR #7 1349573

#9 #5 AND #8 377

PubMed

Search number	Query	Results
5	(("Radiodermatitis"[Mesh]) OR ((((((((((((((((((Radiodermatitis[Title/Abstract]) OR (Radiodermatitides[Title/Abstract])) OR (Radiation-Induced Dermatitis[Title/Abstract])) OR (Radiation Induced Dermatitis[Title/Abstract])) OR (Dermatitis, Radiation-Induced[Title/Abstract])) OR (Dermatitides, Radiation-Induced[Title/Abstract])) OR (Dermatitis, Radiation Induced[Title/Abstract])) OR (Radiation-Induced Dermatitides[Title/Abstract])) OR (Radiation Recall Dermatitis[Title/Abstract])) OR (Dermatitides, Radiation Recall[Title/Abstract])) OR (Dermatitis, Radiation Recall[Title/Abstract])) OR (Radiation Recall Dermatitides[Title/Abstract])) OR (Radiation Recall Reaction[Title/Abstract])) OR (Radiation Recall Reactions[Title/Abstract])) OR (Reaction, Radiation Recall[Title/Abstract])) OR (Reactions, Radiation Recall[Title/Abstract])) OR (Recall Reaction, Radiation[Title/Abstract])) OR (Recall Reactions, Radiation[Title/Abstract]))) AND (((((((((prevention[Title/Abstract]) OR (control[Title/Abstract])) OR (preventive[Title/Abstract])) OR (prophylaxis[Title/Abstract])) OR (reduce[Title/Abstract])) OR (precautions[Title/Abstract])) OR (prophylactic[Title/Abstract])) OR (preventable[Title/Abstract])) OR (prevent[Title/Abstract]))	754

4	(((((((((prevention[Title/Abstract]) OR (control[Title/Abstract])) OR (preventive[Title/Abstract])) OR (prophylaxis[Title/Abstract])) OR (reduce[Title/Abstract])) OR (precautions[Title/Abstract])) OR (prophylactic[Title/Abstract])) OR (preventable[Title/Abstract])) OR (prevent[Title/Abstract])	4,896,927
3	("Radiodermatitis"[Mesh]) OR ((((((((((((((((((Radiodermatitis[Title/Abstract]) OR (Radiodermatitides[Title/Abstract])) OR (Radiation-Induced Dermatitis[Title/Abstract])) OR (Radiation Induced Dermatitis[Title/Abstract])) OR (Dermatitis, Radiation-Induced[Title/Abstract])) OR (Dermatitides, Radiation-Induced[Title/Abstract])) OR (Dermatitis, Radiation Induced[Title/Abstract])) OR (Radiation-Induced Dermatitides[Title/Abstract])) OR (Radiation Recall Dermatitis[Title/Abstract])) OR (Dermatitides, Radiation Recall[Title/Abstract])) OR (Dermatitis, Radiation Recall[Title/Abstract])) OR (Radiation Recall Dermatitides[Title/Abstract])) OR (Radiation Recall Reaction[Title/Abstract])) OR (Radiation Recall Reactions[Title/Abstract])) OR (Reaction, Radiation Recall[Title/Abstract])) OR (Reactions, Radiation Recall[Title/Abstract])) OR (Recall Reaction, Radiation[Title/Abstract])) OR (Recall Reactions, Radiation[Title/Abstract]))	3,176
2	((((((((((((((((Radiodermatitis[Title/Abstract]) OR (Radiodermatitides[Title/Abstract])) OR (Radiation-Induced Dermatitis[Title/Abstract])) OR (Radiation Induced Dermatitis[Title/Abstract])) OR (Dermatitis, Radiation-Induced[Title/Abstract])) OR (Dermatitides, Radiation-Induced[Title/Abstract])) OR (Dermatitis, Radiation Induced[Title/Abstract])) OR (Radiation-Induced Dermatitides[Title/Abstract])) OR (Radiation Recall Dermatitis[Title/Abstract])) OR (Dermatitides, Radiation Recall[Title/Abstract])) OR (Dermatitis, Radiation Recall[Title/Abstract])) OR (Radiation Recall Dermatitides[Title/Abstract])) OR (Radiation Recall Reaction[Title/Abstract])) OR (Radiation Recall Reactions[Title/Abstract])) OR (Reaction, Radiation Recall[Title/Abstract])) OR (Reactions, Radiation Recall[Title/Abstract])) OR (Recall Reaction, Radiation[Title/Abstract])) OR (Recall Reactions, Radiation[Title/Abstract])	1,495
1	"Radiodermatitis"[Mesh]	2,574

Embase

No.	Query	Results	Date
#5.	#3 AND #4	2,284	6 Jun 2023
#4.	'prevention'/exp OR 'prevention' OR 'control'/exp OR 'control' OR 'preventive' OR 'prophylaxis'/exp OR 'prophylaxis' OR 'reduce' OR 'precautions' OR 'prophylactic' OR 'preventable' OR 'prevent'	9,334,872	6 Jun 2023
#3.	#1 OR #2	5,623	6 Jun 2023
#2.	'radiodermatitis'/exp OR 'radiodermatitis' OR 'radiodermatitides' OR 'radiation-induced dermatitis' OR 'radiation induced dermatitis' OR 'dermatitis, radiation-induced' OR 'dermatitides, radiation-induced' OR 'dermatitis, radiation induced' OR 'radiation-induced dermatitides' OR 'radiation recall dermatitis'/exp OR 'radiation recall dermatitis' OR 'dermatitides, radiation	5,623	6 Jun 2023

recal' OR 'dermatitis, radiation recall' OR 'radiation recall dermatitides' OR 'radiation recall reaction'/exp OR 'radiation recall reaction' OR 'radiation recall reactions' OR 'reaction, radiation recall' OR 'reactions, radiation recall' OR 'recall reaction, radiation' OR 'recall reactions, radiation'

#1. 'radiodermatitis'/exp OR radiodermatitis 5,418 6 Jun 2023

Web of Science

#	Search details	Results
1	((((((((((((((((TS=(Radiodermatitis)) OR TS=(Radiodermatitides)) OR TS=(Radiation-Induced Dermatitis)) OR TS=(Radiation Induced Dermatitis)) OR TS=(Dermatitis, Radiation-Induced)) OR TS=(Dermatitides, Radiation-Induced)) OR TS=(Dermatitis, Radiation Induced)) OR TS=(Radiation-Induced Dermatitides)) OR TS=(Radiation Recall Dermatitis)) OR TS=(Dermatitides, Radiation Recal)) OR TS=(Dermatitis, Radiation Recall)) OR TS=(Radiation Recall Dermatitides)) OR TS=(Radiation Recall Reaction)) OR TS=(Radiation Recall Reactions)) OR TS=(Reaction, Radiation Recall)) OR TS=(Reactions, Radiation Recall)) OR TS=(Recall Reaction, Radiation)) OR TS=(Recall Reactions, Radiation) and Preprints (excluded - database)	6899
2	((((((((TS=(prevention)) OR TS=(control)) OR TS=(preventive)) OR TS=(prophylaxis)) OR TS=(reduce)) OR TS=(precautions)) OR TS=(prophylactic)) OR TS=(preventable)) OR TS=(prevent) and Preprints (excluded - database)	46645951
3	#1 AND #2 and Preprints (excluded - database)	3383