International Society of Nurses in Cancer Care

EVIDENCE-BASED GUIDELINES FOR THE

Prevention & Management of Radiation Dermatitis

REPORT

2021

International Society for Nurses in Cancer Care

CONTENTS

1. BACKGROUND

Over 50% of patients with cancer should receive radiation therapy at some stage throughout the course of their disease.[1] While high doses of radiation effectively treat patients with cancer with curative or palliative intent, collateral damage to nearby tissues is common, producing localised side-effects such as adverse skin reactions and organ damage, or general side-effects such as gastrointestinal symptoms, or cancer-related fatigue, culminating in reduced quality of life (QoL).[2] These side effects often occur during or after the course of treatment, persisting for a few weeks, months or even years after treatment is complete.[3] It is therefore essential to ensure these side effects are managed in an effective, optimal and evidence-based manner.

Radiation dermatitis (RD) is the most common side-effect of radiation therapy. Approximately 85 to 95% of all cancer patients treated with radiation experience some level of dermatitis at the treated area.[4-6] RD develops 2-3 weeks after the first fraction of radiation therapy commences and can last up to 4 weeks after treatment ends.[5] It is especially commonly experienced by people with breast cancer, head and neck cancer, and sarcoma due to the superficial position of these cancers and higher radiation doses to the skin.[6] There are various degrees of RD experienced by patients, characterised by redness (erythema), peeling, and dry and wet desquamation.[7] In most patients, RD is mild to moderate; however approximately 15 to 25% of patients experience severe reactions.[8] RD severity can be graded using several grading systems including the Common Terminology Criteria for Adverse Events (CTCAE), Radiation Therapy Oncology Group (RTOG) toxicity scoring system and the Radiation Induced Skin Reaction Assessment Scale (RISRAS).[9,10] Acute RD presents as faint erythema and dry desquamation (Mild), tender or bright erythema combined with moist desquamation (Moderate), moist desquamation not confined to skin folds (Severe), and can result in ulceration. Symptomatically, patients may experience tenderness, discomfort, pain or burning in skin surrounding the treated region, which is detrimental to their QoL.[10,11]

RD management seeks to minimise irritants through active treatment with topical preparations and wound dressings.[12] However, there is a lack of standardised, evidence-based approach for the management of RD at present. Consequently, management of RD is inconsistent across radiation treatment centres.[13,14] Recognising the need for clinical consistency and accuracy in treatment for RD, the International Society of Nurses in Cancer Care (ISNCC), in collaboration with an international and interdisciplinary group of experts in radiation oncology, develop evidence-based recommendations in a clinical guideline to inform the management of RD. This project sought to: (1) provide an updated systematic review on the management of radiation-induced skin reactions (RISR)[13], and (2) identify effective topical interventions in the management of RD. These recommendations target patients receiving radiation therapy who experience RD and are tailored towards practitioners in their clinical practice.

2. METHODOLOGY

Objectives

- To update a previous systematic review on prevention and management of radiation-induced skin reactions (RISRs)[13]
- To develop evidence-based clinical guidelines for use of topical interventions in the prevention and management of radiation dermatitis.

Part 1. Literature Review

Eligibility Criteria

A literature search was conducted in April 2020, only including studies that were not included in the earlier publication[13] which concluded its search in November 2012, to provide an overview of the literature on interventions to prevent and manage RISR. Only randomised controlled trials (RCTs) investigating the effects of topical interventions in the management of RD in patients with cancer were included. Studies including the development of RISRs, levels of RISRs, and their symptom severity as primary outcomes were eligible. Secondary outcomes were time taken to develop erythema or dry desquamation; quality of life; time taken to heal; various skin reaction and symptom severity measures; participant satisfaction; ease of use; and adverse effects. Studies were excluded if they evaluated or compared non-topical interventions; reported insufficient data on the effects of the intervention; or were pilot studies, reviews, conference abstracts, retrospective studies, descriptive studies, case reports, or case series.

Search Strategy

Relevant articles were identified from November 2012 up to April 2020 using a search strategy replicated from Chan and colleagues (2014)[13] for the following electronic databases: Cochrane CENTRAL, PubMed (MEDLINE), CINAHL, PsycINFO and EMBASE. After obtaining all references, duplicates were excluded using appropriate software (EndNote, v9.3.1; Thomson Reuters, New York, USA).

Study Selection

Two authors screened all search results (titles and abstracts) for relevance, and those selected by both authors were subject to full-text assessment. Any discrepancies were discussed between both authors and an arbiter. Data extraction was undertaken by one author and checked by a second author. For each included study, the following data were extracted: first author; country and year of publication; population characteristics, including type of cancer and sample size; intervention characteristics, including type of intervention, duration of intervention; and outcome measures.

Risk of Bias in Individual Studies

The Risk of Bias 2 (RoB 2) tool[15] was used to critically appraise the RCTs included in the study. Critical appraisals were independently conducted by two authors. Any discrepancies were discussed between both authors and an arbiter.

Part 2. Evidence-based Guidelines

Evidence to Recommendations

Quality of the evidence for topical interventions were based on the ASCO Resource-Stratified Guidelines for systematic review processes, and formal consensus methodology, and included the ratings for the quality domains (i.e., risk of bias, consistency, directness, and precision).[16] The overall strength of the total body of evidence for each topical intervention was rated by two authors (as high quality, intermediate quality, low quality or insufficient) and best practice statements were drafted. The strength of each statement was rated as the following: strong, moderate, or weak.

Delphi Consensus Process

A three-step modified Delphi method was used to establish consensus (Figure 2).[16] Eighteen (n=18) representatives of radiation oncology, including cancer nurses, radiation oncologists, radiation therapists, clinical researchers and evidence-based practice (EBP) researchers participated as panel members. Three panel members involved in this project declared any conflicts of interest relevant to this project. In the first round of the Delphi, draft best practice statements were distributed to the panel (using fillable PDF forms) via email and they were asked to mark “agree” or “disagree” beside each statement and provide written feedback. Panel members were also asked to rate the strength of statements by selecting “strong”, “moderate”, or “weak”. After the first round, statements were grouped and reduced to those that reached *a priori* consensus (defined as agreement by ≥75% of panel members). In the second round, refined statements were re-distributed to confirm consensus. In the final round, any statements that did not reach consensus in previous rounds were revised based on feedback provided by the panel members.

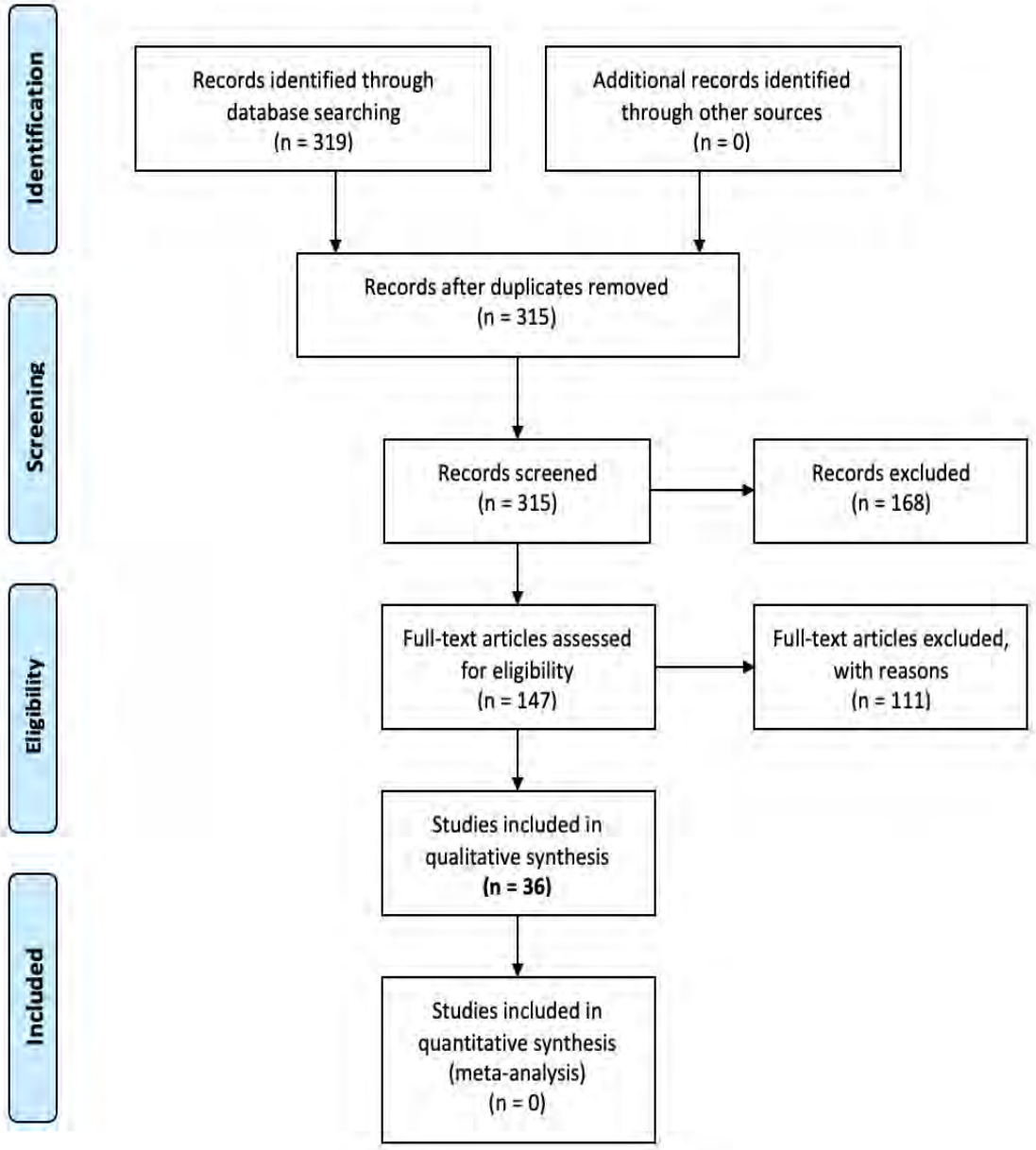

Figure 1 Flow diagram of literature search and selection process (PRISMA)

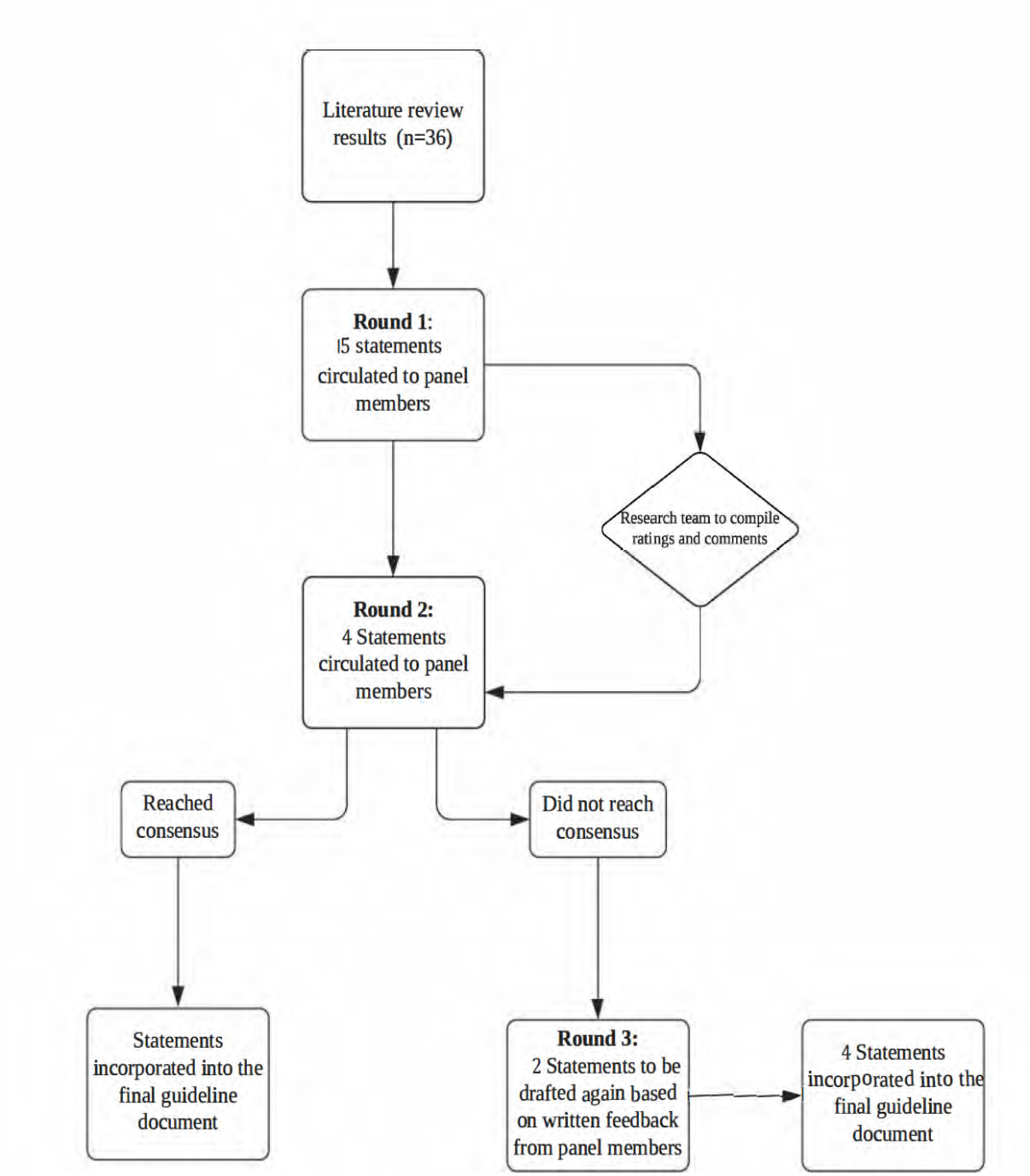

Figure 2 Modified Delphi Methodology

3. RESULTS

Study Selection

In the first phase of study selection, 315 citations were identified from the electronic database searches after removing duplicates. After screening of the titles and abstracts, 147 articles were included for full-text screening in phase two. Of these 147 articles, 36 were included, and 111 were excluded which did not meet the selection criteria.

Risk of Bias

Overall, the risk of bias assessment identified 24 studies with a low risk of bias, while the 12 remaining studies had intermediate or high risk of bias (Appendix C). The domain with the highest rates of high risk of bias were deviations from intended interventions (Domain 2).

Recommendations

Of the 36 included studies, identical topical interventions were grouped accordingly to generate 15 statements for distribution to expert panel members to review (Appendix E). The investigators arrived at recommendations for each intervention based on the availability and quality of the evidence.[16] Panel members supported four statements meeting criteria for agreement consensus (≥75% of panel members) (Appendix F and Appendix G). The panel recommended against topical interventions where there was insufficient evidence to support or refute use. Recommendations were described as weak when there was limited and low-quality evidence. All panel members strongly recommended against the use of aloe vera to manage acute RD. There was moderate confidence that the use of betamethasone 17-valerate cream during radiation therapy to manage acute RD reflected best practice. There was some confidence that the use of silicone-based film forming gel dressing and mometasone furoate cream to manage acute RD offered the next best option in clinical practice.

Steroidal topical ointment/cream

Betamethasone 17-valerate cream

Two trials[17,18] and one systematic review[19] found using Betamethasone 17-valerate significantly reduced the development of acute RD in patients with breast cancer.

Trial recommendation

> Based on previous trials[17-19], betamethasone 17-valerate cream has been found to be effective if applied prophylactically twice daily from the first day of radiation therapy to two weeks after the completion of treatment to prevent and reduce the development of acute RD.

Panel recommendation

The panel makes a moderate recommendation for the use of betamethasone 17-valerate cream during radiation therapy to manage acute RD (High quality of evidence).

Mometasone furoate cream

Three trials[20-22] determined that mometasone furoate cream significantly reduced the incidence of high-grade RD in patients with breast or head and neck cancer. However, one systematic review[23] found that mometasone furoate cream was not superior to placebo.

Trial recommendation

Based on previous trials[20-22], mometasone furoate cream has been found to be effective if applied prophylactically once daily from the first day of radiation therapy to two weeks after the completion of treatment to prevent and reduce the incidence of high-grade RD.

Panel recommendation

The panel makes a weak recommendation for the use of mometasone furoate cream during radiation therapy to treat high-grade RD (Intermediate quality of evidence).

Non-Steroidal ointment/cream

Silicone-based film forming gel dressing

One trial[24] demonstrated that silicone-based film forming gel dressing significantly prevented and delayed the development of Grade 2 and 3 skin toxicity in patients with head and neck cancer.

Pharmaceutical recommendation

Based on a previous trial[24], silicone-based film forming gel dressing has been found to be effective if applied prophylactically twice daily from the first day of radiation therapy to 4 weeks after the completion of treatment to prevent and delay the development of acute RD.

Panel recommendation

The panel makes a weak recommendation for the use of silicone-based film forming gel dressing at the initiation of radiation therapy to prevent and delay the development of acute RD (Intermediate quality of evidence).

Aloe vera

Two trials[25,26] and four previous systematic reviews[27-30] determined that Aloe Vera did not reduce the incidence or severity of RD in patients with breast cancer.

Trial recommendation

Based on previous trials[25,26], aloe vera has not been found to be effective in reducing the incidence or severity of RD.

Panel recommendation

The panel makes a strong recommendation against the use of aloe vera to manage RD (Intermediate quality of evidence).

3. DISCUSSION

The review of the evidence indicates that ongoing research in the prevention and treatment of RD is still required. However, after reviewing the evidence, panel members have recommended three topical interventions for the management of RD (betamethasone 17-valerate cream, mometasone furoate cream and silicone-based film forming gel dressing). Panel members also provided clinical considerations when applying these interventions in practice (Table 1). There were no clinical considerations provided for the use of aloe vera as there is sufficient evidence to refute its use. Topical steroid creams (betamethasone 17-valerate cream and mometasone furoate cream) should be used with utmost caution as panel members have advised that they should not be applied on irritated skin as it can cause a stinging or burning sensation in patients. Furthermore, the panel has advised that topical steroid creams should be ceased once the skin becomes disrupted to avoid any further damage to the skin barrier. Despite the effectiveness of silicone-based form gel dressing, panel members have advised that cancer practitioners should consider the cost-effectiveness in terms of the hospital or patient. Furthermore, unlike other dressings, panel members have advised that silicone-based film-forming gel dressing does not need to be removed prior to each fraction of radiation therapy. Cancer practitioners are encouraged to discuss these management options with each patient and use an individualised approach to determine which topical agent provides the greatest symptomatic relief and is most preferred.

4. CONCLUSION

Recommendations in this guideline provide support to cancer practitioners in their clinical practice to facilitate better supportive cancer care for patients receiving radiation therapy. It is important that topical interventions for the management of RD are continually evaluated to provide optimal patient care. Future studies should include patient-reported experiences and outcome measures to provide further guidance for practitioners.

Table 1. Final recommendations made by the panel through consensus

Recommendations	Strength of recommendation	Agree	Disagree	Clinical considerations recommended by the panel
Aloe Vera is not recommended for patients to manage acute radiation dermatitis.	Strong	17 (94%)	1 (6%)	Not applicable
Betamethasone 17-valerate cream may be recommended for patients during radiation therapy to manage acute radiation dermatitis.	Moderate	16 (89%)	2 (11%)	• Patients should not apply topical steroid cream on the irradiated area during radiation therapy to avoid extra skin dose which may worsen the skin reaction. • Any topical steroid cream should be ceased once the skin becomes disrupted and not intact. • Avoid applying on areas with thin skin e.g., face, axilla, groin.
Mometasone furoate cream may be recommended for patients during radiation therapy to treat high-grade radiation dermatitis.	Weak	16 (89%	2 (11%)	• Avoid applying on irritated skin as it may cause stinging. • Fluorinated topical corticosteroids (such as mometasone furoate) may be associated with other side effects including cutaneous atrophy, telangiectasia formation, and periorificial dermatitis.
Silicone-based film forming gel dressing may be recommended for patients at the initiation of radiation therapy to manage acute radiation dermatitis.	Weak	17 (94%)	1 (6%)	• Regarding the silicone gel preparation: the gel is different to other dressings and does not require removal before radiation treatment. • Practitioners should consider the payer's (hospital or patient) ability to afford the costs of the silicone-based film forming gel dressing.

Table 2. ISNCC radiation dermatitis prevention and management recommendations

Topical interventions	Recommendation	Not recommended	Insufficient evidence to support or refute	Type of recommendation	Strength of recommendation
Atorvastatin 1%			✓	N/A	N/A
Betamethasone 17-valerate cream	✓			Evidence-based	Moderate
Hydrocortisone cream			✓	N/A	N/A
Mometasone furoate cream	✓			Evidence-based	Weak
Aloe Vera		✓		Evidence-based	Strong
Doxepin cream			✓	N/A	N/A
Heparinoid moisturiser			✓	N/A	N/A
Topical lactokine-based R1 and R2			✓	N/A	N/A
Silicone-based film forming gel dressing	✓			Evidence-based	Weak
Silver sulfadiazine cream			✓	N/A	N/A
Silymarin-based cream			✓	N/A	N/A
3M Cavilon no-string barrier film			✓	N/A	N/A
Mepilex Lite dressings			✓	N/A	N/A
Mepitel film			✓	N/A	N/A
Silver Nylon dressing			✓	N/A	N/A

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6. APPENDICES

Appendix A. Expert Stakeholder Group

	Panel member	Discipline	Country	Declaration of conflict of interest
1	Ms Andi Agbejule	Radiation Therapist	Australia	No conflict of interest declared
2	Dr Cathy Hargrave	Radiation Therapist	Australia	*CH is currently the principal investigator of an RCT investigating the efficacy of StrataXRT gel to manage RD. This RCT receives partial funding from Stratpharma AG.
3	Dr David Chia	Radiation Oncologist	Singapore	*DC serves on the advisory board for Janssen (J&J), Astellas, Astra Zaneca. *DC owns shares/equity in Pfizer, ISRG, Merck, GSK, Beckton-Dickinson, AbbVie, Abbott at various times.
4	Dr Francis James	Radiation Oncologist	India	No conflict of interest declared
5	Ms Fumiko Schwarz	Oncology Nurse (Medical)	Japan	No conflict of interest declared
6	Ms Gu Fen	Oncology Nurse	China	No conflict of interest declared
7	Dr Jeanne Erikson	Clinical/EBP* Researchers	USA	No conflict of interest declared
8	Dr Jonathon Teh	Radiation Oncologist	Singapore	No conflict of interest declared
9	Ms Karen Benstead	Radiation Oncology NUM	Australia	No conflict of interest declared
10	Dr Lorraine Drapek	Nurse Practitioner	USA	No conflict of interest declared
11	Mr Omare Solomon	Oncology Nurse	Kenya	No conflict of interest declared
12	Dr Pauline Rose	Radiation Oncology Clinical Nurse Consultant	Australia	No conflict of interest declared
13	Dr Saxon Smith	Onco-Dermatologist	Australia	No conflict of interest declared

14	Dr Shiow-Ching Shun	Clinical/EBP* Researchers	Taiwan	No conflict of interest declared
15	Ms Suzanne Mak	Nurse consultant (Oncology)	Hong Kong	No conflict of interest declared
16	Dr Tracy Gosselin	Senior Administrators/professionals responsible for procurement	USA	*TG has recent experience with the Oncology Nursing Society (ONS) team on a paper related to radiation skin reactions.
17	Dr Vinante Lorenzo	Radiation Oncologist (Medical)	Italy	No conflict of interest declared
18	Ms Vina Vallabh	Radiotherapy Clinical Nurse Specialist	UK	No conflict of interest declared

Note. All panel members made declarations of interest in line with the conflict-of-interest policy; *and relevant to this clinical guideline project.

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Appendix B. Evidence to Recommendations (Quality Domains)

Intervention	Summary of evidence (Click here for data extraction table)	Quality assessment (based on ASCO guidelines)				Quality of evidence	Rationale
1. Steroidal topical ointment/cream		**Risk of bias (ROB)** *Low, Intermediate, High*	**Consistency** *Consistent, Minor inconsistencies, Inconsistent*	**Directness** *Direct, Somewhat direct, Indirect*	**Precision** *Precise, Somewhat precise, Imprecise*	*High, Intermediate, Low, Insufficient*	
1.1 Mometasone furoate cream (MMF) Hindley 2014 Ho 2018 Liao 2019 **Previous Systematic Review (SR):** Miller 2011	Three trials (n=124, n=120, n=24) found MMF cream significantly reduced acute radiation dermatitis in patients with cancer. Two trials were conducted in patients with breast cancer whereas one trial looked at patients with head & neck cancer. One previous systematic review found that MMF cream was not superior to placebo.	Intermediate	Minor inconsistencies (effect size could not be calculated for 1 study)	Direct	Somewhat precise (1 study has a wide CI)	Intermediate	Quality of evidence is reduced due to intermediate ROB in terms of study design, minor inconsistencies, and varied precision across studies.
1.2 Betamethasone 17-valerate cream Ulff 2017 Ulff 2013 **Previous SR:** Omidvari 2007	Two trials (n=202, n=102) and one previous systematic review found using Betamethasone 17-valerate significantly reduced the development of radiation dermatitis	Low	Consistent	Direct	Precise	High	No concerns regarding quality assessments.

	in patients with breast cancer.						
1.3 Topical atorvastatin 1% Ghasemi 2019	One trial (n=70) found that topical atorvastatin significantly reduced itching, breast oedema, and pain in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.
1.4 1% hydrocortisone cream Meghrajani 2016	One trial (n=50) found hydrocortisone cream significantly delayed the onset of radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.
2. Non-steroidal ointment/cream							
2.1 Cavilon Durable Barrier Cream Laffin 2015	One trial (n=255) found Cavilon Durable Barrier Cream significantly reduced moist desquamation and skin toxicities in patients with breast cancer.	Intermediate	Cannot be determined (only 1 study)	Direct	Cannot be determined (no CIs)	Low	Quality of evidence is reduced due to intermediate ROB in terms of study design, there is only one study and no CIs are provided. Further research may better inform the topic.
2.2 A silicone-based film forming gel dressing (StrataXRT) Chan 2019	One trial (n=197) found StrataXRT significantly delayed the development of grade 2 and 3 skin toxicity in patients with head & neck cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.

2.3 Boswellia cream Togni 2015	One trial (n=114) found Boswellia cream significantly reduced erythema in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Imprecise	Low	Quality of evidence is reduced as there is only one study and the results are imprecise. Further research may better inform the topic.
2.4 Topical silver sulfadiazine cream Hemati 2012	One trial (n=110) found topical silver sulfadiazine cream significantly reduced the severity of radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.
2.5 Silymarin-based cream Karbasforooshan 2019	One trial (n=101) found Silymarin-based cream significantly reduced the severity of radiation dermatitis in patients with breast cancer.	Intermediate	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.
2.6 Topical lactokine-based R1 and R2 Manas 2014	One trial (n=98) found topical R1 and R2 significantly reduced the severity of radiation dermatitis in patients with breast and head & neck cancer.	Intermediate	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced due to intermediate ROB in terms of study design and there is only one study. Further research may better inform the topic.
2.7 Heparinoid moisturiser Sekiguchi 2018 Sekiguchi 2015	Two trials (n=48, n=62) found Heparinoid moisturiser significantly reduced skin desquamation and acute radiation	Low	Consistent	Somewhat direct (primary outcomes are different in both studies)	Imprecise	Intermediate	Quality of evidence is reduced due to different primary outcomes and imprecise results.

	dermatitis in patients with breast cancer.						
2.8 Aloe Vera Ahmadloo 2017 Hoopfer 2015 **Previous SR:** Merchant 2007 Heggie 2002 Olsen 2001 Williams 1996	Two trials (n=237, n=100) and four previous systematic reviews found Aloe Vera did not reduce the incidence and severity of radiation dermatitis in patients with breast cancer.	Low	Consistent	Direct	Somewhat imprecise (1 study has a wide CI)	Intermediate	Quality of evidence is reduced as precision varies across both studies.
2.9 Hyaluronic serum Pinnix 2012 **Previous SR:** Kirova 2011 Leonardi 2008 Primavera 2006 Liguori 1997	One trial (n=74) and two previous systematic reviews showed that Hyaluronic serum was not beneficial for prophylaxis of radiation-induced skin toxicity in patients with breast cancer. However, two other systematic reviews showed that Hyaluronic serum was beneficial in terms of RISR severity and maximum RISR.	Low	Inconsistent (3 studies show no benefits and 2 studies show benefits)	Direct	Imprecise	Low	There are conflicting results across available studies. Further research may better inform the topic.
2.10 Natural oil-based emulsion containing Allantoin (MooGoo Udder cream) Chan 2014	One trial (n=174) showed that MooGoo Udder cream has similar effects for managing skin toxicity compared with aqueous cream in patients with lung,	Low	Cannot be determined (only 1 study)	Direct	Cannot be determined (no CIs)	Low	There is only one study and no CIs are provided. Further research may better inform the topic.

	breast or head & neck cancer. Aqueous cream was the more preferred option.						
2.11 Calendula offinalis Schneider 2015	One trial (n=51) found that Calendula offinalis may be effective in managing radiation dermatitis in patients with cancer.	Low	Cannot be determined (only 1 study)	Direct	Imprecise	Low	Quality of evidence is reduced as the results are imprecise. Further research may better inform the topic.
2.12 Alpha ointment Ansari 2013	One trial (n=60) found Alpha ointment significantly reduced the severity of radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Imprecise	Low	Quality of evidence is reduced as there is only one study and the results are imprecise. Further research may better inform the topic.
2.13 Doxepin cream Shariati 2020	One trial (n=48) found that Doxepin cream significantly reduced the incidence of grade 2 or higher radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.
2.14 Melatonin containing emulsion Ben-David 2016	One trial (n=47) found that Melatonin containing emulsion significantly reduced radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Imprecise	Low	Quality of evidence is reduced as there is only one study and the results are imprecise. Further research may better inform the topic.
2.15 Trolamine cream Abbas 2011	One trial (n=30) found that Trolamine cream significantly reduced acute	Low	Inconsistent (different results to previous studies)	Direct	Imprecise	Low	There are conflicting results across available studies. Further research may better inform the topic.

Previous SR: Zhang 2011 Gosselin 2010 Ribet 2008 Elliott 2006 Pommier 2004 Fisher 2000	radiation dermatitis in patients with head & neck cancer. However, four previous systematic reviews showed that Trolamine may not be beneficial (not significant). Two other systematic reviews showed that patient satisfaction was significant.						
2.16 Topical regenerating agent (RGTA) Tao 2017	One trial (n=76) found that topical OTD70DERM did not reduce the incidence and severity of radiation dermatitis in patients with head & neck cancer.	Intermediate	Cannot be determined (only 1 study)	Direct	Imprecise	Low	Quality of evidence is reduced due to intermediate ROB in terms of study design, there is only one study and the results are imprecise. Further research may better inform the topic.
3. Dressings							
3.1 Mepitel film Yan 2020 Moller 2018 Herst 2014	Three trials (n=101, n=80, n=57) found that Mepitel film significantly reduced radiation dermatitis in patients with cancer. Different populations were looked at across studies (different cancers). Furthermore, one of these trials (n=57) found that Mepitel film was	High	Minor inconsistencies (patients did not tolerate in 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced due to high ROB in terms of study design and minor inconsistencies across studies.

	unsatisfactory tolerated by patients.						
3.2 3M Cavilon no-string barrier film Lam 2019 Shaw 2015	Two trials (n=55, n=39) found that Barrier film significantly reduced radiation dermatitis in patients with breast cancer.	Low	Consistent	Direct	Somewhat precise (one study has a wide CI)	Intermediate	Quality of evidence is reduced as the results are imprecise for one study.
3.3 Mepilex Lite dressings Zhong 2013 **Previous SR:** Paterson 2012	One trial (n=88) found that Mepilex Lite dressings significantly reduced time-to-wound healing in patients with nasopharyngeal carcinoma. One other previous study found that Mepilex Lite reduced the overall severity of skin reactions and the average moist desquamation score.	Low	Consistent	Somewhat direct (primary outcomes are different in current and previous studies)	Imprecise	Intermediate	Quality of evidence is reduced as the results are imprecise. Further research may better inform the topic.
3.4 Hydrofilm polyurethane film dressings Schmeel 2018	One trial (n=62) found Hydrofilm polyurethane film dressings significantly reduced radiation dermatitis in patients with breast cancer.	High	Cannot be determined (only 1 study)	Direct	Precise	Low	Quality of evidence is reduced due to high ROB in terms of study design and there is only one study. Further research may better inform the topic.
3.5 Silver Nylon dressing Niazi 2012	One trial (n=40) found Silver Nylon dressing significantly reduced radiation dermatitis in patients	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.

	with anal/advanced rectal cancer.						
4. Other interventions							
4.1 Hydrosorb spray Bazire 2015	One trial (n=278) found that there was no significant difference between Hydrosorb spray and simple water spray in treating radiation dermatitis in patients with breast cancer.	Low	Cannot be determined (only 1 study)	Direct	Precise	Intermediate	Quality of evidence is reduced as there is only one study. Further research may better inform the topic.

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Appendix C. Risk of Bias Assessment

References	Overall risk of bias
1. Ulff 2017	LOW
2. Ghasemi 2019	LOW
3. Liao 2019	INTERMEDIATE
4. Meghrajani 2016	LOW
5. Hindley 2014	LOW
6. Ulff 2013	LOW
7. Ho 2018	INTERMEDIATE
8. Abbas 2011	LOW
9. Hemati 2012	LOW
10. Graham 2013	INTERMEDIATE
11. Ansari 2013	LOW
12. Ahmadloo 2017	LOW
13. Schneider 2015	LOW
14. Togni 2015	LOW
15. Hoopfer 2015	LOW
16. Tao 2017	INTERMEDIATE
17. Pinnix 2012	LOW
18. Manas 2014	INTERMEDIATE
19. Sekiguchi 2015	LOW
20. Sekiguchi 2018	LOW
21. Shariati 2020	LOW
22. Chan 2019	LOW
23. Karbasforooshan 2019	INTERMEDIATE
24. Laffin 2015	INTERMEDIATE
25. Chan 2014	LOW
26. Zhong 2013	LOW
27. Herst 2014	HIGH
28. Moller 2018	INTERMEDIATE
29. Schmeel 2018	HIGH
30. Rades 2019	INTERMEDIATE
31. Shaw 2015	LOW
32. Niazi 2012	LOW
33. Yan 2020	HIGH
34. Bazire 2015	LOW
35. Ben-David 2016	LOW
36. Lam 2019	LOW

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Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ulff 2017	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ghasemi 2019	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Liao 2019	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Unclear-baseline characteristics were not compared across groups
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measured in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-19 patients who withdrew from the study was not included in analysis.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Meghrajani 2016	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- it is mentioned in text that the two groups were well balanced with regards to patient characteristics.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, High*	LOW
Quality Criterion	**Rating**

	Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant
Hindley 2014	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes-8 participants missed 1 or more assessment visits.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ulff 2013	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value provided for comparison between intervention groups but appears to be similar.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ho 2018	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-19 participants dropped out
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Abbas 2011	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Unclear-does not specify whether assessors were blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Hemati 2012	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially- due to the smell and colour of the SSD cream, the assessors were not able to be blinded.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Graham 2013	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value but appears to be similar across treatment groups
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-data for 15 patients was not available
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ansari 2013	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Unclear-not specified whether assessors were blinded or not
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ahmadloo 2017	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no baseline characteristics compared between groups
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	No-participants were aware of their assigned intervention and not specified whether assessors were blinded.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Schneider 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Partially- small sample size
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-No baseline characteristics were compared across groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Togni 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Partially- universal grading scale was not used and visual grading scale was subjective.
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Hoopfer 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Unclear-not mentioned within text (11 patients were withdrawn following randomisation)
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Tao 2017	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-2 patients did not receive any cutaneous applications
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS	INTERMEDIATE

Low, Intermediate, high	

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Pinnix 2012	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially-participants were informed not to discuss treatment with assessors.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes-2 participants did not use the agents for more than 9 days, 1 applied the agents only twice daily.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Manas 2014	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Partially- small sample size
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no baseline characteristics were compared across groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Unclear-it was not specified whether participants and assessors were blinded.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS	INTERMEDIATE

Low, Intermediate, high	

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Sekiguchi 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no comparison between baseline characteristics
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Partially- different skin scoring systems were used
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Sekiguchi 2018	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- no comparison between baseline characteristics.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Shariati 2020	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Partially- small sample size
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Chan 2019	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Karbasforooshan 2019	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-5 patients excluded as they did not complete the study.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	Rating *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Laffin 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value provided but baseline characteristics appear to be similar across both groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-5 participants excluded as they did not complete RT

9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Chan 2014	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Zhong 2013	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Yes
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes

OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Herst 2014	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value provided however seems to be similar across both areas (breast and chest wall).
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	No-RT and participants were not blinded as film was in situ for days at a time.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-2 participants were excluded from analysis
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	HIGH

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Moller 2018	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially-participants were not blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-19 participants were withdrawn due to side effects and 3 participants had incomplete questionnaires.
9.Insignificant COIs	Yes

The risk for potential conflicts of interest is minimal.	
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Schmeel 2018	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value provided but comparison between groups seems to be similar.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	No-RT and participants were not blinded as patients acted as their own controls with visible film-dressings.
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No- 6 patients stopped using film due to side effects.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	HIGH

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Rades 2019	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially-no p value provided but baseline characteristics appear to be similar across groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	No-Trial was stopped prematurely

8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	INTERMEDIATE

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Shaw 2015	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- no comparison between baseline characteristics
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially-participants were not blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Niazi 2012	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- no p value but appears to be similar across groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs	Yes

The risk for potential conflicts of interest is minimal.	
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Yan 2020	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- no comparison between groups
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	No-both researcher and patients were not blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	No-5 participants were excluded due to not following protocol, skin reaction and not completing RT.
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	HIGH

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Bazire 2015	
1.***Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially-participants were not blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant

9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Ben-David 2016	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Yes
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Partially-outcome assessors were not blinded
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant
9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Quality Criterion	**Rating** *Yes (indicates a low risk of bias), No (indicates high risk of bias), Partially, (indicates an intermediate risk of bias), Unclear (indicates insufficient detail and/or unknown risk of bias), or Not relevant*
Lam 2019	
1***.Adequate Randomisation*** An adequate method is used to randomize subjects to treatment.	Yes
2.Concealed Allocation An adequate method is used to conceal allocation to treatment arms.	Yes
3.Sufficient sample size The sample size is sufficient to detect differences.	Yes
4.Comparable Groups The only difference between groups is the treatment under investigation.	Partially- no p values provided but baseline characteristics appears to be similar across groups.
5.Blinded Subjects, investigators, and assessors are unaware of treatment arm.	Yes
6.Validated and Reliable measures The intervention(s) and outcomes are clearly defined and measure in a standardized, valid, reliable, and consistent way.	Yes
7.Adequate Follow-up There is an adequate follow-up period to assess outcomes, and loss to follow-up is appropriately assessed and addressed.	Yes
8.Intention to Treat Analysis	Not relevant

9.Insignificant COIs The risk for potential conflicts of interest is minimal.	Yes
OVERALL RISK OF BIAS *Low, Intermediate, high*	LOW

Appendix D. Data Extraction Table (*RC 2014 Systematic Review)

Comparison of interventions	Reference citation	Sample size	Population	Aim of study	Duration	Outcome type	Outcome	Results/ effect size	Conclusion
1. Skincare Practices (Washing Practices and Deodorant Use)									
*1.1 Washing with Soap versus No Washing	Campbell, 1992; Roy, 2001	N=167	Previous SR	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/No) (Roy, 2001)	OR 0.32, 95% CI 0.01 to 8.05, p=0.49	Previous SR
							Secondary: Itch at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992)	Week 6-MD -0.43, 95% CI -0.97 to 0.11, p=0.12, Week 8-MD-0.40, 95% CI -0.81 to 0.01, p=0.06 (Favouring washing with soap)	
							Erythema at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992)	Week 6-MD-0.40 95% CI -0.77 to -0.03, p=0.03, Week 9-MD -0.21, 95% CI -0.52 to 0.10, p=0.18	
							Desquamation at the end of treatment (week six) and the two-	Week 6-MD -0.47, 95% CI -0.83 to -0.11, p=0.01, Week 8-	

							week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992)	MD- -0.82, 95% CI -1.16 to -0.48, p<0.00001 (Favouring washing with soap)	
*1.2 Washing with Water versus No Washing	Campbell, 1992	N=58	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Itch at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) Erythema at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992) Desquamation at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992)	Week 6- MD -0.27, 95% CI -0.83 to 0.29, p=0.35, Week 8- MD -0.46, 95% CI -0.83 to -0.09, p=0.01 (Favouring washing with water) Week 6- MD -0.34, 95% CI -0.69 to 0.01, p=0.06, Week 8 - MD -0.44, 95% CI -0.72 to -0.16, p=0.002 (Favouring washing with water) Week 6- MD -0.59, 95% CI -0.94 to -0.24, p=0.001, Week 8- MD -0.62, 95% CI -0.96 to -0.28, p=0.0004 (Favouring washing with water)	Previous SR

*1.3 Washing with Water versus Washing with Soap	Campbell, 1992	N=64	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Itch at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) Erythema at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992) Desquamation at the end of treatment (week six) and the two-week follow-up (week eight) (EORTC/RTOG criteria, with a possible score of 0-3) (Campbell, 1992)	Week 6- MD 0.16, 95% CI -0.35 to 0.67, p=0.54, Week 8- MD -0.06, 95% CI -0.39 to 0.27, p=0.72 Week 6- MD 0.06, 95% CI -0.26 to 0.38, p=0.71, Week 8- MD -0.44, 95% CI -0.72 to -0.16, p=-.001 (Favouring washing with water) Week 6- MD -0.12, 95% CI -0.51 to 0.27, p=0.54, Week 8- MD 0.20, 95% CI -0.16 to 0.56, p=0.27	Previous SR
*1.4 Deodorant versus No Deodorant	Bennett, 2009; Gee, 2000; Theberge, 2009; Watson, 2012	N=509	Previous SR	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/No) (Bennett, 2009 & Gee, 2000) Development of RISR in patients	Meta-analysis: OR 0.80, 95% CI 0.47 to 1.37, p=0.42	Previous SR

with axilla treated (Yes/No) (Bennett, 2009)	OR 0.06, 95% CI 0.01 to 0.60, p=0.02
Secondary: RISR at the end of radiation treatment and at the two-week follow-up (CTCAE criteria version 3, with a possible range of 0-3) (Watson, 2012)	End of treatment- MD 0.01, 95% CI -0.17 to 0.19, p=0.91, Two-week follow-up- MD 0.01, 95% CI -0.21 to 0.23, p=0.93
Maximum RISR rated by researcher (RTOG criteria, with a possible range of 0-3) (Bennett, 2009)	MD=-0.74, 95% CI -1.22 to -0.26, p=0.003 (Favouring deodorant)
Moderate-to-severe pain at the end of radiation treatment and at the two-week follow-up (Yes/No) (Theberge, 2009)	End of treatment- OR 0.77, 95% CI 0.29 to 2.09, p=0.61, Two-week follow-up- OR 2.16, 9% CI 0.65 to 7.14, p=0.21
Pruritus at the end of radiation treatment and at the two-week follow-up (Yes/No) (Theberge, 2009)	End of treatment- OR 2.62, 95% CI 1.01 to 6.78, p=0.05, Two-week follow-up- OR 1.47, 95%

							Sweating at the end of radiation treatment and at the two-week follow-up (Yes/No) (Theberge, 2009)	CI 0.57 to 3.77, p=0.42 End of treatment -OR 0.34, 95% CI 0.12 to 0.93, p=0.04, Two-week follow up- OR 0.70, 95% CI 0.25 to 1.99, p=0.51	
2. Steroidal Topical Ointment/Cream									
*2.1 Topical Corticosteroid Plus Antibiotics versus No Treatment	Halnan, 1962	N=20	Previous SR	Previous SR	Previous SR	Prevention	**Primary:** Development of RISR (Yes/ No)	There was an equal proportion of people developing a RISR (summary statistics not estimated)	Previous SR
*2.2 Topical Corticosteroid Plus Antibiotics versus Corticosteroid Alone	Halnan, 1962	N=20	Previous SR	Previous SR	Previous SR	Prevention	**Primary:** Development of RISR (Yes/ No)	OR 0.07, 95% CI 0.01 to 0.84, p=0.04 (Favouring topical corticosteroid plus antibiotics)	Previous SR
*2.3 Topical Corticosteroid versus Another Topical Corticosteroid	Glees, 1979	N=53	Previous SR	Previous SR	Previous SR	Prevention	**Primary:** Development of RISR (Yes/ No)	OR 3.35, 95% CI 0.13 to 86.03, p=0.46	Previous SR
*2.4 Topical Corticosteroid versus Dexpanthenol	Schmuth, 2002	N=21	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Levels of RISR at the end of radiation treatment (week six) (The clinical	MD -0.10, 95% CI-0.57 to 0.37, p=0.68	Previous SR

							symptom score with a possible range of 0-3)		
							Levels of RISR at the two-week follow-up after the end of radiation treatment (week eight) (The clinical symptom score with a possible range of 0-3)	MD -1.40, 95% CI—1.97 to -0.83, p<0.00001(Favouring topical corticosteroid)	
*2.5 Topical Betamethasone Cream versus Placebo	Omidvari, 2007	N=36	Breast cancer patients, Iran	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/No)	There was an equal proportion of people developing a RISR (summary statistics not estimated)	Previous SR
							Secondary: RISR at the end of treatment (week five) and the two-week follow-up (week seven) (RTOG criteria, with a possible range of 0-4)	End of treatment- MD -0.10, 95% CI -0.28 to 0.08, p=0.28, two-week follow-up- MD -0.55, 95% CI -0.71 to -0.39, p<0.00001(Favouring topical betamethasone)	
							Maximum level of RISR (RTOG criteria, with a possible range of 0-4)	MD -1.62, 95% CI -2.03 to -1.21, p<0.00001 (Favouring	

								topical betamethasone cream).	
*2.6 Topical betamethasone versus no topical treatment	Omidvari, 2007	N=36	Breast cancer patients, Iran	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/No)	There was an equal proportion of people developing a RISR (summary statistics not estimated)	
							Secondary: RISR at the end of treatment (week five) and the two-week follow-up (week seven) (RTOG criteria, with a possible range of 0-4)	End of treatment- MD -0.40, 95% CI -0.62 to -0.15, p=0.002, two-week follow-up- MD -0.30, 95% CI -0.53 to -0.07, p=0.01 (Favouring topical betamethasone cream)	
							Maximum level of RISR (RTOG criteria, with a possible range of 0-4	MD -0.27, 95% CI -0.75 to 0.21, p=0.27	
*2.7 Topical 0.1% Mometasone Furoate Cream versus Placebo	Miller, 2011	N=166	Breast cancer patients, Minnesota	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/ No)	OR 0.60, 95% CI 0.28 to 1.31, p=0.20	Previous SR
							Secondary: RISR at the two-week follow-up after the completion of radiation treatment (CTCAE criteria	MD -0.39, 95% CI -0.80 to 0.02, p=0.06	

							version 3.0, with a possible range of 0-3)		
							Maximum RISR level (CTCAE criteria version 3.0, with a possible range of 0-3)	MD -0.10, 95% CI -0.35 to 0.15, p=0.43	
2.8 Betamethasone-17-valerate cream versus two emollients, Essex cream and Canoderm cream	Ulff 2013	N=102	Breast cancer patients, Sweden	To investigate whether the potent steroid betamethasone-17-valerate reduces ARD better than two emollients	7 weeks	Prevention	**Primary**: development of RISR (RTOG) **Secondary**: patients' symptoms (itching, burning, irritation)	**Primary**: OR 0.10, 95% CI 0.02 to 0.47, p<0.05 (Favouring steroid cream) Effect size: 2.90 **Secondary**: NS	Betamethasone + Essex cream is more efficient than moisturizers for the control of ARD.
2.9 Mometasone Furoate Cream versus D cream (control)	Hindley 2014	N=120	Breast cancer patients, UK	To confirm the benefit of MMF in preventing ARD.	6 weeks	Treatment	**Primary:** mean skin dermatitis score (RTOG) **Secondary**: time taken to reach the maximum RTOG score, maximum RTOG score, mean erythema measurement and quality of life.	**Primary:** MD 0.123, 95% CI 0.002 to 0.244, p=0.046 (Favouring MMF cream). Effect size: 0.182 **Secondary:** mean erythema scores MD 8.98, 95% CI 2.02 to 15.94, p<0.012 (Favouring MMF cream).	MMF cream significantly reduces RD when applied to the breast during and after radiation therapy. This treatment should be considered the standard of care for severe dermatitis.
2.10 1% hydrocortisone cream versus prophylactic placebo cream	Meghrajani 2016	N=50	Breast cancer patients, Philippines	To determine whether the application of 1% hydrocortisone	6 weeks	Prevention	**Primary:** occurrence of moist desquamation	**Primary:** NS **Secondary:** ARD MD 0.16, 95% CI 0.14 to 0.18,	Prophylactic use of a mild topical corticosteroid was able to delay the onset

				cream during radiation therapy can prevent the occurrence of moist desquamation.			**Secondary:** mean ARD scores, onset of ARD, subjective symptoms (pruritus, burning, pain) and quality of life.	p = 0.024 (Favouring Hydrocortisone) Effect size: 2.01	of RD and reduce the overall ARD scores.
2.11 Betamethasone-17-valerate cream versus Essex cream	Ulff 2017	N=202	Breast cancer patients, Sweden	To test the hypothesis that preventive topical steroid treatment instituted from start of radiotherapy can ameliorate acute radiation dermatitis (ARD)	2 weeks after Tx	Prevention	**Primary:** Development of RD (RTOG) **Secondary:** itching, burning and irritation of skin	**Primary:** OR 0.20, 95% CI 0.09 to 0.46, p<0.05 (Favouring steroid) Effect size: 3.8 **Secondary:** NS	Prophylactic treatment with a strong local steroid is efficient for the prevention and control of ARD.
2.12 0.1% Mometasone furoate versus Eucerin Original (E) cream	Ho 2018	N=124 (Phase 3 RCT)	Breast cancer patients, Boston	To evaluate the efficacy of 0.1% MMF versus E cream in preventing the development of moderate to severe ARD.	7-7.5 weeks	Prevention	**Primary:** skin toxicity (CTCAE) **Secondary**: patient reported outcomes	**Primary:** Moist desquamation- OR 0.39, 95% CI 0.19 to 0.81, p=0.012 (Favouring MMF cream) Effect size: 2.5 **Secondary**: NS	MMF reduced the incidence of high-grade ARD. Moderate strength steroid creams are a low-risk and affordable intervention strategy that can be adopted into most clinical practices.

2.13 Topical atorvastatin (ATV) 1% versus placebo gel	Ghasemi 2019	N=70	Breast cancer patients, Iran	To investigate the preventive effect of topical administration of atorvastatin on the acute radiation-induced skin toxicity	6 weeks	Prevention	**Primary:** skin toxicities (RTOG) **Secondary:** breast swelling/oedema, pain, itching	**Primary:** MD: 0.86, 95% CI 0.83 to 0.89, NS Effect size: 2.0 **Secondary:** oedema; MD 0.65, 95% CI 0.61 to 0.69, p=0.02, itching; MD 1.53, 95% CI 1.45 to 1.60, p<0.05, pain; MD 1.45, 95% CI 1.17 to 1.72, p<0.05 (All favouring ATV)	Atorvastatin was able to reduce significantly itching, breast oedema, and pain in patients during radiotherapy.
2.14 Mometasone furoate cream (MMF) versus control	Liao 2019	N=41	Head & neck cancer patients, China	To evaluate the effect of MMF local application on RD.	2 weeks after Tx	Treatment	**Primary:** maximal RTOG score, pain severity, and itching stages	**Primary:** maximal RTOG score p=0.039, itch and pain p<0.01 (Favouring MMF) The trial authors did not provide mean scores.	MMF inunction after high-dose radiotherapy (>50 Gy) can prevent ARD, especially when the radiation dose is <6000 cGY.
3. Non-Steroidal Ointment/Cream									
	Maiche, 1994	N=44	Previous SR	Previous SR	Previous SR	Previous SR	Previous SR		Previous SR

*3.1 Sucralfate Cream versus Placebo Cream								Maiche 1994 compared sucralfate cream and placebo cream. The trial authors reported that "grade 1 and grade 2 reactions appeared significantly later on the areas treated with sucralfate cream. Grade 2 reactions were observed highly significantly more often at four weeks (p=0.01) and at five weeks (p<0.05) in favour of sucralfate. No allergic reactions were observed in either group. No other data were available after attempts to contact trial authors for more information.	
*3.2 Aloe Vera Gel versus Placebo	Williams, 1996	N=194	Breast cancer patients, USA	Previous SR	Previous SR	Previous SR	Previous SR	Williams 1996 reported that "skin dermatitis scores were virtually identical on both treatment arms, and that, aloe	Previous SR

								vera gel does not protect against radiation treatment-induced dermatitis". However, this study did not contain data or summary statistics concerning the outcome measures.	
*3.3 Sucralfate mixed with Sorbolene (10% w/w (50g of sucralfate crushed in 500g of sorbolene) versus Sorbolene cream	Delaney, 1997	N=39	Previous SR	Previous SR	Previous SR	Previous SR	Previous SR	The trial authors of Delaney 1997 reported that mean time to healing for the sucralfate and control groups, respectively were 14.8 days (coefficient of variation (c.v.=70%) and 14.2 days (c.v.=75%). The ratio of mean times to healing was 1.043 and was not statistically different from 1. (p=0.86, 95% CI 0.65, 1.67). Estimates of the SD could not be calculated as it was unsure	Previous SR

								whether the c.v. data presented by the authors was based on the log transformed time-to-heal data or the untransformed data. The trial authors reported that "there was no statistically significant difference was found between the two arms in either from randomisation to healing or improvement in pain score". We could not extract data from this study. The trial authors were contacted for further information. However, no replies were received at the time of publishing this review.	
*3.4 Aloe Vera Gel and Soap versus Soap Alone	Olsen, 2001	N=73	Cancer patients, Caucasians (74%) & African-	Previous SR	Previous SR	Previous SR	Previous SR	Olsen 2001 reported that "when the cumulative of radiation dose was high	Previous SR

			Americans (26%)					(>2700cGy), the median time was given weeks prior to any skin changes in the aloe/soap arm versus three weeks in the soap only arm. When cumulative dose increases over time, there seems to be a protective effect of adding aloe to the soap regimen." However, this study did not contain data or summary statistics concerning the outcomes as defined by this review.	
*3.5 Aloe Vera versus Aqueous Cream	Heggie, 2002	N=225	Breast cancer patients, Australia	Previous SR	Previous SR	Previous SR	Previous SR	Heggie 2002 reported that "aqueous cream was significantly better than aloe vera in reducing dry desquamation and pain related to treatment". However, this study did not contain data or summary	Previous SR

								statistics concerning the outcomes as defined by this review.	
*3.6 Trolamine versus Calendula	Pommier, 2004	N=254	Breast cancer patients, France	Previous SR	Previous SR	Treatment	**Secondary:** Ease of use (measured as difficult to use- yes or no) Allergic reaction (yes/no)	OR 7.68, 95% CI 3.07 to 19.17, p<0.0001 (Favouring trolamine) OR 0.11, 95% CI 0.01 to 2.05, p=0.14	Previous SR
*3.7 Sucralfate cream versus aqueous cream	Wells, 2004	N=357	Previous SR	Previous SR	Previous SR	Previous SR	Previous SR	Wells 2004 compared Sorbolene and aqueous cream. We could not extract data from this study. The trial authors did not provide SE, SD or 95% CI for the mean scores reported. However, the authors reported that no statistically significant differences were found in the severity of skin reactions suffered by patients in either of the treatment arms.	Previous SR

*3.8 Trolamine versus Usual Care as Per Institutional Preference	Elliott, 2006; Fisher, 2000	N=462	Squamous Cell Carcinoma patients, Canada	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (yes/no) (Elliot 2006) **Secondary:** Maximum levels of RISR (NCI CTC criteria and RTOG criteria, with a possible range of 0-4) (Eilott, 2006 & Fisher,2000)	OR 0.40, 95% CI 0.08 to 2.11, p=0.28 Meta-analysis: MD 0.00, 95% CI -0.13 to 0.13, p=0.97	Previous SR
*3.9 Sorbolene versus Wheatgrass Extract Cream	Wheat, 2006; Wheat, 2007	N=50	Previous SR	Previous SR	Previous SR	Previous SR	Previous SR	Wheat 2006 (n=30) and Wheat 2007 (n=20) compared Sorbolene and wheatgrass extract cream. We could not extract data from these two studies. The trial authors did not provide SE, SD or 95% CI for the	Previous SR

								mean scores reported. The trial authors were contacted for further information. However, no replies were received at the time of publishing this review. Both studies reported that there were no statistically significant differences between the two arms with respect to the peak RISR severity or time to peak RISR rating. The trial authors reported a statistically significant improvement in quality of life of patients in the wheatgrass group at week five and week six of radiation treatment.	
*3.10 Aloe Vera Gel versus an Anionic Phospholipid-Based (APP) Cream	Merchant, 2007	N=194	Cancer patients (Hodgkins disease, CNS tumor,	Previous SR	Previous SR	Previous SR	Previous SR	Merchant 2007 (n=194) reported that statistically significant	Previous SR

			pediatric sarcoma, neuroblastoma) USA					differences were found favouring the APP cream over the aloe vera gel in a number of outcomes including skin comfort, RISR skin severity. However, this study did not contain data or summary statistics concerning the outcome measures.	
*3.11 Topical Lian Bai Liquid versus No Lian Bai Liquid	Ma, 2007	N=126	Previous SR	Previous SR	Previous SR	Prevention	**Primary:** Development of RISR (yes or no)	OR 0.04, 95% CI 0.01 to 0.12, p<0.00001 (Favouring topical lian bai liquid)	Previous SR
*3.12 Trolamine versus ETA Gel (99% Avene Thermal Spring Water)	Ribet, 2008	N=54	Breast and/or head & neck cancer patients, France	Previous SR	Previous SR	Treatment	**Secondary:** RISR severity at the end of radiation treatment (NCI CTC criteria, with a possible range of 0	MD -0.14, 95% CI -0.58 to 0.30, p=0.53	Previous SR

*3.13 Non-steroidal Restitutio restructuring cream formula A and non-steroidal restitutio restructuring cream formula B	Garibaldi, 2009	N=64	Previous SR	Previous SR	Previous SR	Prevention	**Primary:** Development of RISR (yes/no)	OR 0.64, 95% CI 0.22 to 1.88, p=0.41	Previous SR
*3.14 Trolamine versus Placebo	Gosselin, 2010	N=102	Breast cancer patients, USA	Previous SR	Previous SR	Prevention/Treatment	**Secondary:** Patient satisfaction (Scoring system developed by authors, with a possible range of 0-5, 5-best satisfaction) Ease of use (Scoring system developed by authors, with a possible range of 0-5, 5-highest level of ease)	MD 1.12, 95% CI 0.56 to 1.68, p<0.00001 (Favouring trolamine) MD 0.44, 95% CI 0.01 to 0.87, p=0.04 (Favouring trolamine)	Previous SR
*3.15 Aquaphor ointment versus placebo	Gosselin, 2010	N=106	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Patient satisfaction (Scoring system developed by	MD 0.59, 95% CI 0.04 to 1.15, p=0.04 (Favouring	Previous SR

							authors, with a possible range of 0-5, 5-best satisfaction)	aquaphor ointment)	
							Ease of use (Scoring system developed by authors, with a possible range of 0-5, 5-best level of ease)	MD -0.10, 95% CI -0.61 to 0.41, p=0.70	
*3.16 RadiaCare Gel versus Placebo	Gosselin, 2010	N=106	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Patient satisfaction (Scoring system developed by authors, with a possible range of 0-5, 5-best satisfaction)	MD 0.91, 95% CI 0.36 to 1.46, p=0.001 (Favouring radiacare gel)	Previous SR
							Ease of use (Scoring system developed by authors, with a possible range of 0-5, 5-best level of ease)	MD 0.16, 95% CI -0.30 to 0.62, p=0.49	
*3.17 Formulation A Topical Cream (capprais spinosa, opuntia coccinellifera and olive leaf extract) versus No Treatment	Rizza, 2010	N=44	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Maximum RISR over eight weeks (modified RTOG criteria, with a possible range of 0-5, 5-best level of ease)	MD -01.17, 95% CI -1.59 to -0.75, p<0.00001 (Favouring formulation A topical cream)	Previous SR

*3.18 Formulation B Topical Cream (non-steroidal water-based emulsion) versus No Treatment	Rizza, 2010	N=42	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Maximum RISR over eight weeks (modified RTOG criteria, with a possible range of 0-5, 5-best level of ease)	MD -0.79, 95% CI -1.21 to -0.37, p<0.00001 (Favouring formulation B topical cream)	Previous SR
*3.19 Formulation A Topical Cream (capprais spinosa, opuntia coccinellifera and olive leaf extract) versus Formulation B Topical Cream (non-steroidal water-based emulsion)	Rizza, 2010	N=50	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Maximum RISR over eight weeks (modified RTOG criteria, with a possible range of 0-5, 5-best level of ease)	MD -0.38, 95% CI -0.69 to -0.07, p=0.02 (Favouring formulation A topical cream)	Previous SR
*3.20 Trolamine versus Topical Qingdiyou Medication	Zhang, 2011	N=72	Head & neck carcinoma patients, China	Previous SR	Previous SR	Previous SR	Previous SR	Zhang 2011 compared trolamine and topical qingdiyou medication. We could not extract data from this study. The trial authors reported that patients who received qingdiyou medication had significantly less severe RISR (p<0.05). The trial authors did not provide a time point as to when the assessments	Previous SR

								were undertaken. We attempted contacted authors for further information. However, no further information was provided.	
*3.21 WO1932 Oil in Water Emulsion versus Usual Care/Untreated	Jenson, 2011 N=66	N=66	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** RISR severity at the end of radiation treatment (Oncology Nursing Society Skin Reaction Scoring System, with a possible range of 0-3)	MD -0.21, 95% CI -0.43 to 0.01, p=0.07	Previous SR
*3.22 Hyaluronic acid versus placebo cream	Kirova, 2011; Leonardi, 2008; Liguori, 1997; Primavera, 2006	N=384	Breast cancer patients, France	Previous SR	Previous SR	Prevention/Treatment	**Primary:** Development of RISR (Yes/No) (Leonardi, 2008) **Secondary:** Severe pain (>2) at week one, week two and week three of radiation treatment (as defined as >2 on a visual analogue scale, Yes/No) (Kirova 2011) Quality of life at week four of radiation	OR 0.39, 95% CI 0.01 to 10.10, p=0.57 Week One: OR 1.25, 95% CI -6.75 to 6.55, p=0.98, Week Two- OR 1.79, 95% CI 0.97 to 3.27, p=0.06 to 2.59, p=0.45 MD -0.10, 95% CI -6.75 to 6.55, p=0.98	Previous SR

treatment (EORTC CLC Q30) (Kirova 2011)	
RISR severity at the end of radiation treatment (Scoring system developed by authors, with a possible range of 0-6) (Liguori 1997)	MD -0.73, 95% CI -1.04 to -0.42, p<0.00001 (Favouring hyaluronic acid)
RISR at four weeks after radiation treatment completion (Scoring system developed by authors, with a possible range of 0-6) (Liguori 1997)	MD -0.35, 95% CI -0.68 to -0.02, p=0.04 (Favouring hyaluronic acid)
Maximum RISR over the duration of radiation treatment (CTCAE, with a possible range of 0-4) (Leonardi 2008)	MD -0.95, 95% CI -1.23 to -0.67, p<0.00001 (Favouring hyaluronic acid)
Pain, itching and burning at four weeks of radiation treatment (0-	Pain- MD -0.50, 95% CI -1.72 to 0.72, p=0.42, Itching- MD -0.18, 95% CI -1.39 to 1.03, p=0.77, Burning- MD -0.91, 95% CI

							10cm visual analogue scale, with a possible range of 0-10) (Leonardi, 2008). Adverse effects (yes/no) (Leonardi, 2008).	-2.01 to -0.19, p=0.10 OR 0.17, 95% CI 0.02 to 1.65, p=0.13	
3.23 Trolamine versus usual supportive care	Abbas 2011	N=30 (Phase 3 RCT)	Head & neck cancer patients, Egypt	To test trolamine emulsion compared with the usual supportive care	10 weeks	Treatment	**Primary:** reduction of grade III or higher skin toxicity (RTOG criteria)	**Primary:** OR 0.22, 95% CI 0.04 to 1.11, p< 0.01 (Favouring Trolamine emulsion) Effect size: 1.84	Reduced intensity of ARD with trolamine cream.
3.24 Topical silver sulfadiazine (SSD) cream versus control	Hemati 2012	N=110	Breast cancer patients, Iran	To evaluate the effectiveness of SSD cream in preventing ARD.	5 weeks	Treatment	**Primary**: skin injuries (RTOG criteria)	**Primary**: MD 6.35, 95% CI 6.18 to 6.51, p < 0.001 (Favouring SSD cream) Effect size: 2.00	Reduced severity of radiation-induced skin injury with SSD cream. Future trials should also focus on the patients' quality of life.
3.25 Topical hyaluronic acid versus petroleum-based substance (control)	Pinnix 2012	N=74 (Phase 3 RCT)	Breast cancer patients, Houston	To determine the efficacy of an emulsion containing hyaluronic acid compared with best supportive care.	>9 days	Treatment	**Primary:** skin toxicity (CTCAE)	**Primary**: OR 1.75, 95% CI 0.87 to 3.53, p=0.027 (Favouring petroleum gel) Effect size: 1.58	Topical hyaluronic acid is not beneficial for prophylaxis of radiation-induced skin toxicity.

3.26 Moisturizing durable barrier cream (MDBC) versus Sorbolene cream	Graham 2013	N=318	Breast cancer patients, Australia	To ascertain whether peak and overall skin reactions may be reduced by the moisturizing durable barrier cream compared with Sorbolene.	6 weeks	Treatment	**Primary:** peak and overall skin reactions (CTCAE) **Secondary:** pruritus and discomfort	**Primary:** NS **Secondary:** NS	MDBC did not reduce skin reactions compared to Sorbolene. This may be related to the difference in the formulation of the cream compared with the film formulation.
3.27 Alpha ointment versus topical hydrocortisone cream (1%)	Ansari 2013	N=60 (Phase 2 RCT)	Breast cancer patients, Iran	To compare topical Alpha ointment and topical hydrocortisone cream (1%) in terms of their efficacy in the healing of RD.	6 weeks	Treatment	**Primary:** dermatitis grade (CTCAE), the rate of dermatitis healing **Secondary:** skin burning, pain, and pruritus, and amount of skin discharge change	**Primary**: MD 63.2, 95% CI 60.3 to 66.1, p<0.001(Favoured Alpha ointment) Effect size: 2.0 **Secondary**: pain p<0.001, pruritus p=0.009, discharge p=0.010 (Favoured Alpha ointment)	Topical Alpha ointment was more effective on the healing of RD than topical hydrocortisone cream (1%). Further evaluation with larger numbers of patients is required.
3.28 Topical R1 and R2 versus standard topical treatment	Manas 2014	N=98	Breast and head & neck cancer, Madrid	To investigate the use of the topical Lactokine-based R1 and R2 system as a prophylactic treatment of ARD.	8 weeks	Prevention	**Primary:** incidence of ARD grade 3 or 4. **Secondary:** overall response rates, quality of life.	**Primary:** Second follow up; OR 0.06, 95% CI 0.02 to 0.16, p<0.0001(Favouring R1 and R2), Effect size: 5.57, Third follow up; OR 0.0138, 95% CI 0.0008 to	Topical skin treatment with the R1 and R2 system has been shown to be effective in preventing, reducing the onset, and reducing the

								0.2362, p<0.0001(Favouring R1 and R2) Effect size: 2.956	degree of RD in head and neck and breast cancer patients treated with chemoradiation.
3.29 Natural oil-based emulsion containing Allantoin (MooGoo Udder cream) versus aqueous cream	Chan 2014	N=174 (Phase 3 RCT)	Lung, breast or head & neck cancer patients, Australia	To investigate the effects of a natural oil-based emulsion containing allantoin versus aqueous cream for preventing and managing RISR.	4 weeks	Treatment	**Primary:** severity of skin reaction (CTCAE) **Secondary:** QOL, pain, itching, treatment interruptions, adverse events	**Primary:** Week 3; p<0.05 (Favouring MooGoo Udder cream), Week 7,8,9-p<0.001 (Favouring aqueous cream) **Secondary:** Week 3-pain p<0.05, itching p <0.046 (Favouring aqueous cream) The trial authors did not provide mean scores.	Aqueous cream seems to be a more preferred option.
3.30 Cavilon Durable Barrier Cream versus Sorbelene cream	Laffin 2015	N=255	Breast cancer patients, Australia	To compare the effectiveness of Cavilon Durable Barrier Cream and 100% Pure Sorbolene Cream at preventing moist desquamation	8-10 weeks	Prevention	**Primary:** Incidence of moist desquamation **Secondary:** patient reported outcomes (cream acceptability)	**Primary:** Var= 3.93, p=0.047 (SD=1.98) (Favouring barrier cream) The trial authors did not provide mean scores.	Structured discharge planning and patient education need to include information about factors that contribute to the development of moist desquamation.

3.31 Calendula officinalis versus Essential Fatty Acids (EFA)(control)	Schneider 2015	N=51	Head & neck cancer patients, Brazil	To evaluate the efficacy of Calendula officinalis in relation to EFA.	7 months	Prevention/Treatment	**Primary:** development of RD (RTOG)	**Primary:** OR 0.21, 95% CI 0.05 to 0.87, p=0.012 (Favouring calendula) Effect size: 2.15	Calendula showed better therapeutic response than the EFA in the prevention and treatment of RD.
3.32 Heparinoid moisturiser versus control (no topical moisturiser)	Sekiguchi 2015	N=62	Breast cancer patients, Japan	To investigate the effect of heparinoid moisturizer, use after acute skin damage	3.5 months	Treatment	**Primary:** Measurement of skin WC **Secondary:** signs of acute RD, itching and pain	**Primary:** MD 0.23, 95% CI 0.19 to 0.27, p<0.01 (Favouring Group M) Effect size: 1.00 **Secondary**: skin toxicity data not available (NS).	Heparinoid moisturizer for 2 weeks following whole-breast radiotherapy significantly increased water content and helped improve skin dryness and desquamation compared with no use of moisturizer.
3.33 Boswellia cream versus base cream (placebo)	Togni 2015	N=114	Breast cancer patients, Italy	To evaluate the safety and the efficacy of the application of a base cream contaning Boswellic acids in a proprietary formulation (Bosexil(R)) for the prevention and relief of radiation-induced adverse effects	Not specified	Prevention/Treatment	**Primary:** grade of intensity of erythema	**Primary:** OR 0.711, 95% CI 0.327 to 1.545, p=0.009 (Favouring Boswellia cream)	Further studies comparing Boswellia cream with other topical agents will be appropriate to confirm the effectiveness of this treatment for breast cancer patients under radiation therapy.

3.34 Aloe and placebo cream versus powder as skin treatment	Hoopfer 2015	N=237 (Phase 3 RCT)	Breast cancer patients, Canada	To test the efficacy of quality-tested aloe extract in reducing the severity of radiation-induced skin injury	4 weeks	Treatment	**Primary:** acute skin reaction severity **Secondary:** severity of dryness, itchiness, burning, and pain	**Primary:** MD: 6.74, 95% CI 6.70 to 6.78, p=0.0227 (Favouring powder) **Secondary:** NS	No evidence was found to support prophylactic application of quality aloe extract or cream to improve the symptoms or reduce the skin reaction severity.
3.35 Doxepin cream versus placebo	Shariati 2015	N=48 (Phase 2 RCT)	Breast cancer patients, Iran	To evaluate the effects of Doxepin therapy on RD.	5 weeks	Treatment	**Primary**: ARD (grade 2 or higher) $p \leq 0.0001$, $Z\alpha = 1.96$ at 95% confidence interval (Favouring Doxepin)	Doxepin cream prevents RD grade 2 or higher during post-operative breast irradiation. Doxepin cream is easy to use, affordable and prevents pain and irritation.	
3.36 Melatonin containing emulsion versus placebo cream	Ben-David 2016	N=47 (Phase 2 RCT)	Breast cancer patients, Israel	To evaluate the efficacy of melatonin-containing cream in minimising ARD.	7 weeks	Treatment	**Primary:** maximum levels of RISR (RTOG criteria) **Secondary:** pain, burning sensation, pruritus, tingling, stinging, roughness, dryness and softness	**Primary:** OR 0.23, 95% CI 0.05 to 0.97, p=0.038 (Favouring Melatonin) Effect size: 2.00 **Secondary:** NS	Reduced RD with melatonin in comparison with placebo. A larger study is required.

3.37 Aloe vera gel versus control	Ahmadloo 2017	N=100	Breast cancer patients, Iran	To understand whether the adjunctive use of aloe vera gel might reduce the prevalence and/or severity of RD.	5 weeks	Treatment	**Primary:** severity of dermatitis	**Primary:** OR 0.61, 95% CI 0.27 to 1.36, p=0.224 (NS)	Aloe vera exerted no positive effect on prevalence or severity of RD in this study.
3.38 Topical OTD70DERM (RGTA) versus placebo	Tao 2017	N=76	Head & neck cancer patients, France	To evaluate the effect of topical RGTA on RD in patients with head and neck cancer.	4.75 months	Treatment	**Primary:** skin toxicities (CTCAE)	**Primary:** OR 0.91, 95% CI 0.29 to 2.83, p=0.91 (NS) Effect size: 0.50	RGTA did not reduce the incidence and severity of RD in patients with head and neck cancer.
3.39 Heparinoid moisturiser versus control	Sekiguchi 2018	N=48	Breast cancer patients, Japan	To investigate the preventive efficacy of heparinoid moisturizer for ARD.	3 months after Tx	Prevention	**Primary**: skin water content **Secondary:** ARD signs and symptoms	**Primary:** MD 34.4, 95% CI 33.1 to 35.6, p<0.001 (favouring heparinoid moisturiser) Effect size: 2.0 **Secondary:** erythema NS, pain p<0.030 (Favouring heparinoid moisturiser) The trial authors did not provide mean scores.	Heparinoid moisturizer has the potential of reducing skin desquamation and dryness in patients receiving radiotherapy.

3.40 A silicone-based film-forming gel dressing versus Sorbolene cream	Chan 2019	N=197	Head & neck cancer patients, Australia	To investigate the effects of StrataXRT versus 10% Glycerine (Sorbolene cream) for preventing and managing RD.	4 weeks after Tx	Prevention/Treatment	**Primary:** severity of skin toxicity **Secondary:** skin related quality of life, pain and itching	**Primary:** grade 2 skin toxicity; RRR = 0.88, 95% CI: 0.78 to 0.99, p = 0.031 (Favouring Silicon based gel), grade 3 skin toxicity; RRR = 0.65, 95% CI: 0.44 to 0.95, p = 0.025 (Favouring Silicon based gel) **Secondary:** NS	Silicon based gel is effective for preventing and delaying the development of grade 2 and 3 skin toxicity.
3.41 Topical silymarin gel versus placebo	Karbasforoosha n 2019	N=40	Breast cancer patients, Iran	To investigate the efficacy of silymarin gel in prevention of RD.	5 weeks	Treatment	**Primary:** development of RD (RTOG) **Secondary:** adverse drug reactions	**Primary:** Week 3; 0 (0-1) vs 1(0-2), 95% CI 0.033 to 0.041, Week 4; 1(0-1) vs 1 (0-2), 95% CI 0.033 to 0.041; Week 5; 1(1-1) vs 1(1-3), 95% CI 0.001 to 0.003, p<0.05(Favouring silymarin) The trial authors did not provide mean scores only median scores. **Secondary:** NS	Prophylactic administration of silymarin gel could significantly reduce the severity of RD and delay its occurrence after 5 weeks of application.
4. Dressings									
*4.1 MVP Dressings versus Lanolin Dressing	Shell, 1986	N=16	Previous SR	Previous SR	Previous SR	N/A	Previous SR	Shell 1986 compared moisture vapour permeable (MVP dressing)	Previous SR

								compared with lanolin dressings. We were unable to extract data from the study. Insufficient information was provided in relation to the time to healing outcome as well as the RISR scores (no SD provided). The trial authors reported "the trend to faster healing in the MVP group was not statistically significant".	
*4.2 Gentian Violet Dressing versus Non-Adherent Dressing	Mak, 2005	N=39	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Time to heal (days) Pain at week two after the application of dressing (Scoring system developed by authors, with a possible range of 0-5) RISR severity at the end of radiation treatment (CTCAE criteria version 4, with a	HR 0.73, 95% CI 0.52 to 1.03, p=0.07	Previous SR

							possible range of 0-4)		
*4.3 Hydrogel Dressing versus Gentian Violet Dressing	Gollins, 2008	N=20	Previous SR	Previous SR	Previous SR	Treatment	**Secondary:** Time to heal (days) Adverse events (measured as stinging, yes or no)	OR 7.95, 95% CI 2.20 to 28.68, p=0.002 (Favouring hydrogel dressing)	Previous SR
*4.4 Mepilex Lite Dressing versus Aqueous Cream	Paterson, 2012	N=74	Breast cancer patients, New Zealand	Previous SR	Previous SR	Previous SR	Previous SR	Paterson 2012 compared Mepilex lite dressing with aqueous cream alone. We were unable to extract data from the study. However, the trial authors reported that "Mepilex Lite dressings did not significantly reduce the incidence of moist desquamation but did reduce the overall severity of skin reactions by 41% (p<0.001), and the average moist desquamation score by 49% (p=0.043)." The trial authors were contacted for	Previous SR

								further information. However, no replies were received at the time of publishing this review.	
4.5 Silver Nylon Dressing versus Standard Care	Niazi, 2012	N=40 (Phase 3 RCT) N=40	Anal/advanced rectal cancer patients, Canada	To compare the efficacy of SCND with that of standard skin care	8 weeks	Treatment	**Primary:** skin toxicity (RTOG criteria) **Secondary:** RISR severity at the end of radiation treatment (CTCAE criteria version 4, with a possible range of 0-4)	**Primary:** MD 2.1, 95% CI 1.97 to 2.23, p=0.01 (Favouring SCND) Effect size: 2	Reduced severity of RID with SCND. Previous SR
4.6 Mepilex Lite dressings versus usual care	Zhong 2013	N=88	Nasopharyngeal carcinoma patients (NPC), China	To compare the effectiveness of Mepilex Lite dressings and the usual care in the healing of RD.	7 weeks	Treatment	**Primary**: time-to-wound healing	**Primary:** median 16, 95% CI 12 to 19 vs median 23, 95% CI 19 to 27, p=0.009 (Favouring Mepilex Lite)	Mepilex Lite dressing provides a promising alternative to RD of NPC patients.

4.7 Mepitel film (MEP) versus aqueous cream	Herst 2014	N=80	Breast cancer patients, New Zealand	To investigate the prophylactic use of another Safetac product, MEP, on moist desquamation rates.	4 weeks	Treatment	**Primary:** skin reaction severity and incidence of moist desquamation.	**Primary:** Moist desquamation; OR 0.018, 95% CI 0.001 to 0.307, p<0.0001 (Favouring MEP) Effect size: 2.780	MEP completely prevented moist desquamation and reduced skin reaction severity by 92%.
4.8 3M Cavilon no-string barrier film (BF) versus mometasone furoate	Shaw 2015	N=39	Breast cancer patients, Taiwan	To investigate the effect of BF and topical corticosteroids on irradiated skin.	11 weeks	Treatment	**Primary:** grade 1 pruritus, pain score of 3 and grade 2 RD **Secondary:** incidence of grade 3 RD and total pain scores.	**Primary:** time to occurrence for grade 2 RD; MD 48.95, 95% CI 47.6 to 50.4, p <0.002 (Favouring BF) Effect size: 2 **Secondary:** NS	The effectiveness of corticosteroid on prevention of RD should be further investigated under a larger randomized trial.
4.9 Mepitel film (MEP) versus control	Moller 2018	N=101	Breast cancer patients, Denmark	To investigate patient-reported symptoms related to RD and to examine patient preferences using MEP.	4 months	Prevention	**Primary:** patient-reported outcomes	**Primary:** pain p < 0.001, itching p = 0.005, burning sensation p = 0.005, oedema p = 0.017, reduced sensitivity p <0 .001 (favouring MEP) The trial authors did not provide mean scores.	Patients reported reduced symptoms from the skin with MEP. Women treated after mastectomy had a significantly lower level of RD and preferred the film over standard care.
4.10 Hydrofilm polyurethane film dressings versus control	Schmeel 2018	N=62	Breast cancer patients, Germany	To compare prophylactically applied Hydrofilm dressings with our standard	Not specified	Prevention	**Primary:** maximum severity of RD (RTOG) **Secondary:**	**Primary:** MD 0.84, 95% CI 0.71 to 0.97, p<0.001 (Favouring hydrofilm)	There is a favorable cost–benefit ratio and an easy and quick application

				skin care using moisturizing 5% urea lotion.			patient reported outcomes	Effect size: 2 Secondary: itching; MD 0.66, 95% CI 0.57 to 0.75, p<0.001, pain; MD 0.64, 95% CI 0.58 to 0.69, p<0.04.	can reduce or even prevent RD.
4.11 3M Cavilon Barrier film (BF) versus standard skin care	Lam 2019	N=55 (Phase 3 RCT)	Breast cancer patients, Canada	To assess the efficacy of BF in preventing and/or delaying the onset of grade two RD and reducing patient-reported sensation scores.	Throughto ut Tx	Treatment	**Primary:** development of RD **Secondary:** patient-reported outcomes improvements in the time-to-onset	**Primary:** MD 1.06, 95% CI 1.02 to 1.10, p=0.0408 (Favouring BF)	A larger study using a more reliable scoring method is required to clarify the effect of BF on radiation-association skin toxicity.
4.12 Mepitel film (MEP) versus standard care	Rades 2019	N=57	Head & neck cancer patients, Germany	To compare MEP to standard skin care for prevention of grade 2 RD.	Stopped prematurel y	Treatment	**Primary:** grade 2 RD at 50Gy (CTCAE), **Secondary:** grade 2 RD at 60Gy, pain	Trial was stopped prematurely	MEP was unsatisfactorily tolerated by patients.
4.13 Mepitel film (MEP) versus Biafine cream (standard of care)	Yan 2020	N=44 (Phase 2 RCT)	Head & neck cancer patients, China	To compare the effect of MEP and Biafine cream on (1) overall skin reaction severity and (2) on the rates of moist desquamation.	9 weeks	Prevention/Treatme nt	**Primary:** overall skin reaction severity, incidence of moist desquamation **Secondary:** skin dose and patient acceptability	**Primary:** skin reaction severity; MD 3.43, 95% CI 3.29 to 3.56, p<0.001 Effect size: 2 ; moist desquamation; MD 16, 95% CI 14.2 to 17.8, p<0.001) (Favouring MEP) **Secondary:** NS	MEP was superior to Biafine cream in reducing the severity of acute RISR and moist desquamation incidence.

5. Other interventions 5.1 Hydrosorb versus water-based spray (control)	Bazire 2015	N=278	Breast cancer patients, France	To report the efficacy of Hydrosorb versus control (water-based spray) as topical treatment of grade 1–2 RD.	5 weeks	Treatment	**Primary:** presence of grade 1 or 2 RD **Secondary:** Quality of life	**Primary**: MD 4.1, 95% CI 4.09 to 4.11, p=0.36 (NS) **Secondary:** NS	No significant difference between Hydrosorb and simple water spray in the treatment of ARD.

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Appendix E. Round 1 Rating Form

Recommendations	Agree	Disagree	Strength of recommendation				Comments
	%	%	*Strong*	*Moderate*	*Weak*	**Overall**	*Please see the expert stakeholder group's comments below:*
1.Topical atorvastatin may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	50%	50%	0%	6%	61%	*Weak*	• Only 1 study, small numbers (<100) and breast cancer only. • Primary endpoint dermatitis did not reach significance. • Too little research • Haven't heard to use this for Radiation Dermatitis • RTOG grading difference not statistically significant. • Although used, quality of evidence is lacking, few literatures to support it. • Insufficient evidence • Although using Atorvastatin 1% can prevent the acute radiation-induces skin toxicity and symptoms including itching, breast oedema and pain, the evidence is weak due to suggestion only based on 1 study with small sample size (n=70) and concerning minor inconsistencies with one study could not calculated effect size.
2.Bethmethasone 17-valerate cream is recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	89%	11%	44%	33%	6%	*Strong*	• Although the rating for quality of evidence is high, and the summary of evidence showed that using this cream reduced the development of radiation dermatitis, however, the primary outcome from previous SR showed that "there was an equal proportion of people developing a RISR (summary statistics not estimated)", in addition, the duration of intervention in two studies are various, so how to define the quality assessment is consistent? • Not to be used for Head and Neck areas though. Also, should be commenced after 2weeks of Radiotherapy to minimise potential steroid-induced telangiectasia. • All breast cancer patients.
3.Hydrocortisone cream may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	72%	28%	6%	17%	56%	*Weak*	• Only one study available with a small sample size (<100) • Can be used if the radiation dermatitis is itchy. • The strength of recommendation rates "weak" due to recommendation of statement only based on 1 study with small sample size (n=50), and although using this cream significantly

							delayed the onset of radiation dermatitis, its' primary outcome: "occurrence of moist desquamation" showed none significance. • Can be used Head and Neck areas. Will likely be too weak for body/limb areas though. To be commenced 2 weeks into therapy to avoid steroid-induced telangiectasia.
4.Mometasone furoate cream may be recommended for patients at the initiation of radiation therapy until completion to treat high-grade radiation dermatitis.	78%	22%	0%	44%	33%	*Moderate*	• Inconsistent results • Intermediate risk of bias • Agreed with reservation. contradicting results, with previous study, risk of study design bias in one study high. might require panel formal consensus. • Rating "moderate" was based on one previous study found that MMF cream was not superior to placebo. Besides, Different from other interventions, it specially mentioned "high-grade radiation dermatitis". Besides, only one reference pointed out that " MMF inunction after high-dose radiotherapy (>50 Gy) can prevent ARD, especially when the radiation dose is <6000 cGY.". Because of limited evidence, it's not strong to confirm this effect. • I would caution against Mometasone in cream vehicle as they all cause stinging on application. Also, to be limited to body/limbs and avoid on the face. Mometasone has a very high association with the development of periorificial dermatitis. • Some risk of bias due to study design and minor inconsistencies.
5. Aloe Vera is not recommended for patients to manage acute radiation dermatitis.	84%	16%	37%	32%	5%	*Strong*	• 2 negative studies • No significance. • It can cause cooling but cannot stop radiation dermatitis. • The strength of recommendation rates "strong" due to Two studies (n=237, n=100) and four other previous studies using Aloe Vera did not reduce the incidence and severity of radiation dermatitis in patients with breast cancer (which showed the same statement as the Appendix A- "summary of evidence" & "rational"). • Aloe vera is a known strong contact sensitizer. Coupled with the skin barrier impairment radiation dermatitis, this may result in the induction of allergic contact dermatitis or irritant contact dermatitis. • can be drying

6.Doxepin cream may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	44%	56%	0%	11%	56%	*Weak*	• Only 1 study (<100) with small numbers • Doxepin was started only after weeks of RT for treatment and not at initiation for prevention. • Used for oral mucositis. • Application started at week 5 only. • Doxepin cream is only recommended for short term use by the manufacturer. recommended for post radiotherapy treatment. • The strength of recommendation rates "weak" due to suggestion only based on 1 study with small sample size (n=48). It's not strongly enough to generalize the intervention that can use in reducing the incidence of grade 2 or higher radiation dermatitis in patients with breast cancer. • Further investigation required. Only applied for 7 days of treatment not throughout.
7. Heparinoid moisturizer may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	44%	56%	11%	6%	56%	*Weak*	• Study endpoint was skin moisture content not dermatitis. • 2 studies with different primary outcomes, imprecise data. • Inconsistent outcome parameters. • Results are imprecise and the actual study focused on measuring the water content on the skin as opposed to efficacy in skin toxicity. • "Disagree" was based on different primary outcomes and the results are imprecise in two studies (This statement also showed in Appendix A - the summary of evidence & rationale.) • Further investigation required. Not compared with any other accepted cream/dressing (anything is better than nothing?)
8. Topical lactokine-based R1 and R2 may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	67%	33%	0%	6%	61%	*Weak*	• Only 1 study • Risk of bias due to study design (no mention of blinding) • Not clear results in a similar study. • Evidence is very weak. in my clinical setting we have had patient using out of choice and it did not manage the RD. • Although using this kind of interventions can reduce the severity of radiation dermatitis, the evidence is too weak due to suggestion only based on 1 study with small sample size(n=98) and no baseline characteristics were compared across groups.
9. Silicone-based film forming gel dressing may be	89%	11%	11%	22%	44%	*Weak*	• Only 1 study • Other studies by Quills (2018) and Ahn (2020)-*not RCTs*

recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.							• Another study published in 2020 supports the evidence. (Ahn,2020). • Only used to prevent friction during radiotherapy when treating areas where skin folds are involved. • Should be commenced from the outset of radiotherapy.
10. Silver sulfadiazine cream may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	72%	28%	6%	11%	67%	*Weak*	• Contained mineral is not recommended during RT in Japan. • Applied only during non-radiation days. assessor not truly blinded. • More studies needed for comparative and consensus building. • The strength of recommendation rates "weak" due to recommendation of statement only based on 1 study (sample size n=110). • High risk of silver staining of skin due to the impaired skin barrier from radiation. uncommon cases of silver toxicity due to unpredictable absorption of silver through impaired skin barrier if treating a large body surface area. • Any cream containing a metal can affect absorbed radiation dose. Two studies measuring this effect have slightly different recommendations. More data on this is required. effects of creams with metals.
11. Silymarin-based cream may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	56%	44%	11%	0%	56%	*Weak*	• Only 1 study with small sample size (n=40), with risk of bias • No recommendation during RT, after RT. • No data about period about dermatitis grade in period just after radiotherapy. • Previous study supports the evidence (Martina, 2011)-*observational study not an RCT* • Further investigation required due to ROB. Compared to placebo gel but not sure what it was.
12. 3M Cavilon no-string barrier film may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	61%	39%	0%	39%	22%	*Moderate*	• Inconsistent results • Studies too small and imprecise outcomes. • One study of low quality with risk of bias not able to be determined. This is a costly product and needs more evidence. • 1 study wide CI, 1 study intermediate risk of bias. • Often used with good results. • Used very often to protect skin from RD.

							• The results are imprecise in one study with wide CI, and (2) another study did not show the results of secondary outcome- "patient-reported outcomes", and (3) two studies both with small sample size (n=39, 55). It's not strongly enough to generalize the results can use to prevent and delay the onset of grade 2 RD. • Could be commenced at initiation of radiotherapy.
13. Mepilex Lite dressings may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	61%	39%	0%	22%	44%	*Weak*	• One study, imprecise results, this product is too costly to use when there is not enough evidence. • Application only occurred when radiation wounds or erythema developed. • Outcome was time to healing rather than occurrence / severity of radiation dermatitis. • Poorly tolerated among some patients for head and neck. Data inconsistencies and risk of bias is high. efficient for managing wounds. • The strength of recommendation rates "weak" due to that primary outcomes are different in current (time-to-wound healing) and previous (do not reported clearly), and the results are imprecise (which have contacted authors for further information, but no replies were received). • Practically speaking as radiation dermatitis worsens, it becomes more difficult for mepilex dressings to have the required contact with the skin due to haemoserous ooze and crusting. • Removal for treatment.
14. Mepitel film may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	72%	28%	0%	50%	22%	*Moderate*	• Inconsistent outcome measures in one study. • Quite conflicting results between studies as patients did not tolerate in one study. • Superior when used prophylactically as compared to curative. • The strength of recommendation rates "moderate" due to high ROB in two studies in terms of study design and minor inconsistencies across studies (patients did not tolerate in 1 study). Besides, one study (4.12 Rades, 2019) lacked to include in the Appendix A-table 2 which found that Mepitel film was unsatisfactory tolerated by patients, so this intervention totally has four studies.

							• 3 studies found it reduces radiation dermatitis, but one study found not tolerated by patients. This product can interfere with skin marks used to set patients up and in warm humid weather needs constant replacing (anecdotal evidence).
15. Silver Nylon dressing may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	44%	56%	0%	17%	50%	*Weak*	• One study with a small sample size (<100) • Pelvic radiation patients only/ For anorectal only. • Again, this is too expensive without enough evidence. • No metal dressing recommended during Radiotherapy. • The study was mainly conducted in anal/rectal cancer only, that the pelvic site usually has somewhat different RT skin reaction thus different healing process as compared to other irradiated sites such as head and neck or chest wall. • Important to note that it should be removed (i.e, not in place) for each radiation treatment (due to silver component). See Aquino-Parsons2010_Phase III Study of Silver Leaf Nylon Dressing vs Standard Care. Did not reduce radiation dermatitis study with n=196 breast patients.

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Appendix F. Round 2 Rating Form

Group 1- consensus reached (>75%)	Strength of recommendation	Agree	Disagree	Additional comments
Aloe Vera is not recommended for patients to manage acute radiation dermatitis.	Strong	17 (94%)	1 (6%)	-For comfort only -Possible options for poorer countries but can be drying on the skin -I strongly agree with putting a botanical on barrier impaired skin. --This will lead to a significant chance of developing allergic contact dermatitis and should be avoided. Note that Aloe Vera is a strong sensitiser.
Silicone-based film forming gel dressing may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	Weak	17 (94%)	1 (6%)	-It's relatively new-but promising results -Possibly the best option but most expensive -Remark should be made on the recommendation that any topical application of materials must be removed during irradiation to avoid extra skin dose which will worsen the skin reaction.
Group 2- consensus not reached (<75%)				
Bethmethasone 17-valerate cream is recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	Strong	13 (72%)	5 (28%)	-Based on the comments and the mixed responses about the strength of the recommendation, I don't think this can be strongly recommended. Should it be moderate or even weak? There's also the comment about the timing and the location for the cream to

				be used. Should the wording be "may be recommended"? -Agree with the statement but think the strength of recommendation should be moderate given comments provided in previous rating round. -Not at initiation and not for areas with thin skin e.g., face, axilla, groin -Stopped before completion in some cases -Unsafe on broken areas; a corticosteroid -Remark should be made on the recommendation that any topical steroid cream must be withheld once the skin becomes disrupted and not intact, otherwise it will worsen the skin reaction. -Based on the comments (concerning about minor inconsistencies and all for breast cancer from references), the strength of recommendation with “moderate” is more suitable.
Mometasone furoate cream may be recommended for patients at the initiation of radiation therapy until completion to treat high-grade radiation dermatitis.	Moderate	13 (72%)	5 (31%)	-It looks like there is a good amount of reservation for using this cream. Should the recommendation be weak? -Stopped before completion in some cases -Fluoronated topical corticosteroids (such as mometasone furoate) are associated with higher rates of side

				effects including cutaneous atrophy, telangiectasia formation, and periorificial dermatitis. -Furthermore, cream vehicles of this particular TCS cause a lot of stinging on irritated skin which should be avoided as well.

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Appendix G. Round 3 Rating Form

Group 1- consensus reached (>75%)	Strength of recommendation	Agree	Disagree	Additional comments
Revised recommendation 1: Betamethasone 17-valerate cream may be recommended for patients during radiation therapy to manage acute radiation dermatitis.	Moderate	16 (89%)	2 (11%)	-I would only agree that there is WEAK evidence for both these preparations. -We really need to also consider what is the best preparation for poorer countries to use, so there may need to be various levels of recommendations. -I accept the two revised recommendations; however, emphasis must be added on that any topical steroid cream must be stopped once the skin becomes disrupted and not intact, otherwise it will worsen the skin reaction as observed in my previous clinical trials conducted in earlier year. -Due to the principle of physics, we should add reminder in our recommendation that patient should not put any topical application of materials including whatever product in cream or gel form, or dressing materials, on the irradiated area during irradiation to avoid extra skin dose which will worsen the skin reaction. For product in cream or gel form, we usually simply teach patients to
Revised recommendation 2: Mometasone furoate cream may be recommended for patients during radiation therapy to treat high-grade radiation dermatitis.	Weak	16 (89%)	2 (11%)	

				avoid apply on the irradiated skin prior to irradiation.
Aloe Vera is not recommended for patients to manage acute radiation dermatitis.	Strong	17 (94%)	1 (6%)	
Silicone-based film forming gel dressing may be recommended for patients at the initiation of radiation therapy until completion to manage acute radiation dermatitis.	Weak	17 (94%)	1 (6%)	-Regarding the silicone gel preparation: the gel is different to the dressing and does not require removal before radiation treatment. -The use of a moisturiser e.g., Sorbolene is non-expensive and may assist in reducing dryness in intact skin. Best practice may well be silicone gel, but only for those that can afford it. If this is to be an international guideline there needs to be a range of interventions to suit all.

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