ONS RADIODERMATITIS SYSTEMATIC REVIEW

Supplementary Material

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6. Characteristics of included studies

1. PICO Questions

Population	Intervention(s)	Comparator	Outcomes
Care for patients receiving radiation therapy			
Patients receiving radiation therapy for cancer in the breast/chest region	Deodorant/antiperspirant in addition to normal washing	Normal washing	Time to development of radiodermatitis (e.g. rash, desquamation, necrosis)
Care to minimize radiodermatitis			
Patients receiving radiation therapy for cancer	Aloe vera lotion	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity
Patients receiving radiation therapy for cancer	Emu oil	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity

Patients receiving radiation therapy for cancer	Oral curcumin	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity
Patients receiving radiation therapy for cancer	Topical nonsteroidal interventions (creams, lotions, ointments)	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity
Patients receiving radiation therapy for cancer	Topical calendula	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis

			Intervention adherence and fidelity
Patients receiving radiation therapy for cancer	Topical steroidal creams	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity
Patients receiving radiation therapy for cancer	Semipermeable dressings	Standard of care	Pain Pruritis Dry skin Quality of life Cost Time to develop radiodermatitis Intervention adherence and fidelity
Care to treat radiodermatitis			
Patients with radiodermatitis symptoms receiving radiation therapy for cancer	Topical nonsteroidal interventions (creams, lotions, ointments)	Standard of care	Pain Symptom severity Quality of life Cost

			Breaks/discontinuation in radiation treatment Secondary infections Time to resolution of radiodermatitis Protocol adherence and fidelity
Patients with radiodermatitis symptoms receiving radiation therapy for cancer	Topical steroidal creams	Standard of care	Pain Symptom severity Quality of life Cost Breaks/discontinuation in radiation treatment Secondary infections Time to resolution of radiodermatitis Intervention adherence and fidelity
Patients with radiodermatitis symptoms receiving radiation therapy for cancer	Semipermeable dressings	Standard of care	Pain Symptom severity Quality of life Cost Breaks/discontinuation in radiation treatment Secondary infections

			Time to resolution of radiodermatitis Intervention adherence and fidelity

2. Search Strategies

Search strategies replicated from Chan, Webster, et al., 2014, to update the literature search through August 2019

OVID MEDLINE

1. exp Radiodermatitis/ or radiodermatitis.mp.
2. radiation induced skin reaction.mp.
3. erythema.mp. or exp Erythema/
4. Desquamation.mp.
5. ulceration.mp.
6. redness.mp. or exp Skin Pigmentation/
7. exp Fibrosis/ or fibrosis.mp.
8. burning.mp.
9. rash.mp.
10. swell$3.mp.
11. itch$.mp.
12. (skin reaction$ or skin alter$ or skin toxic$ or skin change$).mp.
13. exp Radiation Injuries/

14. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15. exp Radiotherapy/

16. exp Radiation Oncology/

17. (radiother$ or radiat$ or irradiat$ or radiochemo$ or chemoradiat$).mp.

18. 15 or 16 or 17

19. (cancer$ or oncolog$ or neoplasm$ or carcinom$ or tumor$ or tumour$ or malignan$ or hematooncological or hematolo$).mp.

20. hemato oncological.mp.

21. exp Neoplasms/

22. (lymphom$ or sarcom$ or ewing$ or osteosarcom$ or wilms or nephroblastom$ or neuroblastom$ or rhabdomyosarcom$ or teratom$ or hepatom$ or hepatoblastom$ or PNET or medulloblastom$ or retinoblastom$ or meningiom$ or gliom$).mp.

23. (neuroectodermal tumor$ primitive or T-cell or B-cell or brain tumor$ or brain tumour$ or brain neoplasm$ or central nervous system neoplasm$ or central nervous system tumor$ or central nervous system tumour$ or brain cancer$ or brain neoplasm$ or intracranial neoplasm$ or leukemia lymphocytic acute).mp.

24. 19 or 20 or 21 or 22 or 23

25. randomized controlled trial.pt.

26. controlled clinical trial.pt.

27. randomized controlled trial.pt.

28. controlled clinical trial.pt.

29. randomized.ab.

30. placebo.ab.

31. clinical trials as topic.sh.

32. randomly.ab.

33. trial.ti.

34. 27 or 28 or 29 or 30 or 31 or 32 or 33

35. exp animals/ not humans.sh.

36. 34 not 35

37. 14 and 18 and 24 and 36

OVID EMBASE

1 radiodermatitis.mp. or exp radiation dermatitis/

2 radiation induced skin reaction.mp.

3 erythema.mp. or exp ERYTHEMA/

4 DESQUAMATION/ or desquamation.mp.

5 ulceration.mp.

6 redness.mp. or exp SKIN REDNESS/

7 exp FIBROSIS/ or fibrosis.mp.

8 burning.mp.

9 exp RASH/ or rash.mp.

10 swell$3.mp.

11 itch$.mp.

12 (skin adj (reaction$ or alter$ or toxic$ or change$)).mp.

13 exp radiation injury/

14 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13

15 exp RADIOTHERAPY/

16 radiation oncology.mp.

17 (radiother$ or radiat$ or irradiat$ or radiochemo$ or chemoradiat$).mp.

18 15 or 16 or 17

19 (cancer$ or oncolog$ or neoplasm$ or carcinom$ or tumor$ or tumour$ or malignan$ or hematooncological or hematolo$).mp.

20 hemato oncological.mp.

21 exp neoplasm/

22 (lymphom$ or sarcom$ or ewing$ or osteosarcom$ or wilms or nephroblastom$ or neuroblastom$ or rhabdomyosarcom$ or teratom$ or hepatom$ or hepatoblastom$ or PNET or medulloblastom$ or retinoblastom$ or meningiom$ or gliom$).mp.

23 (neuroectodermal tumor$ primitive or T-cell or B-cell or brain tumor$ or brain tumour$ or brain neoplasm$ or central nervous system neoplasm$ or central nervous system tumor$ or central nervous system tumour$ or brain cancer$ or brain neoplasm$ or intracranial neoplasm$ or leukemia lymphocytic acute).mp.

24 19 or 20 or 21 or 22 or 23

25 crossover procedure.sh.

26 double-blind procedure.sh.

27 single-blind procedure.sh.

28 (crossover$ or cross over$).tw.

29 placebo$.tw.

30 (doubl$ adj blind$).tw.

31 allocat$.tw.

32 trial.ti.

33 randomized controlled trial.sh.

34 random$.tw.

35 or/25-34

36 (ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/) and HUMAN/

37 ANIMAL/ or NONHUMAN/ or ANIMAL EXPERIMENT/

38 37 not 36

39 35 not 38

40 14 and 18 and 24 and 39

41 limit 40 to yr="2012 -Current"

42 remove duplicates from 41

43 limit 40 to dc=20120101-20181205

44 remove duplicates from 43

EBSCO CINAHL

S1 (MH "Radiodermatitis") OR radiodermatitis

S2 erythema or desquamation or ulceration or redness or fibrosis or burning or rash or swell or itch

S3 radiation induced skin reaction

S4 "skin reaction*" or "skin alter*" or "skin toxic*" or "skin change*"

S5 (MH "Erythema+")

S6 (MH "Fibrosis")

S7 ((MH "Fibrosis")) and (S1 and S2 and S3 and S4 and S5 and S6)

S8 ((MH "Fibrosis")) and (S1 and S2 and S3 and S4 and S5 and S6)

S9 S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8

S10 (MH "Radiotherapy+")

S11 (MH "Radiation Oncology")

S12 radiother* or radiat* or irradiat* or radiochemo* or chemoradiat*

S13 s10 or s11 or s12

S14 (MH "Neoplasms+")

S15 cancer* or oncolog* or neoplasm* or carcinom* or tumor* or tumour* or malignan* or hematooncological or hematolo* or lymphoma* or sarcoma* or ewing* or osteosarcoma* or wilms or nephroblastoma* or neuroblastoma* or rhabdomysarcoma*or teratom* or hepatom* or hepatoblastom* or pnet or medulloblastom* or retinoblastom* or meningiom* or gliom* or "hemato oncological"

S16 "neuroectodermal tumor* primitive" or "t cell" or "b cell" or "brain tumor" or "brain tumour" or "brain neoplasm" or "central nervous system neoplasm*" or "central nervous system tumour" or "central nervous system tumor" or "brain cancer" or "brain neoplasm" or "intracranial neoplasm*" or "leukemia lymphocytic acute"

S17 S14 or S15 or S16

S18 S9 and S13 and S17

S19 (MH "Clinical Trials+")

S20 PT clinical trial

S21 TX (clinic* n1 trial*)

S22 (MH "Random Assignment")

S23 TX random* allocat*

S24 TX placebo*

S25 (MH "Placebos")

S26 (MH "Quantitative Studies")

S27 TX allocat* random*

S28 "randomi#ed control* trial*"

S29 Singl* n5 blind* or doubl* n5 blind* or trebl* n5 blind* or tripl* n5 mask* or singl* n5 mask* or doubl* n5 mask* or trebl* n5 mask* or tripl* n5 mask*

S30 S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29

S31 S18 and S30

Wiley Cochrane Library

ID	Search
#1	MeSH descriptor: [Radiation Injuries] explode all trees
#2	MeSH descriptor: [Fibrosis] explode all trees
#3	MeSH descriptor: [Erythema] explode all trees
#4	MeSH descriptor: [Radiodermatitis] explode all trees
#5	(radiodermatitis) (Word variations have been searched)
#6	((radiation next induced next skin next reaction)) (Word variations have been searched)
#7	(erythema) (Word variations have been searched)
#8	(desquamation) (Word variations have been searched)
#9	(ulceration) (Word variations have been searched)
#10	(redness) (Word variations have been searched)
#11	(fibrosis) (Word variations have been searched)
#12	(burning) (Word variations have been searched)
#13	(rash) (Word variations have been searched)
#14	(itch) (Word variations have been searched)
#15	(swell) (Word variations have been searched)
#16	MeSH descriptor: [Radiotherapy] explode all trees
#17	MeSH descriptor: [Radiation Oncology] explode all trees
#18	((radiother* or radiat* or irradiat* or radiochemo* or chemoradiat*)) (Word variations have been searched)

#19 ("skin reaction" or "skin alteration" or "skin toxic" or "skin change") (Word variations have been searched)

#20 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #19

#21 #16 OR #17 OR #18

#22 (lymphoma* or sarcoma* or ewing* or osteosarcom* or wilms or nephroblastom* or neuroblastom* or rhabdomyosarcom* or teratom* or hepatom* or hepatoblastom* or pnet or medulloblastom* or retinoblastom* or meningiom* or gliom*) (Word variations have been searched)

#23 ("neuroectodermal tumor* primitive" or "t cell" or "b cell" or "brain tumor*" or "brain tumour*" or "brain neoplasm*" or "central nervous system neoplam*" or "central nervous system tumour*" or "central nervous system tumor*" or "brain cancer" or "brain neoplasm" or "intracranial neoplasm" or "leukemia lymphocytic acute") (Word variations have been searched)

#24 MeSH descriptor: [Neoplasms] explode all trees

#25 (cancer or oncolog* or neoplasm* or carcinom* or tumor* or tumour* or malignan* or hematooncological or hematolo* or "hemato oncological") (Word variations have been searched)

#26 #22 OR #23 OR #24 OR #25

OVID PsycINFO

1. double-blind.tw.

2. random$ assigned.tw.

3. control.tw.

4. 1 or 2 or 3

5. exp Radiation Therapy/ or radiation.mp.

6. cancer.mp. or exp Neoplasms/

7. skin.mp.

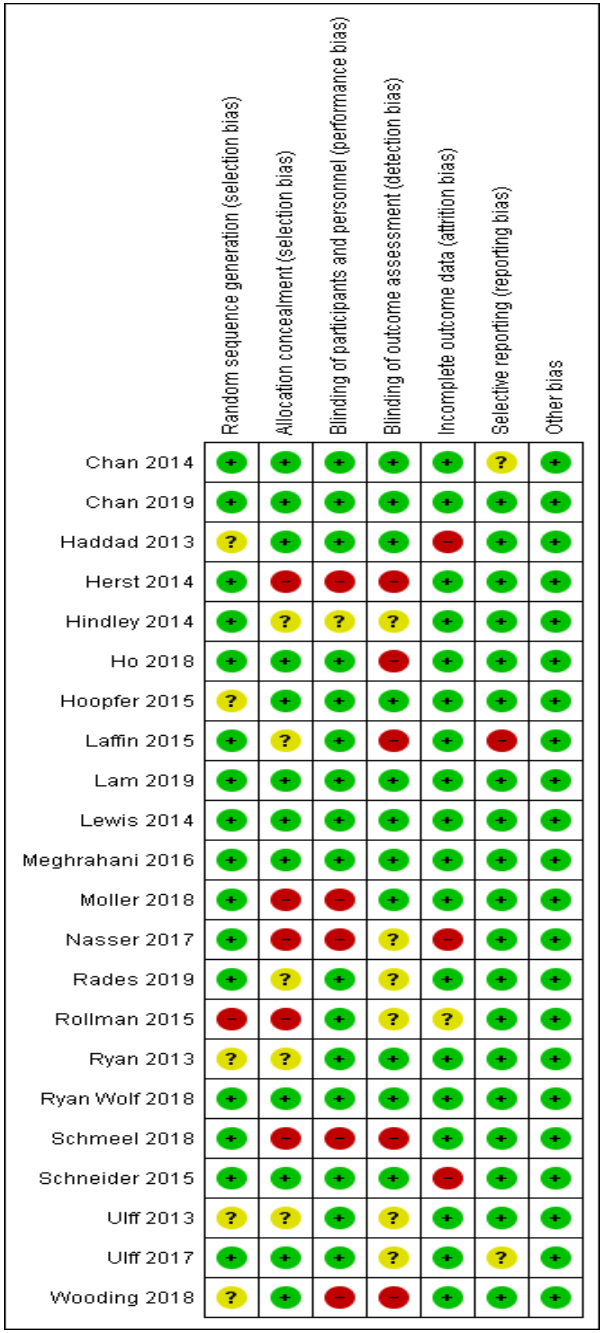
8. 5 and 6 and 7

9. 4 and 8

LILACS

((Pt:"RANDOMIZED CONTROLLED TRIAL" OR Pt:"CONTROLLED CLINICAL TRIAL" OR Mh:"RANDOMIZED CONTROLLED TRIALS" OR Mh:"RANDOM ALLOCATION" OR Mh:"DOUBLE-BLIND METHOD" OR Mh:"SINGLE-BLIND METHOD" OR Pt:"MULTIcentre STUDY") OR ((tw:ensaio or tw:ensayo or tw:trial) and (tw:azar or tw:acaso or tw:placebo or tw:control$ or tw:aleat$ or tw:random$ or (tw:duplo and tw:cego) or (tw:doble and tw:ciego) or (tw:double and tw:blind)) and tw:clinic$)) AND NOT ((CT:ANIMALS OR MH:ANIMALS OR CT:RABBITS OR CT:MICE OR MH:RATS OR MH:PRIMATES OR MH:DOGS OR MH:RABBITS OR MH:SWINE) AND NOT (CT:HUMAN AND CT:ANIMALS)) and (radiation or radiacion) and (skin or piel)

3. Evidence risk of bias figure (Developed using Review Manager Web (RevMan Web) [Systematic review software]. (2019). https://revman.cochrane.org.)



Reviewers' ratings of risk of bias for each study

4. Evidence tables (Developed using GRADEpro GDT: GRADEpro Guideline Development Tool [Software]. McMaster University, 2015 (developed by Evidence Prime, Inc.). Available from gradepro.org.)

- Deodorant/antiperspirant in addition to normal washing vs. normal washing
- Aloe vera lotion vs. standard of care
- Emu oil vs. standard of care
- Oral curcumin vs. standard of care
- Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care
- Calendula vs. standard of care
- Topical steroidal creams vs. standard of care
- Semipermeable dressings vs. standard of care

Deodorant/antiperspirant in addition to normal washing vs. normal washing

Question: Should deodorant/antiperspirant in addition to normal washing be used rather than normal washing alone in patients receiving radiation therapy for cancer in the breast/chest region?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Deodorant plus standard skin care/standard of care	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of Grade 2 RD												
3 [1,2,3]	randomized trials	not serious	not serious [a]	not serious	very serious [b,c]	none	133/302 (44.0%)	75/215 (34.9%)	**RR 0.99** (0.76 to 1.29)	**3 fewer per 1,000** (from 84 fewer to 101 more)	⊕⊕◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Deodorant plus standard skin care/standard of care	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of Grade 3 RD												
3 [1,2,3]	randomized trials	not serious	not serious [a]	not serious	very serious [b,c]	none	11/302 (3.6%)	11/215 (5.1%)	**RR 0.74** (0.27 to 2.02)	**13 fewer per 1,000** (from 37 fewer to 52 more)	⊕⊕◯◯ LOW	CRITICAL
Pruritis at end of radiation treatment												
1 [4]	randomized trials	serious [d]	not serious	not serious	very serious [c,e]	none	28/39 (71.8%)	26/41 (63.4%)	**OR 2.62** (1.01 to 6.78)	**185 more per 1,000** (from 2 more to 287 more)	⊕◯◯◯ VERY LOW	CRITICAL
Moderate-to-severe pain at end of radiation treatment												
1 [4]	randomized trials	serious [d]	not serious	not serious	very serious [b,c]	none	9/39 (23.1%)	5/41 (12.2%)	**OR 0.77** (0.29 to 2.09)	**25 fewer per 1,000** (from 83 fewer to 103 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Deodorant plus standard skin care/standard of care	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Sweating at end of radiation treatment												
1 [4]	randomized trials	serious [d]	not serious	not serious	very serious [c]	none	8/39 (20.5%)	11/41 (26.8%)	**OR 0.34** (0.12 to 0.93)	**157 fewer per 1,000** (from 226 fewer to 14 fewer)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio; **MD:** Mean difference

Explanations

a. Analysis included comparisons using both aluminum and non-aluminum containing deodorant. No serious inconsistency was seen (I^2=35%).

b. The 95% CI includes the potential for both benefit and harm.

c. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

d. Theberge 2009 had some concerns with allocation concealment, patient blinding, and incomplete outcome reporting.

e. The 95% CI may not include meaningful harm.

References

1. Bennett, C. (2009). An investigation into the use of a non-metallic deodorant during radiotherapy treatment: A randomised controlled trial. *Journal of Radiotherapy in Practice*, *8*, 3–9. https://doi.org/10.1017/S146039690800647X

2. Gee, A., Moffitt, D., Churn, M., & Errington, R. D. (2000). A randomised controlled trial to test a non-metallic deodorant used during a course of radiotherapy. *Journal of Radiotherapy in Practice*, *1*, 205–212. https://doi.org/10.1017/S1460396999000321

3. Lewis, L., Carson, S., Bydder, S., Athifa, M., Williams, A.M., & Bremner, A. (2014). Evaluating the effects of aluminum-containing and non-aluminum containing deodorants on axillary skin toxicity during radiation therapy for breast cancer: A 3-armed randomized controlled trial. *International Journal of Radiation Oncology* Biology* Physics*, *90*, 765–771. https://doi.org/10.1016/j.ijrobp.2014.06.054

4. Théberge, V., Harel, F., & Dagnault, A. (2009). Use of axillary deodorant and effect on acute skin toxicity during radiotherapy for breast cancer: A prospective randomized noninferiority trial. *International Journal of Radiation Oncology* Biology* Physics*, *75*, 1048–1052. https://doi.org/10.1016/j.ijrobp.2008.12.046

Aloe vera lotion vs. standard of care

Question: Should aloe vera lotion rather than standard of care be used to minimize the development of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aloe vera lotion	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of RD grade 2 or 3 at wk 5 RT												
1 [1]	randomized trials	not serious [a]	not serious	not serious	very serious [b,c]	none	4/53 (7.5%)	18/53 (34.0%)	**RR 0.22** (0.08 to 0.61)	**265 fewer per 1,000** (from 312 fewer to 132 fewer)	⨁⨁◯◯ LOW	CRITICAL
Moist desquamation (<50% of field; CSSP score 9-10)												
1 [2]	randomized trials	not serious	not serious	not serious	very serious [b,c]	none	11/81 (13.6%)	6/77 (7.8%)	**RR 1.74** (0.68 to 4.48)	**58 more per 1,000** (from 25 fewer to 271 more)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Aloe vera lotion	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Adverse events related to treatment discontinuation												
1 [1]	randomized trials	not serious	not serious	not serious	very serious [c]	none	No treatment-related adverse event reported in either arm (0/53 vs 0/53)				⨁⨁◯◯ LOW	CRITICAL
Skin Rash												
1 [2]	randomized trials	not serious	not serious	not serious	very serious [b,c]	none	24/81 (29.6%)	12/77 (15.6%)	**RR 1.90** (1.02 to 3.53)	**140 more per 1,000** (from 3 more to 394 more)	⨁⨁◯◯ LOW	CRITICAL
Pain												
1 [2]	randomized trials	not serious	not serious	not serious	very serious [b,c]	none	21/81 (25.9%)	25/77 (32.5%)	**RR 0.80** (0.49 to 1.30)	**65 fewer per 1,000** (from 166 fewer to 97 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Haddad 2013 has some concerns with incomplete outcome data; however, may contribute to the imprecision.

b. The 95% CI includes the potential for both benefit and harm.

c. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

References:

1. Haddad, P., Amouzgar–Hashemi, F., Samsami, S., Chinichian, S., & Oghabian, M.A. (2013). Aloe vera for prevention of radiation-induced dermatitis: A self-controlled clinical trial. *Current Oncology*, *20*, e345–e348. http://dx.doi.org/10.3747/co.20.1356

2. Hoopfer, D., Holloway, C., Gabos, Z., Alidrisi, M., Chafe, S., Krause, B., ... Hanson, J. (2015). Three-arm randomized phase III trial: Quality aloe and placebo cream versus powder as skin treatment during breast cancer radiation therapy. *Clinical Breast Cancer*, *15*, 181–190. http://dx.doi.org/10.1016/j.clbc.2014.12.006

Emu oil vs. standard of care

Question: Should emu oil rather than standard of care be used to minimize the development of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Emu oil	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of RD grade 2 or higher												
1 [1]	randomized trials	serious [a]	not serious	serious [b]	very serious [c]	none	1/28 (3.6%)	0/14 (0.0%)	**RR 1.55** (0.07 to 35.83)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
QoL												
1 [1]	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	28	14	-	MD **3.2 lower** (9.08 lower to 2.68 higher)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. Rollman 2015 has some concerns with successful randomization and allocation concealment.

b. Rollman 2015 reports on the outcome of development of radiodermatitis grade 3, not grade 2; therefore, may be an indirect assessment for this outcome.

c. The 95% CI includes the potential for both benefit and harm. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

Reference:

1. Rollmann, D.C., Novotny, P.J., Petersen, I.A., Garces, Y.I., Bauer, H.J., Yan, E.S., ... Laack, N.N.I. (2015). Double-blind, placebo-controlled pilot study of processed ultra emu oil versus placebo in the prevention of radiation dermatitis. *International Journal of Radiation Oncology* Biology* Physics*, *92*, 650–658. http://dx.doi.org/10.1016/j.ijrobp.2015.02.028

Oral curcumin vs. standard of care

Question: Should oral curcumin rather than standard of care be used to minimize the development of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Curcumin	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of radiodermatitis grade 2 or higher (assessed with: moist desquamation)												
2 [1,2]	randomized trials	very serious [a]	not serious [b]	serious [c]	serious [d,e]	none	31/366 (8.5%)	49/364 (13.5%)	**RR 0.64** (0.42 to 0.96)	**48 fewer per 1,000** (from 78 fewer to 5 fewer)	⊕◯◯◯ VERY LOW	CRITICAL
RD at end of treatment												
1 [1]	randomized trials	serious [a]	not serious	not serious	very serious [d]	none	14	16	-	MD **0.8 lower** (1.36 lower to 0.23 lower)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Curcumin	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Pain as measured by SF-MPQ												
1 [1]	randomized trials	serious [a]	not serious	not serious	serious [f]	none	344	342	-	MD **0.007 higher** (0.023 lower to 0.034 higher) [g]	⨁⨁◯◯ LOW	CRITICAL
HRQoL Symptom subscale from Skindex-29 (assessed with: Composite score at end of RT)												
1 [1]	randomized trials	serious [a]	not serious	not serious	serious [f]	none	344	342	-	MD **0.741 higher** (0.394 lower to 0.021 higher)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations

a. Ryan Wolf 2018 has concerns with incomplete outcome data (15% dropped out after randomization), selective reporting (did not use a validated scale and demonstrated unreliable identification of moist desquamation).

b. Some heterogeneity suspected (I^2 = 69%); however, likely contributes to imprecision and is accounted for within that domain.

c. Ryan 2013 and Ryan Wolf 2018 reported on moist desquamation, used here as an indirect measure of the critical outcome development of radiodermatitis.

d. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

e. The 95% CI may not include meaningful benefit.

f. The 95% CI includes the potential for both benefit and harm.

g. Ryan 2013 reported a similar finding when measuring SF-MQP among 35 patients (MD: 1.77, 95% CI: -0.93, 4.47). Based on the presentation of results in Ryan Wolf 2018, the results could not be pooled, so that estimate from the larger study was reported.

References:

1. Ryan, J.L., Heckler, C.E., Ling, M., Katz, A., Williams, J.P., Pentland, A.P., & Morrow, G.R. (2013). Curcumin for radiation dermatitis: A randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. *Radiation Research*, *180*, 34–43. https://doi.org/10.1667/RR3255.1

2. Ryan Wolf, J., Heckler, C.E., Guido, J.J., Peoples, A.R., Gewandter, J.S., Ling, M., ... Pentland, A.P. (2018). Oral curcumin for radiation dermatitis: A URCC NCORP study of 686 breast cancer patients. *Supportive Care in Cancer*, *26*, 1543–1552. https://doi.org/10.1007/s00520-017-3957-4

Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care

Question: Should topical nonsteroidal interventions (creams, lotions, ointments) rather than standard of care be used for the minimization or treatment of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical nonsteroidal	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of RD grade 2 or higher												
3 [1,3]	randomized trials	serious [a]	not serious	not serious [b]	not serious	none	315/341 (92.4%)	232/341 (68.0%)	**RR 1.29** (1.06 to 1.57)	**197 more per 1,000** (from 41 more to 388 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Moist desquamation												
1 [2]	randomized trials	serious [c]	not serious	not serious [b]	very serious [d,e]	none	16/120 (13.3%)	20/125 (16.0%)	**RR 0.84** (0.46 to 1.56)	**26 fewer per 1,000** (from 86 fewer to 90 more)	⊕◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical nonsteroidal	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Pruritis												
3 [1,2]	randomized trials	serious [c]	not serious	not serious [b]	serious [f]	none	179/437 (41.0%)	172/444 (38.7%)	**RR 1.09** (0.95 to 1.24)	**35 more per 1,000** (from 19 fewer to 93 more)	⊕⊕◯◯ LOW	CRITICAL
Pain												
2 [1]	randomized trials	not serious	not serious	not serious [b]	serious [d]	none	122/318 (38.4%)	111/318 (34.9%)	**RR 1.10** (0.90 to 1.35)	**35 more per 1,000** (from 35 fewer to 122 more)	⊕⊕⊕◯ MODERATE	CRITICAL
Relief of itching												
1 [2]	randomized trials	serious [c]	not serious	not serious [b]	very serious [e,g]	none	65/90 (72.2%)	73/86 (84.9%)	**RR 0.85** (0.73 to 0.99)	**127 fewer per 1,000** (from 229 fewer to 8 fewer)	⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations:

a. Nasser 2017 has concerns with allocation concealment, blinding of participants and outcome assessors, and incomplete outcome data. Possibly this contributes or explains the heterogeneity (I^2=78%) in the analysis.

b. SoC arms (using Gosselin 2010 because no difference between Aquafor and water) then in the recent studies of cream, aqueous cream and sorbolene would be a comparable comparison group without rating down for indirectness.

c. Laffin 2015 has some concerns with blinding of outcome assessors and selective reporting.

d. The 95% CI includes the potential for both benefit and harm.

e. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

f. The 95% CI includes the potential for both benefit and harm; however, the optimal information size is met.

g. The 95% CI may not include meaningful benefit.

References:

1. Chan, R.J., Mann, J., Tripcony, L., Keller, J., Cheuk, R., Blades, R., ... Walsh, C. (2014). Natural oil-based emulsion containing allantoin versus aqueous cream for managing radiation-induced skin reactions in patients with cancer: A phase 3, double-blind, randomized, controlled trial. *International Journal of Radiation Oncology* Biology* Physics*, *90*, 756–764. https://doi.org/10.1016/j.ijrobp.2014.06.034

2. Laffin, N., Smyth, W., Heyer, E., Fasugba, O., Abernethy, G., & Gardner, A. (2015). Effectiveness and acceptability of a moisturizing cream and a barrier cream during radiation therapy for breast cancer in the tropics: A randomized controlled trial. *Cancer Nursing*, *38*, 205–214. https://doi.org/10.1097/NCC.0000000000000161

3. Nasser, N. J., Fenig, S., Ravid, A., Nouriel, A., Ozery, N., Gardyn, S., ... Fenig, E. (2017). Vitamin D ointment for prevention of radiation dermatitis in breast cancer patients. *NPJ Breast Cancer*, *3*, 10. https://doi.org/10.1038/s41523-017-0006-x

Calendula vs. standard of care

Question: Should calendula rather than standard of care be used to minimize the development of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calendula	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of Grade 2 or greater												
2 [1,2]	randomized trials	not serious [a]	not serious	not serious	very serious [b]	none	47/227 (20.7%)	40/235 (17.0%)	**RR 1.21** (0.83 to 1.77)	**36 more per 1,000** (from 29 fewer to 131 more)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations:

a. Schneider had some concerns with incomplete outcome reporting; however, only contributes 5% to the meta-analysis.

b. The 95% CI includes the potential for both benefit and harm. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

References:

1. Schneider, F., Danski, M.T.R., & Vayego, S.A. (2015). Usage of Calendula officinalis in the prevention and treatment of radiodermatitis: A randomized double-blind controlled clinical trial. *Revista da Escola de Enfermagem da USP*, *49*, 221–228. https://doi.org/0.1590/S0080-623420150000200006

2. Sharp, L., Finnilä, K., Johansson, H., Abrahamsson, M., Hatschek, T., & Bergenmar, M. (2013). No differences between Calendula cream and aqueous cream in the prevention of acute radiation skin reactions--Results from a randomised blinded trial. *European Journal of Oncology Nursing*, *17*, 429–435. http://dx.doi.org/10.1016/j.ejon.2012.11.003

Topical steroidal creams vs. standard of care

Question: Should topical steroidal creams rather than standard of care be used for the minimization or treatment of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical steroids	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of RD grade 2 or higher												
6 [1,2,3,4,5,6]	randomized trials	not serious [a]	serious [b]	not serious	not serious	none	150/394 (38.1%)	223/389 (57.3%)	**RR 0.64** (0.42 to 0.96)	**224 fewer per 1,000** (from 338 fewer to 57 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Moist desquamation												
3 [2,3,6]	randomized trials	not serious [a]	serious [c]	not serious	serious [d,e]	none	41/195 (21.0%)	75/200 (37.5%)	**RR 0.57** (0.29 to 1.12)	**161 fewer per 1,000** (from 266 fewer to 45 more)	⊕⊕◯◯ LOW	IMPORTANT
Pain during radiation treatment (Severe VAS rating of itching, burning, irritation)												
1 [6]	randomized trials	not serious	not serious	not serious	very serious [e,f]	none	0/101 (0.0%)	7/99 (7.1%)	**RR 0.12** (0.02 to 0.98)	**62 fewer per 1,000** (from 69 fewer to 1 fewer)	⊕⊕◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Topical steroids	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Pain after radiation treatment (Severe VAS rating of itching, burning, irritation)												
1 [6]	randomized trials	not serious	not serious	not serious	serious [e]	none	0/98 (0.0%)	18/96 (18.8%)	**RR 0.05** (0.01 to 0.39)	**178 fewer per 1,000** (from 186 fewer to 114 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Treatment-related adverse events												
1 [3]	randomized trials	not serious	not serious	not serious	very serious [d,e]	none	2/23 (8.7%)	1/27 (3.7%)	**RR 2.35** (0.23 to 24.26)	**50 more per 1,000** (from 29 fewer to 861 more)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations:

a. Ho 2018 has some concerns with blinding of outcome assessors; however, outcome is objective.

b. Inconsistency present (I^2=84%); however, all studies demonstrate reduction in radiodermatitis with receipt of topical steroids.

c. Some unexplained inconsistency (I^2=60) present.

d. The 95% CI includes the potential for both benefit and harm.

e. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

f. The 95% CI may not include meaningful values.

References:

1. Hindley, A., Zain, Z., Wood, L., Whitehead, A., Sanneh, A., Barber, D., & Hornsby, R. (2014). Mometasone furoate cream reduces acute radiation dermatitis in patients receiving breast radiation therapy: results of a randomized trial. *International Journal of Radiation Oncology* Biology* Physics*, *90*, 748–755. http://dx.doi.org/10.1016/j.ijrobp.2014.06.033

2. Ho, A.Y., Olm-Shipman, M., Zhang, Z., Siu, C.T., Wilgucki, M., Phung, A., ... Powell, S.N. (2018). A randomized trial of mometasone furoate 0.1% to reduce high-grade acute radiation dermatitis in breast cancer patients receiving postmastectomy radiation. *International Journal of Radiation Oncology* Biology* Physics*, *101*, 325–333. https://doi.org/10.1016/j.ijrobp.2018.02.006

3. Meghrajani, C.F., Co, H.S., Arcillas, J.G., Maano, C.C., & Cupino, N A. (2016). A randomized, double-blind trial on the use of 1% hydrocortisone cream for the prevention of acute radiation dermatitis. *Expert Review of Clinical Pharmacology*, *9*, 483–91. http://dx.doi.org/10.1586/17512433.2016.1126506

4. Miller, R. C., Schwartz, D. J., Sloan, J. A., Griffin, P. C., Deming, R. L., Anders, J. C., ... Atherton, P. J. (2011). Mometasone furoate effect on acute skin toxicity in breast cancer patients receiving radiotherapy: a phase III double-blind, randomized trial from the North Central Cancer Treatment Group N06C4. *International Journal of Radiation Oncology* Biology* Physics*, *79*, 1460–1466. https://doi.org/10.1016/j.ijrobp.2010.01.031

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Semipermeable dressings vs. standard of care

Question: Should semipermeable dressings rather than standard of care be used for the minimization or treatment of radiodermatitis?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dressings	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of RD grade 2 or higher												
7 [2,3,4,6,7]	randomized trials	serious [a,b,c]	serious [d]	not serious	not serious [e,f]	none	84/353 (23.8%)	165/353 (46.7%)	**RR 0.52** (0.26 to 1.03)	**224 fewer per 1,000** (from 346 fewer to 14 more)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dressings	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Development of moist desquamation												
5 [1,2,6,7]	randomized trials	serious [a,c]	serious [g]	not serious	not serious	none	41/266 (15.4%)	94/262 (35.9%)	**RR 0.43** (0.32 to 0.58)	**205 fewer per 1,000** (from 244 fewer to 151 fewer)	⨁⨁◯◯ LOW	CRITICAL
Tenderness, discomfort, or pain												
1 [4]	randomized trials	serious [b]	not serious	not serious	serious [h]	none	7/78 (9.0%)	20/78 (25.6%)	**RR 0.35** (0.16 to 0.78)	**167 fewer per 1,000** (from 215 fewer to 56 fewer)	⨁⨁◯◯ LOW	IMPORTANT
Pruritis												
1 [4]	randomized trials	serious [b]	not serious	not serious	very serious [e,h]	none	11/77 (14.3%)	16/77 (20.8%)	**RR 0.69** (0.34 to 1.38)	**64 fewer per 1,000** (from 137 fewer to 79 more)	⨁◯◯◯ VERY LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dressings	Standard of care	Relative (95% CI)	Absolute (95% CI)		
Adverse events leading to treatment discontinuation												
2 [5,6]	randomized trials	not serious [i]	not serious	not serious	serious [h]	none	19/90 (21.1%)	0/91 (0.0%)	**RR 20.40** (2.82 to 147.52)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL
Patient-reported QoL												
2 [7]	randomized trials	serious [a]	not serious	not serious	very serious [h,j]	none	33	33	-	MD **0.4 lower** (0.75 lower to 0.05 lower)	⊕◯◯◯ VERY LOW	CRITICAL
Skin sensitivity												
1 [4]	randomized trials		not serious	not serious		none	6/78 (7.7%)	15/78 (19.2%)	**RR 0.40** (0.16 to 0.98)	**115 fewer per 1,000** (from 162 fewer to 4 fewer)	-	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio; **MD:** Mean difference

Explanations:

a. Wooding 2018 has some concerns with blinding of patients and outcome assessors.

b. Moller 2018 has some concerns with blinding of patients and outcome assessors.

c. Herst 2014 and Schmeel 2018 have concerns with allocation concealment and blinding of participants and outcome assessors.

d. Heterogeneity present (I^2=93%), may be explained by difference in cancer site receiving radiation; however, studies within radiation treatment site subgroups also demonstrate heterogeneity. All studies are in the direction of reduced radiodermatitis development within group receiving dressings.

e. The 95% CI includes the potential for both benefit and harm.

f. Imprecision likely explained by high heterogeneity and rated down in domain for inconsistency.

g. Some heterogeneity present (I^2=61%), may be explained by difference in cancer site receiving radiation.

h. Few events reported do not meet the optimal information size and suggest fragility in the estimate.

i. Schmeel 2019 has some concerns with allocation concealment and blinding of participants and outcome assessors; however, demonstrates a similar, but more conservative, estimate to Rades 2019.

j. The 95% CI may not include a meaningful benefit.

References:

1. Chan, R.J., Blades, R., Jones, L., Downer, T.R., Peet, S.C., Button, E., ... Yates, P. (2019). A single-blind, randomised controlled trial of StrataXRT®–A silicone-based film-forming gel dressing for prophylaxis and management of radiation dermatitis in patients with head and neck cancer. *Radiotherapy and Oncology*, *139*, 72–78. https://doi.org/10.1016/j.radonc.2019.07.014

2. Herst, P.M., Bennett, N.C., Sutherland, A.E., Peszynski, R.I., Paterson, D.B., & Jasperse, M.L. (2014). Prophylactic use of Mepitel Film prevents radiation-induced moist desquamation in an intra-patient randomised controlled clinical trial of 78 breast cancer patients. *Radiotherapy and Oncology*, *110*, 137–143. http://dx.doi.org/10.1016/j.radonc.2014.01.005

3. Lam, A.C., Yu, E., Vanwynsberghe, D., O'Neil, M., D'Souza, D., Cao, J., & Lock, M. (2019). Phase III randomized pair comparison of a barrier film vs. standard skin care in preventing radiation dermatitis in post-lumpectomy patients with breast cancer receiving adjuvant radiation therapy. *Cureus*, *11,* e4807. https://doi.org/10.7759/cureus.4807

4. Møller, P. K., Olling, K., Berg, M., Habæk, I., Haislund, B., Iversen, A. M., ... & Brink, C. (2018). Breast cancer patients report reduced sensitivity and pain using a barrier film during radiotherapy–A Danish intra-patient randomized multicentre study. *Technical Innovations & Patient Support in Radiation Oncology*, *7*, 20–25. https://doi.org/10.1016/j.tipsro.2018.05.004

5. Rades, D., Narvaez, C. A., Splettstößer, L., Dömer, C., Setter, C., Idel, C., ... Schild, S. E. (2019). A randomized trial (RAREST-01) comparing Mepitel® Film and standard care for prevention of radiation dermatitis in patients irradiated for locally advanced squamous cell carcinoma of the head-and-neck (SCCHN). *Radiotherapy and Oncology*, *139*, 79–82. https://doi.org/10.1016/j.radonc.2019.07.023

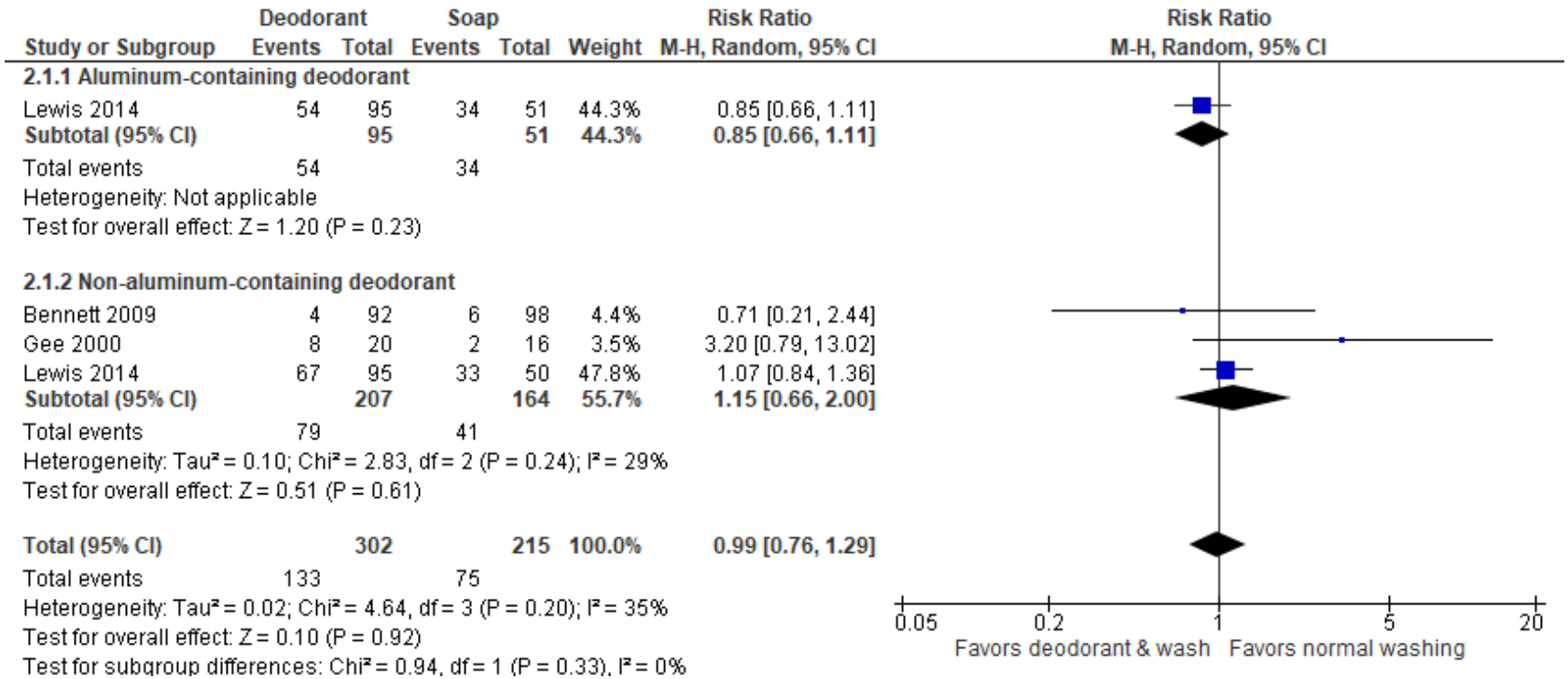
6. Schmeel, L.C., Koch, D., Stumpf, S., Leitzen, C., Simon, B., Schüller, H., ... Garbe, S. (2018). Prophylactically applied Hydrofilm polyurethane film dressings reduce radiation dermatitis in adjuvant radiation therapy of breast cancer patients. *Acta Oncologica*, *57*, 908–915. https://doi.org/10.1080/0284186X.2018.1441542

7. Wooding, H., Yan, J., Yuan, L., Chyou, T. Y., Gao, S., Ward, I., & Herst, P. M. (2018). The effect of Mepitel Film on acute radiation-induced skin reactions in head and neck cancer patients: A feasibility study. *The British Journal of Radiology*, *91*, 20170298. https://doi.org/ 10.1259/ bjr.20170298

5. Evidence forest plots (Developed using Review Manager Web (RevMan Web) [Systematic review software]. (2019). https://revman.cochrane.org)

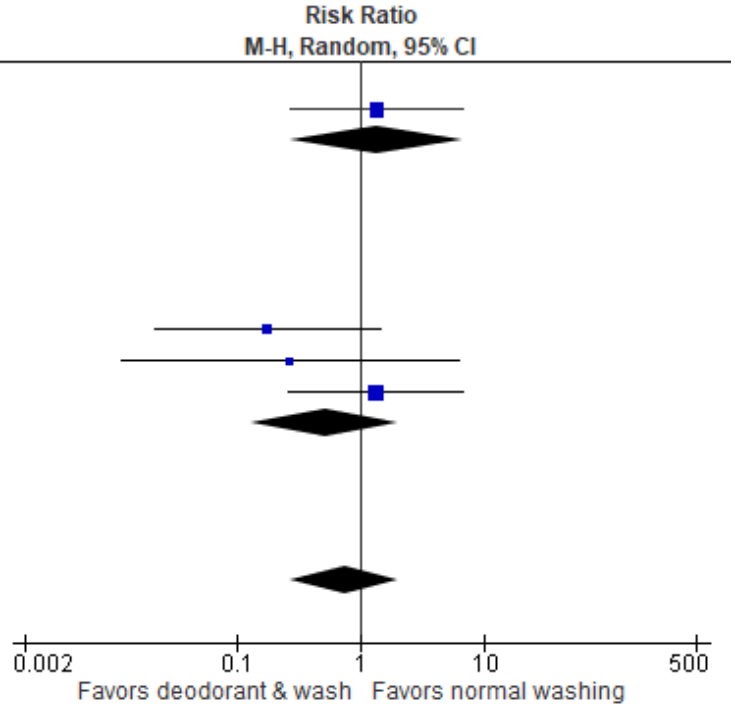
- Deodorant/antiperspirant in addition to normal washing vs. normal washing: Grade 2 radiodermatitis
- Deodorant/antiperspirant in addition to normal washing vs. normal washing: Grade 3 radiodermatitis
- Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care: Grade 2 or higher radiodermatitis
- Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care: Pruritis
- Calendula vs. standard of care: Grade 2 or higher radiodermatitis
- Topical steroidal creams vs. standard of care: Grade 2 or higher radiodermatitis
- Topical steroidal creams vs. standard of care: Moist desquamation
- Semipermeable dressings vs. standard of care: Grade 2 or higher radiodermatitis
- Semipermeable dressings vs. standard of care: Moist desquamation
- Semipermeable dressings vs. standard of care: Adverse events leading to discontinuation

Deodorant/antiperspirant in addition to normal washing vs. normal washing: Grade 2 radiodermatitis



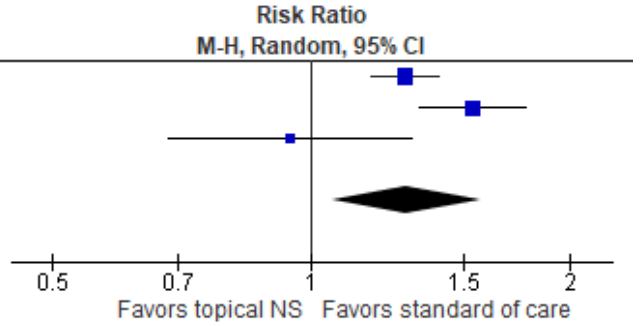
Deodorant/antiperspirant in addition to normal washing vs. normal washing: Grade 3 radiodermatitis

Study or Subgroup	Deodorant Events	Deodorant Total	Soap Events	Soap Total	Weight	Risk Ratio M-H, Random, 95% CI
2.2.1 Aluminum-containing deordorant						
Lewis 2014	5	95	2	51	34.4%	1.34 [0.27, 6.68]
Subtotal (95% CI)		**95**		**51**	**34.4%**	**1.34 [0.27, 6.68]**
Total events	5		2			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.36 (P = 0.72)						
2.2.2 Non-aluminum-containing deodorant						
Bennett 2009	1	92	6	98	21.2%	0.18 [0.02, 1.45]
Gee 2000	0	20	1	16	9.9%	0.27 [0.01, 6.21]
Lewis 2014	5	95	2	50	34.5%	1.32 [0.26, 6.54]
Subtotal (95% CI)		**207**		**164**	**65.6%**	**0.52 [0.13, 2.02]**
Total events	6		9			
Heterogeneity: Tau² = 0.31; Chi² = 2.50, df = 2 (P = 0.29); I² = 20%						
Test for overall effect: Z = 0.95 (P = 0.34)						
Total (95% CI)		**302**		**215**	**100.0%**	**0.74 [0.27, 2.02]**
Total events	11		11			
Heterogeneity: Tau² = 0.09; Chi² = 3.27, df = 3 (P = 0.35); I² = 8%						
Test for overall effect: Z = 0.59 (P = 0.56)						
Test for subgroup differences: Chi² = 0.79, df = 1 (P = 0.37), I² = 0%						



Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care: Grade 2 or higher radiodermatitis

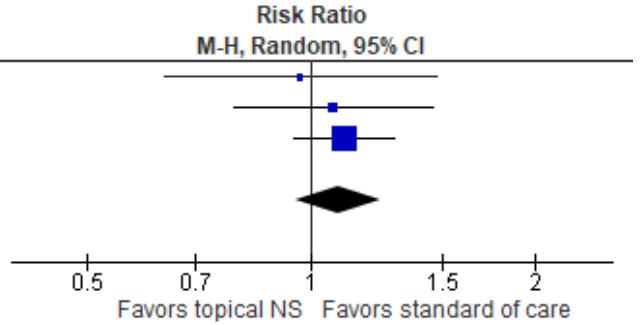
Study or Subgroup	Topical nonsteroidal Events	Topical nonsteroidal Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Chan 2014 (lateral)	153	157	122	161	42.1%	1.29 [1.17, 1.41]
Chan 2014 (medial)	145	161	92	157	37.4%	1.54 [1.33, 1.77]
Nasser 2017	17	23	18	23	20.6%	0.94 [0.68, 1.31]
Total (95% CI)		**341**		**341**	**100.0%**	**1.29 [1.06, 1.57]**
Total events	315		232			
Heterogeneity: Tau² = 0.02; Chi² = 9.20, df = 2 (P = 0.01); I² = 78%						
Test for overall effect: Z = 2.53 (P = 0.01)						



Topical nonsteroidal interventions (creams, lotions, ointments) vs. standard of care: Pruritis

	Topical nonsteroidal		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI
Chan 2014 (lateral)	33	157	35	161	9.9%	0.97 [0.63, 1.47]
Chan 2014 (medial)	56	161	51	157	18.4%	1.07 [0.79, 1.46]
Laffin 2015	90	119	86	126	71.7%	1.11 [0.95, 1.30]
Total (95% CI)		**437**		**444**	**100.0%**	**1.09 [0.95, 1.24]**
Total events	179		172			

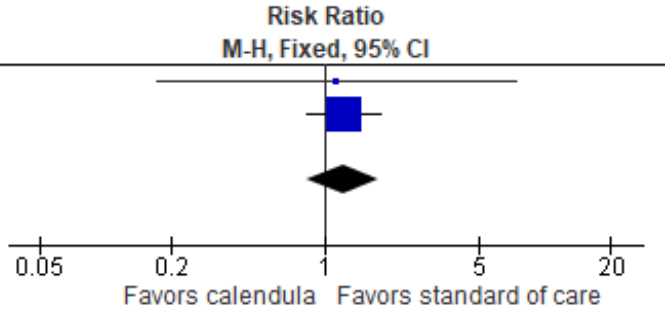
Heterogeneity: Tau² = 0.00; Chi² = 0.43, df = 2 (P = 0.81); I² = 0%
Test for overall effect: Z = 1.22 (P = 0.22)



Calendula vs. standard of care: Grade 2 or higher radiodermatitis

	Calendula		Standard of care			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
Schneider 2015	2	24	2	27	4.8%	1.13 [0.17, 7.38]
Sharp 2013	45	203	38	208	95.2%	1.21 [0.82, 1.79]
Total (95% CI)		**227**		**235**	**100.0%**	**1.21 [0.83, 1.77]**
Total events	47		40			

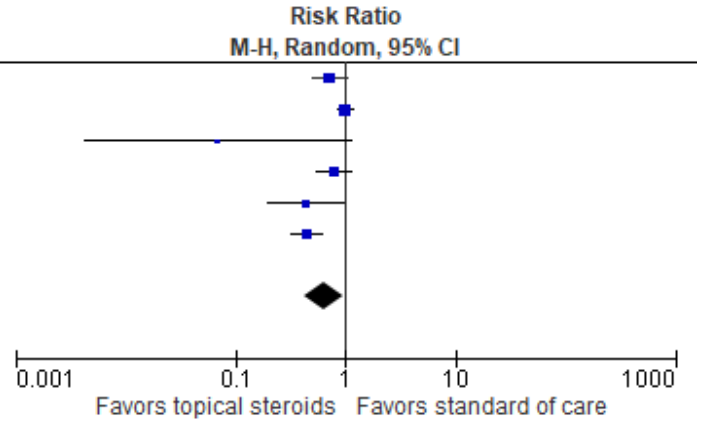
Heterogeneity: Chi² = 0.01, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.98 (P = 0.33)



Topical steroidal creams vs. standard of care: Grade 2 or higher radiodermatitis

Study or Subgroup	Topical steroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Hindley 2014	26	62	34	58	20.4%	0.72 [0.50, 1.03]
Ho 2018	55	70	58	73	23.3%	0.99 [0.84, 1.17]
Meghrahani 2016	0	23	8	27	2.0%	0.07 [0.00, 1.13]
Miller 2011	30	84	37	82	20.3%	0.79 [0.54, 1.15]
Ulff 2013	7	53	15	49	12.6%	0.43 [0.19, 0.97]
Ulff 2017	32	102	71	100	21.3%	0.44 [0.32, 0.60]
Total (95% CI)		**394**		**389**	**100.0%**	**0.64 [0.42, 0.96]**
Total events	150		223			

Heterogeneity: Tau² = 0.18; Chi² = 32.02, df = 5 (P < 0.00001); I² = 84%
Test for overall effect: Z = 2.14 (P = 0.03)



Topical steroidal creams vs. standard of care: Moist desquamation

Study or Subgroup	Topical steroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
9.2.1 Hypofraction RT						
Ulff 2017	0	32	2	29	4.7%	0.18 [0.01, 3.64]
Subtotal (95% CI)		**32**		**29**	**4.7%**	**0.18 [0.01, 3.64]**
Total events	0		2			

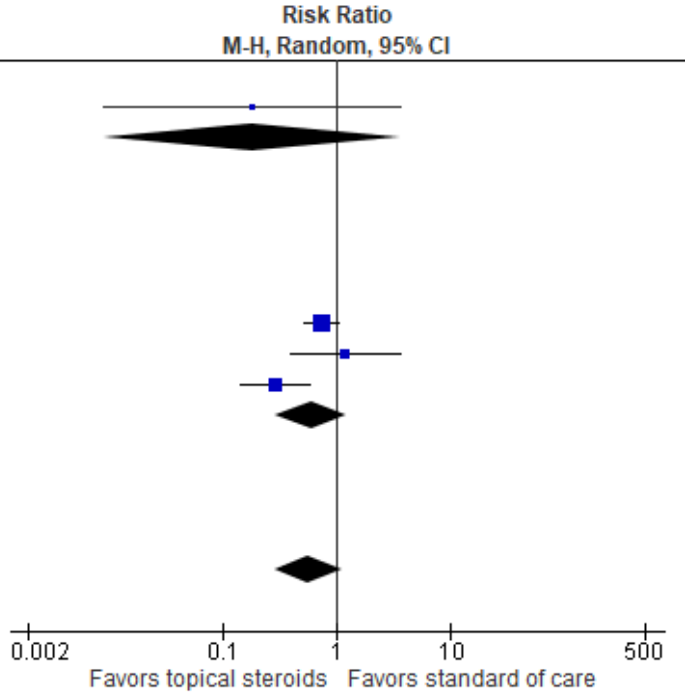
Heterogeneity: Not applicable
Test for overall effect: Z = 1.12 (P = 0.26)

9.2.2 Conventional RT						
Ho 2018	28	70	40	73	42.5%	0.73 [0.51, 1.04]
Meghrahani 2016	5	23	5	27	21.2%	1.17 [0.39, 3.55]
Ulff 2017	8	70	28	71	31.5%	0.29 [0.14, 0.59]
Subtotal (95% CI)		**163**		**171**	**95.3%**	**0.60 [0.29, 1.23]**
Total events	41		73			

Heterogeneity: Tau² = 0.28; Chi² = 6.71, df = 2 (P = 0.03); I² = 70%
Test for overall effect: Z = 1.39 (P = 0.16)

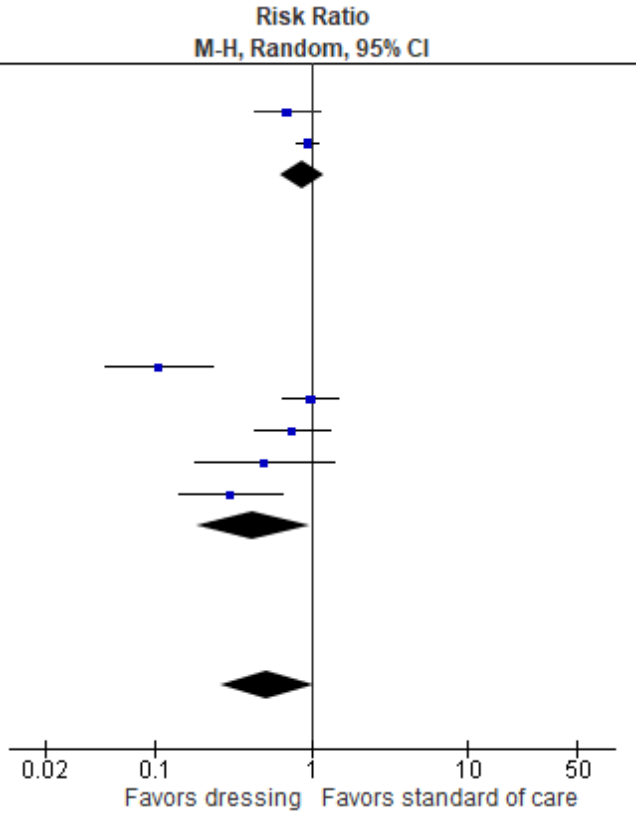
Total (95% CI)		**195**		**200**	**100.0%**	**0.57 [0.29, 1.12]**
Total events	41		75			

Heterogeneity: Tau² = 0.25; Chi² = 7.47, df = 3 (P = 0.06); I² = 60%
Test for overall effect: Z = 1.64 (P = 0.10)
Test for subgroup differences: Chi² = 0.57, df = 1 (P = 0.45), I² = 0%

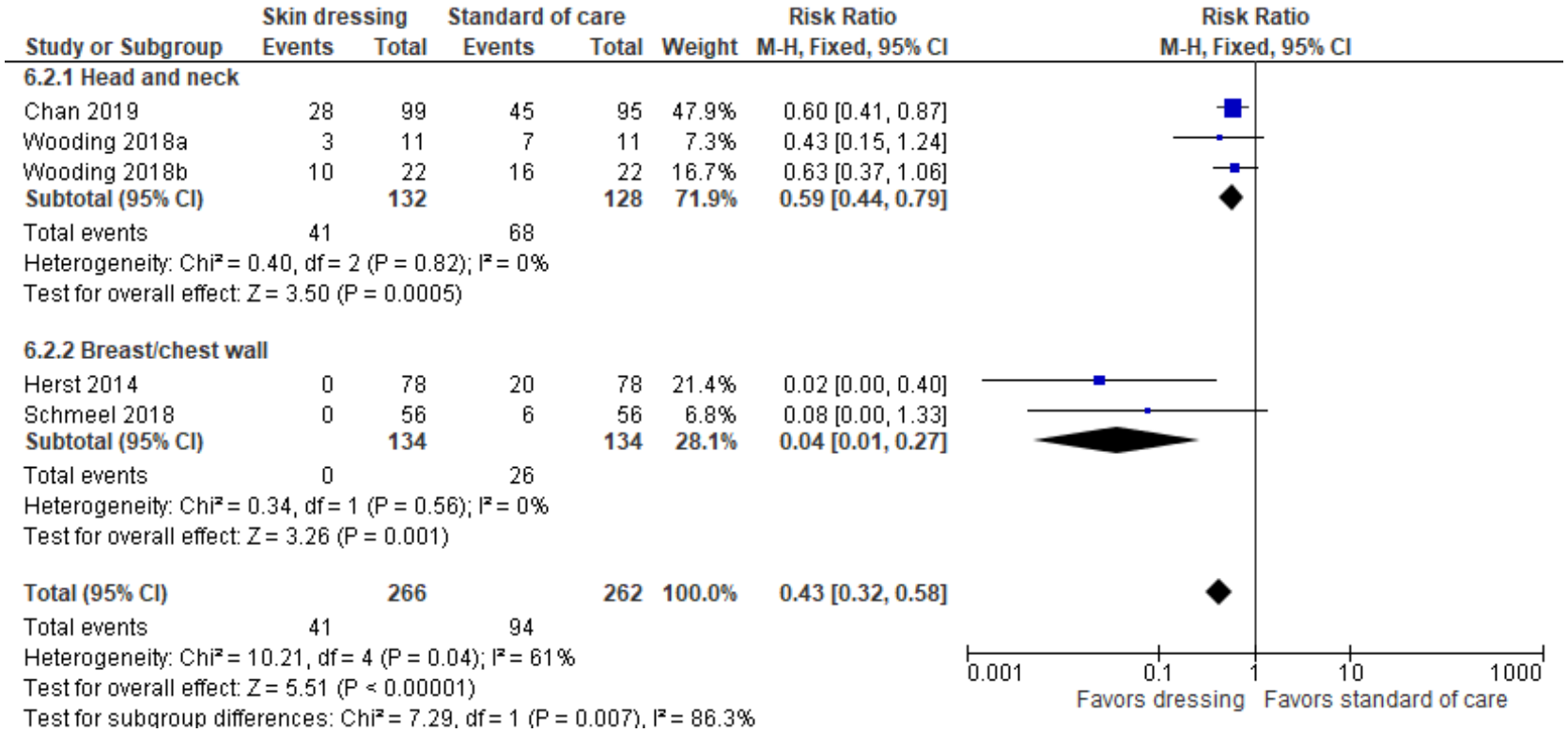


Semipermeable dressings vs. standard of care: Grade 2 or higher radiodermatitis

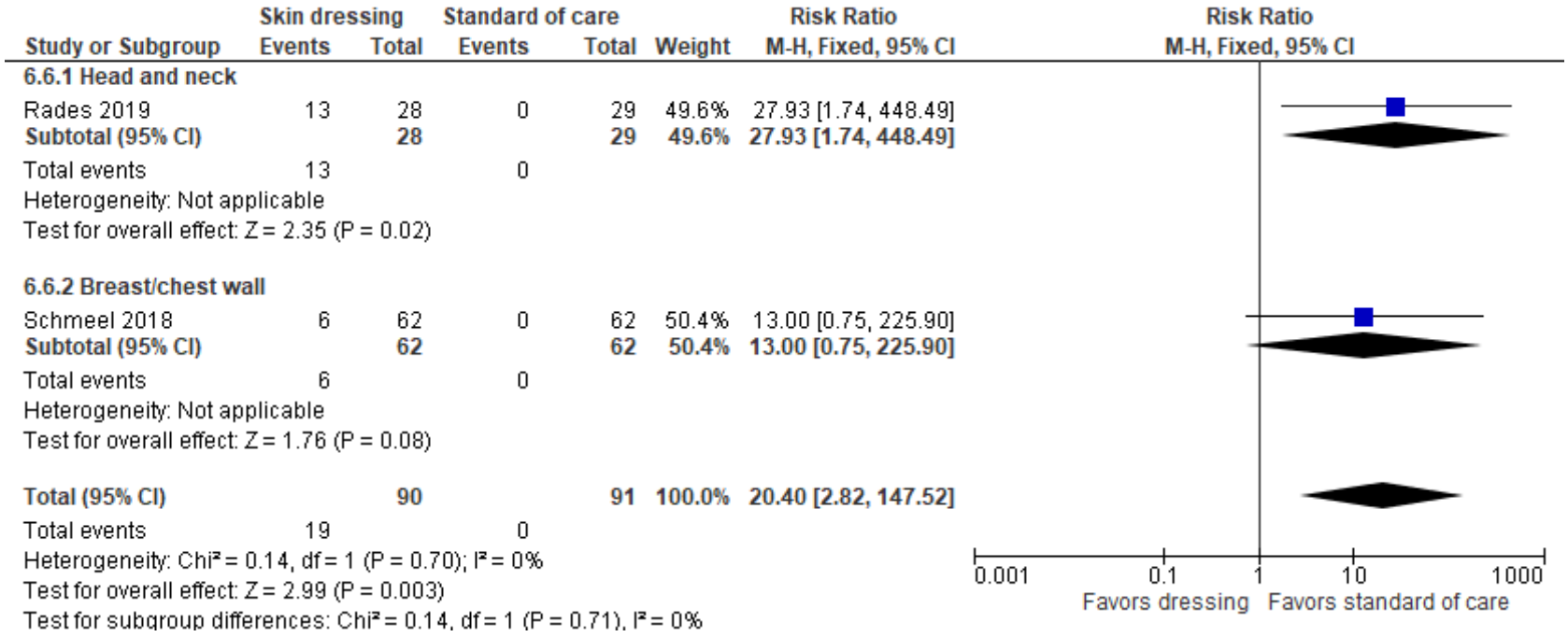
Study or Subgroup	Skin dressing Events	Total	Standard of care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
6.1.1 Head and neck						
Wooding 2018a	7	11	10	11	15.0%	0.70 [0.43, 1.14]
Wooding 2018b	20	22	21	22	16.1%	0.95 [0.81, 1.12]
Subtotal (95% CI)		**33**		**33**	**31.2%**	**0.87 [0.63, 1.21]**
Total events	27		31			
Heterogeneity: Tau² = 0.03; Chi² = 1.97, df = 1 (P = 0.16); I² = 49%						
Test for overall effect: Z = 0.84 (P = 0.40)						
6.1.2 Breast/chest wall						
Herst 2014	6	78	56	78	13.4%	0.11 [0.05, 0.23]
Lam 2019 (lateral)	23	52	26	58	15.3%	0.99 [0.65, 1.50]
Lam 2019 (medial)	16	58	19	52	14.7%	0.75 [0.44, 1.31]
Moller 2018	5	76	10	76	11.9%	0.50 [0.18, 1.39]
Schmeel 2018	7	56	23	56	13.5%	0.30 [0.14, 0.65]
Subtotal (95% CI)		**320**		**320**	**68.8%**	**0.43 [0.19, 0.98]**
Total events	57		134			
Heterogeneity: Tau² = 0.77; Chi² = 32.27, df = 4 (P < 0.00001); I² = 88%						
Test for overall effect: Z = 2.01 (P = 0.04)						
Total (95% CI)		**353**		**353**	**100.0%**	**0.52 [0.26, 1.03]**
Total events	84		165			
Heterogeneity: Tau² = 0.74; Chi² = 87.35, df = 6 (P < 0.00001); I² = 93%						
Test for overall effect: Z = 1.86 (P = 0.06)						
Test for subgroup differences: Chi² = 2.43, df = 1 (P = 0.12), I² = 58.9%						



Semipermeable dressings vs. standard of care: Moist desquamation



Semipermeable dressings vs. standard of care: Adverse events leading to discontinuation



6. Characteristics of included studies

Study Characteristics Table

RT – radiation
NR – not reported
Gy – Grey

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
Chan, 2014	Australia	RCT	In: >18 years with a definitive diagnosis of breast, lung, or head and neck cancer and receiving RT either as primary treatment or postoperative treatment to their chest, breast/ axilla, or head and neck Ex: preexisting skin rash, ulceration, or open wound in the treatment area, known skin allergy or other systemic skin disease (even if not directly affecting irradiated fields), any known allergic reaction to any ingredient of either the	N=174 NOCA cream n=89 Aqueous cream n=85	Mean NR NOCA cream 60.03 Aqueous cream 60.74	66.3	Breast, lung, head and neck cancer	>50 Gy	NOCA cream	Aqueous cream	Weekly during RT and weekly x 4 post RT	Development of radiodermatitis

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			NOCA or the aqueous cream									
Chan, 2019	Australia	RCT	In: aged 18 years or older with a definitive diagnosis of head and neck cancer receiving RT (>50 Gy) either as a primary or postoperative treatment to their head and neck were eligible. Ex: pre-existing skin rash or had an open wound in the treatment area. Patients were also excluded if they had known allergic and other systemic skin diseases, any known allergic reactions towards any ingredient of either the StrataXRT or Sorbolene or failed the patch test	N=197 StrataXRT n=100 Sorbolene n=97	Strata mean age 64, Sorbolene mean age 63.6	Strata 23%, Sorbo-lene 21%	Head and Neck With or without systemic therapy	Radiotherapy (>50 Gy) either as a primary or postopera-tive treatment to head and neck	StrataXRT	Sorbolene	Weekly during RT and up to 4 weeks post RT	Development of radiodermatitis Pain Pruritis Quality of life Treatment discontinuation
Haddad, 2013	Iran	RCT (self-control)	In: Adults; H&N, breast, pelvic cancers; anatomic RT area could be divided into two symmetrical halves with no	N=60	Mean 52 (range 21-78)	67	Head and neck, pelvic, other Radiation plus	40- 70 Gy, (mean 54 Gy)	Aloe Vera	Standard of care	Weekly during RT and at 2 and 4 weeks post RT	Development of radiodermatitis

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			difference in the radiation dose prescribed for each half. Ex: previous history of RT, presence of skin diseases in the treatment area, underlying diseases such as diabetes leading to increased susceptibility of patients to skin problems				systemic therapy					
Herst, 2014	Australia /New Zealand	RCT (intra-patient con-trolled)	In: Patients receiving RT for breast cancer, able to return to the hospital after treatment for follow-up for up to four weeks. Ex: Previous RT to the ipsilateral chest wall, metastatic disease, breast reconstruction, impaired mobility, and a Karnofsky performance status of less than 70	N=80	Range 30-94 Mean age 59.9	97	Breast, radiation only	40-54 Gy	Mepilex	Aqueous cream	3x weekly during RT followed by weekly x4 weeks post RT	Development of radiodermatitis Adverse events
Hindley, 2014	UK	RCT	In: Patients receiving RT to breast or chest wall alone Ex: NR	N=120 Mometa-sone n=62	Mean age Mean age mometa-sone 59	100	Breast cancer with or without surgery	40 Gy in 15 fractions in 3 weeks	Mometa-sone	Diprobase	Weekly during RT and 2 weeks post RT	Development of radiodermatitis Quality of life

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
				Diprobase n=58	Mean age diprobase 60		and/or systemic therapy					Adverse events
Ho, 2018	US	RCT	In: 18 or older with ECOG status of 0 or 1 and a pathologic diagnosis of breast cancer receiving PMRT. Ex: Patients with gross disease within intended field, prior RT to ipsilateral chest wall or thorax, chest wall boost, palliative or preoperative RT with concurrent chemotherapy (biologic agents allowed), pre-existing > grade 1 skin toxicity, cellulitis or incompletely healed wounds at intended site of cream application, comorbid conditions such as uncontrolled infections, uncontrolled diabetes, or connective tissue disease	N=143 Mometa-sone n=70 Eucerin n=73	Median age 48 Mometa-sone median age 49 Eucerin median age 47.5	100	Breast cancer with or without systemic therapy	50 Gy/25 fractions or 50.4 Gy/28 fractions delivered over 5 to 5.5 weeks	Mometa-sone	Eucerin	Weekly during RT and 2 weeks post RT	Development of radiodermatitis Quality of life Adverse events

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
Hoopfer, 2015	Canada	RCT	In: age ≥ 18 years, nonmetastatic breast cancer, previous mastectomy or segmental resection Ex: uncontrolled diabetes, uncontrolled eating disorders, acquired immunodefi-ciency syndrome, active lupus or scleroderma, a known allergy to pure aloe	N=248 Powder n=79 Aloe cream n=81 Placebo n=77	5 subjects </=35; 147 subjects 36-59; 85 subjects >/=60	100	Breast cancer Radiation plus systemic therapy and/or surgery	45 Gy in 20 fractions or 50 Gy in 25 fractions.	Powder (non-metallic baby or cornstarch or aloe cream)	Placebo cream	Weekly during RT and at 1, 2 and 4 weeks post RT	Development of radiodermatitis Pain
Laffin, 2015	Australia	RCT	In: 18 years or older, having external beam RT for carcinoma of the breast Ex: receiving RT other than standard protocols or for palliative reasons, had an allergy to either study cream	N=250 Cavilon n=119 Sorbolene n=126)	Mean age 55.5 Cavilon mean 55.66 Sorbolene mean 55.38)	100	Breast cancer, Radiation following surgery	42 Gy in 16 fractions or 50 Gy in 25 fractions	Cavilon double barrier cream	Sorbolene	Weekly during RT and 4 weeks post RT	Moist desquamation Pruritis
Lam, 2019	Canada	RCT (self-control)	In: women aged 18-90 who had undergone a lumpectomy and had been prescribed a standard dose (42.5 Gy in 16	N=55	Mean age 62.1	100	Breast cancer with or without systemic therapy and/or surgery	42.5 to 50 Gy	3M Cavilon Barrier Film (BF) Lateral and Medial	Standard of care	Weekly during RT and 7-10 days post RT	Development of radiodermatitis Pain Pruritis

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			fractions or 50 Gy in 25 fractions) of adjuvant tangential RT, without the need for a boost or bolus. Ex: NR									
Lewis, 2014	Australia	RCT	In: Female 18 years or older scheduled to undergo 2-, 3-, or 4- field breast RT Ex: Concomitant chemo; hypofractionated RT; intraoperative RT; previous ipsilateral breast or chest wall RT; tumor with skin involvement; pregnant or lactating; known allergy or hypersensitivity to deodorant; or hyperhidrosis	N=333, Aluminum deodorant = 107 Non-aluminum deodorant =109 Soap only N=117	Range 31-88 Aluminum deodorant mean=53.5 Non-aluminum deodorant mean=56.5 Soap only mean=57.0	100	Breast cancer, Radiation only	Total dose NR	Aluminum-containing deodorant, non-aluminum containing deodorant	Soap only	Weekly during RT and one month post RT	Development of radiodermatitis Pruritis Adverse events
Meghrajani, 2016	Philli-pines	RCT	In: age 19-80, radical mastectomy, completed chemotherapy for stage I to III breast cancer, scheduled for RT Ex: Known connective tissue disease, concurrent	N=50 Hydro-cortisone n=23 Placebo n=27	Hydro-cortisone mean age 50.48 Placebo mean age n=51.78	100	Breast cancer with or without surgery	50 Gy total in 25 fractions	Hydro-cortisone	Placebo	Weekly during RT to the end of RT	Development of radiodermatitis Quality of life Adverse events

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			chemotherapy, systemic corticosteroids									
Moller, 2018	Den-mark	RCT	In: women referred to postoperative adjuvant RT for breast cancer Ex: Lack of compliance, not understanding Danish, or inclusion in a separate trial	N=101, Mepitel film=79 Standard care=79	Mean 61.9	100	Breast, Radiation plus systemic therapy	40 Gy/15 fractions in 3 weeks	Mepitel film	Standard care	At end of RT and 2 weeks post RT	Development and resolution of radio-dermatitis Pain Pruritis Adverse events
Nasser, 2017	Israel	RCT	In: women aged 18 to 75 years with a confirmed histological diagnosis of localized breast cancer. All patients were after breast lumpectomy, and scheduled to receive adjuvant RT Ex: scleroderma, large breast with an inter-field of more than 25 cm, or prior RT to the same breast. Patients with indication to lymph node irradiation were not included in this study	N=23	Mean age 63	100	Breast cancer, Radiation with or without surgery	42.72 Gy in 16 fractions or 50 Gy in 25 fractions	Daivonex (Vitamin D) ointment	Aqua cream	Weekly during RT and at 2 weeks post RT	Development of radiodermatitis

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
Rades, 2019	Ger-many	RCT	NR	N=57, Mepitel n=28, Standard of care n=29	N=13 older than 63, N=15 younger than 62 N=15 older than 63, N=14 younger than 62	38.6	Head and neck, radiation, radiation and systemic	Max of 50 Gy to primary tumor region and bilateral lymph nodes	Mepitel film	Standard care	Interim analysis—trial stopped early	Development of radiodermatitis Pain Pruritis Adverse events
Rollman, 2015	USA	RCT	In: adults (age 18 years) with primary invasive breast carcinoma or ductal carcinoma in situ, planned course of continuous, definitive, or adjuvant external beam and who had an Eastern Cooperative Oncology Group performance status of 0, 1, or 2. Ex: Patients with inflammatory carcinoma of the breast, a history of prior RT to the area being treated, or bilateral breast carcinoma; who were receiving partial (<75%) breast treatment,	N=42, Emu oil n=28, Cotton-seed oil (placebo) n=14	NR	100	Breast cancer, radiation with or without surgery	45-55 Gy	Emu oil	Cotton-seed oil (placebo)	Weekly during RT and at 6 weeks post RT	Development of radiodermatitis Quality of life Adverse events

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			or who had a known allergy to Ultra Emu Oil or cottonseed oil									
Ryan, 2013	USA	RCT	In: >/= 18 years old, diagnosed with breast cancer or carcinoma in situ and prescribed RT without chemotherapy Ex: bilateral breast cancer, previous RT to the chest or breast area, inflammatory breast cancer, reconstruction and/or expanders prior to RT, taking anticoagulant therapy or anti-epidermal growth factor receptor (EGFR) therapy or receiving partial breast irradiation	N=35 Curcumin n=15 Placebo n=16	Mean age 58.1 Curcumin 54.6 Placebo, 61.1	100	Breast cancer, with or without surgery	Total dose of >/=42Gy	Curcumin	Placebo	Weekly during RT and at 1 and 6 months post RT	Development of radiodermatitis Pain Adverse events
Ryan Wolf, 2018	USA	RCT	In: females >17 with breast cancer or carcinoma in situ, prescribed conventional or Canadian fractionated RT without concurrent chemotherapy	N=686 Curcumin n=344 Placebo n=342	Mean age 57.6 Curcumin 57.6 Placebo 57.7	100	Breast cancer, radiation with or without surgery	48-51 Gy	Curcumin	Placebo	Weekly during RT and at 1 week post RT	Pain Quality of life Adverse events

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			Ex: previous RT to the chest or breast area, partial breast irradiation, anticoagulant therapy, epidermal growth factor receptor inhibitor therapy, history of radiosensitivity disorder or collagen vascular disease, unhealed surgical wounds, and/or breast infections in the RT area									
Schmeel, 2018	Ger-many	RCT (self-control)	In: >18 years old, breast-preserving surgery for breast cancer Ex: Neoadjuvant or concomitant chemotherapy, active smoking status, metastatic disease, previous RT to the ipsilateral chest wall, breast reconstruction, active dermatitis, treatment with topical or oral corticosteroids, mastectomy, different	N=56	Range 36-82 Median 62	100	Breast, Radiation with or without surgery	50 Gy in 25 fx	Hydro film	Urea lotion	Weekly during RT and at end of RT	Development of radiodermatitis Pain Pruritis Adverse events

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
			fractionation regimens									
Schneider, 2015	Brazil	RCT	In: >18 y.o., diagnosis of H&N cancer Ex: Presence of H&N tumor wounds, hx of RT in same field, allergy to EFA or calendula, use of other skin product at treatment during study, lack of adherence and follow-up	N=51 Calendula n=24 Essential fatty acids n=27	Calendula mean age 62.4 Essential fatty acids mean age 60.44	NR	Head and neck cancer, radiation plus systemic therapy	Unclear as reported	Calendula	Essential fatty acids	Weekly during RT and at 30 days post RT	Development of radiodermatitis
Ulff, 2013	Sweden	RCT	In: age >18 years, surgical intervention for carcinoma of the breast with or without lymph node metastases, treatment with 3-D planned RT Ex: Pregnancy, breastfeeding, concomitant chemotherapy, trastuzumab treatment or previous RT to the area, any kind of generalized dermatitis and treatment with local or oral steroids	N=104 Betameth-asone/Ess-ex n=53, Essex n=24 Canoderm n=25	Median age 62 Betametha-sone/Essex median age 63 Essex median age 64 Canoderm median age 60	100	Breast cancer, radiation with or without surgery	2 Gy/day, total dose of 50 Gy	Betametha-sone + Essex, Essex cream alone	Canoderm cream alone	Weekly during RT and 2 weeks post RT	Development of radiodermatitis Patient-reported symptoms

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
Ulff, 2017	Sweden	RCT	In: age >18 years, surgical intervention for carcinoma of the breast with or without lymph node metastases and treatment either with cRT or hRT. Ex: pregnancy, breastfeeding, concomitant chemotherapy, previous RT to the treated area, active dermatitis or treatment with local or oral corticosteroids	N=202 Betameth-asone-17-valerate (steroid) n=102 Essex n=100	NR	100	Breast cancer, radiation plus systemic therapy	42.56 Gy (hRT) or 50 Gy (cRT)	Betametha-sone-17-valerate cream	Essex	Radioderm-atitis at end of RT, adverse events weekly and 1 week after RT	Development of radiodermatitis Pruritis Adverse events
Wooding (China), 2018	China and New Zealand	RCT	In: all patients receiving RT for nasopharyngeal cancer, able to return to the hospital for follow-up for up to 4 weeks after treatment. Ex: Previous RT to the H&N region, metastatic disease, facial hair in the research area and a Karnofsky performance status score of 70 or less	N=12	NR	9	Naso-pharyngal carcinoma, radiation plus systemic therapy	74 Gy in 37 fractions	Mepitel film	Biafine	3 times weekly during RT then weekly for 4 weeks post RT	Development of radiodermatitis

Author, Year	Country	Design	Inclusion/ exclusion criteria	N (arm1/ arm2)	Age in yrs (mean arm 1/ arm 2)	% female	Cancer type and treatment	Radiation dose	Intervention	Control	Follow up	Outcomes reported
Wooding (NZ), 2018	China and New Zealand	RCT	In: patients receiving RT for mucosal squamous cell carcinoma of the H&N region. Ex: Previous RT to the H&N region, metastatic disease, facial hair in the research area and a Karnofsky performance status score of 70 or less	N=24	NR	23	Mucosal squamous cell carci-noma, radiation plus systemic therapy	66 Gy in 30 fractions for definitive txmt and 60 Gy in 30 fractions for postopera-tive txmt	Mepitel film	Dermasoft sorbolene cream	3 times weekly during RT then weekly for 4 weeks post RT	Development of radiodermatitis