ONS RADIODERMATITIS SYMPTOM MANAGEMENT GUIDELINE

Supplementary Material

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1. Guideline panel conflict of interest disclosures

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2. 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	Semipermeable dressings	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
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

3. Evidence-to-Decision Frameworks (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 (breast/chest region radiation therapy)
- Aloe vera 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 steroid creams vs. standard of care
- Semipermeable dressings vs. standard of care

Deodorant/antiperspirant in addition to normal washing vs. normal washing (breast/chest region radiation therapy)

RECOMMENDATION

Should deodorant/antiperspirant in addition to normal washing be used rather than normal washing alone in persons receiving radiation therapy for cancer in the breast/chest region?	
POPULATION:	Individuals receiving radiation therapy in the breast/chest region
INTERVENTION:	Deodorant/antiperspirant in addition to normal washing
COMPARISON:	Normal washing
MAIN OUTCOMES:	Time to development of necrosis (e.g., rash, desquamation, necrosis)
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	See table below	The panel noted that there may be some differences in quality of life. The use of deodorant/anti-perspirant is more important to persons in warm climates. The panel discussed whether the desirable effects were small or trivial but decided on trivial.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with soap	Risk difference with Deodorant
Development of Grade 2 RD	517 (3 RCTs [1,2,3])	⨁⨁◯◯ LOW[a,b]	**RR 0.99** (0.76 to 1.29)	Study population	
				349 per 1,000	**3 fewer per 1,000** (84 fewer to 101 more)

Development of Grade 3 RD	517 (3 RCTs [1,2,3])	⨁⨁◯◯ LOW[a,b]	**RR 0.74** (0.27 to 2.02)	Study population	
				51 per 1,000	**13 fewer per 1,000** (37 fewer to 52 more)
Pruritis at end of radiation treatment	80 (1 RCT [4])	⨁◯◯◯ VERY LOW[b,c,d]	**OR 2.62** (1.01 to 6.78)	Study population	
				634 per 1,000	**185 more per 1,000** (2 more to 287 more)
Moderate-to-severe pain at end of radiation treatment	80 (1 RCT [4])	⨁◯◯◯ VERY LOW[a,b,c]	**OR 0.77** (0.29 to 2.09)	Study population	
				122 per 1,000	**25 fewer per 1,000** (83 fewer to 103 more)
Sweating at end of radiation treatment	80 (1 RCT [4])	⨁◯◯◯ VERY LOW[b,c]	**OR 0.34** (0.12 to 0.93)	Study population	
				268 per 1,000	**157 fewer per 1,000** (226 fewer to 14 fewer)

Explanations:

a. The 95% CI includes the potential for both benefit and harm.
b. Few events reported do not meet the optimal information size and suggest fragility in the estimate.
c. Theberge 2009 had some concerns with allocation concealment, patient blinding, and incomplete outcome reporting.
d. 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 In a Canadian randomized controlled trial (Watson, Gies, Thompson, & Thomas, 2012) of aluminum-based anti-perspirant use in patients with breast cancer undergoing radiotherapy, there was no difference in quality of life between the anti-perspirant use and the control (washing only) groups. In an Australian 3-arm randomized controlled study (Lewis et al., 2014) of the effects of deodorant with and without aluminum on axillary skin toxicity during radiotherapy for breast cancer, 91 patients using aluminum-containing deodorant, 90 patients using non-aluminum-containing deodorant, and 104 no-deodorant-use patients completed the study. The aluminum-containing group had significantly less perspiring than the control. The odds of the aluminum-containing group experiencing perspiring that was barely tolerable and frequently or always interfering with daily activities was reduced by 85%.	

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know		The panel determined the magnitude of the harms to be trivial based on the reported events of axillary pruritus reported in Théberge et al., 2009, (3/40 in deodorant arm vs. 9/44 in non-deodorant arm) and the trivial different in itch reported in both the aluminum and non-aluminum deodorant arms compared with soap in Lewis et al., 2014 (adjusted change in rating score: -0.04; 95% CI: -0.21, 0.13 and adjusted change in rating score: 0.06; 95% CI -0.11, 0.23, respectively).

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				268 per 1,000	**157 fewer per 1,000** (226 fewer to 14 fewer)

	Explanations: a. The 95% CI includes the potential for both benefit and harm. b. Few events reported do not meet the optimal information size and suggest fragility in the estimate. c. Theberge 2009 had some concerns with allocation concealment, patient blinding, and incomplete outcome reporting. d. 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 5. Watson, L.C., Gies, D., Thompson, E., & Thomas, B. (2012). Randomized control trial: Evaluating aluminum-based antiperspirant use, axilla skin toxicity, and reported quality of life in women receiving external beam radiotherapy for treatment of Stage 0, I, and II breast cancer. *International Journal of Radiation Oncology* Biology* Physics*, *83*, e29–e34. https://doi.org/10.1016/j.ijrobp.2011.12.006 In a Canadian randomized controlled trial (Watson, Gies, Thompson, & Thomas, 2012) of aluminum-based anti-perspirant use in patients with breast cancer undergoing radiotherapy, there was no difference in quality of life between the anti-perspirant use and the control (washing only) groups. In an Australian 3-arm randomized controlled study (Lewis et al., 2014) of the effects of deodorant with and without aluminum on axillary skin toxicity during radiotherapy for breast cancer, 91 patients using aluminum-containing deodorant, 90 patients using non-aluminum-containing deodorant, and 104 no-deodorant-use patients completed the study. The aluminum-containing group had significantly less perspiring than the control. The odds of the aluminum-containing group experiencing perspiring that was barely tolerable and frequently or always interfering with daily activities was reduced by 85%.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		The certainty in the estimates for deodorant/antiperspirant use was judged as low and very low due to concerns with risk of bias and for few events.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence identified	The panel determined that people value the prevention of sweating and body odor but that their preference can depend on the severity of the itching. Some may put greater value on avoiding itching, and some may place greater value on using deodorant. However, people still place value on not increasing the severity of radiodermatitis and the ability to a prevent a change in lifestyle. The panel noted that a group exists of people who do not use deodorant in normal practice. The panel noted that the population is predominantly females with breast cancer.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		In determining the balance of effects, the panel discussed the very low certainty in the evidence of harms and that there may be additional benefit from deodorant in addressing body odor. They also noted the trivial desirable and undesirable effects.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	No research evidence identified	The panel determined that there would be no additional cost to their routine with use of the intervention. They measured it against the cost of soap/water.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	The panel determined there would probably be no impact on health equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In an English randomized controlled trial (Bennett, 2009) comparing non-metallic deodorant use and no deodorant use during radiotherapy, 63 questionnaires were distributed that included questions about reactions to the study. Twenty-seven patients reported using the deodorant. All of them said it was easy to use, would use again, and preferred using it over forgoing deodorant. Fourteen percent of the no-deodorant group made positive comments about forgoing deodorant.	The panel decided that the patients are the main key stakeholder and that for healthcare providers, there would require a change in practice.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that the intervention would be feasible to implement.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know

	JUDGEMENT						
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	●	○	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation treatment to the breast/chest region, the ONS Guidelines panel *suggests* either deodorant/antiperspirant use in addition to standard washing/skin care regimen or standard washing/skin care regimen alone (conditional recommendation for either; very low certainty of evidence).

Remarks: This decision will be driven by the values and preferences of the patient. Education should include that antiperspirants/deodorant do not seem to cause harm, sweating is decreased, and the risk of Grade 2 or 3 radiodermatitis is not increased.

Justification

Based on the evidence, the panel issued a conditional recommendation for either deodorant or antiperspirant use in addition to normal washing or normal washing alone for patients receiving radiation therapy to the breast or chest fields. The panel determined that whether to wear deodorant or antiperspirant or not is unlikely to impact the risk of radiodermatitis, so patients receiving radiation to the chest/breast can follow their normal routine. This recommendation suggests that patients have the autonomy to decide whether or not to wear deodorant or antiperspirant during their treatment.

Subgroup considerations

No subgroup considerations

Implementation considerations

Patient education and healthcare provider education around the use of antiperspirants in addition to deodorant would be required because this will be a chance in practice.

Monitoring and evaluation

Current practice versus practice after guideline dissemination should be monitored.

Research priorities

No research priorities identified

IN-TEXT CITED REFERENCES

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Aloe vera vs. standard of care

RECOMMENDATION

Should aloe vera rather than standard of care be used to minimize the development of radiodermatitis?	
POPULATION:	Individuals receiving radiation therapy for cancer
INTERVENTION:	Aloe vera
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; time to development of radiodermatitis; pruritis; dry skin; quality of life; cost; intervention adherence and fidelity
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest	

	within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	See table below	Chan et al. (2014) had identified Heggie et al., 2002, Merchant et al., 2007, Olsen et al., 2001, and Williams et al., 1996 in reviewing non-steroidal topicals, but those studies did not effectively address the evidence base for this guideline, so the panel's decision was informed by the Hoopfer et al. (2015) and Haddad et al. (2013) studies that were found in the update systematic review (Ginex et al., 2020). The panel noted a reduction in pain and a large reduction of the relative risk of grade 2 and 3 at week 5. However, when taking the Hoopfer et al., 2015, results using the modified 10-point Catterall scale (CSSP) into account for grade 2 and 3, the panel determined that the magnitude of the desirable effect of grade 2 and 3 reduction may be reduced because CSSP results cannot be combined with the Radiation Therapy Oncology Group (RTOG) results in Haddad et al. (2013). In Hoopfer et al., 2015, the aloe cream arm had 81 randomized patients and the placebo arm had 77. The panel noted the lack of a standardized formula and a lack of reported evidence (reporting bias). The availability of so many aloe products makes the formulation of the product more important; therefore, the panel decided that "don't know" best represented the decision for desirable and undesirable.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Aloe vera lotion
Development of RD grade 2 or 3 at wk 5 RT	106 (1 RCT [1])	⨁⨁◯◯ LOW[a,b,c]	**RR 0.22** (0.08 to 0.61)	Study population	
				340 per 1,000	265 fewer per 1,000 (312 fewer to 132 fewer)
Moist desquamation (<50% of field; CSSP score 9-10)	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 1.74** (0.68 to 4.48)	Study population	
				78 per 1,000	58 more per 1,000 (25 fewer to 271 more)
Adverse events related to treatment discontinuation	106 (1 RCT [1])	⨁⨁◯◯ LOW[b]	-	No treatment-related adverse event reported in either arm (0/53 vs 0/53).	
Skin Rash	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 1.90** (1.02 to 3.53)	Study population	
				156 per 1,000	140 more per 1,000 (3 more to 394 more)

Pain	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 0.80** (0.49 to 1.30)	Study population	
				325 per 1,000	65 fewer per 1,000 (166 fewer to 97 more)

Explanations

a. The 95% CI includes the potential for both benefit and harm.
b. Few events reported do not meet the optimal information size and suggest fragility in the estimate
c. Haddad 2013 has some concerns with incomplete outcome data, however, may contribute to the imprecision

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

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know		The panel considered the outcomes of moist desquamation and skin rash. The panel questioned how reported improvement in grades 2 and 3 could be possible if there is moist desquamation. The panel noted that the CSSP categories of 9 and 10 are not the same as grade 3. Hoopfer et al. (2015) used aloe and other ingredients in the topical preparation, so the panel decided that evidence was indirect. The panel also noted that Hoopfer et al. (2015) used powder as the standard of care.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Aloe vera lotion
				Study population	

Development of RD grade 2 or 3 at wk 5 RT	106 (1 RCT [1])	⨁⨁◯◯ LOW[a,b,c]	**RR 0.22** (0.08 to 0.61)	340 per 1,000	265 fewer per 1,000 (312 fewer to 132 fewer)
Moist desquamation (<50% of field; CSSP score 9-10)	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 1.74** (0.68 to 4.48)	Study population	
				78 per 1,000	58 more per 1,000 (25 fewer to 271 more)
Adverse events related to treatment discontinuation	106 (1 RCT [1])	⨁⨁◯◯ LOW[b]	-	No treatment-related adverse event reported in either arm (0/53 vs 0/53).	
Skin Rash	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 1.90** (1.02 to 3.53)	Study population	
				156 per 1,000	140 more per 1,000 (3 more to 394 more)
Pain	158 (1 RCT [2])	⨁⨁◯◯ LOW[a,b]	**RR 0.80** (0.49 to 1.30)	Study population	
				325 per 1,000	65 fewer per 1,000 (166 fewer to 97 more)

Explanations

a. The 95% CI includes the potential for both benefit and harm.
b. Few events reported do not meet the optimal information size and suggest fragility in the estimate.
c. Haddad 2013 has some concerns with incomplete outcome data, however, may contribute to the imprecision.

	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	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		The certainty in the evidence was rated as very low due to the imprecision, risk of bias, inconsistency, indirectness, and publication bias (selective reporting of outcomes).

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence identified.	The panel noted the perception among patients that topical aloe may be sticky and dry the skin. Also, aloe may irritate the skin. They noted a difference in gel versus cream preparations. The panel determined that aloe may appeal to people wanting a natural product or a cooling product (when stored in the refrigerator).

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● Don't know		

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of aloe was estimated from results of an Internet search.	The panel determined that aloe preparations would cost patients $5–10 per bottle.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified.	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	The panel determined there would probably be no impact on health equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that patients would accept the intervention and that clinicians would probably accept it. They noted that a standardized formula is needed

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that the intervention would be feasible to implement.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	**Don't know**
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**Don't know**
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation therapy for cancer, the ONS Guidelines panel recommends aloe vera and aloe vera formulations only *in the context of a clinical trial* (no recommendation, knowledge gap).

Justification

Limited consistent evidence exists to support a recommendation for aloe vera for the treatment of radiodermatitis in patients with cancer. Based on the low quality of the evidence and the lack of standardization in the formulas included in the research, the guideline panel was unable to determine the benefits or harms and made no recommendation for aloe vera and identified this intervention as an evidence gap that warrants further research.

Subgroup considerations

No subgroup considerations

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations

Research priorities

Standardized formulation is required

IN-TEXT CITED REFERENCES

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Emu oil vs. standard of care

RECOMMENDATION

Should emu oil rather than standard of care be used to minimize the development of radiodermatitis?	
POPULATION:	Individuals receiving radiation treatment for cancer
INTERVENTION:	Emu oil
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to development of radiodermatitis; intervention adherence and fidelity
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation – Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012)
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al., 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	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	Rollman et al. (2015) used the Skindex-16 for patient-reported outcomes. The panel noted that emu oil may improve quality of life but that the difference between the area under the curve scores of 7.2 for emu oil patients and 10.4 for the placebo patients was probably not meaningful. Cottonseed oil was used as the placebo, but the panel did not know much about it.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	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	In the Rollman et al. (2015) study, patients using emu oil had a slightly worse score for maximum Common Terminology Criteria (CTC) grade (the difference was not significant). One patient using emu oil had an instance of grade 3 CTC moist desquamation. The panel noted a potential for an increased risk of G2+ by using emu oil.

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		The certainty in the estimates for emu oil were judged to be very low due to risk of bias, indirectness (i.e., only reported on grade 3 or above radiodermatitis) and imprecision.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability		The panel decided there would probably be no important uncertainty or variability in how much people value the main outcomes.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		The panel considered the trivial benefits versus trivial harms.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of emu oil was estiimated from results of an Internet search.	The panel noted that the cost of emu oil would be about $20 per treatment, based on the regimen followed in Rollmann et al. (2015). Patients were asked to use 1.5 ml of oil two times a day. And the cost of 16 oz. (475 ml) is about $40.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	The panel determined there may be a decrease in equity due to accessibility issues.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that clinicians would accept the intervention and that patients probably would accept it--some patients would object to the use of an animal product.

Feasibility Is the intervention feasible to implement?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence identified	The panel noted that it would be difficult to apply such a small amount of the emu oil. They determined that formulation, dosing, and acquisition of the product are concerns.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	**Does not favor either the intervention or the comparison**	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation therapy for cancer, the ONS Guidelines panel *suggests* against emu oil in addition to standard washing/skin care regimen (conditional recommendation; very low certainty in the evidence).

Justification

The panel acknowledged the limited evidence for emu oil and the trivial benefits and harms. In addition, emu oil may have moderate cost, possibly reduced accessibility, acceptability, and feasibility of implementation. Based on this evidence, the ONS Guidelines panel issued a conditional recommendation suggesting against use of emu oil for the management of radiodermatitis in patients with cancer receiving radiation therapy.

Subgroup considerations

No subgroup considerations.

Implementation considerations

No implementation considerations.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

Standardized formulation is required.

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Oral curcumin vs. standard of care

RECOMMENDATION

Should oral curcumin rather than standard of care be used to minimize the development of radiodermatitis?	
POPULATION:	Individuals receiving radiation therapy for cancer
INTERVENTION:	Oral curcumin
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to development of radiodermatitis; intervention adherence and fidelity
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest	

within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT

○ Trivial
● Small
○ Moderate
○ Large
○ Varies
○ Don't know

RESEARCH EVIDENCE

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Curcumin
Development of radiodermatitis grade 2 or higher assessed with: moist desquamation	730 (2 RCTs [1,2])	⨁◯◯◯ VERY LOW[a,b,c,d,e]	**RR 0.64** (0.42 to 0.96)	Study population	
				135 per 1,000	**48 fewer per 1,000** (78 fewer to 5 fewer)
RD at end of treatment	30 (1 RCT [1])	⨁◯◯◯ VERY LOW[a,d]	-	The mean RD at end of treatment was **0**	MD **0.8 lower** (1.36 lower to 0.23 lower)
Pain as measured by SF-MPQ	686 (1 RCT [1])	⨁⨁◯◯ LOW[a,f]	-[g]	The mean pain as measured by SF-MPQ was **0**	MD **0.007 higher** (0.023 lower to 0.034 higher)[g]
HRQoL Symptom subscale from Skindex-29 assessed with:	686 (1 RCT [1])	⨁⨁◯◯ LOW[a,f]	-	The mean hRQoL Symptom subscale from Skindex-29 was **0**	MD **0.741 higher** (0.394 lower to 0.021 higher)

ADDITIONAL CONSIDERATIONS

The panel decided that the outcome of moist desquamation was an indirect measure of development of radiodermatitis grade 2 or higher therefore was renamed and rated down for indirectness in the evidence profile.

Composite score at end of RT						

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

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In a systematic review (Vaughn, Branum, & Sivamani, 2016) of the effects of turmeric on skin health, including radiodermatitis, the authors noted that it is important to consider the dosages used in studies when considering curcumin use. They said that curcumin typically has poor bioavailability. The authors referenced Shah et al., 1999, in saying that curcumin may have an inhibitory effect on platelet aggregation and could interact with anticoagulation and antiplatelet medications. They referenced Rasyid and Lelo, 1999, in saying that curcumin can stimulate gallbladder contractions, thereby exacerbating symptoms in patients with gallstones.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT

- ○ Large
- ○ Moderate
- ○ Small
- ● Trivial
- ○ Varies
- ○ Don't know

RESEARCH EVIDENCE

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Curcumin
Development of radiodermatitis grade 2 or higher assessed with: moist desquamation	730 (2 RCTs [1,2])	⨁◯◯◯ VERY LOW[a,b,c,d,e]	**RR 0.64** (0.42 to 0.96)	Study population	
				135 per 1,000	**48 fewer per 1,000** (78 fewer to 5 fewer)
RD at end of treatment	30 (1 RCT [1])	⨁◯◯◯ VERY LOW[a,d]	-	The mean RD at end of treatment was **0**	MD **0.8 lower** (1.36 lower to 0.23 lower)
Pain as measured by SF-MPQ	686 (1 RCT [1])	⨁⨁◯◯ LOW[a,f]	-[g]	The mean pain as measured by SF-MPQ was **0**	MD **0.007 higher** (0.023 lower to 0.034 higher)[g]
HRQoL Symptom subscale from Skindex-29 assessed with: Composite score at end of RT	686 (1 RCT [1])	⨁⨁◯◯ LOW[a,f]	-	The mean hRQoL Symptom subscale from Skindex-29 was **0**	MD **0.741 higher** (0.394 lower to 0.021 higher)

ADDITIONAL CONSIDERATIONS

The undesirable effects considered by the panel are based on the results from the pain and HRQoL scales.

The panel determined that participants would have been excluded from these studies if on anticoagulants because there may be increased risks if used among persons with a risk of bleeding. This has not been studied.

	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 In a systematic review (Vaughn, Branum, & Sivamani, 2016) of the effects of turmeric on skin health, including radiodermatitis, the authors noted that it is important to consider the dosages used in studies when considering curcumin use. They said that curcumin typically has poor bioavailability. The authors referenced Shah et al., 1999, in saying that curcumin may have an inhibitory effect on platelet aggregation and could interact with anticoagulation and antiplatelet medications. They referenced Rasyid and Lelo, 1999, in saying that curcumin can stimulate gallbladder contractions, thereby exacerbating symptoms in patients with gallstones.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Very low ○ Low ○ Moderate ○ High ○ No included studies		The panel had very low certainty in the evidence of effects based on the harms, risk of bias due to lack of a standardized scale, and conflicting readings on the development of moist desquamation.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence identified.	The panel decided there was probably no important uncertainty or variability in how much people value the main outcomes.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● Don't know		In trying to determine the balance of effects, the panel noted some uncertainty in the pain and HRQoL scales and low certainty of benefits. The studies eliminated people who could be harmed. In Ryan Wolf et al. (2018), there was discrepancy in classifying moist desquamation from pictures. Radiation dermatitis severity (RDS) score was used, which is not standardized, so there were concerns about risk of bias. Ryan Wolf et al. (2018) was a multi-site study, so there was no interrater reliability. The report on the benefit is flawed, so the panel was not able to balance the effects.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of curcumin oral supplements was estimated from prices found in an Internet search.	The panel decided that given the over-the-counter price for a bottle of oral curcumin (varies between $5 and $20) and the requirement that 4 pills be taken by the person 3 times per day, this would be a moderate cost.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified.	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified.	The panel determined that accessibility to curcumin supplements may be reduced because of cost, which would reduce health equity.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	The panel determined that both clinicians and patients would find curcumin acceptable.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence identified	The panel determined that there are some concerns with the feasibility of taking curcumin: 1) there is no standard formulation or dosing, 2) the drug-drug interactions are not known, and 3) the patients may experience pill fatigue taking 4 pills 3 times a day, especially when combined with other medical regimens.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	**Very low**	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**Don't know**
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know

	JUDGEMENT						
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	○	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation therapy for cancer, the ONS Guidelines panel recommends oral curcumin only *in the context of a clinical trial* (no recommendation, knowledge gap).

Justification

The panel acknowledged the measurement of moist desquamation concerns in the studies and the potential for harms, particularly interactions with other medications used for cancer treatment. Based on this evidence, the ONS Guidelines panel made no recommendation for curcumin and identified this intervention as an evidence gap.

Subgroup considerations

No subgroup considerations

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

Standardized formulation is required

IN-TEXT CITED REFERENCES

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Should specialty topical nonsteroidal interventions (e.g., creams, lotions, ointments) vs. standard of care

RECOMMENDATION

Should specialty topical nonsteroidal interventions (e.g., creams, lotions, ointments, etc.) rather than standard of care be used to minimize radiodermatitis?	
POPULATION:	Individuals with cancer receiving radiation therapy without symptoms of radiodermatitis
INTERVENTION:	Specialty topical non-steroidal interventions (e.g., creams, lotions, ointments)
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to development of radiodermatitis; intervention adherence and fidelity; symptom severity; breaks/discontinuation in radiation treatment; secondary infections; time to resolution of radiodermatitis; protocol adherence and fidelity
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).

CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	This question is addressing all topical non-steroidal skin treatments: NOCA / 3M Cavilon Durable Barrier Cream / Daivonex (vitamin D) When discussing the standard of care arms, the panel noted that in Gosselin, Schneider, Plambeck, & Rowe (2010), no difference was found between Aquaphor and water/placebo (n = 106: 53 vs 49) in the proportion of grade 2 – 4 progression from week 3 to 6. So then in the recent studies of cream, aqueous cream and sorbolene would be a comparable comparison group without rating down for indirectness.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Trivial ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know	<table><tr><th rowspan="2">Outcomes</th><th rowspan="2">№ of participants (studies) Follow up</th><th rowspan="2">Certainty of the evidence (GRADE)</th><th rowspan="2">Relative effect (95% CI)</th><th colspan="2">Anticipated absolute effects* (95% CI)</th></tr><tr><th>Risk with placebo</th><th>Risk difference with Topical nonsteroidal</th></tr><tr><td></td><td></td><td></td><td></td><td colspan="2">Study population</td></tr></table>	The panel considered the effects on relief of itching and moist desquamation (benefit found in the chest wall region) when deciding upon trivial effect.

Development of RD grade 2 or higher	682 (3 RCTs [1,3])	⨁⨁⨁◯ MODERATE[a]	**RR 1.29** (1.06 to 1.57)	680 per 1,000	**197 more per 1,000** (41 more to 388 more)
Moist desquamation	245 (1 RCT [2])	⨁◯◯◯ VERY LOW[b,c,d]	**RR 0.84** (0.46 to 1.56)	Study population	
				160 per 1,000	**26 fewer per 1,000** (86 fewer to 90 more)
Pruritis	881 (3 RCTs [1,2])	⨁⨁◯◯ LOW[b,e]	**RR 1.09** (0.95 to 1.24)	Study population	
				387 per 1,000	**35 more per 1,000** (19 fewer to 93 more)
Pain	636 (2 RCTs [1])	⨁⨁⨁◯ MODERATE[c]	**RR 1.10** (0.90 to 1.35)	Study population	
				349 per 1,000	**35 more per 1,000** (35 fewer to 122 more)
Relief of itching	176 (1 RCT [2])	⨁◯◯◯ VERY LOW[b,d,f]	**RR 0.85** (0.73 to 0.99)	Study population	
				849 per 1,000	**127 fewer per 1,000** (229 fewer to 8 fewer)

Explanations

a. Nasser 2017 has concerns with allocation concealment, blinding of participants and outcome assessors, and incomplete outcome data. Possibly this contributes to or explains the heterogeneity (I^2=78%) in the analysis.
b. Laffin 2015 has some concerns with blinding of outcome assessors and selective reporting.
c. The 95% CI includes the potential for both benefit and harm.
d. Few events reported do not meet the optimal information size and suggest fragility in the estimate.
e. The 95% CI includes the potential for both benefit and harm; however, the optimal information size is met.

f. 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

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know		This consideration is led by development of grade 2 radiodermatitis (other benefits include less relief of itching, pruritis).

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with placebo	Risk difference with Topical nonsteroidal
Development of RD grade 2 or higher	682 (3 RCTs [1,3])	⨁⨁⨁◯ MODERATE[a]	**RR 1.29** (1.06 to 1.57)	Study population	
				680 per 1,000	**197 more per 1,000** (41 more to 388 more)
Moist desquamation	245 (1 RCT [2])	⨁◯◯◯ VERY LOW[b,c,d]	**RR 0.84** (0.46 to 1.56)	Study population	
				160 per 1,000	**26 fewer per 1,000** (86 fewer to 90 more)

Pruritis	881 (3 RCTs [1,2])	⨁⨁◯◯ LOW[b,e]	**RR 1.09** (0.95 to 1.24)	Study population	
				387 per 1,000	**35 more per 1,000** (19 fewer to 93 more)
Pain	636 (2 RCTs [1])	⨁⨁⨁◯ MODERATE[c]	**RR 1.10** (0.90 to 1.35)	Study population	
				349 per 1,000	**35 more per 1,000** (35 fewer to 122 more)
Relief of itching	176 (1 RCT [2])	⨁◯◯◯ VERY LOW[b,d,f]	**RR 0.85** (0.73 to 0.99)	Study population	
				849 per 1,000	**127 fewer per 1,000** (229 fewer to 8 fewer)

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. Laffin 2015 has some concerns with blinding of outcome assessors and selective reporting.
c. The 95% CI includes the potential for both benefit and harm.
d. Few events reported do not meet the optimal information size and suggest fragility in the estimate.
e. The 95% CI includes the potential for both benefit and harm; however, the optimal information size is met.
f. 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	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ● Moderate ○ High ○ No included studies		The panel judged the certainty in the overall evidence of effects to be moderate due to the harm of developing grade 2 radiodermatitis or higher.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence identified	The panel decided that there would be variability in patient preferences: some patients may want to actively do something (use cream), and some patients may favor doing nothing until the presentation of radiodermatitis.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		The panel considered the intervention's trivial benefits, moderate harms, and moderate certainty in those outcomes when determining the balance of effects.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	No research evidence identified	The panel decided there would be moderate savings if the standard of care (potentially water) were recommended.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	The panel determined that the standard of care may increase equity (It could potentially be water.).

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	In an Australian randomized controlled trial (Laffin et al., 2015) on the effectiveness and acceptability of Sorbolene moisturizing cream and Cavilon barrier cream, patients completed an acceptability survey. Data analysis was based on 245 participants. Cavilon (95.8%) had higher acceptability than Sorbolene (85.7%). Sixty-five percent of the Cavilon users found it easy to apply versus 45% of the Sorbolene users. A small portion (6.4%) of Cavilon users said it built up on the skin versus 27.9% of Sorbolene users. At follow-up, 42.3% of Cavilon of users found it acceptable versus 28.9% of Sorbolene users.	The panel decided that doing nothing would be acceptable to patients if they are provided with the information and reassurance that doing nothing is appropriate. The panel decided that clinicians and radiation therapy technicians would probably accept doing nothing.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that doing nothing would be easy to implement with the correction education.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know

	JUDGEMENT						
UNDESIRABLE EFFECTS	Large	**Moderate**	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	**Moderate**	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	**Favors the comparison**	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
●	○	○	○	○

CONCLUSIONS

Recommendation

Among individuals with cancer receiving radiation therapy without symptoms of radiodermatitis, the ONS Guidelines panel *recommends* standard washing and skin care regimen rather than specialty topical nonsteroidal interventions to minimize radiodermatitis (strong recommendation, moderate certainty in the evidence).

Remark: This evidence for this recommendation evaluated specialty topical interventions. General emollient creams and lotions are part of a standard washing and skin care regimen.

Justification

The panel acknowledged there is sufficient evidence to identify important differences between topical non-steroidal creams to minimize the development of radiodermatitis and standard washing/skin care. Based on this evidence, the ONS Guidelines panel issued a strong recommendation suggesting standard washing/skin care rather than topical non-steroidal creams to minimize the development of radiodermatitis. The panel considered that general emollient creams can be used as part of standard washing and skin care, but specialty/barrier creams demonstrated harms, added additional expense, and can lead to inequity due to increased cost.

Subgroup considerations

No subgroup considerations

Implementation considerations

Preparation for a change in practice would be needed.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

No research priorities

IN-TEXT CITED REFERENCES

Aistars, J. (2006). The validity of skin care protocols followed by women with breast cancer receiving external radiation. *Clinical Journal of Oncology Nursing, 10*, 487–492. https://doi.org/10.1188/06.CJON.487-492

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Bryant, A.K., Banegas, M.P., Martinez, M.E., Mell, L.K., & Murphy, J.D. (2017). Trends in radiation therapy among cancer survivors in the United States, 2000–2030. *Cancer Epidemiology, Biomarkers & Prevention, 26*, 963–970. https://doi.org/10.1158/1055-9965.EPI-16-1023

Gewandter, J.S., Walker, J., Heckler, C.E., Morrow, G.R., & Ryan, J.L. (2013). Characterization of skin reactions and pain reported by patients receiving radiation therapy for cancer at different sites. *The Journal of Supportive Oncology, 11*, 183–189. https://doi.org/10.12788/j.suponc.0009

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Schnur, J.B., Zivin, J.G., Mattson, D.M., Green, S., Jandorf, L.H., Wernicke, A.G., & Montgomery, G.H. (2012). Acute skin toxicity-related, out-of-pocket expenses in patients with breast cancer treated with external beam radiotherapy. *Supportive Care in Cancer*, *20*, 3105–3113. 10.1007/s00520-012-1435-6

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Vaz, A., Pinto-Neto, A., Conde, D., Costa-Palva, L., Morais, S., & Esteves, S. (2007). Quality of life of women with gynecologic cancer: Associated factors. *Archives of Gynecology and Obstetrics, 276*, 583–589. https://doi.org/10.1007/s00404-007-0397-2

Calendula vs. standard of care

RECOMMENDATION

Should calendula rather than standard of care be used to minimize the development of radiodermatitis?	
POPULATION:	Individuals receiving radiation therapy for cancer
INTERVENTION:	Calendula

COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to development of radiodermatitis; intervention adherence and fidelity
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation-induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	The panel noted that a standardized formula for calendula is needed.

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know	See table below	No studies identified reported on benefits, so the panel could not judge their substantial nature.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Calendula
Development of Grade 2 or greater	462 (2 RCTs [1,2])	⨁⨁◯◯ LOW[a,b]	**RR 1.21** (0.83 to 1.77)	Study population	
				170 per 1,000	**36 more per 1,000** (29 fewer to 131 more)

Explanations:

a. Schneider had some concerns with incomplete outcome reporting; however, it 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

In a French, randomized, phase III study (Pommier et al., 2004) of prophylactic calendula ointment versus trolamine for radiotherapy in patients with breast cancer, 226 patients completed self-administered questionnaires regarding satisfaction. Thirty percent of patients using calendula and 5% of patients using trolamine found the application to be difficult. Two of the patients using calendula quit using the intervention due to that difficulty. More trolamine (1.62 times more) was used than calendula.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know	See table below	The panel based their decision on the development of grade 2+ radiodermatitis.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Calendula
Development of Grade 2 or greater	462 (2 RCTs [1,2])	⨁⨁◯◯ LOW[a,b]	**RR 1.21** (0.83 to 1.77)	Study population	
				170 per 1,000	**36 more per 1,000** (29 fewer to 131 more)

Explanations:

a. Schneider had some concerns with incomplete outcome reporting; however, it 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

In a French, randomized, phase III study (Pommier et al., 2004) of prophylactic calendula ointment versus trolamine for radiotherapy in patients with breast cancer, 226 patients completed self-administered questionnaires regarding satisfaction. Thirty percent of patients using calendula and 5% of patients using trolamine found the application to be difficult. Two of the patients using calendula

	quit using the intervention due to that difficulty. More trolamine (1.62 times more) was used than calendula.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies		The panel judged the certainty in the overall evidence of effects to be low due to concerns with imprecision and the potential for both benefits and harms.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	No research evidence identified	

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know		The panel decided that, based on the harms for calendula, the balance of effects probably favors the comparison.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ○ Moderate costs ● Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The cost of calendula cream was estimated from results found in an Internet search.	The panel based their judgement on an approximate cost of $11 for 2.5 oz. of calendula cream.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ● Probably reduced ○ Probably no impact		The panel determined that equity would probably be reduced because the calendula would be an out-of-pocket cost.

○ Probably increased ○ Increased ○ Varies ○ Don't know		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	No research evidence identified	The panel decided that patients would find calendula acceptable and that clinicians would probably find it acceptable (There would be some geographic variability.).

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified.	The panel judged calendula to be feasible because it is available in stores and online.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	**Don't know**
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			

	JUDGEMENT						
BALANCE OF EFFECTS	Favors the comparison	**Probably favors the comparison**	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	**Negligible costs and savings**	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	**Probably reduced**	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	**Probably yes**	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	●	○	○	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation therapy for cancer, the ONS Guidelines panel *suggests* against calendula in addition to a standard washing/skincare regimen to minimize the development of radiodermatitis (conditional recommendation, low certainty of evidence).

Justification

The panel acknowledged the limited evidence for calendula and the unknown benefits with trivial harms. In addition, calendula may have moderate cost, possibly reduced accessibility, acceptability, and feasibility of implementation. Based on this evidence, the ONS Guidelines panel issued a conditional recommendation suggesting standard of care rather than calendula for the management of radiodermatitis in patients with cancer receiving radiation therapy.

Subgroup considerations

No subgroup considerations

Implementation considerations

No implementation considerations.

Monitoring and evaluation

No monitoring and evaluation considerations.

Research priorities

Consistent product formulation

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Semipermeable dressings vs. standard of care

RECOMMENDATION

Should semipermeable dressings rather than standard of care be used to minimize the development of radiodermatitis?	
POPULATION:	Individuals receiving radiation therapy
INTERVENTION:	Semipermeable dressings
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to develop radiodermatitis; intervention adherence and fidelity; symptom severity; breaks/discontinuation in radiation treatment; secondary infections; time to resolution of radiodermatitis
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012).
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN®

Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010). Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention. Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).	

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	<table><tr><th rowspan="2">Outcomes</th><th rowspan="2">№ of participants (studies) Follow up</th><th rowspan="2">Certainty of the evidence (GRADE)</th><th rowspan="2">Relative effect (95% CI)</th><th colspan="2">Anticipated absolute effects* (95% CI)</th></tr><tr><th>Risk with standard of care</th><th>Risk difference with Dressings</th></tr><tr><td rowspan="2">Development of RD grade 2 or higher</td><td rowspan="2">706 (7 RCTs [2,3,4,6,7])</td><td rowspan="2">⨁⨁◯◯ LOW[a,b,c,d,e,f]</td><td rowspan="2">RR 0.52 (0.26 to 1.03)</td><td colspan="2">Study population</td></tr><tr><td>467 per 1,000</td><td>224 fewer per 1,000</td></tr></table>	The panel decided that the size of the desirable effects for the recommendation for minimization is large based on the reduction in the development of radiodermatitis grade 2 or higher and the reduction in development of moist desquamation. The panel made this decision by lumping the results from the outcome of development of grade 3 radiodermatitis from Chan et al., 2019.

					(346 fewer to 14 more)
Development of moist desquamation	528 (5 RCTs [1,2,6,7])	⨁⨁◯◯ LOW[d,f,g]	**RR 0.43** (0.32 to 0.58)	Study population	
				359 per 1,000	**205 fewer per 1,000** (244 fewer to 151 fewer)
Tenderness, discomfort, or pain	156 (1 RCT [4])	⨁⨁◯◯ LOW[e,h]	**RR 0.35** (0.16 to 0.78)	Study population	
				256 per 1,000	**167 fewer per 1,000** (215 fewer to 56 fewer)
Pruritis	154 (1 RCT [4])	⨁◯◯◯ VERY LOW[a,e,h]	**RR 0.69** (0.34 to 1.38)	Study population	
				208 per 1,000	**64 fewer per 1,000** (137 fewer to 79 more)
Adverse events leading to treatment discontinuation	181 (2 RCTs [5,6])	⨁⨁⨁◯ MODERATE[h,i]	**RR 20.40** (2.82 to 147.52)	Study population	
				0 per 1,000	**0 fewer per 1,000** (0 fewer to 0 fewer)
Patient-reported QoL	66 (2 RCTs [7])	⨁◯◯◯ VERY LOW[d,h,j]	-	The mean patient-reported QoL was **0**	MD **0.4 lower** (0.75 lower to 0.05 lower)

Explanations:

a. The 95% CI includes the potential for both benefit and harm.
b. Imprecision likely explained by high heterogeneity and rated down in domain for inconsistency.

	c. 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 the group receiving dressings. d. Wooding 2018 has some concerns with blinding of patients and outcome assessors. e. Moller 2018 has some concerns with blinding of patients and outcome assessors. f. Herst 2014 and Schmeel 2018 have concerns with allocation concealment and blinding of participants and outcome assessors. 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 2018 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	

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In an intra-patient, randomized controlled clinical trial (Herst, 2014) in New Zealand to prevent moist desquamation due to radiotherapy, none of 78 patients experienced moist desquamation in the skin area where Mepitel Film was used. Aqueous cream was the control. An average of 5 film strips per patient and 5 – 10 minutes of radiation therapist time per dressing application was used. For moist desquamation that formed in control areas, an additional 11 Mepilex Lite dressings were used.

In a prospective, intra-patient controlled, randomized clinical study in Germany (Schmeel et al., 2018), prophylactically Hydrofilm was compared to prophylactic Eucerin Urea Repair PLUS lotion 5% (control). Of 62 patients enrolled, 56 completed the study. The Eucerin-covered breast halves caused more frequent patient visits and required more radiation therapist time because of skin injury. The added cost of topical corticosteroids was involved in six of those cases, and one of those patients needed inpatient treatment because of moist desquamation.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know	See table below	The panel decided that the size of the effect for the minimization recommendation is small based on the number of patients who discontinued using dressings in the intervention groups (21%).

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Dressings
Development of RD grade 2 or higher	706 (7 RCTs [2,3,4,6,7])	⨁⨁◯◯ LOW[a,b,c,d,e,f]	**RR 0.52** (0.26 to 1.03)	Study population	
				467 per 1,000	**224 fewer per 1,000** (346 fewer to 14 more)
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				359 per 1,000	**205 fewer per 1,000**

					(244 fewer to 151 fewer)
Tenderness, discomfort, or pain	156 (1 RCT [4])	⨁⨁◯◯ LOW[e,h]	**RR 0.35** (0.16 to 0.78)	Study population	
				256 per 1,000	**167 fewer per 1,000** (215 fewer to 56 fewer)
Pruritis	154 (1 RCT [4])	⨁◯◯◯ VERY LOW[a,e,h]	**RR 0.69** (0.34 to 1.38)	Study population	
				208 per 1,000	**64 fewer per 1,000** (137 fewer to 79 more)
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				0 per 1,000	**0 fewer per 1,000** (0 fewer to 0 fewer)
Patient-reported QoL	66 (2 RCTs [7])	⨁◯◯◯ VERY LOW[d,h,j]	-	The mean patient-reported QoL was **0**	MD **0.4 lower** (0.75 lower to 0.05 lower)

Explanations:

a. The 95% CI includes the potential for both benefit and harm.
b. Imprecision likely explained by high heterogeneity and rated down in domain for inconsistency.
c. 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.
d. Wooding 2018 has some concerns with blinding of patients and outcome assessors.
e. Moller 2018 has some concerns with blinding of patients and outcome assessors.
f. Herst 2014 and Schmeel 2018 have concerns with allocation concealment and blinding of participants and outcome assessors.

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 2018 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

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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

In an intra-patient, randomized controlled clinical trial (Herst, 2014) in New Zealand to prevent moist desquamation due to radiotherapy, none of 78 patients experienced moist desquamation in the skin area where Mepitel Film was used. Aqueous cream was the control. An average of 5 film strips per

	patient and 5 – 10 minutes of radiation therapist time per dressing application was used. For moist desquamation that formed in control areas, an additional 11 Mepilex Lite dressings were used. In a prospective, intra-patient controlled, randomized clinical study in Germany (Schmeel et al., 2018), prophylactically Hydrofilm was compared to prophylactic Eucerin Urea Repair PLUS lotion 5% (control). Of 62 patients enrolled, 56 completed the study. The Eucerin-covered breast halves caused more frequent patient visits and required more radiation therapist time because of skin injury. The added cost of topical corticosteroids was involved in six of those cases, and one of those patients needed inpatient treatment because of moist desquamation.	

Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies		The panel judged the certainty in the overall evidence of effects for prophylactic use of semipermeable dressings to be low due to concerns with risk of bias and imprecision. The panel judged the certainty in the overall evidence of effects for treatment of moist desquamation with semipermeable dressings to be very low due to concerns with risk of bias, indirectness of the comparison between saline solution to the current standard of care of Silvadene, and imprecision.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability	In a Danish intra-patient, randomized multicenter study (Krause Møller et al., 2018) of Mepitel film use during radiotherapy in patients with cancer, there were 79 evaluable patients. Of 19 patients who dropped out of the study, 2 dropped out because of problems handling the Mepitel film; 2 patients wanted to have the film removed. In an intra-patient randomized controlled trial (Wooding et al., 2018) conducted in New Zealand and China on prophylactic and management use of Mepitel film for acute radiation-induced skin reactions in patients with head and neck cancer, 33 patients complied with the protocol. During application of the film by the researcher, care was taken not to stretch or overlap the pieces. If the film curled in small areas, the researcher cut them off. Most of the patients who completed an exit questionnaire favored Mepitel over the control intervention (Sorbolene or Biafine), though problems with film adherence to the skin, itchiness, discomfort, and tightness were issues for some.	The panel determined there was probably no important uncertainty or variability. The panel noted that four patients dropped out of the Krause Møller et al., 2018, study because of problems with Mepitel.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know		The panel decided the balance of effects favors the intervention based on the magnitude of the desirable effect, low certainty of evidence, and adverse events.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The estimated cost of semipermeable dressings was based on Internet search results.	The panel determined that the intervention would cost about $54 for 1 – 3 days. The panel decided the cost would be large based on the assumption that the entire region is covered for the entirety of treatment.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ● Varies ○ No included studies	Minimization: No research evidence identified Treatment: Blades et al. (2019) analyzed the cost-effectiveness of StrataXRT. They reported a 36% probability that StrataXRT would be cost-neutral or would lead to net savings for a healthcare organization.	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
● Reduced ○ Probably reduced ○ Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	The panel decided that equity would be reduced because of the cost of the intervention.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ○ Yes ● Varies ○ Don't know	No research evidence identified	The panel decided that acceptability of the intervention varies among clinicians, patients, and radiation therapy technicians because of the type of dressing and the type of application (physical film vs cream/dressing).

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes	No research evidence identified	The panel decided that feasibility varies based on the type of dressing used (physical film vs cream/dressing).

○ Yes ● Varies ○ Don't know		

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	**Small**	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
RESOURCES REQUIRED	**Large costs**	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	**Varies**	No included studies
EQUITY	**Reduced**	Probably reduced	Probably no impact	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		**Varies**	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Among individuals receiving radiation therapy, the ONS Guidelines panel *suggests* semipermeable dressings in addition to standard washing/skincare regimen rather than standard washing/skincare regimen alone to minimize the development of radiodermatitis (conditional recommendation, low certainty of evidence)

Justification

The panel acknowledged the large benefits of dressings and the small harms for minimization of radiodermatitis. Based on this evidence, the ONS Guidelines panel issued a conditional recommendation suggesting semipermeable dressings rather than standard of care for the minimization of radiodermatitis. The panel did not make a recommendation for semipermeable dressings for treatment of moist desquamation due to the lack of evidence that compared dressings to Silvadene which the panel considered standard of care. The panel tabled this recommendation and will reconsider as new evidence becomes available.

Subgroup considerations

No subgroup considerations

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations

Research priorities

No research priorities

IN-TEXT CITED REFERENCES

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Topical steroid creams vs. standard of care

RECOMMENDATION

Should topical steroid creams rather than standard of care be used for the minimization or treatment of radiodermatitis?	
POPULATION:	Individuals with cancer receiving radiation therapy (for minimization); Individuals with radiodermatitis symptoms (for treatment)
INTERVENTION:	Topical steroid creams
COMPARISON:	Standard of care
MAIN OUTCOMES:	Pain; pruritis; dry skin; quality of life; cost; time to develop radiodermatitis; intervention adherence and fidelity; symptom severity; breaks/discontinuation in radiation treatment; secondary infections; time to resolution of radiodermatitis
SETTING:	Clinical care
PERSPECTIVE:	Clinical recommendation - Population perspective
BACKGROUND:	Radiation-induced skin reactions can have minimal to significant impact on a patient's quality of life and may also have associated out of pocket costs (Schnur et al., 2012)
CONFLICT OF INTERESTS:	ONS conflict of interest declaration and management policies were applied and the following panel members were voting panel members (determining the direction and strength of the recommendation): Tracy Gosselin, PhD, RN, AOCN®, NEA-BC, FAAN, Susan D. Bruce, MSN, RN, OCN®, AOCNS®, Andrea Hutton, Carol M. Marquez, MD, FACR, Anne Shaftic, DNP, RN, NP-C, AOCNP®, Lauren V. Suarez, MSN, RN, OCN®, CBCN® Panel members recused as a result of risk of conflicts of interest: None

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	In the year 2000 about 24% of cancer survivors received radiation, and in 2020 that number is expected to increase to 29% (Bryant et al., 2017). This increase was seen across cancer sites with the largest increases for patients being treated for breast or prostate cancer (Bryant et al., 2017). Radiation induced skin reactions are one of the most commonly reported side effects of radiation therapy that can impact up to 95% of patients, and it is known to vary across treatment sites (Gewandter, Walker, Heckler, Morrow, & Ryan, 2013; Gosselin, Schneider, Plambeck, Rowe, 2010).	The evidence is for the treatment of symptoms related to radiodermatitis and not moist desquamation.

Due to this high risk, interventions for radiodermatitis are aimed at minimizing the severity or delaying progression to higher grades, rather than prevention.

Skin changes from radiation are caused by disruption to the normal process of cell division and repair due to ionizing radiation therapy (Bray et al., 2016). Radiodermatitis can range from mild erythema to dry desquamation and moist desquamation (Singh et al., 2016). These skin changes usually manifest within two to three weeks of radiation initiation and can persist for up to four weeks following the completion of treatment (Naylor & Mallett, 2001). Radiodermatitis can be painful and uncomfortable to patients and affects quality of life (Aistars, 2006; Vaz et al, 2007). If severe, it can also lead to changes in radiation treatment schedules (McQuestion, 2006).

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT

- ○ Trivial
- ○ Small
- ○ Moderate
- ● Large
- ○ Varies
- ○ Don't know

RESEARCH EVIDENCE

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Topical steroids
Development of RD grade 2 or higher	783 (6 RCTs [1,2,3,4,5,6])	⨁⨁⨁◯ MODERATE[a,b]	**RR 0.64** (0.42 to 0.96)	Study population	
				573 per 1,000	224 fewer per 1,000 (338 fewer to 57 fewer)
Moist desquamation	395 (3 RCTs [2,3,6])	⨁⨁◯◯ LOW[a,c,d,e]	**RR 0.57** (0.29 to 1.12)	Study population	
				375 per 1,000	161 fewer per 1,000 (266 fewer to 45 more)
Pain during radiation treatment (Severe VAS rating of itching, burning, irritation)	200 (1 RCT [6])	⨁⨁◯◯ LOW[e,f]	**RR 0.12** (0.02 to 0.98)	Study population	
				71 per 1,000	62 fewer per 1,000

ADDITIONAL CONSIDERATIONS

Minimization:

The panel decided that the desirable effects were large based on the reduction in pain after radiation therapy and the decrease of grade 2 or higher radiodermatitis.

Treatment:

The panel decided that the desirable effects were large based on the reduction in pain after radiation therapy and the decrease of grade 2 or higher radiodermatitis.

					(69 fewer to 1 fewer)
Pain after radiation treatment (Severe VAS rating of itching, burning, irritation)	194 (1 RCT [6])	⊕⊕⊕◯ MODERATE[e]	**RR 0.05** (0.01 to 0.39)	Study population	
				188 per 1,000	178 fewer per 1,000 (186 fewer to 114 fewer)
Treatment-related adverse events	50 (1 RCT [3])	⊕⊕◯◯ LOW[d,e]	**RR 2.35** (0.23 to 24.26)	Study population	
				37 per 1,000	50 more per 1,000 (29 fewer to 861 more)

Explanations:

a. Ho 2018 has some concerns with blinding of outcome assessors; however, outcome is fairly objective
b. Inconsistency present (I^2=81%); 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.

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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS

o Large
o Moderate
o Small
● Trivial
o Varies
o Don't know

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with standard of care	Risk difference with Topical steroids
Development of RD grade 2 or higher	783 (6 RCTs [1,2,3,4,5,6])	⨁⨁⨁◯ MODERATE[a,b]	**RR 0.64** (0.42 to 0.96)	Study population	
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Moist desquamation	395 (3 RCTs [2,3,6])	⨁⨁◯◯ LOW[a,c,d,e]	**RR 0.57** (0.29 to 1.12)	Study population	
				375 per 1,000	161 fewer per 1,000

Minimization:

The panel decided the undesirable effects were trivial based on the intervention-related adverse events.

Treatment:

The panel decided the undesirable effects were trivial based on the intervention-related adverse events.

					(266 fewer to 45 more)
Pain during radiation treatment (Severe VAS rating of itching, burning, irritation)	200 (1 RCT [6])	⨁⨁◯◯ LOW[e,f]	**RR 0.12** (0.02 to 0.98)	Study population	
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Pain after radiation treatment (Severe VAS rating of itching, burning, irritation)	194 (1 RCT [6])	⨁⨁⨁◯ MODERATE[e]	**RR 0.05** (0.01 to 0.39)	Study population	
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Explanations:

a. Ho 2018 has some concerns with blinding of outcome assessors; however, outcome is fairly objective.
b. Inconsistency present (I^2=81%); however, all studies demonstrate reduction in radiodermatitis with receipt of topical steroids
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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.

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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ● Low ○ Moderate ○ High ○ No included studies		The panel judged the certainty in the evidence of effects to be low due to inconsistency with data due to blinding of outcome assessors and imprecision in that the confidence interval may not include meaningful data.

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability	No research evidence identified	Minimization:

○ No important uncertainty or variability		The panel decided there was probably no important uncertainty or variability in values. Treatment: The panel decided there was probably no important uncertainty or variability in values.

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know		Minimization: The panel decided the balance of effects favors the intervention due to the large benefit and trivial harms. Treatment: The panel decided the balance of effects favors the intervention due to the large benefit and trivial harms.

Resources required

How large are the resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know	The estimated cost of the intervention was based on results of an Internet search.	The cost of steroidal cream was determined to be approximately $15. The panel noted that consideration was needed as to whether the patient had conventional insurance or Medicare (which would make the intervention more costly for the patient). Minimization: The panel decided that the resources required would be of moderate cost. Treatment: The panel decided that the resources required would be of moderate cost.

Certainty of evidence of required resources

What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Very low ○ Low ○ Moderate ○ High ● No included studies	No research evidence identified	

Cost effectiveness

Does the cost-effectiveness of the intervention favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ● No included studies	No research evidence identified	

Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Reduced ○ Probably reduced ● Probably no impact ○ Probably increased ○ Increased ○ Varies ○ Don't know	No research evidence identified	Minimization: The panel determined that there would probably be no impact on equity because the intervention is accessible. Treatment: The panel determined that there would probably be no impact on equity because the intervention is accessible.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	Minimization: The panel noted that use of steroidal cream for minimization would be a change in practice. The panel decided that clinicians and patients would find the intervention to be acceptable. Treatment: The panel noted that steroidal cream is currently used for treatment. The panel decided that clinicians and patients would find the intervention to be acceptable.

Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	No research evidence identified	Minimization: The panel decided that the intervention would be feasible to implement. Treatment: The panel decided that the intervention would be feasible to implement.

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	**Yes**		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	**Large**		Varies	Don't know

	JUDGEMENT						
UNDESIRABLE EFFECTS	Large	Moderate	Small	**Trivial**		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	**Probably no important uncertainty or variability**	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
RESOURCES REQUIRED	Large costs	**Moderate costs**	Negligible costs and savings	Moderate savings	Large savings	Varies	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			**No included studies**
COST EFFECTIVENESS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	**No included studies**
EQUITY	Reduced	Probably reduced	**Probably no impact**	Probably increased	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	Conditional recommendation for the intervention	Strong recommendation for the intervention
○	○	○	●	○

CONCLUSIONS

Recommendation

Minimize development - Among individuals with cancer receiving radiation therapy, the ONS Guidelines panel *suggests* topical steroids in addition to standard washing/skincare regimen rather than standard washing/skincare regimen alone for the minimization of radiodermatitis (conditional recommendation; low certainty of evidence).

Remarks: Studies reported on topical steroid creams, both prescription and over-the-counter. If cost is a concern, the over-the-counter option is feasible. If coverage or availability are a concern, then available steroid cream is acceptable.

Treatment of symptoms - Among individuals with radiodermatitis symptoms (e.g., pain, itching, etc.), the ONS Guidelines panel *suggests* the addition of topical steroids **to intact skin** with a standard washing/skincare regimen rather than standard washing/skincare regimen alone (conditional recommendation; low certainty of evidence).

Remarks: Studies reported on topical steroid creams, both prescription and over-the-counter. If cost is a concern, the over-the-counter option is feasible. If coverage or availability are a concern, then available steroid cream is acceptable.

Justification

The panel acknowledged the large benefits of topical steroids and the trivial harms for both minimization of radiodermatitis and the treatment of radiodermatitis symptoms. Based on this evidence, the ONS Guidelines panel issued a conditional recommendation suggesting topical steroid creams in addition to standard washing/skin care rather than standard washing/skin care alone for the minimization of radiodermatitis and topical steroid creams (on intact skin only) for the treatment of radiodermatitis symptoms in patients with cancer receiving radiation therapy.

Subgroup considerations

No subgroup considerations

Implementation considerations

No implementation considerations

Monitoring and evaluation

No monitoring and evaluation considerations

Research priorities

No research priorities

IN-TEXT CITED REFERENCES

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