View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Repository@Nottingham

Cochrane Library

Cochrane Database of Systematic Reviews

Interventions to reduce Staphylococcus aureus in the management of eczema (Review)

George SMC, Karanovic S, Harrison DA, Rani A, Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC

George SMC, Karanovic S, Harrison DA, Rani A, Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC.
Interventions to reduce Staphylococcus aureus in the management of eczema.
Cochrane Database of Systematic Reviews 2019, Issue 10. Art. No.: CD003871.
DOI: 10.1002/14651858.CD003871.pub3.

www.cochranelibrary.com

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

WILEY

TABLE OF CONTENTS

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

[Intervention Review]

Interventions to reduce Staphylococcus aureus in the management of eczema

Susannah MC George[1], Sanja Karanovic[2], David A Harrison[3], Anjna Rani[4], Andrew J Birnie[5], Fiona J Bath-Hextall[6], Jane C Ravenscroft[7], Hywel C Williams[8]

[1]Department of Dermatology, Brighton and Sussex University Hospitals NHS Trust, Brighton General Hospital, Brighton, UK. [2]Department of Dermatology, Queen Elizabeth Hospital Birmingham, Birmingham, UK. [3]Intensive Care National Audit & Research Centre, London, UK. [4](c/o) Cochrane Skin Group, Centre of Evidence Based Dermatology, Nottingham, UK. [5]Department of Dermatology, East Kent Hospitals University Foundation NHS Trust, Canterbury, UK. [6]School of Health Sciences, University of Nottingham, Nottingham, UK. [7]Dermatology, Nottingham University Hospitals NHS Trust, Nottingham, UK. [8]Centre of Evidence Based Dermatology, University of Nottingham, Nottingham, UK

Contact address: Susannah MC George, Department of Dermatology, Brighton and Sussex University Hospitals NHS Trust, Brighton General Hospital, Brighton General Hospital, Elm Grove, Brighton, BN2 3EW, UK. susannah@susannahgeorge.net.

Editorial group: Cochrane Skin Group
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 10, 2019.

Citation: George SMC, Karanovic S, Harrison DA, Rani A, Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC. Interventions to reduce Staphylococcus aureus in the management of eczema. *Cochrane Database of Systematic Reviews* 2019, Issue 10. Art. No.: CD003871. DOI: 10.1002/14651858.CD003871.pub3.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Staphylococcus aureus (*S. aureus*) can cause secondary infection in eczema, and may promote inflammation in eczema that does not look infected. There is no standard intervention to reduce *S. aureus* burden in eczema. It is unclear whether antimicrobial treatments help eczema or promote bacterial resistance. This is an update of a 2008 Cochrane Review.

Objectives

To assess the effects of interventions to reduce *S. aureus* for treating eczema.

Search methods

We updated our searches of the following databases to October 2018: Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, Embase and LILACS. We searched five trials registers and three sets of conference proceedings. We checked references of trials and reviews for further relevant studies. We contacted pharmaceutical companies regarding ongoing and unpublished trials.

Selection criteria

Randomised controlled trials of products intended to reduce *S. aureus* on the skin in people diagnosed with atopic eczema by a medical practitioner. Eligible comparators were a similar treatment regimen without the anti-staphylococcal agent.

Data collection and analysis

We used standard methodological procedures expected by Cochrane. Our key outcomes were participant- or assessor-rated global improvement in symptoms/signs, quality of life (QOL), severe adverse events requiring withdrawal, minor adverse events, and emergence of antibiotic-resistant micro-organisms.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Main results

We included 41 studies (1753 analysed participants) covering 10 treatment categories. Studies were conducted mainly in secondary care in Western Europe; North America; the Far East; and elsewhere. Twelve studies recruited children; four, adults; 19, both; and six, unclear. Fifty-nine per cent of the studies reported the mean age of participants (range: 1.1 to 34.6 years). Eczema severity ranged from mild to severe. Many studies did not report our primary outcomes. Treatment durations ranged from 10 minutes to 3 months; total study durations ranged from 15 weeks to 27 months. We considered 33 studies at high risk of bias in at least one domain.

We present results for three key comparisons. All time point measurements were taken from baseline. We classed outcomes as short-term when treatment duration was less than four weeks, and long-term when treatment was given for more than four weeks.

Fourteen studies evaluated topical steroid/antibiotic combinations compared to topical steroids alone (infective status: infected (two studies), not infected (four studies), unspecified (eight studies)). Topical steroid/antibiotic combinations may lead to slightly greater global improvement in good or excellent signs/symptoms than topical steroid alone at 6 to 28 days follow-up (risk ratio (RR) 1.10, 95% confidence interval (CI) 1.00 to 1.21; 224 participants; 3 studies, low-quality evidence). There is probably little or no difference between groups for QOL in children, at 14 days follow-up (mean difference (MD) -0.18, 95% CI -0.40 to 0.04; 42 participants; 1 study, moderate-quality evidence). The subsequent results for this comparison were based on very low-quality evidence, meaning we are uncertain of their validity: severe adverse events were rare (follow-up: between 6 to 28 days): both groups reported flare of dermatitis, worsening of the condition, and folliculitis (325 participants; 4 studies). There were fewer minor adverse events (e.g. flare, stinging, itch, folliculitis) in the combination group at 14 days follow-up (218 participants; 2 studies). One study reported antibiotic resistance in children at three months follow-up, with similar results between the groups (65 participants; 1 study).

Four studies evaluated oral antibiotics compared to placebo (infective status: infected eczema (two studies), uninfected (one study), one study's participants had colonisation but no clinical infection). Oral antibiotics may make no difference in terms of good or excellent global improvement in infants and children at 14 to 28 days follow-up compared to placebo (RR 0.80; 95% CI 0.18 to 3.50; 75 participants; 2 studies, low-quality evidence). There is probably little or no difference between groups for QOL (in infants and children) at 14 days follow-up (MD 0.11, 95% CI -0.10 to 0.32, 45 participants, 1 study, moderate-quality evidence). The subsequent results for this comparison were based on very low-quality evidence, meaning we are uncertain of their validity: adverse events requiring treatment withdrawal between 14 to 28 days follow-up were very rare, but included eczema worsening (both groups), loose stools (antibiotic group), and Henoch-Schönlein purpura (placebo group) (4 studies, 199 participants). Minor adverse events, including nausea, vomiting, diarrhoea, and stomach and joint pains, at 28 days follow-up were also rare and generally low in both groups (1 study, 68 infants and children). Antibiotic resistance at 14 days was reported as similar in both groups (2 studies, 98 infants and children).

Of five studies evaluating bleach baths compared to placebo (water) or bath emollient (infective status: uninfected (two studies), unspecified (three studies)), one reported global improvement and showed that bleach baths may make no difference when compared with placebo at one month follow-up (RR 0.78, 95% CI 0.37 to 1.63; 36 participants; low-quality evidence). One study showed there is probably little or no difference in QOL at 28 days follow-up when comparing bleach baths to placebo (MD 0.90, 95% CI -1.32 to 3.12) (80 infants and children; moderate-quality evidence). We are uncertain if the groups differ in the likelihood of treatment withdrawals due to adverse events at two months follow-up (only one dropout reported due to worsening itch (placebo group)) as the quality of evidence was very low (1 study, 42 participants). One study reported that five participants in each group experienced burning/stinging or dry skin at two months follow-up, so there may be no difference in minor adverse events between groups (RR 1.00, 95% CI 0.35 to 2.87, 36 participants, low-quality evidence). Very low-quality evidence means we are also uncertain if antibiotic resistance at four weeks follow-up is different between groups (1 study, 80 participants ≤ 18 years).

Authors' conclusions

We found insufficient evidence on the effects of anti-staphylococcal treatments for treating people with infected or uninfected eczema. Low-quality evidence, due to risk of bias, imprecise effect estimates and heterogeneity, made pooling of results difficult. Topical steroid/antibiotic combinations may be associated with possible small improvements in good or excellent signs/symptoms compared with topical steroid alone. High-quality trials evaluating efficacy, QOL, and antibiotic resistance are required.

PLAIN LANGUAGE SUMMARY

Treatments to reduce infection with the bacteria *Staphylococcus aureus* in eczema

Background

The skin of people with eczema (atopic dermatitis) often contains high numbers of a type of bacteria called *Staphylococcus aureus* (*S. aureus*), which can cause skin infections.

Eczema treatments intended to reduce *S. aureus* on the skin include antibiotics, treatments put on the skin, and antibacterial soaps/baths. It is unclear which treatments are helpful.

Review question

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

We reviewed the evidence about the effect of treatments aimed at reducing *S. aureus* on the skin in people with atopic eczema. Eligible comparisons were similar treatments without anti-*S. aureus* actions. We included 41 studies involving 1753 participants (evidence is current to October 2018).

Study characteristics

Included studies assessed a range of treatments, which they compared with placebos (an identical but inactive treatment), no treatment, other treatment, vehicle (inactive ingredient(s) which help deliver an active treatment), or textile without the anti-*S.aureus* component.

Studies were conducted worldwide, and included males and females. Twelve studies recruited children; four, adults; 19, both; and six were unclear; where reported, the average participant age ranged from 1.1 to 34.6 years. Eczema severity varied from mild to severe. Treatment durations ranged from 10 minutes to 3 months; total study durations, from 15 weeks to 27 months.

Key results

Outcomes were measured from treatment start. We classed outcomes as short-term when treatment duration was less than four weeks, and long-term when treatment was given for more than four weeks.

People may be more likely to experience slightly increased short-term improvement with topical steroid/antibiotic combinations than with steroid only (low-quality evidence, one study of infected eczema and two studies with unspecified infection). There is probably little or no difference between the combination group and the steroid only groups in short-term impact on quality of life (QoL) (moderate-quality evidence, one study of infected children). Antibiotic resistance was similar between groups in the long term, but we are uncertain of this result due to very low-quality evidence (one study of infected children).

When compared to placebo, oral antibiotics may make no difference to short-term improvement (low-quality evidence, two studies: one in uninfected infants and children; the other in mainly infected infants and children). For short-term QoL, there is probably little or no difference between the groups (moderate-quality evidence, one study of infected infants and children). Short-term antibiotic resistance was similar in both groups, but we are uncertain if there is a true difference as the quality of evidence was very low (two studies of infants and children, infected in one study and uninfected in the other).

Bleach baths may make no difference to short-term improvement when compared to placebo (low-quality evidence, one study of uninfected participants). There is also probably little or no difference in short-term QoL in children of unspecified infective status (one study; moderate-quality evidence); based on the same study, we are uncertain if short-term antibiotic resistance was different between groups (very low-quality evidence).

Side effects bad enough to stop treatment were rare in all studies; however, evidence was very low quality in all three comparisons, so we are uncertain whether there is a difference between groups. Assessment ranged from six days to two months, participants included children and adults with mixed infective status, and causes of withdrawal included worsening of eczema or itch and loose stools.

Participants in the topical steroid/antibiotic combination group experienced fewer minor side effects than those given steroids alone. Comparing oral antibiotics to placebo, participants experienced equally low numbers of minor side effects. However, we are uncertain if their are true differences between groups due to very low-quality evidence. Based on short-term assessment of mixed participants (children and adults, with mixed infective status), reported side effects included sickness, diarrhoea, stomach/joint pains, and itching. For bleach baths versus placebo, some long-term minor side effects (burning/stinging, dry skin) were reported in both groups, so there may be no difference between treatment groups (low-quality evidence, uninfected participants (2 to 30 years)).

Quality of evidence

Evidence quality for improvement in symptoms or signs was low; for improvement in QoL, moderate; for antibiotic resistance, very low; and for side effects, it was almost consistently very low. The studies were small, diverse, and at risk of bias.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Summary of findings for the main comparison. Topical steroid plus topical antibiotic compared with topical steroid for eczema

Topical steroid plus topical antibiotic compared with topical steroid for eczema

Patient or population: children and adults with eczema

Settings: secondary care

Intervention: topical steroid plus topical antibiotic

Comparison: topical steroid

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Topical steroid	Topical steroid plus topical antibiotic				
Global outcome (good or excellent improvement in symptoms or signs, or both) Follow-up: 6-28 days	**Low risk population**		**RR 1.10** (1.00 to 1.21)	224 (3)	⊕⊕⊖⊖ **low**[b]	One further study (n = 28), using a continuous scale, found a result favouring steroid only.
	741 per 1000[a]	**815 per 1000** (741 to 897)				
Change from baseline in quality of life IDQoL ranges from 0 to 30 with higher values indicating more impaired quality of life Follow-up: 14 days	The mean IDQoL in the control group at the end of treatment decreased by 3.46 from the baseline value.	The mean IDQoL in the intervention group decreased by **0.18 less** (0.40 less to 0.04 more).	-	42 (1)	⊕⊕⊕⊖ **moderate**[c]	A different instrument (CDLQI) was used for children aged 4 years and over and showed significantly less reduction among the participants treated with topical antibiotic. There was no significant difference with either instrument at 28 days or at 3 months.
Adverse events requiring withdrawal from treatment Follow-up: 6-28 days	**Low risk population**		**RR 1.24** (0.21 to 7.25)	325 (4)	⊕⊖⊖⊖ **very low**[d]	Rates of adverse events were very low (zero in one study)
	31 per 1000[a]	**38 per 1000**				

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Cochrane Library
Trusted evidence.
Informed decisions.
Better health.

		(7 to 225)				and consequently the result is very uncertain.
Minor adverse events not requiring withdrawal from treatment Follow-up: 14 days	**Low risk population**		**RR 0.30** (0.12 to 0.78)	218 (2)	⊕⊖⊖⊖ **very low**[f]	The risk in the control group varied hugely between the two studies that assessed this outcome.
	36 per 1000[e]	**11 per 1000** (4 to 28)				
	High risk population					
	636 per 1000[e]	**191 per 1000** (76 to 496)				
Emergence of antibiotic-resistant micro-organisms Follow-up: 3 months	See comment	See comment	-	65 (1)	⊕⊖⊖⊖ **very low**[g]	This study reported the proportion of strains of *S. aureus* that were resistant to the antibiotic used - these were similar between the groups. Two other studies reported results that were not able to be compared between individual treatment groups.
Global change in composite ratings scale EASI ranges from 0 to 72, objective SCORAD ranges from 0 to 83 and SCORAD ranges from 0 to 108, with higher values indicating greater severity. Follow-up: 14-56 days	The mean scores in the control groups were 2.5 (standard deviation 5.2 to 5.6) for EASI, 18.8 (standard deviation 13.1) for objective SCORAD, and 25.4 (standard deviation 15.9) for SCORAD.	The mean score in the intervention group was **0.00 standard deviations lower** (0.33 lower to 0.33 higher).	-	256 (4)	⊕⊕⊖⊖ **low**[h]	As a rule of thumb, a value of 0.2 to 0.5 was considered a small effect, therefore the confidence interval suggested there was unlikely to be more than a small effect, either positive or negative.
No of participants in whom *S. aureus* was isolated Follow-up: 7-56 days	**High risk population**		**RR 0.48** (0.27 to 0.84)	298 (7)	⊕⊕⊕⊖ **moderate**[i]	-
	471 per 1000[a]	**226 per 1000** (127 to 396)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

CI: Confidence interval; **RR:** Risk Ratio; **EASI:** Eczema Area and Severity Index; **SCORAD:** SCORing Atopic Dermatitis

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Assumed risk based on the median control group risk across studies
[b]Downgraded two levels due to risk of bias (attrition bias, performance bias, and possible selective reporting) and imprecision of estimate
[c]Downgraded one level due to risk of bias (attrition bias and baseline imbalance)
[d]Downgraded three levels due to risk of bias (attrition and performance bias) and imprecision of estimate (two levels due to very low number of events)
[e]Assumed risk based on lowest and highest control group risk across studies
[f]Downgraded three levels due to risk of bias (attrition bias), imprecision of estimate and heterogeneity in control group risk
[g]Downgraded three levels due to risk of bias (attrition bias and baseline imbalance) and imprecision of estimate (two levels due to very low numbers of events)
[h]Downgraded two levels due to risk of bias (attrition and performance bias) and heterogeneity in control group means
[i]Downgraded one level due to risk of bias (performance bias, possible selective reporting and baseline imbalance)

Summary of findings 2. Oral antibiotic compared with placebo for eczema

Oral antibiotic compared with placebo for eczema

Patient or population: children and adults with atopic dermatitis

Settings: primary and secondary care

Intervention: oral antibiotic

Comparison: placebo

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Placebo	Oral antibiotic				
Global outcome (good or excellent improvement in symptoms or signs, or both) Follow-up: 14-28 days	**Low risk population**		**RR 0.80** (0.18 to 3.50)	75 (2)	⊕⊕⊖⊖ **low**[b]	-
	619 per 1000[a]	**495 per 1000** (111 to 1000)				

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Change from baseline in quality of life IDQoL ranges from 0 to 30 with higher values indicating more impaired quality of life. Follow-up: 14 days	The mean IDQoL in the control group at the end of treatment decreased by 3.46 from the baseline value.	The mean IDQoL in the intervention group decreased by **0.11 less** (0.32 less to 0.10 more).	-	45 (1)	⊕⊕⊕⊖ **moderate**[c]	A different instrument (CDLQI) was used for children aged 4 years and over and also showed no significant difference. There was also no significant difference with either instrument at 28 days or at 3 months.
Adverse events requiring withdrawal from treatment Follow-up: 14-28 days	See comment	See comment	-	199 (4)	⊕⊖⊖⊖ **very low**[d]	Rates of adverse events were very low (with either zero or one event in each arm of each study) and consequently the result was too uncertain to produce a meaningful estimate.
Minor adverse events not requiring withdrawal from treatment Follow-up: 28 days	See comment	See comment	-	68 (1)	⊕⊖⊖⊖ **very low**[d]	One further study reported a number of specific individual adverse events, but not the overall proportion of participants in each group experiencing any adverse event. The events included nausea, vomiting, diarrhoea, stomach pain, joint pains and new rash. Number of events were generally low in both groups.
Emergence of antibiotic-resistant micro-organisms Follow-up: 14 days	See comment	See comment	-	98 (2)	⊕⊖⊖⊖ **very low**[d]	One study reported the proportion of strains of *S. aureus* that were resistant to the antibiotic used - these were similar between the groups. One other study reported an increase in MRSA until 14 days following treatment but did not give numerical results. A third study reported no resistance to the antibiotic used in either treatment group.
Global change in composite ratings scale EASI ranges from 0 to 72 with higher values indicating greater severity.	The mean EASI score in the control group at the end of treatment decreased by	The mean EASI score in the intervention group decreased by **0.20 less** (0.52 less to 0.12 more).	-	68 (1)	⊕⊕⊕⊖ **moderate**[c]	There was also no significant difference in EASI score at 28 days.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Follow-up: 14 days	3.29 from the baseline value.					
No of participants in whom *S. aureus* was isolated Follow-up: 14-28 days	**High risk population**		**RR 0.76** (0.46 to 1.26)	144 (3)	⊕⊕⊖⊖ **low**[b]	-
	824 per 1000[a]	**626 per 1000** (379 to 1000)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio; **IDQoL:** Infants' Dermatology Quality of Life Index; **CDLQI:** Children's Dermatology Life Quality Index; **EASI:** Eczema Area and Severity Index

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Assumed risk based on the median control group risk across studies
[b]Downgraded two levels due to risk of bias (attrition bias) and imprecision of estimate
[c]Downgraded one level due to risk of bias (high risk of attrition bias and baseline imbalance)
[d]Downgraded three levels due to risk of bias (attrition bias and baseline imbalance), and imprecision of estimate (two levels due to very low number of events)

Summary of findings 3. Bleach bath compared with placebo or bath emollient for eczema

Bleach bath compared with placebo or bath emollient for eczema

Patient or population: children and adults with atopic dermatitis

Settings: secondary care

Intervention: bleach bath

Comparison: placebo or bath emollient

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

	Placebo or bath emollient	Bleach bath				
Global outcome (good or excellent improvement in symptoms or signs, or both) Follow-up: 1 month	**High risk population**		**RR 0.78** (0.37 to 1.63)	36 (1)	⊕⊕⊖⊖ **low**[b]	One further study assessed this outcome using the mean IGA score and also found no significant difference.
	500 per 1000[a]	**390 per 1000** (185 to 815)				
Change from baseline in quality of life CDLQI ranges from 0 to 30 with higher values indicating more impaired quality of life. Follow-up: 28 days	The mean CDLQI in the control group at the end of treatment decreased by 1.43 from the baseline value.	The mean CDLQI in the intervention group decreased by **0.90 less** (3.12 less to 1.32 more).	-	80 (1)	⊕⊕⊕⊖ **moderate**[c]	-
Adverse events requiring withdrawal from treatment Follow-up: 2 months	See comment	See comment	-	42 (1)	⊕⊖⊖⊖ **very low**[d]	Rates of adverse events were too low to produce meaningful estimates. One further study reported no adverse events and two other studies also reported very low rates of adverse events requiring withdrawal from treatment but results could not be combined due to differing study designs.
Minor adverse events not requiring withdrawal from treatment Follow-up: 2 months	**Medium risk population**		**RR 1.00** (0.35 to 2.87)	36 (1)	⊕⊕⊖⊖ **low**[b]	Two further studies reported no adverse events and one other study reported adverse events but results could not be combined due to differing study designs.
	278 per 1000[a]	**278 per 1000** (97 to 798)				
Emergence of antibiotic-resistant micro-organisms Follow-up: 4 weeks	See comment	See comment	-	80 (1)	⊕⊖⊖⊖ **very low**[e]	One further study reported no significant difference in antibiotic resistance patterns but no numerical results were presented.
Global change in composite ratings scale EASI ranges from 0 to 72 with higher values indicating greater severity. Follow-up: 1 month	The mean EASI score in the control group at the end of treatment was 13.87[f].	The mean EASI score in the intervention group was **2.48 lower** (7.36 lower to 2.40 higher).	-	54 (2)	⊕⊖⊖⊖ **very low**[g]	One further study assessed this outcome using the change from baseline in mean SCORAD and also found no significant difference between the groups. One study additionally followed up EASI score at 2 months and one study reported

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

						SCORAD at 3 months; both reported significantly lower scores in the intervention group.
No of participants in whom *S. aureus* was isolated	-	-	-	-	-	No studies reported this outcome, although two studies reported no significant difference in *S. aureus* colony counts.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk Ratio; **IGA:** Investigator global assessment; **CDLQI:** Children's Dermatology Life Quality Index; **EASI:** Eczema Area and Severity Index; **SCORAD:** SCORing Atopic Dermatitis

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[a]Assumed risk based on control group of the one study reporting this outcome
[b]Downgraded two levels due to risk of bias (performance bias, baseline imbalance) and imprecision of estimate
[c]Downgraded one level due to imprecision of estimate
[d]Downgraded three levels due to risk of bias (performance bias, baseline imbalance) and imprecision of estimate (two levels due to very low number of events)
[e]Downgraded three levels due to imprecision (small study) and study limitations due to selective reporting of results (two levels as numerical data not reported) so we were unable to obtain an estimate of the effect from the available evidence
[f]Control group mean based on median across the studies reporting this outcome
[g]Downgraded three levels due to risk of bias (performance bias, baseline imbalance), imprecision of estimate and heterogeneity in control group mean

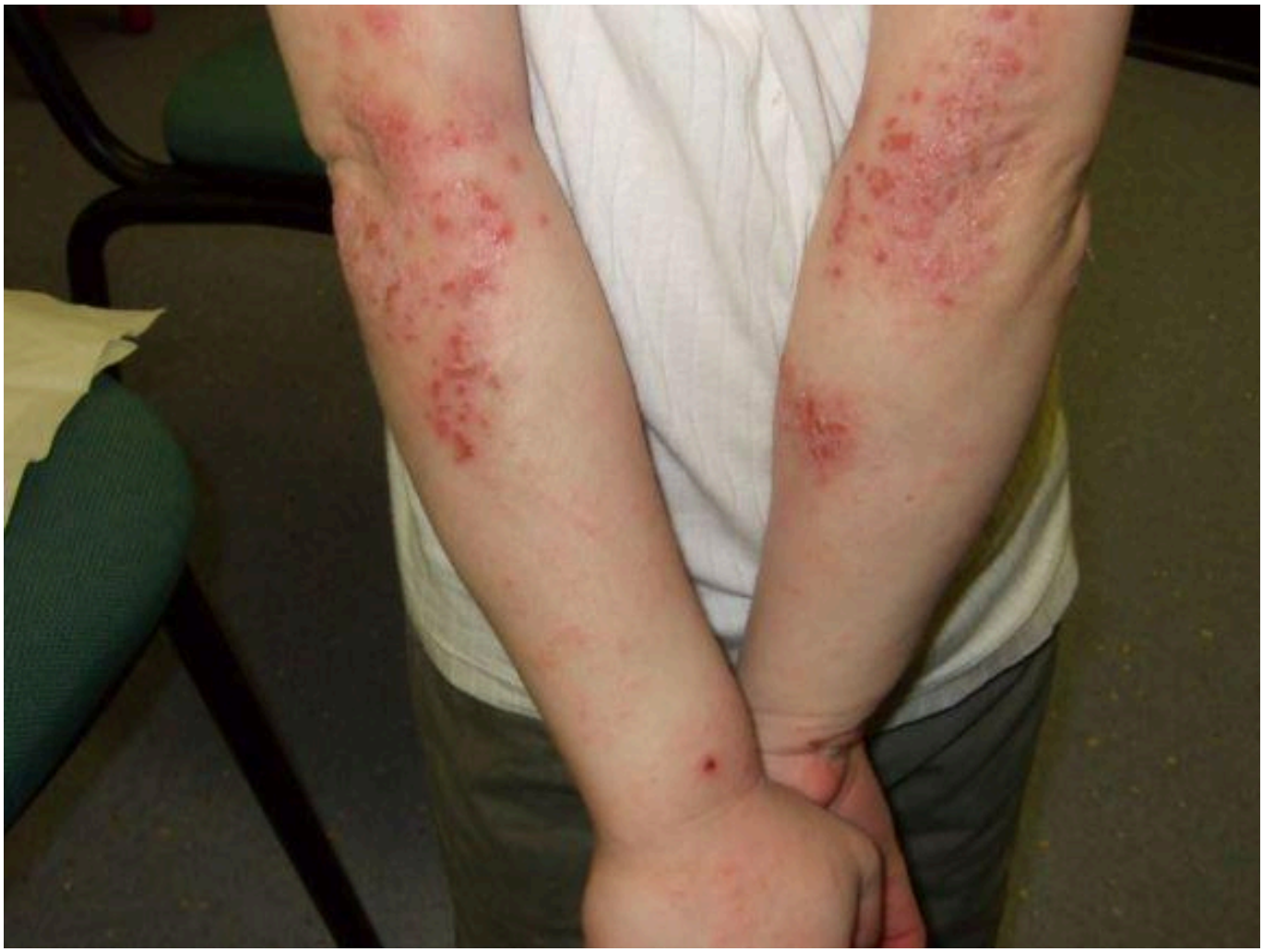
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

BACKGROUND

Description of the condition

Eczema (syn: atopic eczema, atopic dermatitis) is a chronic, relapsing, intensely itchy, inflammatory skin disease (see Figure 1), which involves the skin creases such as the folds of the elbows or behind the knees (Williams 1994). Symptoms usually appear below the age of two years and around 60% of cases will be clear by early adolescence, although some will relapse or continue into adult life. Prevalence ranges from 2 to 20% and varies considerably from one country to another, and also within countries (Odhiambo 2009). The prevalence has also increased substantially across developed and less well developed countries worldwide for reasons that are still unclear (Williams 2008; Deckers 2012). One review suggests that eczema affects around 7% to 10% of adults in the US (Silverberg 2017).

Figure 1. Eczema. Copyright © 2009 Centre of Evidence Based Dermatology: reproduced with permission.



Eczema often occurs in families with atopic diseases including asthma, allergic rhinitis/hay fever (and food allergy), and atopic eczema. These diseases share a common pathogenesis (mechanism of disease), and are frequently present together in the same individual and family. The word atopy refers to the genetic tendency to produce immunoglobulin E (IgE) antibodies in response to small amounts of common environmental proteins such as pollen, house dust mite, and food allergens (Stone 2002; Thomsen 2015). Around 30% of people with eczema develop asthma and 35% develop allergic rhinitis (Luoma 1983). However, it is known that atopy does not concurrently occur in all patients with atopic eczema. In view of this, there have been recent proposals to use the term 'eczema' to define patients both with and without atopy. Various terms are used for eczema; however, despite these synonyms, we will refer to the condition as just 'eczema' throughout the rest of this review. This is in agreement with the 'Revised nomenclature for allergy for global use' (Johansson 2004) and similar to other Cochrane Reviews evaluating eczema therapies (Van Zuuren 2017).

The causes of eczema are not fully understood; however, both genetic and environmental factors are important in determining both the occurrence and the severity of disease (Williams 1992). Skin barrier dysfunction and immunological abnormalities play a role in its pathogenesis (Wollenberg 2014; Benetti 2015). The identification of mutations in the gene coding for the skin barrier protein, filaggrin, confirmed the role of an underlying genetic predisposition (Irvine 2006), however, filaggrin mutations do not occur in all cases of eczema and other genes are likely to play a role. Environmen-

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

tal factors are important in the initial development of the condition and in triggering flares (George 2015).

Staphylococcus aureus and eczema

An association between *S. aureus* and eczema has been recognised for many years. It has been demonstrated that *S. aureus* can be isolated from 70% of eczema skin lesions (Totté 2016) and the density of *S. aureus* tends to increase with the clinical severity (Williams 1990). In contrast, *S. aureus* is rarely found on healthy skin (< 5%), and it is less common to have severe colonisation or infection in other skin diseases, so eczema does appear to be a special case. Whilst this association is well recognised, the role of *S. aureus* in causing eczema or making it worse, as opposed to simply colonising the skin, is still under debate. However, there is increasing experimental evidence for its role in the pathogenesis of eczema.

Clinically infected eczema

At one end of the spectrum, there is undoubtedly a clinical condition of 'infected eczema' manifest by oozing, crusting and presence of pus spots overlying the areas of pre-existing eczema. This corresponds with heavy growth of bacteria in the laboratory on swabs taken from the affected areas, usually of *S. aureus*, but there are also reports of beta-haemolytic streptococci (a type of streptococci that can split open red blood cells; some types can cause skin infections, while others live harmlessly on the skin) being isolated either alone or in combination with *S. aureus* (Ong 2016). In this situation, the overt infection responds to antibiotic treatment, although the eczema itself may not. Clinical infection is a major problem for some eczema sufferers (David 1986). It has been reported that flares in eczema are preceded by a decrease in microbial diversity and that *S. aureus* is the main species found during a flare (Ong 2016).

Staphylococcus aureus and non-clinically infected eczema: coloniser or pathogen?

In eczema that is not overtly clinically infected, the role of *S. aureus* is much less clear. It may be that *S. aureus* simply colonises the skin, taking advantage of a favourable environment for growth. This is supported by the fact that treatment of the underlying eczema with topical steroid alone drastically reduces the number of colonies of *S. aureus* (Stalder 1994).

The role of *S. aureus* in eczema has been discussed in several review articles (Lin 2007; Lee 2014; Ong 2016; Hepburn 2017). There are numerous ways in which *S. aureus* may potentially contribute to the pathogenesis of eczema, including via production of various proteins such as superantigens and proteases (Lee 2014). Superantigens penetrate the skin barrier and cause chronic inflammation through a variety of mechanisms, including:

1. stimulation of cytokine (a type of protein used for signalling in the immune system) release from T-cells;
2. acting as an allergen by induction of IgE antibodies, which cause release of inflammatory mediators from mast cells (cells that release histamine during inflammatory or allergic reactions) and basophils (a type of white blood cell)
3. stimulation of antigen-presenting cells and keratinocytes (a type of skin cell) to release pro-inflammatory cytokines, thereby increasing T-cell infiltration;
4. increasing cutaneous lymphocyte-associated antigen receptor (a skin-homing receptor) on T-cells, causing migration to the skin and increasing inflammation; and
5. increasing skin inflammation caused by other allergens.

Superantigens also increase adherence of *S. aureus* to the skin by exposing extracellular matrix adhesins (a type of protein) and cause corticosteroid resistance (Lee 2014; Benetti 2015). In a clinical study, application of one specific superantigen to the skin has been shown to induce skin changes of erythema (redness) and thickening of the skin (Strange 1996).

S. aureus also produces proteases, which cause skin barrier breakdown, allowing penetration of allergens and irritants. *S. aureus*-derived proteases cleave endogenous protease inhibitors (proteins produced by the body that prevent the breakdown of proteins by enzymes called proteases), induce pro-inflammatory and pro-allergic responses, promote Th2 immune response and result in IgE production (Lee 2014).

Other *S. aureus*-derived proteins may also contribute to skin inflammation in eczema. Phenol-soluble modulins (a type of bacterial toxin) attract and lyse (break up) neutrophils (a type of white blood cell), making *S.aureus* more likely to cause harm (Benetti 2015; Syed 2015). Fibronectin-binding protein, a type of protein produced by *S. aureus* that enables it to stick to and enter cells of the host organism, activates T–cells (a type of cell from the immune system, that plays a key role in skin inflammation). This activation results in the release of chemical messengers called cytokines that also promote skin inflammation (Reginald 2011).

Description of the intervention

A number of products with anti-staphylococcal properties have been developed for the treatment of eczema, both clinically infected and uninfected, ranging from antibacterial soaps, impregnated clothing, to additives such as bath oils and topical corticosteroids. Some of these treatments are classed as antiseptics, substances applied to the skin which either kill or inhibit the growth of microorganisms, and others are antibiotics, which have specific effects on certain bacteria.

Common anti-staphylococcal interventions that are used in clinical practice include oral antibiotics, topical antibiotics used alone or in combination with a topical steroid (e.g. “Fucidin H” fusidic acid and hydrocortisone), and topical antiseptics, which can be used as a leave-on emollient (moisturiser), soap or bath additive. Any of these interventions may be used in a primary or secondary care setting.

The decision to use an anti-staphylococcal intervention may be made on the observation of overt signs of clinical infection such as oozing on a background of intense erythema and pus spots, or during a flare of eczema, when staphylococcal colonisation is confirmed on bacterial culture from a skin swab. Exact regimens for topical preparations used in eczema are likely to vary depending on the patient’s condition and clinician experience. However, more specific recommendations for staphylococcal skin infection suggest using fusidic acid cream three to four times per day (BNF 2019). Combination steroid and antibiotic preparations are popular in the UK and are usually prescribed at a maximum frequency of twice daily for two weeks (NICE 2013).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

For more widespread or severely infected eczema, oral antibiotics may be chosen. For an adult, this would usually be flucloxacillin at a dose of 250 mg or 500 mg four times per day for a week. For patients allergic to flucloxacillin, a macrolide antibiotic, e.g. erythromycin, can be used. Flucloxacillin commonly causes gastrointestinal side effects, such as nausea and diarrhoea (BNF 2019). Other less common side effects include hypersensitivity reactions, skin reactions and thrombocytopenia (low blood platelet count) (BNF 2019). Flucloxacillin can potentially interact with numerous other drugs, which can increase the risk of hepatotoxicity (liver damage) (BNF 2019).

Many emollients are available which contain an antiseptic ingredient, such as chlorhexidine and benzalkonium chloride, present in brands such as Dermol. Some of the products are intended to be used as leave-on emollients, which would usually be used twice a day and either prescribed for overt or suspected infection or as part of a normal emollient regimen regardless of infective status. Others are used as soap substitutes or bath additives when bathing. Skin irritation or allergic reactions may occur to the active ingredients or excipients (i.e. other inactive ingredients in the topical preparation such as a vehicle).

Bath additives may also contain antiseptic ingredients such as chlorhexidine and benzalkonium chloride. These may be recommended for use when bathing, often as part of a normal skin care regimen for patients with eczema, especially those with recurrent skin infections. Skin irritation or allergic reactions may occur to the active ingredients or excipients. “Bleach baths” with dilute sodium hypochlorite solution are recommended for twice weekly use (St John's Institute of Dermatology 2016). These may be recommended for patients with overt, suspected or frequently infected eczema.

Therapeutic textiles with anti-staphylococcal properties, although described in clinical trials, are not routinely used in a clinical setting for treating eczema.

How the intervention might work

The aim of treatment with anti-staphylococcal interventions in eczema is to decrease bacterial load, thereby decreasing the amount of *S. aureus* superantigen, proteases and other protein products produced, which result in damage and inflammation of the skin barrier.

Possible concern about anti-staphylococcal treatment in eczema

Quite apart from the fundamental question of whether anti-staphylococcal therapies work in eczema, there are special concerns about their routine use in non-clinically infected eczema. For the individual patient, irritant and allergic contact dermatitis can occur from topically-applied antiseptics or antibiotic-containing preparations. For example, allergic contact dermatitis is increasingly recognised to occur with benzalkonium chloride (Hann 2007) and chlorhexidine (Koch 2014) with rare reports of anaphylaxis with the latter (Moka 2015). One study found that triclosan, a commonly used microbial agent, acted as a liver tumour promoter in mice (Yueh 2014).

The potential for development of bacterial resistance to antibiotics, which may be needed for systemic treatment of serious infections, is also important. An increase in the prevalence of fusidic acid resistant *S. aureus* has been observed in several areas of the UK (Reed 1999; Ravenscroft 2000; Simpson-Dent 2000; Brown 2002). In Harrogate, UK, fusidic acid resistance has been shown to be associated with intensive use of oral and topical fusidic acid-containing preparations such as those marketed for eczema (Ravenscroft 2000). A subsequent study from Singapore confirmed an association between recent use of fusidic acid and fusidic acid-resistant *S. aureus* (Heng 2013). Widespread use in dermatological practice may limit the use of fusidic acid combination therapies for the treatment of more serious diseases including staphylococcal bone and joint infections and systemic methicillin-resistant *S. aureus* (MRSA) infections.

Resistant organisms also have implications for patients with eczema. The prevalence of MRSA is increasing in patients with eczema (Jagadeesan 2014; Chaptini 2015). Furthermore, the presence of resistant *S. aureus* was found to be associated with increased disease severity (Jagadeesan 2014). Mupirocin may also be used to reduce *S. aureus* carriage in patients with eczema. The use of mupirocin has also been found to correlate with mupirocin-resistant *S. aureus* in paediatric dermatology patients (Antonov 2015).

Why it is important to do this review

There is a plausible theoretical rationale for use of anti-staphylococcal agents in eczema, especially if it appears to be clinically infected. Yet existing evidence to support clinical benefit of anti-staphylococcal agents appears to be conflicting. There are concerns regarding adverse event issues, e.g. contact and irritant dermatitis, and promoting wider drug resistance in the community. Despite these concerns, anti-staphylococcal products are widely marketed and used by the clinical community.

This is an update of a review 'Interventions to reduce *Staphylococcus aureus* in the management of atopic eczema' (Birnie 2008). The previous review found that most studies were poorly reported and study differences limited pooling of results. The authors failed to find clear evidence of benefit for antimicrobial interventions for people with eczema, despite their widespread use.

OBJECTIVES

To assess the effects of interventions to reduce *S. aureus* for treating eczema.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs), including cross-over trials and randomised within-patient trials.

Types of participants

Anyone who has been diagnosed with atopic eczema by a medical practitioner. We regarded diagnostic criteria such as the Hanifin and Rajka definition (Hanifin 1980) or the UK refinement (Williams 1994) as acceptable, as was diagnosis of atopic eczema by a dermatologist using the terms 'atopic eczema' or 'atopic dermatitis'. We only accepted the term 'eczema' when referring to children. Any other terms, such as 'Besnier's prurigo' or 'neurodermatitis' had to have additional descriptive evidence of atopic eczema in the flexures before inclusion. It was noted whether the participants were described as 'clinically infected' or otherwise.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Studies in which not all participants had atopic eczema were only included if separate results were reported for the participants with atopic eczema.

Types of interventions

1. Oral antibiotic known to be active against *staphylococcus*
2. Topical antiseptic/antibiotic
3. Topical steroid plus antiseptic/antibiotic
4. Topical steroid plus antibiotic and antifungal
5. Topical calcineurin inhibitor plus antibiotic
6. Antibacterial soap
7. Antibacterial bath additive
8. Antibacterial bath additive plus antibiotic
9. Therapeutic textile
10. Protease inhibitor

We accepted as comparators a similar treatment regimen without the anti-staphylococcal agent, i.e. placebo, no treatment, vehicle only, or untreated textile where the intervention was an anti-staphylococcal agent alone, or an active compound where the intervention consisted of the active compound plus an anti-staphylococcal agent (e.g. topical steroid/antibiotic combination compared against the same topical steroid without the antibiotic). On this final point, it was agreed that a vehicle was not an appropriate comparator for a steroid/antibiotic combination as it is well recognised that topical steroids are an effective treatment for inflamed eczema and thus one could not establish whether it was the addition of the antibiotic, or the steroid itself that had efficacy.

For studies with two treatment groups of interventions from different categories compared against a single comparator group, the relevant treatment group and the same comparator group were included in both categories.

Types of outcome measures

Primary outcomes

(a) Global degree of improvement in symptoms or signs, or both, as rated by the participant or medical practitioner, i.e. percentage with good or excellent improvement. We included both short-term (less than or equal to a month) improvement and long-term (more than one month) benefit.
(b) Improvement in Quality of Life questionnaires.

Secondary outcomes

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation.
(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.
(c) Emergence of antibiotic-resistant micro-organisms. Only *S. aureus* was considered, and we only included studies if swab data before and after the intervention were available. It was planned to take duration of treatment into account when these data were interpreted.

Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale.
(b) Changes in the individual signs of eczema as assessed by a physician, e.g. erythema (redness), papules (spots that protrude from the skin surface), vesicles (water blisters), scaling.
(c) Duration of remission and/or prevention of subsequent flares.
(d) Change in isolation rate of *S. aureus*, i.e. isolated or not isolated.
(e) Change in bacterial counts of *S. aureus*, i.e. an assessment of quantity of *S. aureus*.

The Harmonising Outcome Measures for Eczema (HOME) initiative recommends a core outcome set of four domains for trials in eczema (Schmitt 2012):

1. Clinician-reported signs, with core outcome instrument Eczema Area & Severity Index (EASI) (Schmitt 2014). This would be included in our tertiary outcome, global changes in composite rating scales, with individual signs also captured as a separate tertiary outcome.
2. Patient-reported symptoms, with core outcome instrument Patient Oriented Eczema Measure (POEM) (Spuls 2017). This would also be included in our tertiary outcome, global changes in composite rating scales.
3. Quality of life. This was one of our primary outcomes. HOME has yet to recommend a core outcome instrument.
4. Long-term control. HOME recommends that this should be captured by repeated measurement of the other three domains. We assessed all reported outcomes in both short- and long-term timeframes.

Search methods for identification of studies

We aimed to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

Electronic searches

For this update, we revised all our search strategies in line with current Cochrane Skin practices. Details of the previous search strategies are available in Birnie 2008.

We searched the following databases up to 29 October 2018:

- the Cochrane Skin Group Specialised Register using the following search terms: (dermatitis or eczema or neurodermatitis or besnier*) and (staphylococc*)
- the Cochrane Central Register of Controlled Trials (CENTRAL); 2018, Issue 9, in the Cochrane Library using the search strategy in Appendix 1;
- MEDLINE via Ovid (from 1946) using the strategy in Appendix 2;
- Embase via Ovid (from 1974) using the strategy in Appendix 3; and
- LILACS (Latin American and Caribbean Health Science Information database, from 1982) using the strategy in Appendix 4.

Trials registers

We searched the following trials registers up to 16 November 2018:

Trial registry	Search terms

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ClinicalTrials.gov (www.clinicaltrials.gov)	("Eczema" OR "Dermatitis") AND "Staphylococcus"
the ISRCTN registry (www.isrctn.com/)	("Eczema" OR "Dermatitis") AND "Staphylococcus"
the EU Clinical Trials Register (www.clinicaltrialsregister.eu/)	("Eczema" OR "Dermatitis") AND "Staphylococcus"
the Australian New Zealand Clinical Trials Registry (www.anzctr.org.au)	("Eczema" OR "Dermatitis") AND "Staphylococcus"
the World Health Organization International Clinical Trials Registry Platform (ICTRP) (apps.who.int/trialsearch/)	eczema AND staphylococcus OR dermatitis AND staphylococcus

Searching other resources

References lists

We checked the bibliographies of all of the studies that were obtained for further references to relevant trials.

Correspondence

Where possible we corresponded with trial authors (Table 1), and we contacted pharmaceutical companies who produce relevant products, in order to identify unpublished and ongoing trials. For the current update, the following companies were contacted:

- Dermal (Dermol 600, Dermol 200, Dermol wash emulsion, Dermol cream, Dermol 500, Emulsiderm);
- GSK (Trimovate, Bactroban, Retapamulin);
- Amdipharm mercury (Aureocort);
- Leo (Fucidin H, Fucibet, Fucidin);
- Typharm (Nystaform- HC);
- Alliance (Terra-Cortril, Timodene);
- Derma UK (Synalar N);
- PLIVA Pharma Ltd (TEVA) (Polyfax);
- Smith & Nephew (Flamazine);
- Genus (Eczmol);
- Stiefel (Oilatum Plus);
- Thornton and Ross (Zerolatum Plus).

Grey literature

Conference proceedings from the following meetings were checked for RCTs and, where appropriate, the trial authors were contacted for further information:

- British Association of Dermatologists annual meeting (from 1980 to 2018);
- American Academy of Dermatology annual meeting (2006 to 2018); and
- Congresses of the European Academy of Dermatology and Venereology were searched using the term “staphylococcus aureus” for the following years: 1995, 1998, 1999, 2002, 2003, 2005, 2006, 2008-2018.

Data collection and analysis

Selection of studies

Two authors independently checked the titles and abstracts identified from the searches (JR and JP or AB for the original; SG and SK or DH for the update). If it was clear that the study did not refer to a RCT on eczema, it was excluded. If it was unclear, then the full text of the study was obtained for independent assessment by two authors (AB and HCW for the original; SG and SK or DH for the update). The authors decided which trials fitted the inclusion criteria. For the original review, any disagreement was resolved by discussion between AB and HCW and it was not necessary to refer to a third author. For the update, any disagreement was resolved by discussion between SG and SK or DH; in some cases, a consensus among all authors was obtained. We recorded excluded studies and reasons for exclusion in the Characteristics of excluded studies table.

Data extraction and management

This was performed by two authors (AB and HCW for the original; SG and SK or DH for the update), who independently entered data onto a data extraction form. AB and HCW (SG and SK for the update) discussed discrepancies between themselves. Missing data were obtained from trial authors, where possible. Data were checked and entered into RevMan by AB and FBH (SG and DH for the update). The authors were not blinded to the names of trial authors, journal or institutions.

In the original published protocol, outcomes were considered at the end of treatment and this was considered short-term where treatment had been given for two weeks or less and long-term for periods of one month or greater. After discussion (between AB and HCW) however, it was decided that studies of a month's duration or less would be considered as reflecting short-term benefit and those of greater than a month as a reasonable minimal time to reflect some disease chronicity. Where the patient-rated global assessment was not available, the medical practitioner global rating was used. Both measures were taken into account where both were available. No attempt was made to combine these measures, as they are often not well correlated. In the published protocol, skin irritation was to be reported separately as well as within the minor participant adverse events. After discussion (between AB and HCW), it was decided that it was not necessary to report on skin irritation twice and thus it was included in the "minor patient-reported adverse events" section only.

Assessment of risk of bias in included studies

For the update, two authors (SG and either DH or SK) independently assessed the risk of bias of each study, including those from the original review, using the Cochrane tool for assessing risk of bias (Higgins 2011). Any disagreement was resolved by discussion between these three authors. The risk of bias tool addresses the following domains:

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

- method of sequence generation;
- method of allocation concealment;
- blinding of investigators and participants;
- blinding of outcome assessors;
- presence of incomplete outcome data;
- presence of selective reporting; and
- other bias such as, for example, baseline imbalance.

For each study we categorised each domain as 'low risk of bias', 'high risk of bias' or 'unclear risk of bias'.

Measures of treatment effect

For studies with a similar type of intervention and control (e.g. steroid/antibiotic combinations), a meta-analysis was performed to calculate a weighted treatment effect across trials using a random-effects model. The results were expressed as risk ratio (RR) and 95% confidence intervals (CI) for dichotomous outcomes, rather than odds ratio as the event rates were common and we did not wish to overestimate the effect. Continuous outcomes were expressed as either mean differences (MD and 95% CI) for cases in which the same instrument was used, or standardised mean differences (SMD) for cases in which different instruments were used. Where it had not been possible to perform a meta-analysis, the data were described qualitatively. Where appropriate, we expressed results as number needed to treat for an additional beneficial outcome (NNTB) with 95% CI and the baseline risk to which it applied.

Unit of analysis issues

We did not perform techniques appropriate for paired designs for cross-over studies due to insufficient data; however, where data from the first period were available from a cross-over study, then they were analysed as if it were a parallel study as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). For within-patient trials, we abstracted from the original paper the paired analysis results, if available, and reported these in the review. If cluster-randomised trials had been identified, we would have attempted to include them using the generic inverse-variance method, if appropriate results were reported. Where studies with multiple treatment arms were identified, if two interventions from different categories were compared against the same control group, then both pairwise comparisons were included within the relevant categories.

Dealing with missing data

If results from intention-to-treat analyses were given, then we used them as such (see Characteristics of included studies). Where a per protocol analysis was performed by the study in question or it was clear that the number of participants completing the study were not the same as those randomised, then we performed an available case analysis (i.e. we included only those participants for whom the outcome was reported).

Assessment of heterogeneity

Heterogeneity was assessed using I^2. Where substantial heterogeneity ($I^2 > 50\%$) existed between studies for the primary outcome, we explored reasons for heterogeneity, such as differing inclusion criteria (Higgins 2011).

Assessment of reporting biases

We would have performed funnel plots if greater than 10 pooled studies were available (Higgins 2011).

Data synthesis

A random-effects model was used when conducting a meta-analysis as the studies were deemed to be clinically heterogeneous.

Subgroup analysis and investigation of heterogeneity

We would have performed subgroup analysis where adequate information was given. The planned subgroups were 'clinically infected eczema', 'mixed infection/colonisation with *S. aureus* and beta haemolytic *Streptococcus*', and 'non-infected or unspecified.' Heterogeneity was assessed as above (Assessment of heterogeneity).

Sensitivity analysis

We explored reasons for heterogeneity in studies and, if necessary, we would have performed sensitivity analyses examining the effects of excluding study subgroups, e.g. those studies with low methodological quality.

Summary of findings tables

Summary of findings tables were generated for all comparisons for which we were able to pool evidence. The outcomes selected for inclusion in the 'Summary of findings' tables were all primary and secondary outcomes, and two tertiary outcomes that were considered most important (changes in composite rating scales and changes in *S. aureus* isolation rates). For each outcome included in the 'Summary of findings' tables, the quality of the body of evidence was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (GRADE Working Group 2004), which specifies four levels of quality (high, moderate, low and very low). As all studies included in the review were RCTs, the starting level for all assessments was high quality. The level was then downgraded according to the presence of the following factors: risk of bias; indirectness of evidence; unexplained heterogeneity; imprecision of results; and likelihood of publication bias. The number of levels to downgrade each body of evidence was decided by discussion and agreement between two authors (SG and DH).

RESULTS

Description of studies

Results of the search

We updated the searches to October 2018. We screened 307 records from the following databases: Cochrane Skin Specialised Register, CENTRAL, MEDLINE, Embase, and LILACS. A further 88 records were identified through trial registries (52), the GREAT database (34), correspondence with authors (1), and conference abstracts (1). This gave a total of 395 records.

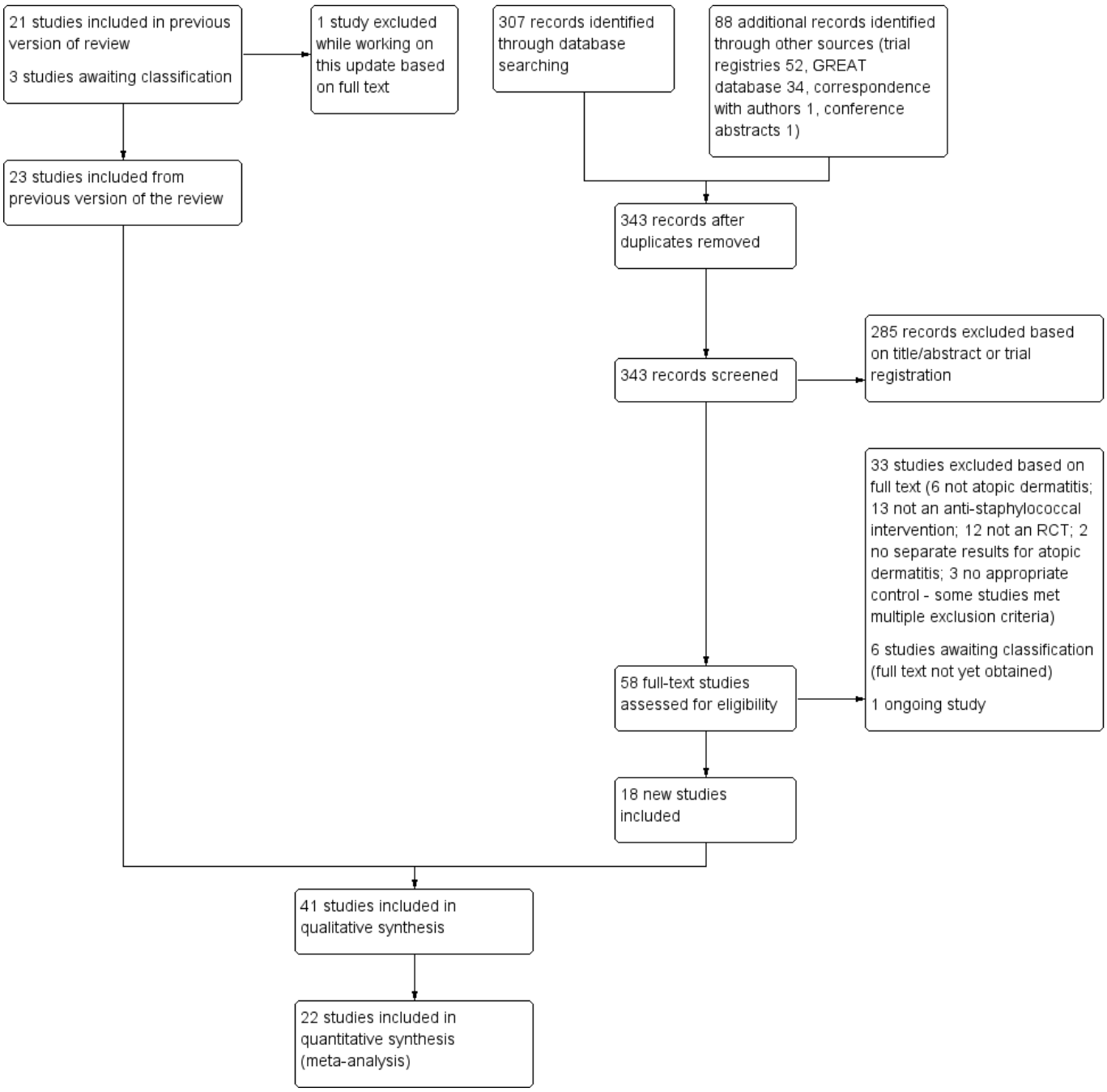
After duplicates were removed, there were 343 records. We excluded 285 records based on titles, abstracts and trial registration records. After screening the remaining 58 records, we included 18 new studies (see Characteristics of included studies), and excluded 33 (Characteristics of excluded studies). We identified one ongoing study, and six studies awaiting classification.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

We combined the new studies with those previously identified for this review, and for this update we have included a total of 41 trials (18 new), and excluded 57 trials (33 new).

A summary of the search results is provided in Figure 2.

Figure 2. Study flow diagram.



Included studies

Twenty-one studies were included in the original review. Of three studies awaiting classification in the original review, two were included for this update (Gauger 2006; Huang 2009), and one was excluded (Senti 2006), giving a total of 23 trials from the original review. From the update searches, 18 additional studies were included, resulting in a total of 41 studies with 1753 evaluable participants included in this review and described in the Characteristics of included studies tables.

Study design

All studies were RCTs: 27 parallel group RCTs (including one 2 x 2 factorial), six cross-over, and eight within-patient studies. The studies involved sample sizes between four and 174 evaluable participants.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Setting

Setting was specified in 38 studies and they were conducted in secondary care, except one study (Francis 2016), which predominantly recruited from primary care. Three studies did not specify the setting. Twenty-one of the studies were conducted in Western Europe, nine were in North America, seven were from the Far East and four elsewhere in the world. Nine of the studies were conducted using multiple centres, 27 were single centre and five did not specify.

Participants

Twelve studies looked specifically at children and four specifically at adults, 19 included both, and, in six studies, it was not clear. Mean age ranged from 1.1 to 34.6 years across the 24 studies that reported this, with a median across studies of 14.9 years (eleven of the studies that did specify whether they recruited adults or children did not report the mean age). All of the studies included both males and females. The proportion of males ranged from 20% to 65% across the 28 studies that reported this, with a median of 48%.

Four studies were in clinically infected eczema, 15 in uninfected eczema, and two reported a mix of infected and uninfected cases, while 20 did not specify infective status. In five studies, colonisation or infection with *S. aureus* was specified as an inclusion criterion, and across the other 18 studies that reported the proportion colonised (usually assessed on lesional skin), this varied from 38% to 100%, with a median of 83%.

Funding sources

In 22 studies, the funding sources were not stated. In one study, funding was reported as "none". Nine studies were commercially funded, five studies were funded by non-commercial research grants or institutions and one study was explicitly reported to have been funded by both a non-commercial research grant and a pharmaceutical company. In three studies, the intervention, placebo or other research support was commercially supplied.

Interventions

The included studies fell into 10 broad categories of interventions:

1. Oral antibiotic (four studies);
2. Topical antiseptic/antibiotic (five studies);
3. Topical steroid plus antiseptic/antibiotic (14 studies);
4. Topical steroid plus antibiotic and antifungal (one study);
5. Topical calcineurin inhibitor plus antibiotic (one study);
6. Antibacterial soap (one study);
7. Antibacterial bath additive (seven studies);
8. Antibacterial bath additive plus antibiotic (one study);
9. Therapeutic textile (eight studies);
10. Protease inhibitor (one study).

One three-arm study had two interventions included in different categories (oral antibiotic and topical steroid plus antiseptic/antibiotic) (Francis 2016), and the factorial trial also had two interventions included in different categories (topical steroid plus antiseptic/antibiotic and topical calcineurin inhibitor plus antibiotic) (Hung 2007). Two further studies included a third randomised arm that was not eligible for inclusion in the review (Wachs 1976; Juenger 2006), one study had two additional randomised arms that were not eligible (Polano 1960) and one study included an additional non-randomised control group (Canpolat 2012). Three of the papers additionally reported a second study, which in all cases was not eligible for inclusion in the review (Leyden 1977; Nilsson 1992; Ramsay 1996).

Control groups for the studies of oral interventions were all oral placebos and topical interventions were compared against vehicle alone, another topical placebo, or no treatment. Studies of topical steroid (or topical calcineurin inhibitor) plus antiseptic/antibiotic (with or without antifungal) were only included if the controls used a topical steroid (or calcineurin inhibitor) without the antiseptic/antibiotic added. Antibacterial bath emollients were compared against the same emollient without the antibacterial component and bleach baths were compared against water or bath emollient. Therapeutic textiles were all compared against untreated placebo textiles.

In 16 studies, plus two arms of the factorial RCT, all participants received topical steroids. In five studies, plus the other two arms of the factorial RCT, topical steroids were not permitted. In seven studies, participants could continue to use topical steroids as needed, and in four studies participants were strongly discouraged from using topical steroids or they were only permitted as 'rescue medication'. The remaining eight studies did not report on use of topical steroids.

Outcomes

The studies had multiple stated outcomes, a number of which were not reported in the results. Twenty studies reported on global improvement and five reported on quality of life, using the DLQI (Dermatology Life Quality Index, Finlay 1994) (two studies), CDLQI (Children's Dermatology Life Quality Index, Lewis-Jones 1995) (two studies), IDQoL (Infant's Dermatology Quality of Life Index, Lewis-Jones 2001) (one study) and DIELH (German Instrument for the assessment of Quality of Life in Skin Diseases, Schafer 2001) (one study). The DLQI, CDLQI and IDQoL range from 0 to 30 and DIELH ranges from 0 to 180, with higher values on all scores indicating more impaired quality of life. Twenty-seven studies reported on either severe and/or minor patient-reported adverse events. A large number of studies looked at microbiological data including resistant organisms (seven studies), isolation rates (19 studies) and colony counts (17 studies) of *S. aureus*. Twenty studies assessed outcomes based on a published named scale including SCORAD (SCORing Atopic Dermatitis, European Task Force on Atopic Dermatitis 1993) (15 studies), EASI (Hanifin 2001) (five studies), SASSAD (Six Area, Six Sign Atopic Dermatitis, Schmitt 2007) (one study) and POEM (Charman 2004) (one study). SCORAD ranges from 0 to 103 (0 to 83 for the objective component), EASI from 0 to 72, SASSAD from 0 to 108, and POEM from 0 to 28, with higher values on all scores indicating greater severity.

For comparisons of oral antibiotic versus placebo and topical steroid plus topical antibiotic versus topical steroid, we were able to pool studies in groups of up to seven studies for some outcome measures. For the remaining categories, either the studies were not sufficiently similar to pool or the studies did not report the same outcome measures. For the initial pooling we did not take into consideration whether it was infected or non-infected eczema that was being treated.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Trial periods

Treatment durations ranged from 10 minutes to 3 months (mean: 26 days). Three studies had less than one week duration of treatment, seven were of one week, 11 of two weeks, one of three weeks, 10 of four weeks, and nine of greater than four weeks duration. Only the nine studies with greater than four weeks treatment duration were considered a reasonable time to reflect disease chronicity (Breneman 2000; Hung 2007; Fluhr 2009; Huang 2009; Tan 2009; Leins 2013; Portela Araujo 2013; Wong 2013; Lopes 2015). We considered the remainder to provide short-term data. Seven studies reported follow-up data beyond the final day of treatment: Breneman 2000 (3 weeks follow-up after 6 weeks treatment); Canpolat 2012 (7 weeks follow-up after 1 week treatment); Ewing 1998 (8 weeks follow-up after 4 weeks treatment); Fluhr 2009 (4 weeks follow-up after 8 weeks treatment); Francis 2016 (3 months follow-up after 1 week treatment); Korting 1994 (4 weeks follow-up after 5 days treatment); and Schuttelaar 2005 (6 weeks follow-up after 2 weeks treatment). Only 15 studies reported the total study duration, ranging from 15 weeks to 27 months (median: 10 months).

Excluded studies

We excluded 57 studies and their details can be found in the Characteristics of excluded studies tables. Twenty-one were not RCTs, and 19 were excluded as they were not studies of atopic eczema or there were no separate results for atopic eczema. Fourteen studies were not of anti-staphylococcal interventions and 11 were excluded as they only compared anti-staphylococcal agents against each other or against an inappropriate control. Some studies were excluded for more than one reason.

Ongoing studies

One study, to evaluate the efficacy of a combination of topical antibiotic, steroid and moisturiser (supiroban 2% cream and fluocinolone acetonide) compared to steroid alone in children aged two to nine years with severe atopic dermatitis (SCORAD 50 or above), was registered on Clinicaltrials.gov in 2017 (NCT03052348). The investigators planned to assess change in SCORAD from baseline to weeks 4, 8 and 12, frequency of atopic dermatitis relapse episodes, and change in IDQoL index from baseline to weeks 4, 8, and 12. However, at the last update of Clinicaltrials.gov in September 2017, this had not yet begun recruitment.

Studies awaiting classification

Six studies are included in the section of studies awaiting classification. ACTRN12610000438055 is a parallel group RCT of participants aged 18 to 50 years with mild to moderate atopic dermatitis (SCORAD 20-50), colonised with *S. aureus*. The intervention was Recombinant Human ß Defensin 2 cream, which was being compared to placebo cream. The study planned to collect data on safety and tolerability, change in local SCORAD at end of treatment (day 14), change in *S. aureus* colonisation rate at end of treatment, change in the colonisation rate of any bacteria at end of treatment, and symptomatic relief using a Likert scale. Recruitment was reported to be complete in September 2011. The trials authors were emailed, but there was no response.

EudraCT 2006-004233-15 is a within-patient (left/right) RCT of patients aged 6 months to 50 years with eczema affecting the limbs with an ESCORAD (SCORAD of extremities) between 5 and 12 and staphylococcus superinfection. The participants were randomised to triclosan cream versus placebo. The trial evaluated changes in ESCORAD from baseline to day 14, changes in log staphylococcus count and changes in ESCORAD from baseline to day 7, changes in single-ESCORAD of erythema, oedema/papulation, oozing/crusting, excoriation, lichenification and clinical and microbiological response rates for day 7 and 14, evaluation of skin parameters, side effects, tolerance, efficacy, and compliance. Recruitment was reported to be complete in May 2009 and, in July 2019, the EU Clinical Trials Register was updated with the addition of a link to the results in German.

EudraCT 2008-005890-37 is a within-patient RCT of patients aged 18 or older with mild to moderate atopic eczema and two comparable lesional areas of 20-50 cm^2 and TEWL (transepidermal water loss) of at least 12 g/m^2h in lesional areas. The study compared K201 cream [Lactic acid (5%), Propylene glycol (20%), Urea (5%)] and placebo. Outcomes assessed were barrier impairment (TEWL measurements), clinical skin condition (corneometric measurements and clinical assessments) and bacterial colonisation of *S. aureus* over a four-week treatment period. Recruitment was reported to be complete in April 2009 and in February 2019 a synopsis of the results was added to the EU Clinical Trials Register.

NCT03009734 is a parallel group RCT of patients aged 18 to 70 years with localised atopic dermatitis with two separate lesions of 10-200 cm^2 each of which has an IGA (Investigator Global Assessment) of 1-3 and an additional localised lesion of the same size and severity range, total localised disease not > 20% BSA (body surface area) and colonisation with *S. aureus*. The trial was comparing a topical antibiotic, ATx201, with placebo. Outcomes were treatment-related adverse events, IGA score, treatment success (100-fold reduction in *S. aureus* colony count), and local dermal tolerability. Recruitment was reported to be complete in March 2018.

NCT03047954 is a parallel group RCT involving children aged 6 months to 7 years with atopic dermatitis with affected BSA 15-70% and SCORAD 25-70. The trial is comparing Broncho-Vaxom 1 capsule (3.5 mg) per day and placebo. Outcomes were number of atopic dermatitis flares and changes in SCORAD over nine months of treatment, area of eczema involvement and amount of corticosteroids used. Recruitment was reported to be complete in December 2006, although the trial was not registered until February 2017.

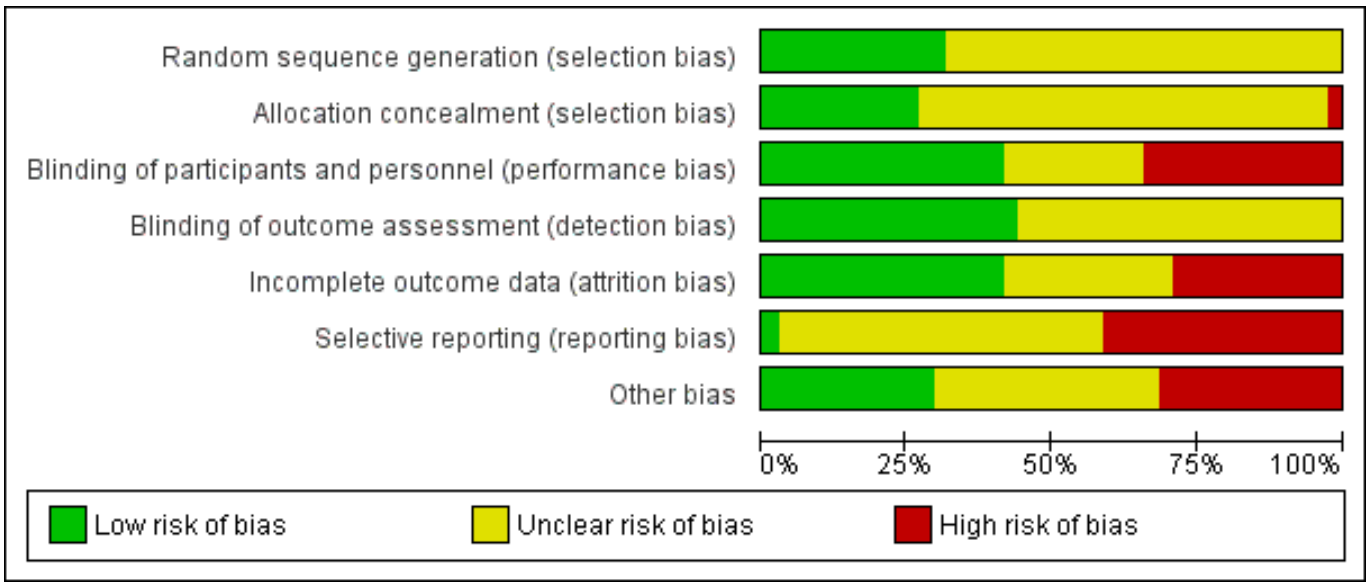
Totté 2017 is a parallel group RCT of adults aged 18 or older with moderate to severe atopic dermatitis (EASI 7.1 to 50). The trial was comparing Staphefekt SA 100 cream (Gladskin) and placebo. The outcomes assessed were corticosteroid use and changes in EASI, POEM, IGA, Pruritus Numerical Rating Scale, Skindex 29, reduction in bacteria and serious adverse events. Recruitment was reported to be complete in February 2018.

Risk of bias in included studies

The overall methodological quality of the studies was variable, and was generally better in more recent studies. 'Risk of bias' assessment for each individual study is reported in the Characteristics of included studies and summarised in Figure 3 and Figure 4. Since no meta-analyses were performed involving more than four studies, sensitivity analysis based on methodological quality was not performed.

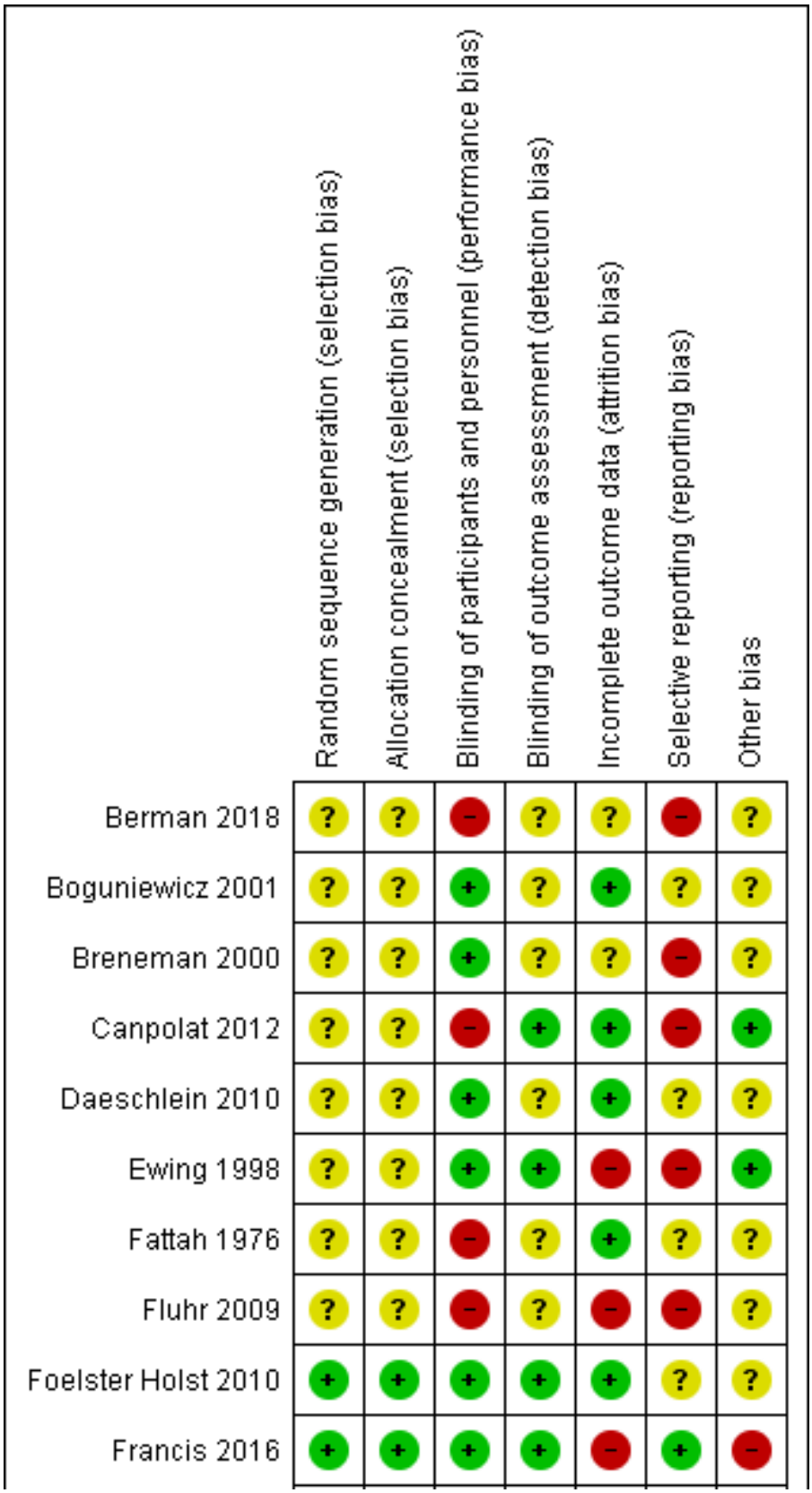
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



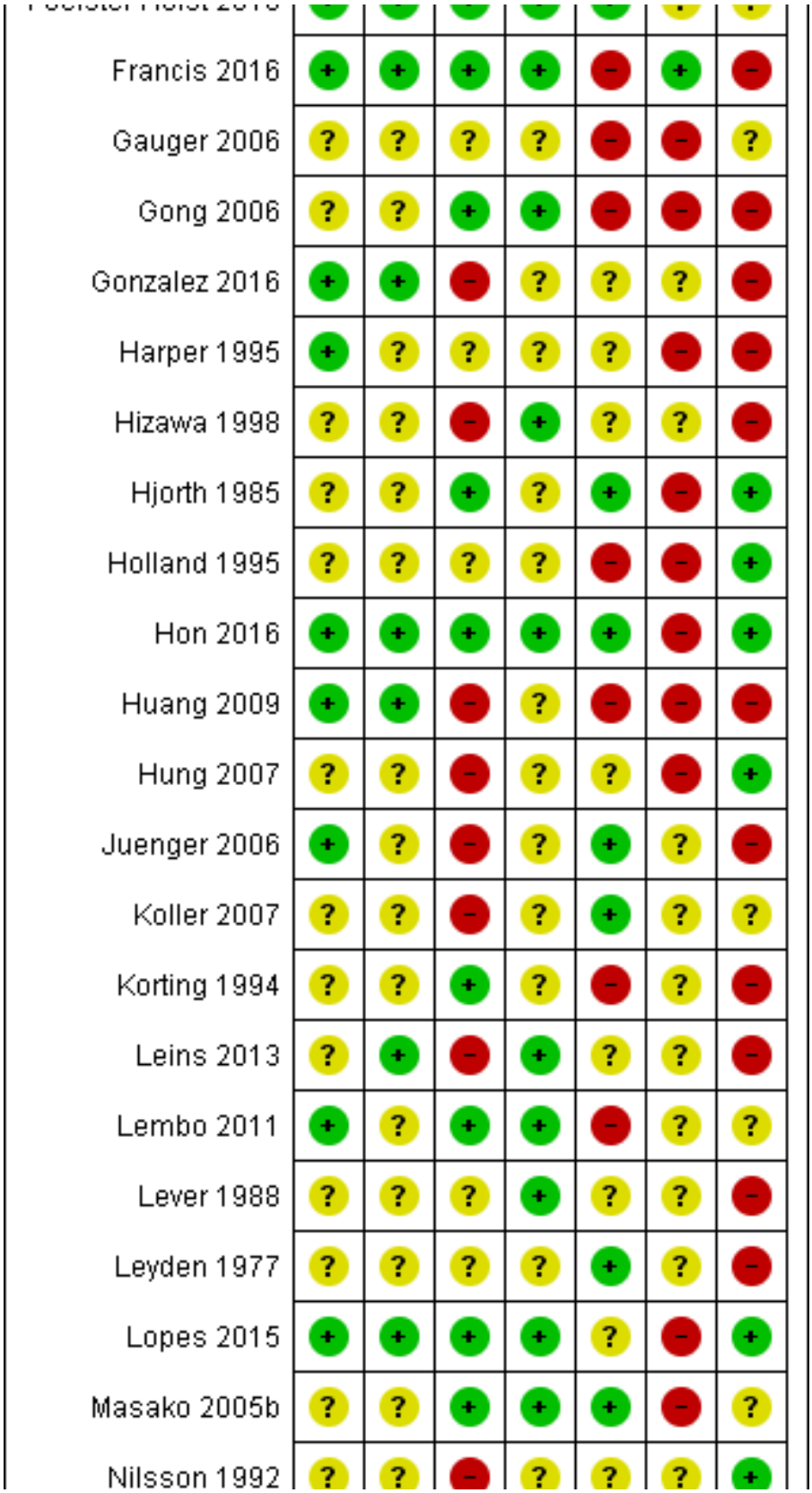
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 4. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



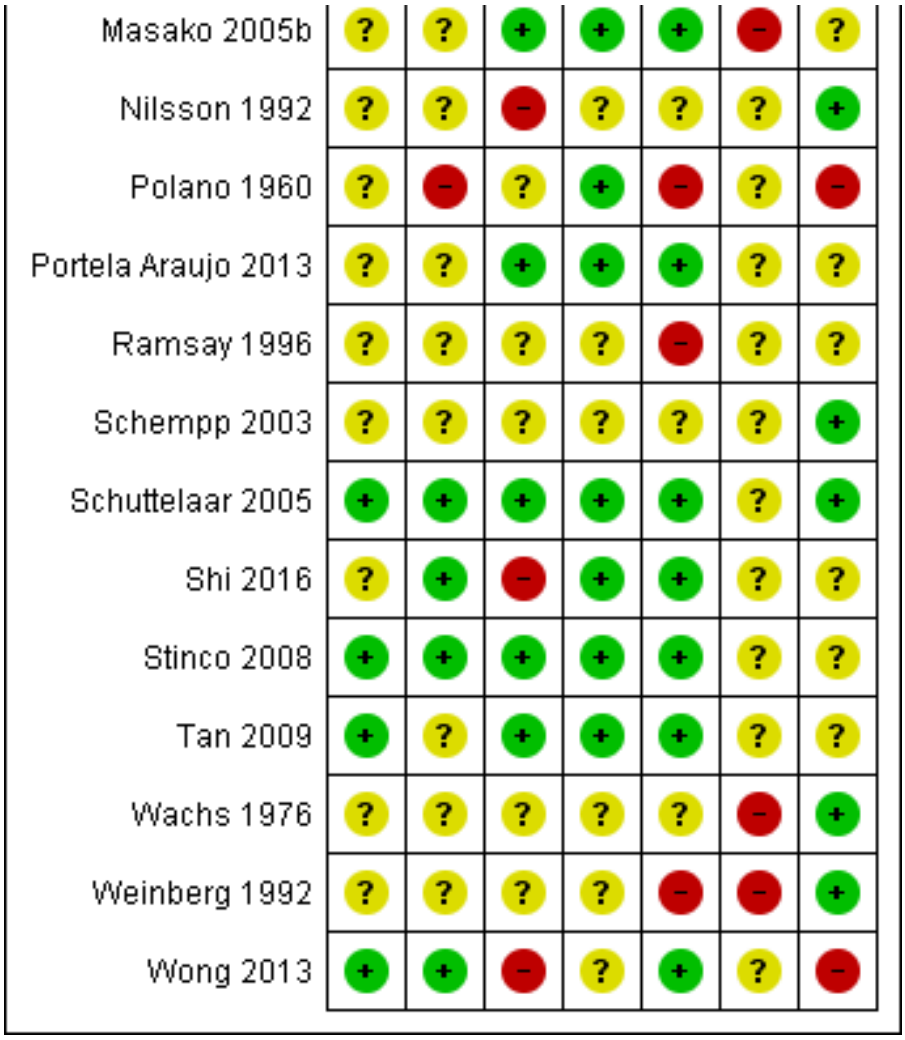
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 4. (Continued)



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Figure 4. (Continued)



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Allocation

The method of random sequence generation was frequently not specified (two-thirds of studies). For the remaining one third of studies (n = 13), random sequence generation was judged to have a low risk of bias.

Eleven of the 41 studies were judged to have a low risk of selection bias from allocation concealment. In one study, risk of bias was assessed as high as one of the investigators had an opportunity to influence the sequence of treatments (Polano 1960). The other 29 studies were considered as having unclear risk of selection bias from allocation concealment.

Blinding

The majority of studies attempted to blind participants and personnel. However, in nine studies, either participants and/or personnel were not blinded and these studies were therefore judged to have a high risk of bias (Nilsson 1992; Hizawa 1998; Juenger 2006; Hung 2007; Koller 2007; Fluhr 2009; Canpolat 2012; Leins 2013; Berman 2018). One study noted that the creams were different colours and was therefore judged to have a high risk of bias (Fattah 1976). Of five studies evaluating bleach baths versus placebo, only one study (Hon 2016) gave an adequate description of how they had attempted to blind participants to the different odours of the bleach and placebo. This study was therefore judged to have a low risk of bias, whereas the other four (Huang 2009; Wong 2013; Gonzalez 2016; Shi 2016) were judged to have a high risk of bias. In addition to Hon 2016, sixteen other studies (Hjorth 1985; Korting 1994; Ewing 1998; Breneman 2000; Boguniewicz 2001; Masako 2005b; Schuttelaar 2005; Gong 2006; Stinco 2008; Tan 2009; Daeschlein 2010; Foelster Holst 2010; Lembo 2011; Portela Araujo 2013; Lopes 2015; Francis 2016) were judged to have a low risk of bias. In the remaining 10 studies, the success of blinding was unclear.

In over half of studies (n = 23), the blinding of outcome assessment was judged to be unclear as the success of blinding of participants could not be guaranteed and the results included patient-reported outcomes. The remaining 18 studies were judged to have a low risk of bias.

Incomplete outcome data

Seventeen studies were judged to have a low risk of bias for incomplete outcome data as either all participants were accounted for in the analysis or numbers of dropouts were low and reasons were similar between the groups. Twelve studies were judged to have a high risk due to very high rates of attrition overall, disproportionately high numbers between the groups, or different reasons for dropouts between the groups (Polano 1960; Weinberg 1992; Korting 1994; Holland 1995; Ramsay 1996; Ewing 1998; Gauger 2006; Gong 2006; Fluhr 2009; Huang 2009; Lembo 2011; Francis 2016). For the remaining 12 studies, the reasons for dropouts or distribution between the groups were unclear.

Selective reporting

Trial registrations were only available for six studies (Huang 2009; Foelster Holst 2010; Leins 2013; Lopes 2015; Francis 2016; Shi 2016). Of these, for only one study (Francis 2016) were all outcomes clearly described in the registration and reported in the paper. This study was therefore judged to have a low risk of bias. For one study (Huang 2009), the primary outcome was changed between the registration and reporting, and for one study (Lopes 2015), a "co-primary outcome" from the registration was reported as a secondary outcome. These two studies were therefore judged to have a high risk of bias. For the other three studies with registrations available, there was insufficient information to make a judgement.

Of the remaining studies, some outcomes described in the methods were frequently either not reported at all (Wachs 1976; Breneman 2000; Masako 2005b; Gauger 2006; Hung 2007; Canpolat 2012), not reported at all stated time points (Wachs 1976; Gauger 2006; Gong 2006; Fluhr 2009; Canpolat 2012), or reported only in terms of statistical significance, precluding pooling (Hjorth 1985; Harper 1995; Holland 1995; Ewing 1998; Masako 2005b; Hon 2016; Berman 2018). All these studies were judged to have a high risk of bias, with the remaining 20 studies judged as unclear.

Other potential sources of bias

Unsurprisingly, given the small sample sizes, substantial imbalance in potentially important baseline characteristics was present in a number of studies. Six studies (Lever 1988; Juenger 2006; Huang 2009; Leins 2013; Francis 2016; Gonzalez 2016) reported baseline imbalance in severity of eczema and three studies (Leyden 1977; Wong 2013; Francis 2016) reported baseline imbalance in presence or colonisation density of *S. aureus*. These were judged to have a high risk of bias. Baseline severity was not reported in 12 studies (Fattah 1976; Leyden 1977; Harper 1995; Ramsay 1996; Breneman 2000; Boguniewicz 2001; Masako 2005b; Daeschlein 2010; Foelster Holst 2010; Shi 2016; Berman 2018) and 17 studies did not report presence of *S. aureus* at baseline (Fattah 1976; Harper 1995; Ramsay 1996; Gauger 2006; Gong 2006; Juenger 2006; Koller 2007; Stinco 2008; Fluhr 2009; Tan 2009; Daeschlein 2010; Foelster Holst 2010; Lembo 2011; Leins 2013; Portela Araujo 2013; Shi 2016; Berman 2018). These were judged to have an unclear risk of bias (unless other potential sources of bias were identified, as described below). The remaining studies, which were well-balanced on both severity and presence of *S. aureus*, were judged to have a low risk of bias (unless other potential sources of bias were identified, as described below).

Gong 2006 performed subgroup analysis at the end of the study which was not part of the predetermined outcomes. Harper 1995 and Hizawa 1998 report statistical comparisons only as significant differences from baseline and not between groups. Korting 1994 changed inclusion criteria after recruitment to exclude participants aged < 18 years. Lever 1988 and Polano 1960 did not include a washout period between treatments in cross-over trials. In addition, Polano 1960 used an unusual (inverse sine) data transformation and it was not clear if this was preplanned. All these studies were therefore graded as having a high risk of bias.

We were unable to assess for publication bias as there were not enough studies to perform a funnel plot. There were two duplicate publications. In both cases, identical results were published in both English and German (Korting 1994 and Schempp 2003).

Effects of interventions

See: **Summary of findings for the main comparison** Topical steroid plus topical antibiotic compared with topical steroid for eczema; **Summary of findings 2** Oral antibiotic compared with placebo for eczema; **Summary of findings 3** Bleach bath compared with placebo or bath emollient for eczema

Please see table of Characteristics of included studies.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Subgroup analysis was not performed due to the limited number of studies available to pool in a meta-analysis.

1. Oral antibiotic - four studies

We included four studies comparing oral antibiotics against placebo; results for this comparison are reported in Summary of findings 2. Boguniewicz 2001 was a cross-over study evaluating cefuroxime axetil among 20 patients (children and adults) with moderate to severe eczema with *S. aureus* isolated from the skin, but excluding overt clinical infection. The duration of the condition was not stated. In this study, participants were randomised to either receiving cefuroxime axetil orally (dose not stated) twice daily or placebo orally twice daily for two weeks, each with one week washout in between. A moderate potency topical steroid was used in all participants.

Ewing 1998 was a parallel group RCT evaluating flucloxacillin in 50 children (46 evaluable) with uninfected eczema. The severity and duration of the condition were not stated. In this study, participants were randomised to receive either flucloxacillin 250 mg four times daily (n = 25) or placebo (n = 25) for four weeks (dose halved for < 10 yrs old). Topical steroids were used as needed.

Francis 2016 was a three-arm parallel group RCT evaluating flucloxacillin and 2% fusidic acid in 113 children (101 evaluable) with clinically infected eczema (70 evaluable children in flucloxacillin and placebo groups included in this category). The severity and duration of the condition was not stated. This study used the following regimens: oral antibiotic (flucloxacillin four times per day for 7 days, 125 mg in 2.5 mL for children aged three months to two years, 250 mg in 5 mL for children aged > two years to < eight years) and topical placebo (n = 36) versus topical antibiotic (2% fusidic acid cream three times per day for seven days) and oral placebo (n = 37) versus oral and topical placebo (n = 40). All treatment groups received topical steroids (clobetasone butyrate 0.05% cream or ointment for use on trunk/limbs and/or hydrocortisone 1% cream or ointment for use on face, applied once daily for 14 days) and were encouraged to use emollients that did not contain antimicrobial agents.

Weinberg 1992 was a parallel group RCT evaluating cefadroxil in 33 children (30 evaluable) with eczema with *S. aureus* isolated from the skin, with 28 of the 30 participants having clinical infection. The severity of the condition was not stated. Patients in the intervention group had eczema for a mean duration of 3.2 years and in the placebo group 2.6 years. Participants were randomised to receive either cefadroxil 50 mg/kg/day in two equal doses (n = 16) or placebo (n = 17) for two weeks. No information was provided on topical steroid use.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by participant or medical practitioner

Two studies (Ewing 1998; Weinberg 1992) reported global degree of improvement in signs and symptoms as rated by the medical practitioner. Ewing 1998 found a significantly lower rate of good or excellent outcomes in the flucloxacillin group compared to placebo, whereas Weinberg 1992 found a non-significant improvement in the cefadroxil group compared to placebo. Pooling these studies gave an estimate of a non-significantly lower rate of good or excellent outcomes with oral antibiotic compared to placebo, with substantial imprecision and statistical heterogeneity (RR 0.80; 95% CI 0.18 to 3.50, I^2 = 92%) (Analysis 1.1). Differences between the studies that may have contributed to the heterogeneity included the use of different antibiotics, although both have activity against *S. aureus*, and also one study recruited only patients with uninfected eczema whereas, in the other study, most patients had clinical infection.

One study (Boguniewicz 2001) reported no change in clinical severity, but provided no data. Francis 2016 did not report any data for this outcome.

(b) Improvement in Quality of Life questionnaires

One study (Francis 2016), comparing flucloxacillin to placebo, reported changes in quality of life using the IDQoL questionnaire for children aged three months to < four years and the CDLQI questionnaire for children aged four years to < eight years. At two weeks, there was no significant difference between the groups in the change from baseline on either IDQoL (MD 0.11; 95% CI -0.10 to 0.32) (Analysis 1.2) or CDLQI (MD 0.43; 95% CI -0.16, 1.02) (Analysis 1.3). The other three studies did not report any data for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

One study (Boguniewicz 2001) reported no adverse events. Ewing 1998 reported one withdrawal in the oral antibiotic group (loose stools) and one withdrawal in the placebo group (Henoch-Schönlein purpura). Francis 2016 reported one withdrawal in each group due to the eczema worsening. Weinberg 1992 reported one withdrawal in the oral antibiotic group due to an adverse event, but the nature of the event was not specified. Pooled analysis of these studies showed no clear differences for adverse events requiring withdrawal (RR 1.43; 95% CI 0.28 to 7.36, I^2 = 0%) (Analysis 1.4).

(b) Minor patient-reported adverse events. These included mild skin irritation not sufficient to require cessation of treatment

One study (Francis 2016) reported minor patient-reported adverse events. There were no clear differences between the groups in any of the adverse events reported (nausea 2/33 versus 3/35, vomiting 4/33 versus 6/35, diarrhoea 5/33 versus 5/35, stomach pain 3/33 versus 2/35, joint pains 1/33 versus 0/35, new rash 4/33 versus 8/35).

(c) Emergence of antibiotic-resistant micro-organisms

See long-term results.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

One study (Francis 2016) reported changes in both the POEM and EASI scores. At two weeks, there was no clear difference between the groups in the change from baseline on either POEM (MD 1.52; 95% CI -1.35 to 4.40) (Analysis 1.5) or EASI (MD 0.20; 95% CI -0.12 to 0.52) (Analysis 1.6).

(b) Changes in the individual signs of eczema as assessed by a physician

Two studies (Weinberg 1992; Ewing 1998) found no significant difference in erythema in the control groups compared to oral antibiotic (MD in erythema scores: 0.40; 95% CI -0.03 to 0.83) (Analysis

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

1.7), (number of people with erythema: RR 0.93; 95% CI 0.38 to 2.28) (Analysis 1.8). The two studies could not be pooled because one used a continuous and the other a dichotomous measure (score). One study (Weinberg 1992) found significantly fewer clinically apparent infections in the treatment group at the end of the study compared to control (RR 0.06; 95% CI 0.00 to 0.94) (Analysis 1.9).

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Two studies (Ewing 1998; Francis 2016) found no significant differences in isolation rates of *S. aureus* for flucloxacillin compared with placebo; one study (Weinberg 1992) found a significantly lower rate of *S. aureus* among participants treated with cefadroxil compared with placebo. The pooled result of all three studies was not significant (RR 0.76; 95% CI 0.46 to 1.26, I^2 = 66%) (Analysis 1.10). A potential source of the heterogeneity in this result was a baseline imbalance in the rate of *S. aureus* colonisation in Francis 2016 resulting in a higher isolation rate of *S. aureus* in the antibiotic group at the end of the study despite a greater reduction from baseline. Francis 2016 reported a change from baseline at two weeks (end of treatment) of -30.4% (95% CI -51.6% to -9.2%) in the flucloxacillin group compared with -15.9% (-39.1% to 7.4%) in the placebo group; the difference between the groups was not statistically significant (mean difference -14.5%; 95% CI -46.0% to 17.0%) (Analysis 1.11). In Ewing 1998, the isolation rates of *S. aureus* from affected skin reduced from 24/24 participants to 15/22 in the flucloxacillin group and from 24/25 to 22/24 in the placebo group, but a change from baseline analysis was not undertaken.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

One study (Ewing 1998) found a non-significant difference in the log *S. aureus* counts/cm^2 in the flucloxacillin group compared to placebo (MD -1.40; 95% CI -3.09 to 0.29) (Analysis 1.12). They reported that the difference between groups in change from baseline among the 18 participants in each group with both baseline and follow-up measurements recorded was statistically significant (P = 0.008), although further details of this analysis were not reported. Another study (Boguniewicz 2001) suggested that addition of an antibiotic resulted in a reduction in colony counts, however, when the antibiotic was discontinued, the skin was quickly recolonised.

Long-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

There were no results given for this outcome in any of the four studies.

(b) Improvement in Quality of Life questionnaires

One study (Francis 2016) continued to follow up participants to three months. There was no significant difference between the groups in the change from baseline on either IDQoL (MD -0.21; 95% CI -0.44 to 0.02) (Analysis 1.13) or CDLQI (MD -0.14; 95% CI -0.97 to 0.69) (Analysis 1.14). The other three studies did not report any data for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation.

There were no results given for this outcome.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

There were no results given for this outcome.

(c) Emergence of antibiotic-resistant micro-organisms

Ewing 1998 reported that the number of methicillin-resistant strains (MRSA) increased in the treatment group up until 14 days after treatment, but did not give numerical results. Any increase in the number of MRSA had returned to almost baseline at day 56. Another study Francis 2016 reported resistance of *S. aureus* to flucloxacillin, erythromycin and fusidic acid at baseline, week two (end of treatment) and three months. Erythromycin was included for participants who were allergic to penicillin, however, no participants received erythromycin. Fusidic acid was included as this was the other active treatment in this three-arm trial. Among participants treated with flucloxacillin with *S. aureus* identified from skin swabs, 1/30, 0/18 and 1/8 strains were resistant to flucloxacillin at baseline, two weeks and three months, respectively. No strains were resistant to flucloxacillin in the placebo group (of 24, 16 and 10 positive skin swabs at each time point). No flucloxacillin-resistant strains were identified from the nose or mouth. Weinberg 1992 reported on resistance to cephadroxil. Of 33 participants, 16 were randomised to receive cephadroxil, but three were withdrawn, in one case due to the presence of a resistant organism at baseline. At the end of the study, none of the participants in either the intervention or placebo group were found to have a resistant organism.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Francis 2016 reported longer term changes in the POEM score. At three months, there was no significant difference between the groups in the change from baseline (MD -0.21; 95% CI -3.12, 2.70) (Analysis 1.15).

(b) Changes in the individual signs of eczema as assessed by a physician

Ewing 1998 reported no significant difference in erythema at 56 days post-treatment with oral flucloxacillin compared to placebo (MD -0.10; 95% CI -0.59, 0.39) (Analysis 1.17).

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Francis 2016 reported a change from baseline in the percentage of participants with *S. aureus* on the skin at three months of -52.6% (95% CI -74.1% to -31.0%) in the flucloxacillin group compared with -20.0% (-45.4% to 5.4%) in the placebo group; the difference between the groups was not statistically significant (mean difference -32.6%; 95% CI -65.9% to 0.7%) (Analysis 1.16).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

In one study (Ewing 1998), bacterial counts returned to almost pre-treatment levels by 14 days after completion of treatment.

2. Topical antiseptic/antibiotic - five studies

Five studies compared topical antiseptics/antibiotics versus placebo. Of these, one study (Lembo 2011) evaluated a topical antibiotic. This was a cross-over study evaluating 1% erythromycin in Vaseline in 38 children (19 evaluable) with uninfected eczema. The severity and duration were not stated. In this study, there was no use of topical or systemic medications during the first week with the intervention beginning from day eight onwards. The intervention was 1% erythromycin (Sigma-Aldrich S.r.l., Milano) in white Vaseline on the whole skin surface twice daily from day 8 to day 21 and Vaseline from day 22 to 35 versus Vaseline from day 8 to 21 on the whole skin surface twice daily and erythromycin from day 22 to 35. Participants did not use topical steroids in this study.

The remaining four studies compared various topical products with antiseptic/antibacterial properties, and no attempt was made to pool them. Berman 2018 was a parallel group RCT evaluating hypochlorous acid compared with no treatment in 30 patients with eczema and itch (infective status not specified). Participants were included if they scored more than 2 on an itch severity scale. The duration of the condition was not stated. In this study, participants were randomised to the application of hypochlorous acid-containing solution twice daily or, as required, for 72 hours versus no treatment. No information was provided on topical steroid use.

Hizawa 1998 was a right-and-left comparison evaluating povidone iodine 10% in 15 children and adults with mild to moderate eczema (without purulent skin infection). The duration of the condition was not stated. Povidone iodine 10% versus an unspecified placebo was applied twice daily for one week. No information was provided on topical steroid use.

Masako 2005b was a right-and-left comparison evaluating 0.2% farnesol + 5% xylitol in 17 patients with mild to moderate eczema (infective status not specified). The duration of the condition was not stated. In this study, participants were randomised to receive either FX cream (0.2% farnesol + 5% xylitol) or a placebo cream (identical in appearance) for seven days. The frequency of application was not stated. No information was provided on topical steroid use.

Schempp 2003 was a right-and-left comparison evaluating hyperforin 1.5% cream in 21 children and adults (18 evaluable) with 'subacute' eczema (infective status not specified) with a SCORAD of < 80. The duration of the condition was not stated. In this study, participants were randomised to receive either hyperforin 1.5% cream or a placebo (identical vehicle with added chromogenic substances to colour the vehicle for the purpose of blinding). These were applied twice daily for four weeks. No participants used concomitant topical steroids.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

None of the studies evaluating a topical antibiotic reported global degree of improvement. Berman 2018 reported that both participant global assessment (PGA) and IGA improved between baseline and 72 hours, in favour of the hypochlorous acid-treated group; however, results were only reported as P values (PGA 0.128, IGA 0.012). Hizawa 1998 reported that there was a statistically significant improvement in the povidone iodine group for appearance of skin lesions; however, no numbers were given and no between-group analysis was done.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome in any of the included studies.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Lembo 2011 reported that none of the participants had any adverse reaction to the 1% erythromycin in Vaseline or placebo.

Berman 2018 reported no treatment-related discontinuations or severe adverse events in either the hypochlorous acid or no treatment-group. Schempp 2003 reported that three participants in the left-and-right comparison of hyperforin 1.5% cream withdrew from treatment due to acute episodes of atopic dermatitis; whether this was present on the actively-treated or placebo-treated side of the body was not specified.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Schempp 2003 reported that one participant developed contact eczema in the placebo group.

(c) Emergence of antibiotic-resistant micro-organisms

There were no results give for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

For the first period of the cross-over study, Lembo 2011 reported a reduction in mean SCORAD from 47.6 (SD 12.0) to 43.2 (11.3) for the 1% erythromycin group compared with a reduction from 45.4 (11.4) to 43.9 (10.6) for the placebo group; this difference was reported to be statistically significant.

Schempp 2003 reported a significant difference in the median reduction in modified SCORAD on the Hyperforin 1.5%-treated side of 6.5 compared to 2.5 on the placebo-treated side.

(b) Changes in the individual signs of eczema as assessed by a physician

Masako 2005b stated that scores of dryness and scaling were significantly improved in both the 0.2% farnesol + 5% xylitol cream and placebo groups, but no data were provided.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Schempp 2003 reported a reduction in colonisation with *S. aureus* from 17/18 to 16/18 on the Hyperforin 1.5%-treated side compared with no change (17/18 to 17/18) on the placebo-treated side.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Hizawa 1998 reported that there was a statistically significant improvement in *S. aureus* colony counts in the povidone iodine group; however, no numbers were given and no between-group analysis was done. Masako 2005b reported that, at end of treatment, there was a significant difference in the number of *S. aureus* in favour of 0.2% farnesol + 5% xylitol cream compared with placebo.

Long-term:

There were no long-term data presented relevant to our outcomes.

3. Topical steroid plus antiseptic/antibiotic - 14 studies

There were 14 studies, with a total of 895 evaluable participants in the relevant arms, comparing topical steroids plus antiseptics/antibiotics versus topical steroids alone. Twelve of these studies compared a topical steroid plus topical antibiotic against topical steroid alone, and results for this comparison are summarised in Summary of findings for the main comparison.

Canpolat 2012 was a parallel group RCT evaluating hydrocortisone plus mupirocin compared with hydrocortisone alone in 53 infants with mild to moderate eczema (infective status not specified). The duration of the condition was not stated. In this study, participants were randomised to hydrocortisone plus mupirocin (n = 27) or hydrocortisone (n = 26) applied twice daily (hydrocortisone in the morning and evening and mupirocin at noon and night) by parents to areas affected with atopic dermatitis at least two hours before bathing for up to seven days.

Francis 2016 was a three-arm parallel group RCT evaluating flucloxacillin and 2% fusidic acid in 113 children (101 evaluable) with clinically infected eczema, in which all children received clobetasone butyrate 0.05% cream or ointment for use on trunk/limbs and/or hydrocortisone 1% cream for use on face (67 evaluable children in fusidic acid and placebo groups included in this category). The duration and severity were not stated. This study used the following regimens: oral antibiotic (flucloxacillin four times per day for seven days, 125 mg in 2.5 mL for children aged three months to two years, 250 mg in 5 mL for children aged > two years to < eight years) and topical placebo (n = 36) versus topical antibiotic (2% fusidic acid cream three times per day for seven days) and oral placebo (n = 37) versus oral and topical placebo (n = 40). All treatment groups received topical steroids (clobetasone butyrate 0.05% cream or ointment for use on trunk/limbs and/or hydrocortisone 1% cream or ointment for use on face, applied once daily for 14 days) and were encouraged to use emollients that did not contain antimicrobial agents.

Gong 2006 was a parallel group RCT evaluating hydrocortisone butyrate plus mupirocin compared with hydrocortisone butyrate plus vehicle ointment in 327 participants (children and adults), of whom 119 had atopic eczema and are included in the review (infective status not specified). The severity and duration of the condition were not stated. In this study, participants were randomised to hydrocortisone butyrate ointment and mupirocin ointment (n = 58) or hydrocortisone butyrate ointment and vehicle ointment (n = 61) applied once daily (with two to three hours between products) for 28 days.

Hjorth 1985 was a right-and-left comparison evaluating 0.1% betamethasone 17-valerate plus 2% microcrystalline fusidic acid compared with 0.1% betamethasone 17-valerate alone in 81 patients (children and adults), of whom 60 had atopic eczema and were included in the review (infective status not specified). The severity and duration of the condition were not stated. Treatments were applied twice daily for seven days.

Hung 2007 was a 2 x 2 factorial RCT comparing fluticasone versus tacrolimus with or without fusidic acid in 60 children and adults (54 evaluable) with moderate to severe uninfected eczema. The duration of the condition was not stated. In this study, the following treatments were compared: 0.05% fluticasone propionate cream (Cutivate) (n = 15) versus 0.05% fluticasone propionate cream with 2% fusidic acid cream (Fucidin) (n = 15) versus 0.03% tacrolimus ointment (Protopic) (n = 15) versus 0.03% tacrolimus ointment with 2% fusidic acid cream (n = 15) applied twice daily for eight weeks. Fusidic acid cream was applied first followed by fluticasone or tacrolimus 20 minutes later without occlusive dressings. Oral antihistamine was given to all participants. Twenty-eight evaluable participants in the fluticasone plus fusidic acid versus fluticasone alone comparison were included in this category.

Lever 1988 was a cross-over study evaluating 0.05% clobetasol butyrate ointment plus either 2% mupirocin or placebo in 49 children and adults (45 evaluable) with eczema (infective status not specified). The duration and severity of the condition were not stated. In this study, 2% mupirocin ointment followed by placebo (polyethylene glycol ointment) or vice versa were applied once daily for two weeks. All participants received 0.05% clobetasol butyrate ointment twice daily during the two-week pre-trial period and once daily while using mupirocin/placebo.

Leyden 1977 was a parallel group RCT evaluating fluocinolone acetonide plus 0.5% neomycin sulphate compared with fluocinolone acetonide cream in 36 patients (mainly children) with 'rather severe' eczema (infective status not specified). The duration of the condition was not stated. In this study, participants were randomised to fluocinolone acetonide plus 0.5% neomycin sulphate (Neo-Synalar) cream (n = 15) versus fluocinolone acetonide (Synalar) cream (n = 21) applied twice daily for one week.

Nilsson 1992 was a parallel group RCT evaluating the betamethasone plus neomycin cream compared with clobetasol in 30 children and adults (28 evaluable) with moderate to severe uninfected eczema. The duration of the condition was not stated. In this study, participants were randomised to betamethasone plus neomycin cream applied to all affected areas except the face twice daily for one week then once daily for one week (n = 15 evaluable) or clobetasol cream applied twice daily on days 1, 2, 3, 4, 8, 9, 12 and 14 (n = 13 evaluable).

Polano 1960 was a four-arm, four-period cross-over study evaluating 0.5% prednisolone plus 0.5% neomycin versus 0.5% prednisolone versus 1% hydrocortisone versus petrolatum base in 24 patients (14 evaluable) with uninfected eczema (the 0.5% prednisolone plus 0.5% neomycin versus 0.5% prednisolone being eligible for the review). The severity of the condition was not stated. Duration was described as “longstanding.” Treatments were applied for one week, or until the ointment was used up. The frequency of application was not stated.

Ramsay 1996 was a parallel group RCT in 186 patients (174 evaluable) with mild to moderate eczema (infective status not specified). The duration of the condition was not stated. In the trial, participants were randomised to fusidic acid 2% plus 1% hydrocortisone

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

cream (n = 91 evaluable) or 1% hydrocortisone cream (n = 83 evaluable) for two weeks. The frequency of application was not stated.

Schuttelaar 2005 was a parallel group RCT in 44 adults with moderate to severe uninfected eczema (SCORAD 25 or more). The duration of the condition was not stated. The study evaluated 0.1% triamcinolone acetonide in oculentum simplex FNA (an ointment base containing cetostearylalcohol, lanolin, vaseline and paraffin) plus 3% tetracycline (n = 22) compared with 0.1% triamcinolone acetonide in oculentum simplex FNA alone (n = 22). The treatments were applied all over the body twice daily for two weeks.

Wachs 1976 was a parallel group RCT in 83 patients (79 evaluable) with moderate to severe clinically infected eczema. The duration of the condition was not stated. The trial randomised participants to betamethasone valerate (Betnovate) plus gentamicin cream (n = 25 evaluable) versus betamethasone valerate cream (n = 27 evaluable) versus gentamicin cream (n = 27 evaluable). Treatments were applied three times daily for 22 days. Only the 52 evaluable participants in the betamethasone valerate plus gentamicin versus betamethasone valerate cream comparison were eligible for the review.

The remaining two studies evaluated antiseptics.

Korting 1994, was a parallel group RCT. The severity and duration of the condition were not stated. The study evaluated prednicarbate 0.25% cream plus the antiseptic didecyldimethylammonium chloride 0.25% compared with prednicarbate 0.25% cream, in 143 adults (117 evaluable) with eczema with heavy *S. aureus* colonisation. The prednicarbate 0.25% cream plus didecyldimethylammonium chloride 0.25% or prednicarbate 0.25% cream were applied twice daily for five days.

Tan 2009 was a parallel group RCT evaluating 0.0025% betamethasone valerate cream plus either 1% triclosan or vehicle alone in 60 patients (children and adults) with mild to moderate eczema (infective status not specified). The median duration of the condition of patients in the intervention group was 12 years and in the control group, 9 years. Participants were randomised to an emollient containing 1% triclosan (n = 30) or the vehicle alone (n = 30) applied twice daily to the whole body for 27 days. Following a washout period of one week, all participants were provided with 0.0025% betamethasone valerate cream for the first 27 days and asked to apply a thin layer of the corticosteroid cream over the eczematous areas for the first 27 days followed by either study cream or vehicle on the whole body. Following this, participants who still had persistent eczema were allowed to continue use of the steroid, if necessary. Participants were provided with emulsifying ointment as cleansers and instructed not to use any systemics or topical antibiotics, antibacterial soap or antibacterial shampoo.

The different studies used a number of different corticosteroid potencies and the majority added an antibiotic to a corticosteroid and compared it to the same corticosteroid. However, Nilsson 1992 evaluated a potent steroid (betamethasone) combined with an antibiotic and compared it against a super-potent steroid (clobetasol). Only two studies (Korting 1994; Tan 2009) evaluated an antiseptic; we did not pool these with studies of antibiotics. Two studies (Polano 1960; Hjorth 1985) gave no data for the outcomes of interest.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

Five studies of antibiotic/steroid combination compared to steroid alone (Wachs 1976; Leyden 1977; Nilsson 1992; Gong 2006; Canpolat 2012) reported global degree of improvement, but results from only three studies could be pooled. The other seven studies did not report global degree of improvement. Three studies (Wachs 1976; Gong 2006; Canpolat 2012) reported non-significantly greater improvements in global outcomes at the end of treatment for steroid plus antibiotic versus steroid alone. When these three studies were pooled (one in clinically infected eczema and two unspecified), the combination treatment showed a borderline improvement compared to steroid alone (RR 1.10; 95% CI 1.00 to 1.21, I^2 = 0%) (Analysis 2.1). Leyden 1977 reported a good or excellent response among 90% of those in the combination group compared with 70% in the steroid-only group, but denominators were not reported and correspondence with the author confirmed that these figures were likely to have been rounded to the nearest 10%, making it impossible to extract the raw values for pooling. Nilsson 1992 found a significant improvement in global outcome in favour of steroid only using a subjective interval scale self-evaluation (MD 1.20; 95% CI 0.25 to 2.15) (Analysis 2.2).

Korting 1994 reported a non-significantly greater improvement in global outcomes at the end of treatment for steroid plus antiseptic versus steroid alone; no numerical results were reported. Tan 2009 did not report global degree of improvement.

(b) Improvement in Quality of Life questionnaires

Francis 2016 reported changes in quality of life using the IDQoL questionnaire for children aged three months to < four years and the CDLQI questionnaire for children aged four years to < eight years. At two weeks, there was no significant difference between the groups in the change from baseline on IDQoL (MD 0.18; 95% CI -0.04 to 0.40) (Analysis 2.3) but significantly less improvement of symptoms in the combined treatment group for CDLQI (MD 0.70; 95% CI 0.12 to 1.28) (Analysis 2.4). None of the other studies reported any data for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Francis 2016 reported five withdrawals in the fusidic acid group (four condition worsened, one intolerant to medication) and one in the placebo group (condition worsened). There were no adverse events requiring withdrawal of treatment in either of the two eligible treatment combinations in Hung 2007. Ramsay 1996 reported one adverse event requiring withdrawal from treatment in the steroid plus antibiotic group ("flare of dermatitis" - no further information provided) and three in the steroid-alone group (two "flare of dermatitis", one burning and soreness). Schuttelaar 2005 reported one adverse event requiring withdrawal from treatment in each group (both folliculitis). Pooled results from these studies showed no clear difference between groups (RR 1.24; 95% CI 0.21 to 7.25, I^2 = 42%) (Analysis 2.5). In addition, Lever 1988 reported that one participant in the cross-over trial reacted adversely to both 2% mupirocin and placebo and stopped treatment.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Tan 2009 reported no withdrawals due to adverse events in either the 1% triclosan or placebo group.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Ramsay 1996 reported two adverse events not requiring cessation of treatment in the steroid plus antibiotic group (one itching, one flare of dermatitis) and three in the steroid-alone group (one stinging and irritation, one folliculitis, one flare of dermatitis). Schuttelaar 2005 reported three minor adverse events in the steroid plus antibiotic group and 13 in the steroid alone group (all folliculitis). Pooled results from these two studies showed significantly fewer minor adverse events not requiring withdrawal from treatment in the combination treatment group compared to the steroid-alone control, (RR 0.30; 95% CI 0.12 to 0.78, I^2 = 0%) (Analysis 2.6). In addition, Francis 2016 reported individual minor patient-reported adverse events; there were no significant differences between the groups in any of the adverse events reported (nausea 1/29 versus 3/35, vomiting 2/29 versus 6/35, diarrhoea 5/29 versus 5/35, stomach pain 3/29 versus 2/35, joint pains 2/29 versus 0/35, new rash 5/29 versus 8/35). This study could not have been included in the pooled result as some participants experienced multiple different events. Lever 1988 reported that, in addition to the one participant that withdrew, one other participant reported stinging and an exacerbation of symptoms with both 2% mupirocin and placebo.

Tan 2009 reported a total of 27 adverse events among 15 participants (not split by group), of which four (three stinging pain after application in the 1% triclosan group, one pruritus after application in the placebo group) were considered treatment-related.

(c) Emergence of antibiotic-resistant micro-organisms

See long-term outcomes.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Francis 2016 reported changes in both the POEM and EASI scores. At two weeks, there was no significant difference between the groups in the change from baseline on POEM (MD 1.49; 95% CI -1.55 to 4.53) (Analysis 2.8). The reduction in EASI in the fusidic acid group was slightly less than that in the placebo group (MD 0.42; 95% CI 0.09 to 0.75) (Analysis 2.7). Gong 2006 reported that both hydrocortisone and mupirocin and hydrocortisone alone showed significant within-group improvement in EASI scores, however, at the end of treatment there was no significant difference. Hung 2007 reported a reduction in mean SCORAD from 50.1 (SD 12.8) to 24.7 (16.5) in the fluticasone plus fusidic acid group compared with 54.8 (16.5) to 25.4 (15.9) with fluticasone alone (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/). Schuttelaar 2005 reported no significant difference in objective SCORAD at the end of treatment between 3% tetracycline plus 0.1% triamcinolone and 0.1% triamcinolone. Pooling results of these four studies for the mean composite rating (using EASI , SCORAD or objective SCORAD) at the end of treatment using the standardised mean difference showed no difference between the groups (SMD -0.00; 95% CI -0.33 to 0.33, I^2 = 38%) (Analysis 2.9). Canpolat 2012 reported no significant difference in SCORAD at the end of treatment but a significant difference in EASI for hydrocortisone and mupirocin compared with hydrocortisone alone; however standard deviations were not reported precluding inclusion in the pooled analysis.

Tan 2009 reported a greater reduction from baseline in mean SCORAD at day 14 for the 1% triclosan group compared with the placebo group (-8.86 versus -4.75; MD -4.11; 95% CI -8.58 to 0.32), but this became non-significant at later time points.

(b) Changes in the individual signs of eczema as assessed by a physician

Wachs 1976 reported a reduction in mean inflammation score (out of 10) from 5.8 to 0.7 (standard deviations not reported) in the betamethasone valerate plus gentamicin group compared with 5.9 to 1.4 in the betamethasone valerate-only group; other individual signs were evaluated but not reported.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Pooled analysis of seven studies (Wachs 1976; Leyden 1977; Lever 1988; Nilsson 1992; Schuttelaar 2005; Hung 2007; Francis 2016) showed a 52% reduction in the isolation rate of *S. aureus* in the combination group compared to steroid-alone at the end of treatment (RR 0.48; 95% CI 0.27, 0.85, I^2 = 47%) (Analysis 2.10). Francis 2016 reported a change from baseline at two weeks (end of treatment) of -31.2% (95% CI -54.8% to -9.2%) in the fusidic acid group compared with -15.9% (-39.1% to 7.4%) in the placebo group; the difference between the groups was not statistically significant (mean difference -15.3%; 95% CI -48.4% to 17.8%) (Analysis 2.11). Nilsson 1992 reported that isolation rates of *S. aureus* reduced from 14/15 in the combination group and 12/13 in the steroid group to zero in both groups. Gong 2006 reported that the rate of *S. aureus* in the entire trial cohort decreased from 59.7% at baseline to 14.8% at day seven of treatment; however, results were not split by treatment group, other than a statement that there was no significant difference between intervention and control groups, or reported for later time points.

Korting 1994 reported that the number of participants with *S. aureus* at an initially lesional site reduced from 47 to 5 in the prednicarbate 0.25% cream plus didecyldimethylammonium chloride 0.25% group and from 54 to 7 in the steroid-only group; denominators were not reported.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

In one study of 30 participants (Nilsson 1992), both steroid plus antibiotic and steroid alone completely cleared *S. aureus* (presented as log counts). Hung 2007 reported a greater decrease in colony counts of *S. aureus* for participants treated with fusidic acid, but results for the individual treatment combinations were not reported. Leyden 1977 reported that the geometric mean counts/cm^2 decreased from 420,000 to 350 for steroid plus antibiotic and from 200,000 to 65,000 for steroid alone.

Korting 1994 reported that the mean colony forming units/cm^2 decreased from 50 (SD 130) to 34 (SD 170) in the prednicarbate 0.25% cream plus didecyldimethylammonium chloride 0.25% group and from 89 (200) to 7.1 (22) in the steroid-only group.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Long-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

There were no results given for this outcome in any of the 14 studies.

(b) Improvement in Quality of Life questionnaires

One study (Francis 2016) continued to follow up participants to three months. There was no significant difference between the groups in the change from baseline on either IDQoL (MD -0.07; 95% CI -0.31 to 0.17) (Analysis 2.12) or CDLQI (MD -0.13; 95% CI -0.96 to 0.70) (Analysis 2.13). None of the other studies reported any data for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

There were no results given for this outcome.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

There were no results given for this outcome.

(c) Emergence of antibiotic-resistant micro-organisms

Francis 2016 reported resistance of *S. aureus* to flucloxacillin, erythromycin and fusidic acid at baseline, week two (end of treatment) and three months. Among participants treated with fusidic acid with *S. aureus* identified from skin swabs, 8/24, 8/11 and 2/8 strains were resistant to fusidic acid at baseline, two weeks and three months, respectively, compared with 6/24, 5/16 and 2/10 in the placebo group. Hung 2007 reported that, of five participants with persistent *S. aureus* colonisation, two (40%) developed fusidic-acid resistant strains after eight weeks of fusidic acid treatment. Results were not broken down into the fluticasone plus fusidic acid and tacrolimus plus fusidic acid groups and no comparative figures were reported for the fluticasone alone or tacrolimus alone groups. Lever 1988 included 45 participants in a cross-over trial of mupirocin versus placebo. *S. aureus* resistant to mupirocin was isolated in one participant four weeks after stopping mupirocin. Lever 1988 reported no cases of MRSA.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Francis 2016 reported longer term changes in the POEM score. At three months, there was no significant difference between the groups in the change from baseline (MD -1.13; 95% CI -4.32 to 2.06) (Analysis 2.14).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Francis 2016 reported a change from baseline in the percentage of participants with *S. aureus* on the skin at three months of -28.6% (95% CI -55.3% to -1.9%) in the flucloxacillin group compared with -20.0% (-45.4% to 5.4%) in the placebo group; the difference between the groups was not statistically significant (mean difference -8.6%; 95% CI -45.4% to 28.2%) (Analysis 2.15).

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

There were no results given for this outcome.

4. Topical steroid plus antibiotic and antifungal - one study

One study (Fattah 1976) compared 0.1% halcinonide with neomycin plus nystatin versus 1% hydrocortisone cream in a right-and-left comparison of eight people with uninfected steroid-responsive dermatoses, of whom four had atopic eczema and were included in the review. The severity of the eczema was not stated. The mean duration of the condition for all participants in the trial was reported to be 14 weeks, but no breakdown of figures was given for those with atopic eczema. In the trial, participants were randomised to 0.1% halcinonide cream with 0.25% neomycin and 100000u/g nystatin versus 1% hydrocortisone both applied three times daily for not more than three weeks.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

The study showed no significant difference in global outcome; out of a total of four participants, three achieved a good or excellent response with the combination treatment and two with hydrocortisone alone.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome.

No results were reported for any of the other outcomes of interest.

Long-term:

There were no long-term data presented relevant to our outcomes.

5. Topical calcineurin inhibitor plus antibiotic - one study

One study (Hung 2007) evaluated a topical calcineurin inhibitor plus antibiotic. This was a 2 x 2 factorial RCT comparing fluticasone versus tacrolimus with or without fusidic acid in 60 children and adults (54 evaluable) with moderate to severe uninfected eczema. The duration of the condition was not stated. In this study, the following treatments were compared: 0.05% fluticasone propionate cream (Cutivate) (n = 15) versus 0.05% fluticasone propionate cream with 2% fusidic acid cream (Fucidin) (n = 15) versus 0.03% tacrolimus ointment (Protopic) (n = 15) versus 0.03% tacrolimus ointment with 2% fusidic acid cream (n = 15) applied twice daily for eight weeks. Fusidic acid cream was applied first followed by fluticasone or tacrolimus 20 minutes later without occlusive dressings. Oral antihistamine was given to all participants. Twenty-six evaluable participants in the tacrolimus plus fusidic acid versus tacrolimus-alone comparison were included in this category.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

There were no results given for this outcome.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Hung 2007 reported that two participants receiving tacrolimus plus fusidic acid withdrew because of intolerance to a burning sensation (RR 5.00; 95% CI 0.26 to 96.13) (Analysis 3.1).

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

There were no results given for this outcome.

(c) Emergence of antibiotic-resistant micro-organisms

Hung 2007 reported that, of five participants with persistent *S. aureus* colonisation, two (40%) developed fusidic acid-resistant strains after eight weeks of fusidic acid treatment. Results were not broken down into the fluticasone plus fusidic acid and tacrolimus plus fusidic acid groups and no comparative figures were reported for the fluticasone-alone or tacrolimus-alone groups.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Hung 2007 reported a reduction in mean SCORAD from 60.0 (SD 15.8) to 31.5 (SD 17.6) in the tacrolimus plus fusidic acid group compared with 56.8 (SD 14.0) to 32.9 (SD 19.4) with tacrolimus alone (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/). The difference in mean SCORAD at the end of treatment was not significant (MD -1.4; 95% CI -15.6 to 12.8) (Analysis 3.2).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Hung 2007 reported that the number of participants with *S. aureus* isolated reduced from 12/13 to 2/13 in the tacrolimus plus fusidic acid group compared with a reduction from 12/13 to 7/13 with tacrolimus alone. The difference at the end of treatment was not significant (RR 0.29; 95% CI 0.07 to 1.13) (Analysis 3.3).

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Hung 2007 reported a greater decrease in colony counts of *S. aureus* for participants treated with fusidic acid, but results for the individual treatment combinations were not reported.

Long-term:

There were no long-term data presented relevant to our outcomes.

6. Antibacterial soap - one study

One very poor quality study (Breneman 2000) compared daily washing with a bar of 1.5% triclocarban soap versus placebo in 50 adults with moderately severe eczema (infective status and the number in each group were not specified) and provided few data to substantiate claims of efficacy. The duration of the condition was not stated. During the trial, participants were required to wash the whole body at least daily for 42 days. Topical steroids were used as needed.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

Global degree of improvement was presented as a mean score on a scale from -5 (severe worsening) to 5 (total clearing) with 0 representing no change from baseline. At the end of treatment, the mean global improvement score was 2.7 in the 1.5% triclocarban soap group compared with 2.2 in the placebo group (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/); standard deviations or CIs were not reported.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

One participant from the 1.5% triclocarban soap group withdrew because of worsening dermatitis.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Other than the one withdrawal, there were no study-related adverse events.

(c) Emergence of antibiotic-resistant micro-organisms

There were no results given for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

There were no results given for this outcome.

(b) Changes in the individual signs of eczema as assessed by a physician

Significant improvements were reported in individual signs, but no numerical values were given.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

There were no results given for this outcome.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(e) Change in bacterial counts of *S. aureus*, i.e. an assessment of quantity of *S. aureus*

Among the 50% of participants with *S. aureus* at baseline, the mean $\log_{10}$ colony forming units reduced from 2.0 to 0.5 in the 1.5% triclocarban soap group and from 2.6 to 1.1 in the placebo group (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/).

Long-term:

There were no long-term data presented relevant to our outcomes.

7. Antibacterial bath additive - seven studies

Two studies compared a mineral oil-based bath emollient incorporating triclosan and benzalkonium chloride (Oilatum Plus) versus the same emollient without the triclosan and benzalkonium chloride (Oilatum) (Harper 1995; Holland 1995). Harper 1995 was a cross-over study of 30 children (26 evaluable) with eczema with recurrent infection and/or frequent exacerbations. The severity of the condition was not stated. The duration of the condition was not stated but, in 19 participants, onset of eczema occurred before one year. In this study, participants were randomised to Oilatum Plus or Oilatum (15 mL in an 8-inch bath of water, soaking for 10 to 15 minutes daily for four weeks). Topical steroids were used as needed.

Holland 1995 was a parallel group RCT of 15 patients (children and adults) with moderate to severe eczema with *S. aureus* isolated from the skin. The duration of the condition was not stated. Participants were randomised to either Oilatum Plus (containing triclosan and benzalkonium chloride) (n = 7) or Oilatum (n = 8) (15 mL in eight inches of water from 10 to 15 minutes, soaking daily for four weeks). Information was not provided on topical steroid use.

Results for the first period of the cross-over study (Harper 1995) were not given which precluded the pooling of results.

Five studies compared sodium hypochlorite (bleach) baths versus placebo (water) (Wong 2013; Gonzalez 2016; Hon 2016; Shi 2016) or bath emollient (Leins 2013), and results for this comparison are summarised in Summary of findings 3.

Gonzalez 2016 was a parallel group RCT of 21 children (18 evaluable) with moderate to severe uninfected eczema. Duration of the condition was not stated. Participants were randomised to receiving either bleach baths (bottle of bleach diluted with bath water 2 times per week to achieve a 0.005% sodium hypochlorite concentration) plus topical corticosteroid (n = 10) or placebo (bottle of water) plus topical corticosteroid (n = 11) for four weeks.

Hon 2016 was a cross-over study of 40 children with moderate to severe eczema (as assessed by SCORAD) with previous *S. aureus* colonisation. The duration of the condition was not stated. Participants were randomised to bleach bath (0.005% sodium hypochlorite) or placebo (water). Participants were instructed to bathe for 10 minutes two to three times per week. There was a four-week treatment period, followed by a four-week washout then a four-week cross-over treatment period. Topical steroids were used as rescue medication only.

Leins 2013 was a parallel group RCT of 19 children with moderate to severe eczema with SCORAD > 25 (infective status not specified). The duration of the condition was not stated. In this study, patients were randomised to bleach bath (sodium hypochlorite 0.005%) three times per week or bath emollient (bath oil containing liquid paraffin 95% volume per volume). All participants received a course of oral antibiotics. Information on topical steroid use was not provided.

Shi 2016 was a right-and-left comparison of 10 patients (children and adults) with eczema (infective status not specified). The severity and duration of the condition were not specified. Participants were randomised to a bleach bath (sodium hypochlorite 0.005%) or placebo (tap water). Each arm was immersed for 10 minutes.

Wong 2013 was a parallel group RCT of 42 children and adults (36 evaluable) with moderate to severe uninfected eczema. The duration of the condition was not stated. Participants were randomised to bleach baths (100 mL of sodium hypochlorite (bleach) in 100 L (or roughly half a tub) of water, sodium hypochlorite 0.005%) (n = 21) or placebo (100 mL of distilled water in 100 L of water) (n = 21). For children under twelve years old, 50 mL bleach was added to a quarter tub of water. Participants were instructed to soak from the neck down in the diluted baths for 10 minutes twice a week for two months, rinsing off with normal tap water after each bath. They were maintained on a stable regimen of topical anti-inflammatory and emollient therapy and used aqueous cream as a soap substitute.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

One study of Oilatum Plus (Harper 1995) suggested, in the text, that there was no statistically significant difference between the treatment groups. The results given are difficult to interpret since baseline data were absent and no firm numbers were given for the individual participant groups. The other study did not report any data for this outcome (Holland 1995).

For bleach baths, two studies reported improvements in both groups but with no significant difference between the groups. In Wong 2013, seven of 18 participants reported being "better" or "much better" in the bleach bath group at one month compared with nine of 18 in the placebo group (RR 0.78; 95% CI 0.37 to 1.63) (Analysis 4.1). Gonzalez 2016 reported results as the mean IGA score at four weeks (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/), with a mean of 0.54 in the bleach bath group compared with 1.08 in the placebo group (MD -0.54; 95% CI -1.79 to 0.71) (Analysis 4.2). The other two studies did not report any data for this outcome.

(b) Improvement in Quality of Life questionnaires

No results on quality of life were reported for the studies of Oilatum Plus. Hon 2016 reported a reduction from baseline (improvement) in the CDLQI of 0.53 following the bleach bath period compared with 1.43 following the placebo period (MD 0.90; 95% CI -1.32 to 3.12) (Analysis 4.3). The other three studies of bleach baths did not report any data for this outcome.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Harper 1995 reported that one participant withdrew from the study due to severe pruritus while receiving Oilatum Plus and one participant withdrew due to a deterioration in eczema severity while receiving Oilatum.

Among the bleach bath studies, Leins 2013 reported no adverse events. Wong 2013 reported that one participant withdrew from the placebo group due to worsening itch; there were no withdrawals due to adverse events in the bleach bath group (RR 0.33; 95% CI 0.01 to 7.74) (Analysis 4.4). Hon 2016 reported that one participant withdrew from treatment during the bleach bath period due to itch and one participant withdrew from treatment during the placebo period due to dryness; however, results were not presented for the first period of the cross-over, so these could not be included in pooled analysis. Shi 2016 reported no adverse events severe enough to require withdrawal of treatment in the left-and-right comparison.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Harper 1995 reported that three participants experienced adverse events (all pruritus) while receiving Oilatum Plus (it was unclear whether this included the one participant that withdrew due to pruritus) and five participants experienced adverse events (four pruritus, one unspecified) while receiving Oilatum (including one participant that experienced pruritus with both preparations).

Among the bleach bath studies, Leins 2013 reported no adverse events. Wong 2013 reported that five participants in each group experienced burning/stinging or dry skin (RR 1.00; 95% CI 0.35 to 2.87) (Analysis 4.5). Hon 2016 reported that seven participants experienced one or more minor adverse events during the bleach bath period (two stinging, three itch, two dry skin, one erythema, one urticaria, one oozing) and 12 participants experienced one or more minor adverse events during the placebo period (four stinging, five itch, one erythema, one urticaria, one dizziness), but these were not reported by period of the cross-over. Shi 2016 reported no adverse events.

(c) Emergence of antibiotic-resistant micro-organisms

Hon 2016 reported no significant difference in antibiotic resistance patterns between the bleach bath and placebo periods; numerical results were not presented.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Both studies of Oilatum Plus used non-standard rating scales. For the bleach bath studies, Wong 2013 reported a significant within-group reduction from baseline in mean EASI score at one month in the bleach bath group but no significant difference between the groups. On correspondence, the numerical values (presented graphically in the paper) were confirmed as a reduction from 29.5 (SD 10.3) to 20.2 (SD 11.8) in the bleach bath group and from 34.3 (SD 14.3) to 25.4 (SD 13.1) in the placebo group. Gonzalez 2016 reported that both EASI and local EASI improved significantly in both groups but there was no difference between the groups, with a mean of 1.38 in the bleach bath group at one month compared with 2.34 in the placebo group (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/). Pooling the results from these two studies confirmed a non-significantly lower EASI score at one month in the bleach bath group compared with the placebo group (MD -2.48; 95% CI -7.36 to 2.40) (Analysis 4.6). Hon 2016 reported a mean change from baseline in objective SCORAD of -0.50 (SD 10.63) during the bleach bath period compared with -3.95 (SD 10.54) during the placebo period; the difference between the groups was not statistically significant (MD 3.45; 95% CI -1.66 to 8.56) (Analysis 4.7).

(b) Changes in the individual signs of eczema as assessed by a physician

Wong 2013 reported that "scores for erythema, papulation, lichenification and excoriation showed a significant improvement" but numerical results were not presented. Shi 2016 reported "no increased erythema or signs of irritation".

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Hon 2016 reported a change in isolation rate of *S. aureus* from 36/40 at baseline to 27/40 during the bleach bath period and 31/40 during the placebo period. This difference was not statistically significant; a treatment effect from a paired analysis was not reported.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Holland 1995 reported a significant within-group reduction in median $\log_{10}$ colony forming units/cm^2 from 4.3 (IQR (interquartile range) 4.2 to 6.8) at baseline to 3.8 (IQR 0.8 to 5.1) at the end of treatment for the Oilatum Plus group and no significant change (from 4.7 (IQR 2.8 to 5.5) to 4.3 (IQR 4.0 to 5.6)) in the Oilatum group; there was no statistically significant difference between the groups.

For bleach baths, Wong 2013 reported a change in mean colony forming units/cm^2 from 16.8 (SD 15.7) at baseline to 9.7 (SD 12.4) at one month in the bleach bath group compared with a change from 7.5 (SD 13.6) to 10.4 (SD 13.6) in the placebo group (MD at one month -0.70; 95% CI -9.20 to 7.80) (Analysis 4.8). Hon 2016 also reported no significant difference in colony counts, but numerical results were not presented. Gonzalez 2016 reported that *S. aureus* counts reduced in both groups in both lesional and non-lesional skin; however, results were reported by sample and not by participant.

Long-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

In Wong 2013, 11 of 18 participants reported being "better" or "much better" in the bleach bath group at two months compared with nine of 18 in the placebo group (RR 0.78; 95% CI 0.37 to 1.63) (Analysis 4.9). None of the other studies reported any long-term results.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome in any of the seven studies.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Leins 2013 reported no adverse events at 12 weeks.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Leins 2013 reported no adverse events at 12 weeks.

(c) Emergence of antibiotic-resistant micro-organisms

There were no results given for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Leins 2013 reported a significant difference in mean SCORAD at 12 weeks between the bleach bath and emollient groups; however, after adjustment for baseline imbalance, the difference was no longer significant. Wong 2013 reported a significant difference in mean EASI score at two months between the bleach bath and placebo groups. Numerical results were confirmed on correspondence with the authors (MD at two months: -12.70; 95% CI -20.06 to -5.34). Pooling results of these two studies resulted in a significant reduction in severity in the bleach bath compared with the placebo/emollient group (SMD -1.11; 95% CI -1.68 to -0.53) (Analysis 4.10).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Leins 2013 reported that bleach baths 'did not eradicate *S. aureus*'; no further results were reported.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Wong 2013 reported a change in mean colony forming units/cm^2 from 16.8 (SD 15.7) at baseline to 7.8 (SD 11.6) at two months in the bleach bath group compared with a change from 7.5 (13.6) to 6.2 (10.7) in the placebo group (MD at two months 1.60; 95% CI -5.69 to 8.89) (Analysis 4.11).

8. Antibacterial bath additive plus antibiotic - one study

One study (Huang 2009), a parallel group RCT, compared bleach and mupirocin versus water and placebo ointment in 31 children (25 evaluable) with moderate to severe infected eczema, as determined by IGA. The duration of the condition was not stated. Participants were randomised to bleach and mupirocin (n = 15) or water and placebo ointment (n = 16). A half cup of 6% bleach (final concentration 0.005%) or water was added to a full bathtub (40 gallons) of water. The amount of administered bleach solution/water was adjusted by the family on the basis of the bath tub size and estimated height of bath tub water. Participants were instructed to bathe in the dilute bleach bath or placebo for five to ten minutes twice weekly. Participants and their household members were instructed to apply mupirocin ointment (Centany (OrthoNeutrogena, Skillman, NJ)) (treatment group) or petrolatum (control group) intranasally twice daily for five consecutive days of each month for three months. Topical steroids were used as needed.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

The study reported significantly lower IGA scores in the treatment group compared with the placebo at one month (P = 0.024) but numerical results were not reported.

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

No participants withdrew from treatment due to adverse events.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

One participant in the treatment group experienced itching and irritation of the skin.

(c) Emergence of antibiotic-resistant micro-organisms

At one month, one participant (of 11) in the treatment group had developed MRSA compared with none (of 13) in the placebo group (RR 3.50; 95% CI 0.16, 78.19) (Analysis 5.1).

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Huang 2009 reported a significantly greater reduction in mean EASI score at one month in the treatment group compared with the placebo group (MD -7.90; 95% CI -14.22, -1.58) (Analysis 5.2).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

At one month, 55% (6/11) in the treatment group had *S. aureus* isolated compared with 77% (10/13) in the placebo group (RR 0.71; 95% CI 0.38 to 1.31) (Analysis 5.3).

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

There were no results given for this outcome.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Long-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

At three months, 67% (6/9) of participants in the treatment group showed reductions in IGA scores compared with 15% (2/13) in the placebo group (RR 4.33; 95% CI 1.12 to 16.82) (Analysis 5.4).

(b) Improvement in Quality of Life questionnaires

There were no results given for this outcome.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

There were no results given for this outcome.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

There were no results given for this outcome.

(c) Emergence of antibiotic-resistant micro-organisms

At three months, one participant (of 8) in the treatment group had developed MRSA compared with one (of 13) in the placebo group (RR 1.63; 95% CI 0.12 to 22.50) (Analysis 5.5).

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Huang 2009 reported a significantly greater reduction in mean EASI score at three months in the treatment group compared with the placebo group (MD -12.10; 95% CI -20.18 to -4.02) (Analysis 5.6).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

At three months, 88% (7/8) in the treatment group had *S. aureus* isolated compared with 77% (10/13) in the placebo group (RR 1.14; 95% CI 0.77 to 1.69) (Analysis 5.7).

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

There were no results given for this outcome.

In summary, the one small study of bleach baths plus antibiotics suggested possible clinical benefit in infected eczema but with one case of antibiotic resistance identified.

9. Therapeutic textile - eight studies

Eight studies, with a total of 265 evaluable participants, compared various treated or impregnated textiles against placebo. Five parallel group RCTs compared clothing impregnated with silver (Gauger 2006; Juenger 2006; Fluhr 2009; Daeschlein 2010; Portela Araujo 2013). Two of the products (Fluhr 2009; Portela Araujo 2013) additionally included seaweed or algae-based fibres/treatment.

Daeschlein 2010 evaluated 16 children and adults with uninfected eczema. The severity and duration were not stated. Participants were randomised to wearing silver-impregnated long vests and long johns (Juzo Skin Protect Silver ®, Julius Zorn, Aichach, Germany) (n = 7) or the same textiles without silver (Juzo Skin Protect) (n = 9). These were worn for four weeks continuously, day and night. The garments were washed every two days and participants brought used garments to clinic once a week for testing. No information was provided on concomitant topical steroid use.

Fluhr 2009 evaluated 37 children and adults with mild to moderate eczema (infective status not specified). Participants who had a score of ten or more on the Erlangen Atopy Score were included in the study. The duration of the condition was not stated. Participants were randomised to wear silver-loaded seaweed-based fibre (SeaCell® Active) as a long-sleeved t-shirt (n = 19) or placebo (cotton; n = 18) for eight weeks. No information was provided on concomitant topical steroid use.

Gauger 2006 evaluated 57 children and adults (of 68 randomised) with moderate to severe eczema with a SCORAD of 20 or more (infective status not specified). Duration of the condition was not stated. Participants were randomised to wear silver-coated textiles as verum (Padycare ®, consisting of micromesh material, 82% polyamide, 18% Lycra, with woven silver filaments with a silver content of 20% in total) as all in one suits for children and long-sleeved and long-legged clothes for adults (n = 37) or placebo (textiles made of pure cotton of equal size) (n = 31). Study clothes were worn daily for two weeks (in the day, like underwear and at night, like pyjamas). Topical steroids were used as needed.

Juenger 2006 evaluated 30 children and adults with uninfected eczema. The severity of the condition in the participants in the study was not reported. The median duration of the condition in the intervention group was 20.5 years and 25.5 years in the control group. Participants were randomised to wearing a long-sleeved undershirt and long underpants with silver thread (n = 10) or identical garment with polyester thread (n = 10) or prednicarbate 0.25% ointment (n = 10) for 14 days. Only comparison of silver textile versus silver-free textile was eligible for this review. Topical steroids were used as needed.

Portela Araujo 2013 evaluated 18 children (of 19 randomised) with eczema (infective status not specified). The severity and duration of the condition were not stated. Participants were randomised to Skintoskin textiles® (70% cotton, 20% cellulose with algae extracts, 10% silver activated algal cellulose; 6000 ppm, 0.6% silver (n = 12) or 100% cotton (woven similarly to the trial textile (n = 7) as babygrows for babies around one year old and pyjamas and socks for older participants. These were worn continuously for seven days following which they were only worn at night (until day 90). Topical steroids were used as rescue medication only.

Two studies (Koller 2007; Stinco 2008) reported right-and-left comparisons of Dermasilk® (sericin-free silk treated with AEGIS AEM5772/5) compared with untreated silk or cotton. Koller 2007 evaluated 22 children with mild to moderate eczema (infective status not specified). The duration of the condition was not stated. Participants were randomised to Dermasilk® (sericin-free silk treated with AEGIS AEM5772/5) for 12 weeks or simple silk fabric

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(sericin-free silk without AEGIS AEM5772/5) for two weeks followed by cotton for 10 weeks. Participants were given three different 'arm tubes'. "For the first 2 wk of the study, parents were advised to dress one arm of their children with simple silk fabric and the other one with the Dermasilk® fabric. After 2 wk - throughout the rest of the study - one arm had to be covered with the cotton and the other with the Dermasilk® tube." No concomitant topical steroids were used.

Stinco 2008 evaluated 26 children and adults (of 30 randomised) with uninfected eczema. The severity and duration of the condition were not stated. Participants were randomised to wear tubular sleeves made from knitted fibrin silk bonded with AEGIS AEM 5772/5 (DermaSilk®) or an identical product without the bonded AEGIS AEM 5772/5. Each participant received four pairs of tubular sleeves (with different coloured seams) and parents/participants were asked to dress their arms with the sleeves all night and day, changing them once a day and washing them with a mild detergent, with the same coloured sleeve always on the same arm. An assigned emollient was permitted and a gentle, non-irritating skin cleanser without antiseptics/antimicrobial products was provided. No topical steroids were used.

One parallel group RCT (Lopes 2015) compared cotton pyjamas coated with the natural biopolymer chitosan with untreated cotton in 78 children and adults (69 evaluable) with uninfected eczema. The severity was not stated. The median duration of eczema in the intervention group was 18 years and in the control group, 12 years. Participants were randomised to cotton pyjamas coated with chitosan (ChitoClear CG-800) (n = 43) or uncoated cotton pyjamas (n = 35). These consisted of long-sleeved top and long pants. Pyjamas were worn at night for the duration of the study (two-week run-in period and eight-week intervention period). Topical steroids were used for rescue medication only.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

Juenger 2006 reported no significant difference in the overall disease control of eczema in the silver textile group compared with the non-silver textile as assessed by the participant or their carer (RR 2.40; 95% CI 0.91 to 6.36) (Analysis 6.1). There were no data reported for this outcome in any of the other seven studies.

(b) Improvement in Quality of Life questionnaires

Gauger 2006 reported within-group improvements in mean quality of life using the DIELH at the end of the intervention (two weeks) from 55.7 to 45.2 for silver textile group and from 53.3 to 44.2 for the placebo group but no significant difference between the groups. There were no short-term data reported for this outcome in any of the other seven studies.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Four studies reported no adverse reactions to silver textiles (Gauger 2006; Portela Araujo 2013) or Dermasilk® (Koller 2007; Stinco 2008). Lopes 2015 reported that one participant withdrew due to an eczema flare in the chitosan-coated textile group compared with no withdrawals in the placebo group (RR 2.45; 95% CI 0.10 to 58.45) (Analysis 6.2).

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Juenger 2006 reported that two out of ten participants in each group reported dryness of skin (RR 1.00; 95% CI 0.17 to 5.77) (Analysis 6.3).

(c) Emergence of antibiotic-resistant micro-organisms

There were no results given for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Five studies (Gauger 2006; Juenger 2006; Koller 2007; Stinco 2008; Portela Araujo 2013) reported short-term changes in SCORAD. Juenger 2006 reported a reduction in the mean SCORAD from baseline to day 14 from 72.7 to 36.1 in the silver textile group and from 51.5 to 45.9 in the placebo group; the difference between groups in change in SCORAD was statistically significant using a non-parametric U-test, however, the mean values at day 14 were not significantly different (mean difference -9.8; 95% CI -27.3 to 7.7) (Analysis 6.4). Gauger 2006 reported a significant within-group reduction in mean SCORAD from baseline to week two from 47.8 to 34.7 in the silver textile group and a non-significant reduction from 45.9 to 38.4 in the placebo group; the difference between groups was not statistically significant (standard deviations and CIs were not reported, precluding pooling). Portela Araujo 2013 also reported a substantial reduction in mean SCORAD from baseline to seven days from 43.8 to 32.5 in the silver/seaweed textile group and from 41.5 to 35.2 in the placebo group (standard deviation and CI were not reported for the placebo group). Koller 2007 reported a significant difference at four weeks in both intensity of itching score and subjective score of SCORAD between the arm treated with Dermasilk and the arm treated with untreated silk/cotton; the median intensity of itching score decreased from 9 to 6.5 in the Dermasilk arm and from 9.5 to 8 in the untreated silk/cotton arm and the median subjective score decreased from 5 to 4 in the Dermasilk arm and increased from 5 to 5.5 in the untreated silk/cotton arm. Stinco 2008 reported a significant reduction in mean local SCORAD from baseline to day 28 from 47.35 to 26.32 in the arm treated with Dermasilk and from 46.68 to 35.70 in the placebo group; the difference in mean reduction from baseline between the groups was statistically significant (mean difference -10.05; 95% CI -13.60 to -6.50) (Analysis 6.5).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

There were no results given for this outcome.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

There were no results given for this outcome.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Juenger 2006 reported no difference in *S. aureus* counts at day 14 in the silver textile and placebo groups (MD 0.0 log CFU/cm^2; 95% CI

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

-0.93 to 0.93) (Analysis 6.6), however, the baseline count in the silver textile group was considerably higher (3.1 versus 1.8 log CFU/cm^2). Daeschlein 2010 reported lower bacterial counts of *S. aureus* after two days in the silver textile group than the placebo group; however, the difference was not statistically significant (MD 9.90k CFU/cm^2; 95% CI -41.83 to 22.03) (Analysis 6.7) and no baseline counts were reported.

Long-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

There were no results given for this outcome in any of the eight studies.

(b) Improvement in Quality of Life questionnaires

Lopes 2015 reported a significant within-group improvement in quality of life using the DLQI at the end of the eight-week study period for chitosan-coated cotton and a non-significant improvement for untreated cotton; the difference between the groups was not statistically significant (MD -0.80; 95% CI -3.32 to 1.72) (Analysis 6.8). There were no long-term data reported for this outcome in any of the other seven studies.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

There were no results given for this outcome.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

There were no results given for this outcome.

(c) Emergence of antibiotic-resistant micro-organisms

There were no results given for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Lopes 2015 reported a significant reduction in mean SCORAD from baseline to end of treatment (eight weeks) from 44.2 (95% CI 34.5 to 53.9) to 29.4 (21.4 to 37.4) in the chitosan-coated textile group and from 41.4 (34.3 to 48.6) to 25.7 (18.3 to 33.1) in the placebo group; the difference between the groups was not statistically significant (MD 3.70; 95% CI -7.20 to 14.60) (Analysis 6.9). Portela Araujo 2013 reported a significant reduction in mean SCORAD from baseline to end of treatment (90 days) from 43.8 (SD 12.1) to 24.0 (SD 12.5) in the silver/seaweed textile group compared with 41.5 (11.6) to 24.2 (12.5) in the placebo group; the difference between the groups was not statistically significant (MD -0.20; 95% CI -12.05 to 11.65) (Analysis 6.10).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

Lopes 2015 reported a median of 0 flares (IQR 0 to 1) during the eight-week study period in both the chitosan-coated textile and placebo groups.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

Lopes 2015 reported no significant difference in the percentage of participants with *S. aureus* isolated at the end of treatment (eight weeks) between the chitosan-coated textile and placebo groups (RR 1.01; 95% CI 0.69, 1.46) (Analysis 6.11).

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

Lopes 2015 reported a small increase in mean $\log_{10}$ colony forming units/cm^2 of *S. aureus* between baseline and end of treatment (eight weeks) from 3.5 (SD 1.4) to 4.0 (SD 1.8) in chitosan-coated textile group and from 3.3 (1.5) to 3.8 (1.6) in the placebo group (data extracted from graph using WebPlotDigitizer, https://automeris.io/WebPlotDigitizer/); neither the within-group changes from baseline nor the difference between the groups was statistically significant (MD 0.20; 95% CI -0.65 to 1.05) (Analysis 6.12).

In summary, therapeutic textiles showed no clear benefit in either infected or uninfected eczema.

9. Protease inhibitor - one study

One study (Foelster Holst 2010), a parallel group RCT, compared a novel protease inhibitor (SRD441) ointment against placebo in 93 adults with mild to moderate eczema, with an IGA of 2 to 3 and a current exacerbation requiring a step up in treatment (infective status not specified). The duration of the condition was not specified. Participants were randomised to receive the study drug SRD441 ointment (mixture of white soft paraffin and Miglyol 812N, a medium chain triglyceride, and 1 mg/g SRD441) (n = 45) or the vehicle ointment (white soft paraffin and Miglyol 812N) (n = 48). The study drug or vehicle were applied to all affected areas and commonly affected body areas up to a maximum of 20% BSA for up to 28 days. Unmedicated emollients and moisturisers were permitted during the screening period and on all nontreated skin during the treatment phase. Topical steroids were used as rescue medication only.

Short-term:

(1) Primary outcome measures

(a) Global degree of improvement in symptoms and/or signs as rated by patient or medical practitioner

The study reported no significant difference in the proportions of participants with a score of 0 (clear) or 1 (almost clear) on a 6-point investigator's global assessment scale (RR 0.89; 95% CI 0.29 to 2.71) (Analysis 7.1).

(b) Improvement in Quality of Life questionnaires

At 28 days, Foelster Holst 2010 reported a decrease in the mean DLQI of 0.8 points in the protease inhibitor group compared with 3.2 points in the placebo group; the difference was not statistically significant (standard deviations and CIs were not reported).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(2) Secondary outcome measures

(a) Severe adverse events, i.e. severe enough to require withdrawal of treatment, including severe skin irritation

Seven participants in the protease inhibitor group (15.6%) and 11 participants in the placebo group (22.9%) experienced an adverse event that resulted in discontinuation of the study medication (RR 0.68; 95% CI 0.68, 1.60) (Analysis 7.2). The most frequent adverse events requiring withdrawal of treatment were application site reaction (n = 6), application site dryness (n = 4), "atopic dermatitis" (despite all participants having this at baseline; hence, we are not clear what this means), application site pruritus and pruritus (all, n = 3), and application site irritation, application site swelling, application site urticaria and pain (all, n = 2). The types of adverse events were not reported by treatment group.

(b) Minor patient-reported adverse events. This included mild skin irritation not sufficient to require cessation of treatment.

Twenty participants in the protease inhibitor group (44.4%) and 23 participants in the placebo group (47.9%) experienced minor adverse events (RR 0.93; 95% CI 0.60, 1.44) (Analysis 7.3). Full details of these adverse events were not reported.

(c) Emergence of antibiotic-resistant micro-organisms

There were no results given for this outcome.

(3) Tertiary outcome measures

(a) Global changes in composite rating scales, using a published named scale

Foelster Holst 2010 reported a 17.2% decrease from baseline in SCORAD in the protease inhibitor group compared with 13.9% in the placebo group; the difference was not statistically significant (standard deviations and CIs were not reported).

(b) Changes in the individual signs of eczema as assessed by a physician

There were no results given for this outcome.

(c) Duration of remission and/or prevention of subsequent flares

Foelster Holst 2010 reported no difference in the number and severity of new exacerbations, but numerical results were not presented.

(d) Change in isolation rate of S. aureus, i.e. isolated or not isolated

There were no results given for this outcome.

(e) Change in bacterial counts of S. aureus, i.e. an assessment of quantity of S. aureus

There were no results given for this outcome.

Long-term:

There were no long-term outcomes reported.

DISCUSSION

Summary of main results

This review included 41 studies with a total of 1753 participants analysed. Of the ten types of intervention considered in this review, we found the most substantial body of evidence for the comparison of topical steroids plus topical antibiotics compared with topical steroids alone (see Summary of findings for the main comparison). In total, 14 studies addressed this comparison of which only three reported the first primary outcome, and pooled analysis indicated that the combination group may lead to a slightly increased proportion with good or excellent global degree of improvement in symptoms or signs, as rated by the patient or medical practitioner (follow-up: 6 to 28 days; one of these studies was in clinically infected eczema and the other two studies did not specify; low-quality evidence). Only one study from this comparison reported the review's second primary outcome of change from baseline in quality of life and there is probably little or no difference between groups (follow-up: 14 days; infected eczema; moderate-quality evidence). Rates of adverse events requiring withdrawal from treatment were extremely low in the four studies from this comparison evaluating this outcome (both groups reported flare of dermatitis, worsening of the condition, and folliculitis), and consequently there is considerable uncertainty in the effect estimate (follow-up: 6 to 28 days; studies' infective status: not stated (one study), uninfected (two studies), infected (one study); very low-quality evidence). Pooled analysis of the two studies reporting minor adverse events not requiring withdrawal from treatment showed fewer adverse events, such as flare of dermatitis, stinging, itch, folliculitis, in the combination group, but we are uncertain of the validity of this result (follow-up: 14 days; studies' infective status: not stated and uninfected; very low-quality evidence). One study in this comparison reported the proportion of strains of *S. aureus* that were resistant to the antibiotic used; these were similar between the groups, but we are not confident in this result (follow-up: three months; infected eczema; very-low quality of evidence).

Of the four studies comparing oral antibiotics with placebo (Summary of findings 2), two studies evaluated good or excellent global improvement and indicated that there may be no difference between the groups (follow-up: 14 to 28 days; studies' infective status: uninfected and mainly infected, low-quality evidence). Only one study in this comparison reported quality of life and there is probably little or no difference between the groups (follow-up: 14 days; infected eczema; moderate-quality evidence). The rates of adverse events requiring withdrawal from treatment were very low (e.g. eczema worsening (both groups), loose stools (antibiotic group), and Henoch-Schönlein purpura (placebo group)) in the four studies that assessed this outcome in this comparison, resulting in an extremely imprecise estimate of the treatment effect. Thus, we are uncertain if there is a difference between groups (follow-up: 14 to 28 days; studies' infective status: uninfected (two studies), infected (one study), mainly infected (one study: 28/30 participants); very low-quality evidence). The only information regarding minor adverse events for this comparison was from one study, which again showed similar results (low number of events) between the groups. However, we are uncertain if there is a difference between groups. Minor adverse events included nausea, vomiting, diarrhoea, and stomach and joint pains (follow-up: 28 days; infected eczema; very low-quality evidence). Based on two studies, antibiotic resistance was found to be similar in both groups, but the evidence was uncertain (follow-up: 14 days; studies' infective status: infected and uninfected; very low-quality evidence).

Of the five studies comparing bleach baths with placebo or bath emollient (Summary of findings 3), one evaluated the percentage of participants with good or excellent global improvement and found there may be no difference between bleach baths or placebo (follow-up: one month; uninfected eczema; low-quality evidence). One study reported change from baseline in quality of life and found

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

that there was probably little or no difference between groups (bleach baths or placebo) (follow-up: at 28 days; unspecified infective status; moderate-quality evidence). One study reported just one dropout due to worsening itch; the numbers of events requiring withdrawal from treatment were very low in the studies within this comparison, and we are uncertain if there is a difference between bleach baths or placebo (follow-up: two months; uninfected eczema; very-low quality evidence). Based on one study in this comparison, some minor adverse events such as burning, stinging, and dry skin were reported by participants in both groups; there may be no difference in this outcome between bleach baths and placebo (follow-up: two months; uninfected eczema; low-quality evidence). Based on one study, we are uncertain if antibiotic resistance was different between groups (bleach baths and placebo) (follow-up: four weeks; unspecified infective eczema; very low-quality evidence).

Quality of life and antibiotic resistance were the most under-represented of our core outcomes. Although other outcomes were more frequently reported, heterogeneity often precluded pooling. Most studies assessed short-term eczema control, so we are uncertain of the effects of included treatments in the long term. Although the included studies assessed iinterventions currently used in clinical practice, many interventions were assessed by single studies; these included the following groups: topical steroid plus antibiotic and antifungal; topical calcineurin inhibitor plus antibiotic; antibacterial soap; antibacterial bath additive plus antibiotic; and protease inhibitor. Although we found moderate-quality evidence for the assessment of quality of life for our three key comparisons, our other key outcomes were mainly reported by trials of low or very low quality.

Antibiotic resistance

Of the 18 studies evaluating antibiotics, only six reported on the emergence of resistant organisms. These included three studies of oral antibiotics (Weinberg 1992; Ewing 1998; Francis 2016), three studies of topical steroids plus topical antibiotics (Lever 1988; Hung 2007; Francis 2016), one study of topical calcineurin inhibitor plus topical antibiotic (Hung 2007) and one study of bleach bath plus antibiotic (Huang 2009), including two studies each reporting on two interventions.

In the studies of oral antibiotics, numbers of resistant organisms to the study drugs were low; however, these were based on small numbers of participants (Weinberg 1992; Francis 2016). One study of flucloxacillin reported an increase in MRSA in the treatment group but did not give numerical results (Ewing 1998).

In the studies of topical steroids or topical calcineurin inhibitor plus topical fusidic acid, cases of resistance to fusidic acid were reported in 25% to 73% of strains isolated from the intervention groups (Hung 2007; Francis 2016); however, these were based on small numbers of participants and, in one of the studies, comparative figures were not given for the participants that did not receive fusidic acid. In the one study that also reported rates of fusidic acid resistance in the control group, 20% to 31% of strains were resistant. In the study of mupirocin, only one participant had a resistant strain of *S. aureus* following treatment (Lever 1988); however, as this was a cross-over trial, it was impossible to produce comparative results for mupirocin versus placebo.

In the study of bleach bath plus mupirocin (Huang 2009), one participant (of 11) developed MRSA in the intervention group compared with none (of 13) in the control group; however, the numbers were too small to draw any meaningful conclusions.

Overall completeness and applicability of evidence

Although we identified studies of relevance to our review question, these were insufficient to address all of the review's objectives. This review included several different interventions designed to reduce *S. aureus* in eczema; however, the studies were generally small and poorly reported. Furthermore, while a broad range of treatment categories were included, covering all anti-staphylococcal interventions currently used in clinical practice, half of these were assessed by single studies:

- four studies of oral antibiotics included a total of 166 participants;
- five studies of topical antiseptics/antibiotics versus placebo included only 99 participants;
- one study of an antibiotic and antifungal combined with a topical steroid compared with topical steroid alone included only four participants with atopic eczema;
- one study included 26 participants evaluating a topical calcineurin inhibitor plus antibiotic compared with topical calcineurin inhibitor alone;
- one study included 50 participants evaluating antibacterial soap;
- seven studies of antibacterial bath additives included a total of 164 participants;
- one study of an antibacterial bath additive (bleach) combined with an antibiotic included 25 participants;
- eight studies, with a total of 265 participants, compared various treated or impregnated textiles against placebo; and
- one study, with 93 participants, compared a novel protease inhibitor (SRD441) ointment against placebo.

The most well-represented treatment group was topical steroids plus antiseptics/antibiotics versus topical steroids alone, which was assessed in 14 studies; these studies (34% of the included studies) contributed over 50% of the review's evaluable participants. However, even when comparisons included an adequate number of studies, variation between studies in the specific interventions and in the outcomes reported precluded any meaningful conclusions regarding their usefulness.

Twenty-one studies were conducted in Western Europe, nine in North America, seven in the Far East, and four elsewhere in the world. Environmental factors may influence the severity of the eczema, bathing behaviour, and tendency to infection. Furthermore, living conditions between different countries influence the usefulness of the intervention in different populations. For example, in Hon 2016, participants did not routinely have bath tubs in their homes and had to be supplied with portable bathtubs in order to participate in the trial. In practice, if most of the population do not have a bath tub, this intervention would be difficult to implement.

The majority of studies, 19, included both children and adults, 12 only included children, four only included adults and in six studies, the age of the participants was not reported. Severity of the eczema, when mentioned, ranged from mild to severe. The method

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

of assessing severity was often not described and, when it was, this ranged from subjective global assessments to objective scoring systems such as SCORAD.

In clinical practice, patients with clinically obvious, infected eczema will often be given antibiotic treatment to clear the infection, leading to an improvement in their eczema. A systematic review found that the pooled prevalence of *S. aureus* amongst patients with eczema was 70% for lesional skin, 39% for non-lesional skin, and 62% for nasal colonisation (Totté 2016). The inclusion criteria of the studies in our review varied widely. Nine studies required evidence of colonisation or infection, with five requiring microbiological evidence of *S. aureus* and another four requiring clinically infected eczema. Fourteen studies excluded participants with acutely infected eczema, or those requiring oral antibiotics, while the remainder (19 studies) did not mention this in their inclusion or exclusion criteria. The differences in inclusion criteria make the studies difficult to compare and it is difficult to draw conclusions about the role of clearing *S. aureus* in clinically infected eczema versus treating *S. aureus* in patients without evidence of clinical infection.

In clinical practice, most people with eczema will use accessory care such as emollients or specific cleansing products; however, other aspects of clinical care were not recorded in the included studies.

Very few trials looked at quality of life, long-term control of eczema, or antibiotic resistance. Just under half of the studies reported on the primary outcome, global improvement. Only five studies addressed quality of life. Twenty-seven studies reported on either severe or minor participant-reported adverse events, or both. Seven studies looked at microbiological data including sensitivity of or resistant organisms (the secondary outcome emergence of antibiotic-resistant micro-organisms).

Few studies reported the same outcome measures, and outcomes were assessed using different instruments and at different time points; therefore, it was impossible to perform pooled analyses for many interventions.

For three of the key comparisons of oral antibiotic versus placebo, topical steroid plus topical antibiotic versus topical steroid, and bleach bath versus placebo, we were able to pool studies in groups of up to seven studies for some outcome measures. For the remaining categories, either the studies were not sufficiently similar to pool or the studies did not report the same outcome measures. For the initial pooling, we did not take into consideration whether it was infected or non-infected eczema that was being treated.

Arguably one of the most important outcomes in the treatment of eczema is long-term control. Only nine studies in our review were longer than one month's treatment duration, which was considered a reasonable time to reflect disease chronicity. The problem of measuring long-term control has been highlighted as part of the HOME initiative (Chalmers 2014). Several different methods of measuring long-term control have been employed in RCTs (Barbarot 2016). More recently there have been attempts to validate measures of long-term control in eczema by assessing "well-controlled weeks" (Langan 2017).

Antibiotic resistance

Of 18 studies evaluating antibiotics, only six reported on antibiotic resistance. The numbers of events were too low and the studies of insufficient duration to establish whether changes were genuine or to draw any meaningful conclusions.

The concern about the use of antibiotics for eczema leading to development of resistant organisms has led clinicians to seek alternative strategies to decrease *S. aureus* in eczema. This review includes five studies of bleach baths and one study in which they were combined with nasal mupirocin. Another strategy to decrease *S. aureus* in eczema is the use of endolysin, a trial of which was recently completed at the time of writing and is yet to report (Totté 2017).

Quality of the evidence

Many of the studies were small, with 37 of the 41 studies including fewer than 100 participants, and two studies (Hjorth 1985; Polano 1960) provided no data for the outcomes of interest. The quality of reporting was frequently poor. More than one-quarter of studies were assessed as having high risk of bias for blinding of participants and personnel, incomplete outcome data and selective reporting.

For the comparison of topical steroid plus topical antibiotic versus topical steroid alone, the evidence regarding the global outcome was judged to be of moderate quality because of the risk of bias in included studies (lack of blinding and possible selective reporting in Canpolat 2012; high risk of attrition bias in Gong 2006; possible selective reporting in Wachs 1976). The evidence regarding change from baseline in quality of life was judged to be of moderate quality because of risk of bias (high risk of attrition bias and baseline imbalance in Francis 2016). The evidence regarding adverse events requiring withdrawal of treatment was judged to be of very low quality because of risk of bias (high risk of attrition bias and baseline imbalance in Francis 2016; lack of blinding in Hung 2007; high risk of attrition bias in Ramsay 1996) and imprecision of the estimate (downgraded two levels due to the very low numbers of events). The evidence regarding minor adverse events was also judged to be of very low quality, this time, because of risk of bias (high risk of attrition bias in Ramsay 1996), imprecision of the estimate and heterogeneity of the control group risk (which varied from 3.6% in Ramsay 1996 to 59.1% in Schuttelaar 2005). The evidence regarding global change in composite rating scales was judged to be of low quality because of risk of bias (high risk of attrition bias and baseline imbalance in Francis 2016; high risk of attrition bias in Gong 2006; lack of blinding in Hung 2007) and heterogeneity in control group means. The evidence regarding *S. aureus* isolation rates was judged to be of moderate quality because of risk of bias (high risk of attrition bias and baseline imbalance in Francis 2016; lack of blinding in Hung 2007; lack of a washout period and baseline imbalance in severity in Lever 1988; baseline imbalance in *S. aureus* colonisation in Leyden 1977; lack of blinding in Nilsson 1992; possible selective reporting in Wachs 1976).

For the comparison of oral antibiotics versus placebo, the evidence regarding the global outcome was judged to be of low quality because of risk of bias (high risk of attrition bias in both Ewing 1998 and Weinberg 1992) and imprecision of the estimate. The evidence regarding change from baseline in quality of life and global change in composite rating scales was judged to be of moderate quality because of risk of bias (high risk of attrition bias and baseline imbalance in severity and rates of *S. aureus* in Francis 2016). The

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

evidence regarding adverse events requiring withdrawal of treatment was judged to be of very low quality because of risk of bias (high risk of attrition bias in Weinberg 1992, Ewing 1998 and Francis 2016, and baseline imbalance in Francis 2016) and imprecision of the estimate (downgraded two levels due to the very low number of events). The evidence regarding *S. aureus* isolation rates was judged to be of low quality because of risk of bias (high risk of attrition bias in Weinberg 1992, Ewing 1998 and Francis 2016 and baseline imbalance in Francis 2016) and imprecision of the estimate.

For the comparison of bleach baths versus placebo, the evidence regarding global outcome and *S. aureus* isolation rates was judged to be of low quality because of risk of bias (likely ineffectiveness of blinding and baseline imbalance in *S. aureus* rates in Wong 2013) and imprecision of the estimate. The evidence regarding change from baseline in quality of life was judged to be of moderate quality because of imprecision of the estimate. The evidence regarding adverse events requiring withdrawal of treatment was judged to be of very low quality because of risk of bias (likely ineffectiveness of blinding and baseline imbalance in *S. aureus* rates in Wong 2013) and imprecision of the estimate (downgraded two levels due to the very low numbers of events). The evidence regarding minor adverse events was judged to be of low quality because of risk of bias (likely ineffectiveness of blinding and baseline imbalance in *S. aureus* rates in Wong 2013) and imprecision of the estimate. The evidence regarding global change in composite rating scales was judged to be of very low quality because of risk of bias (likely ineffectiveness of blinding in both studies, and baseline imbalance in severity in Gonzalez 2016 and *S. aureus* rates in Wong 2013), imprecision of the estimate and heterogeneity in the control group means (from 2.3 in Gonzalez 2016 to 25.4 in Wong 2013).

Potential biases in the review process

Our searches identified a number of studies, which at first may have appeared eligible for the review; however, studies with no placebo group that compared two anti-staphylococcal interventions were ineligible according to our protocol. Exclusion of such studies might potentially have resulted in the omission of additional evidence. To include such studies would require more complex techniques such as network meta-analysis.

The other decision we faced in selection of studies was whether studies which reported reduction in *S. aureus*, but used an intervention that was not specifically anti-staphylococcal (e.g. trials of vitamin D or probiotics) should be included. We opted not to include such studies.

We attempted to conduct a comprehensive search for studies, but the fact that six studies are awaiting classification and have not yet been incorporated may be a source of potential bias. Several of these studies appear to have been completed some time ago but have never been published.

Agreements and disagreements with other studies or reviews

Other than the previous version of this review, there have been no other systematic reviews covering all interventions to reduce *S. aureus* in eczema. A systematic review of bleach baths (Chopra 2017) concluded that "while bleach baths are effective in reducing AD severity, they do not appear to be more effective than water bath alone." However, the finding that bleach baths reduce severity was based on non-randomised, within-group comparisons. The conclusion that bleach baths do not appear more effective than water alone is consistent with our results. A systematic review of functional textiles (Lopes 2013) concluded that recommendation for their use in treating eczema is weak, with low-quality evidence of effectiveness. This is consistent with our findings.

A recent narrative review summarised the current and future treatment strategies (Hepburn 2017). Potential future treatments for *S. aureus* infection include monoclonal antibodies, vaccines, endolysins, vitamin D and probiotics (Hepburn 2017).

AUTHORS' CONCLUSIONS

Implications for practice

The quality of the evidence included in this review was insufficient to address the overall set of objectives and provide definitive guidance for clinical practice. Only a limited number of studies were available to pool in meta-analyses.

We found low-quality evidence that using a topical antibiotic/steroid combination compared with topical steroid alone may be associated with slight improvement in short-term good or excellent improvement in symptoms or signs, or both, but there is probably little or no difference between groups in change from baseline in quality of life.

Similarly, there is probably little or no difference between oral antibiotics or bleach baths and placebo on quality of life (both short-term assessment and based on moderate-quality evidence).

When compared to placebo, oral antibiotics or bleach baths may make no difference to short-term overall good or excellent improvement (low-quality evidence).

Low rates of adverse events were reported for all the interventions considered, but we are uncertain of the effect of our key comparisons on adverse effects (whether or not they required withdrawal from treatment) as we assessed the quality of the evidence as very low for all but one adverse event outcome: there is low-quality evidence that there may be no difference in minor adverse events (burning/stinging or dry skin) between bleach baths and placebo (water). Common adverse events included flare of dermatitis, worsening of the condition, folliculitis, stinging, itch and digestive dysfunction.

We are uncertain of the effect of our three key comparisons on antimicrobial resistance (all evidence was very low quality), which is a potential concern with this intervention. Although there was insufficient evidence to determine the effects of antibiotics to treat infected eczema, this does not preclude their use to treat the infection itself, which was outside the scope of this review.

The six studies in Studies awaiting classification may alter the conclusions of the review, once assessed.

Implications for research

This review highlights the need for further research into the role of treating *S. aureus* in eczema. The trials included in this review were heterogeneous in terms of baseline population, interventions used, and outcomes. First, there is need to establish valid and repeatable criteria for describing clinically infected eczema, perhaps

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

using consensus methods supported by reference images or more objective methods such as colony counts. Whilst there is likely to be good agreement between clinicians on what grossly infected eczema is, there is likely to be a lot of variability between clinicians in deciding a suitable boundary between clinically infected and non-infected eczema. Once this is established, there is a need to clarify whether the study population has clinically infected (or just colonised) eczema or whether the eczema is clinically uninfected. Future studies need to assess for the presence or absence of *S. aureus* infection at baseline and follow-up visits and for the presence of resistant organisms. The results of a trial of an anti-staphylococcal intervention may differ depending on whether the eczema is infected or uninfected at baseline.

In clinical practice, other products such as emollients and washing products are usually used. Information on this has not been documented. Collection of this information would provide a more realistic view on what is going on in clinical practice.

Many of the trials were small leading to imprecise estimates of treatment effects; future studies must be adequately powered to detect clinically meaningful differences in outcomes. Larger trials will also reduce the risk of chance baseline imbalance. In future trials, attempts should be made to blind the participants and personnel, whenever possible; however, for certain interventions, such as bleach baths, adequate blinding may be very difficult to achieve.

Heterogeneity of outcome measures precluded pooling of data in many cases. In future studies, the HOME initiative (Chalmers 2014) will help to standardise outcome measures for use in trials of eczema. As well as objective measures of eczema severity, future studies of anti-staphylococcal interventions should include measures of quality of life. Future studies also need to assess whether any benefit in terms of severity or reduction in flares is sustained following clearance of *S. aureus* (for example, following antibiotic treatment) and whether sustained benefit can be achieved by longer term use of non-antibiotic treatments. Given the time required to recover from severe flares in eczema, follow-up of several months would be required. Every effort should be made to maximise follow-up of participants, as many studies in our review were potentially impacted by attrition bias. Studies should report all relevant adverse events.

Many studies were poorly reported and future studies should be prospectively registered and adhere to CONSORT reporting guidelines (Schulz 2010) to ensure complete and transparent reporting and avoid selective reporting of study results.

In view of the low quality of evidence and lack of information on quality of life and antibiotic resistance, a larger, definitive trial on steroid/antibiotic combination treatment is required. With the increased concerns about antibiotic resistance, other strategies to treat *S. aureus* infection that do not involve antibiotics should be further investigated.

ACKNOWLEDGEMENTS

Dr Finola Delamere for performing the searches for the original review and Liz Doney for performing the searches for the update and inserting the search results into the review.
Prof Masutaka Furue, Prof Markus Mäkinen, and Dr Johanna Mäkinen for help in obtaining full-text papers.
Dr Carsten Flohr for interpreting papers in German (Schempp 2003).
Dr Yukihiro Ohya for extracting data from a paper in Japanese (Hizawa 1998).
Dr Masaki Futamura for evaluating eligibility for one paper in Japanese (Ishibashi 1993) and completing the table of bias for another (Hizawa 1998).
Dr Nadia Terrazzini for help extracting data from a paper in Italian (Lembo 2011).
Dr Maggie Findley and Dr Theresa Stjernholm for translating a paper in Danish (Nielsen 1979).
Dr Vivien Weston for help with the interpretation of the microbiological data for the original review.
Dr Richard Williams and Ms Jacqueline Page for help with the development of the protocol previously published.

The Cochrane Skin editorial base wishes to thank Luigi Naldi, who was the Dermatology Editor for this review; Laurence Le Cleach, who was Methods Editor; the clinical referee, Kachiu Lee; Amanda Roberts, the consumer referee; and Anne Lethaby who copy-edited the review.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

REFERENCES

References to studies included in this review

Berman 2018 *{published data only}*

Berman B, Nestor M. An investigator blinded randomized study evaluating hypochlorous acid (HOCl) in the treatment of atopic dermatitis-associated pruritus. *Journal of Clinical and Aesthetic Dermatology* 2018;**11**(5 Supplement 1):S13.

Boguniewicz 2001 *{published data only}*

* Boguniewicz M, Sampson H, Leung SB, Harbeck R, Leung DYM. Effects of cefuroxime axetil on Staphylococcus aureus colonization and superantigen production in atopic dermatitis. *Journal of Allergy and Clinical Immunology* 2001;**108**(4):651-2. [CENTRAL: CN-00374302]

Breneman 2000 *{published data only}*

* Breneman DL, Hanifin JM, Berge CA, Keswick BH, Neumann PB. The effect of antibacterial soap with 1.5% triclocarban on Staphylococcus aureus in patients with atopic dermatitis. *Cutis* 2000;**66**(4):296-300. [CENTRAL: CN-00372699]

Canpolat 2012 *{published data only* **(unpublished sought but not used)}**

Canpolat F, Erkocoglu M, Tezer H, Kocabas CN, Kandi B. Hydrocortisone acetate alone or combined with mupirocin for atopic dermatitis in infants under two years of age - a randomized double blind pilot trial. *European Review for Medical and Pharmacological Sciences* 2012;**16**(14):1989-93. [CENTRAL: CN-00841489; PUBMED: 23242727]

Daeschlein 2010 {*published and unpublished data}*

Daeschlein G, Assadian O, Arnold A, Haase H, Kramer A, Junger M. Bacterial burden of worn therapeutic silver textiles for neurodermitis patients and evaluation of efficacy of washing. *Skin Pharmacology and Physiology* 2010;**23**(2):86-90. [CENTRAL: CN-00731215; PUBMED: 20016250]

Ewing 1998 *{published data only}*

* Ewing CI, Ashcroft C, Gibbs ACC, Jones GA, Connor PJ, David TJ. Flucloxacillin in the treatment of atopic dermatitis. *British Journal of Dermatology* 1998;**138**(6):1022-9. [CENTRAL: CN-00155038]

Fattah 1976 *{published data only}*

* Fattah AA, El Shiemy S, Faris R. A comparative clinical evaluation of a new topical steroid "Halcinonide" and hydrocortisone in steroid responsive dermatoses. *Journal of International Medical Research* 1976;**4**(4):228-31. [CENTRAL: CN-00697652]

Fluhr 2009 *{published data only* **(unpublished sought but not used)}**

Fluhr JW, Breternitz M, Kowatzki D, Bauer A, Bossert J, Elsner P, et al. Silver-loaded seaweed-based cellulosic fiber improves epidermal skin physiology in atopic dermatitis: safety assessment, mode of action and controlled, randomized single-blinded exploratory in vivo study. *Experimental Dermatology* 2010;**19**(8):e9-15. [CENTRAL: CN-00768275; PUBMED: 19645851]

Foelster Holst 2010 *{published data only}*

Foelster Holst R, Reitamo S, Yankova R, Worm M, Kadurina M, Thaci D, et al. The novel protease inhibitor SRD441 ointment is not effective in the treatment of adult subjects with atopic dermatitis: results of a randomized, vehicle-controlled study. *Allergy* 2010;**65**(12):1594-9. [CENTRAL: CN-00772211; PUBMED: 21039597]

Francis 2016 *{published data only}*

Francis NA, Ridd MJ, Thomas-Jones E, Shepherd V, Butler CC, Hood K, et al. A randomised placebo-controlled trial of oral and topical antibiotics for children with clinically infected eczema in the community: the ChildRen with Eczema, Antibiotic Management (CREAM) study. *Health Technology Assessment* 2016;**20**(19):i-xxiv, 1-84. [CENTRAL: CN-01259966; PUBMED: 26938214]

Gauger 2006 *{published data only}*

Gauger A, Fischer S, Mempel M, Schaefer T, Foelster-Holst R, Abeck D, et al. Efficacy and functionality of silver coated textiles in patients with atopic eczema. *Journal of the European Academy of Dermatology and Venereology* 2006;**20**(5):534-41. [CENTRAL: CN-00565215]

Gong 2006 *{published data only}*

* Gong JQ, Lin L, Lin T, Hao F, Zeng FQ, Bi ZG, et al. Skin colonization by Staphylococcus aureus in patients with eczema and atopic dermatitis and relevant combined topical therapy: a double-blind multicentre randomized controlled trial. *British Journal of Dermatology* 2006;**155**(4):680-7. [CENTRAL: CN-00572111]

Gonzalez 2016 {*published and unpublished data}*

Gonzalez ME, Schaffer JV, Orlow SJ, Gao Z, Li H, Alekseyenko AV, et al. Cutaneous microbiome effects of fluticasone propionate cream and adjunctive bleach baths in childhood atopic dermatitis. *Journal of the American Academy of Dermatology* 2016;**75**(3):481-493.e8. [CENTRAL: CN-01368690; PUBMED: 27543211]

Harper 1995 *{published data only}*

* Harper J. Double-blind comparison of an antiseptic oil-based bath additive (Oilatum Plus) with regular Oilatum (Oilatum Emollient) for the treatment of atopic eczema. In: Lever R, Levy J editor(s). The Bacteriology of Eczema: Round Table Series. Vol. **37**, The Royal Society of Medicine Press Ltd, 1995:42-47. [CENTRAL: CN-00184126]

Hizawa 1998 *{published data only}*

* Hizawa T, Sano H, Endo K, Fukuzumi T, Kataoka Y, Aoki T. Is povidone-iodine effective to the lesions of atopic dermatitis. *Hifu [Skin Research]* 1998;**40**(Suppl 20):134-9. [CENTRAL: CN-00499393]

Hjorth 1985 *{published data only}*

* Hjorth N, Schmidt H, Thomsen K. Fusidic acid plus betamethasone in infected or potentially infected eczema. *Pharmacotheraputica* 1985;**4**(2):126-31. [CENTRAL: CN-00259287]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Holland 1995 *{published data only}*

* Holland KT, Bojar RA, Cunliffe WJ. A comparison of the effect of treatment of atopic eczema with and without antimicrobial compounds. In: Lever R, Levy J editor(s). The Bacteriology of Eczema: Round Table Series. Vol. **37**, The Royal Society of Medicine Press Ltd, 1995:37-40. [CENTRAL: CN-00747631]

Hon 2016 *{published data only}*

Hon KL, Tsang YC, Lee VW, Pong NH, Ha G, Lee ST, et al. Efficacy of sodium hypochlorite (bleach) baths to reduce Staphylococcus aureus colonization in childhood onset moderate-to-severe eczema: a randomized, placebo-controlled cross-over trial. *Journal of Dermatological Treatment* 2016;**27**(2):156-62. [CENTRAL: CN-01132944; PUBMED: 26270469]

Huang 2009 *{published data only}*

* Huang JT, Abrams M, Tlougan B, Rademaker A, Paller AS. Treatment of Staphylococcus aureus colonization in atopic dermatitis decreases disease severity. *Pediatrics* 2009;**123**(5):e808-14. [CENTRAL: CN-00700251; PUBMED: 19403473]

Huang JT, Rademaker A, Paller AS. Dilute bleach baths for Staphylococcus aureus colonization in atopic dermatitis to decrease disease severity. Archives of Dermatology 2011; Vol. 147, issue 2:246-7. [PUBMED: 21339459]

Hung 2007 *{published data only}*

Hung SH, Lin YT, Chu CY, Lee CC, Liang TC, Yang YH, et al. Staphylococcus colonization in atopic dermatitis treated with fluticasone or tacrolimus with or without antibiotics. *Annals of Allergy, Asthma & Immunology* 2007;**98**(1):51-6. [CENTRAL: CN-00574988; MEDLINE: 17225720]

Juenger 2006 *{published data only}*

* Juenger M, Ladwig A, Staecker S, Arnold A, Kramer A, Daeschlein G, et al. Efficacy and safety of silver textile in the treatment of atopic dermatitis (AD). *Current Medical Research and Opinion* 2006;**22**(4):739-50. [CENTRAL: CN-00565217]

Koller 2007 *{published data only* **(unpublished sought but not used)}**

Koller DY, Halmerbauer G, Bock A, Engstler G. Action of a silk fabric treated with AEGIS in children with atopic dermatitis: a 3-month trial. *Pediatric Allergy and Immunology* 2007;**18**(4):335-8. [CENTRAL: CN-00636754; PUBMED: 17346297]

Korting 1994 *{published data only}*

* Korting HC, Zienicke H, Braun-Falco O, Boek K, Milbradt R, Nolting S, et al. Modern topical glucocorticoids and anti-infectives for superinfected atopic eczema: do prednicarbate and didecyldimethylammoniumchloride form a rational combination?. *Infection* 1994;**22**(6):390-3. [CENTRAL: CN-00499406]

Zienicke H. Topical glucocorticoids and anti-infectives: a rational combination?. *Current Problems in Dermatology* 1993;**21**:186-91. [CENTRAL: CN-00098710]

Leins 2013 {*published and unpublished data}*

Leins E, Scullin M. Bleach baths for eczema. *Australasian Journal of Dermatology* 2013;**54**(Suppl 2):55.

Lembo 2011 {*published and unpublished data}*

Lembo C, Patruno C, De Leonibus C, Panariello L, Lembo S, Ayala F. Topical erythromycin in atopic dermatitis [L'eritromicina topica nella terapia della dermatite atopica]. *Annali Italiani di Dermatologia Allergologica Clinica e Sperimentale* 2011;**65**(3):113-8. [CENTRAL: CN-00843852]

Lever 1988 *{published data only}*

* Lever R, Hadley K, Downey D, Mackie R. Staphylococcal colonization in atopic dermatitis and the effect of topical mupirocin therapy. *British Journal of Dermatology* 1988;**119**(2):189-98. [CENTRAL: CN-00055801]

Leyden 1977 *{published data only}*

* Leyden JJ, Kligman AM. The case for steroid-antibiotic combinations. *British Journal of Dermatology* 1977;**96**(2):179-87. [CENTRAL: CN-00569045]

Lopes 2015 *{published data only}*

Lopes C, Soares J, Tavaria F, Duarte A, Correia O, Sokhatska O, et al. Chitosan coated textiles may improve atopic dermatitis severity by modulating skin staphylococcal profile: a randomized controlled trial. *PLOS One* 2015;**10**(11):e0142844. [CENTRAL: CN-01168830; PUBMED: 26618557]

Masako 2005b *{published data only}*

* Masako K, Yusuke K, Hideyuki I, Atsuko M, Yoshiki M, Kayoko M, et al. A novel method to control the balance of skin microflora. Part 2. A study to assess the effect of a cream containing farnesol and xylitol on atopic dry skin. *Journal of Dermatological Science* 2005;**38**(3):207-13. [CENTRAL: CN-00740969]

Nilsson 1992 *{published data only}*

* Nilsson EJ, Henning CG, Magnusson J, Sundsvall BS. Topical corticosteroids and Staphylococcus aureus in atopic dermatitis. *Journal of the American Academy of Dermatology* 1992;**27**(1):29-34. [CENTRAL: CN-00360692]

Polano 1960 *{published data only}*

* Polano MK, De Vries HR, Delver A. Analysis of the results obtained in the treatment of atopic dermatitis with corticosteroid and neomycin containing ointments. *Dermatologica* 1960;**120**:191-9. [CENTRAL: CN-00360818]

Portela Araujo 2013 *{published data only* **(unpublished sought but not used)}**

Araujo CP, Gomes J, Vieira AP, Ventura F, Fernandes JC, Brito C. A proposal for the use of new silver-seaweed-cotton fibers in the treatment of atopic dermatitis. *Cutaneous and Ocular Toxicology* 2013;**32**(4):268-74. [CENTRAL: CN-00918329; PUBMED: 23485342]

Ramsay 1996 *{published data only}*

* Ramsay CA, Savoie JM, Gilbert M, Gidon M, Kidson P. The treatment of atopic dermatitis with topical fusidic acid and hydrocortisone acetate. *Journal of the European Academy*

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

of Dermatology and Venereology 1996;**7**(Suppl 1):S15-22. [CENTRAL: CN-00172818]

Schempp 2003 *{published data only}*

Schempp CM, Hezel S, Simon JC. Topical treatment of atopic dermatitis with St John's wort cream - a randomized, placebo controlled, double blind half-side comparison [Behandlung der subakuten atopischen Dermatitis mit Johanniskraut-Creme. Eine randomisierte, placebokontrollierte Doppelblindstudie im Halbsetendesign]. *Hautarzt* 2003;**54**(3):248-53. [CENTRAL: CN-00509733]

* Schempp CM, Windeck T, Hezel S, Simon JC. Topical treatment of atopic dermatitis with St John's wort cream - a randomized, placebo controlled, double blind half-side comparison. *Phytomedicine* 2003;**10**(Suppl IV):31-7. [CENTRAL: CN-00438398]

Schuttelaar 2005 *{published and unpublished data}*

* Schuttelaar ML, Coenraads P-J. A randomised, double-blind study to assess the efficacy of addition of tetracycline to triamcinolone acetonide (class II corticosteroid) in the treatment of moderate to severe atopic dermatitis. *Journal of the European Academy of Dermatology and Venereology* 2008;**22**(9):1076-82. [CENTRAL: CN-00667932]

Shi 2016 *{published data only}*

Shi VY, Foolad N, Ornelas JN, Hassoun LA, Monico G, Takeda N, et al. Comparing the effect of bleach and water baths on skin barrier function in atopic dermatitis: a split-body randomized controlled trial. *British Journal of Dermatology* 2016;**175**(1):212-4. [CENTRAL: CN-01383031; PUBMED: 26875771]

Stinco 2008 *{published data only}*

Stinco G, Piccirillo F, Valent F. A randomized double-blind study to investigate the clinical efficacy of adding a non-migrating antimicrobial to a special silk fabric in the treatment of atopic dermatitis. *Dermatology* 2008;**217**(3):191-5. [CENTRAL: CN-00668416; PUBMED: 18583910]

Tan 2009 *{published data only}*

Tan WP, Suresh S, Tey HL, Chiam LY, Goon AT. A randomized double-blind controlled trial to compare a triclosan-containing emollient with vehicle for the treatment of atopic dermatitis. *Clinical and Experimental Dermatology* 2010;**35**(4):e109-12. [CENTRAL: CN-00762014; PUBMED: 19843084]

Wachs 1976 *{published data only}*

* Wachs GN, Maibach HI. Co-operative double-blind trial of an antibiotic/corticosteroid combination in impetiginized atopic dermatitis. *British Journal of Dermatology* 1976;**95**(3):323-8. [CENTRAL: CN-00014807]

Weinberg 1992 *{published data only}*

* Weinberg E, Fourie B, Allmann B, Toerien A. The use of cefadroxil in superinfected atopic dermatitis. *Current Therapeutic Research, Clinical and Experimental* 1992;**52**(5):671-6. [CENTRAL: CN-00195530]

Wong 2013 *{published and unpublished data}*

Wong SM, Ng TG, Baba R. Efficacy and safety of sodium hypochlorite (bleach) baths in patients with moderate to severe atopic dermatitis in Malaysia. *Journal of Dermatology* 2013;**40**(11):874-80. [CENTRAL: CN-00915612; PUBMED: 24111816]

References to studies excluded from this review

Alangari 2017 *{published data only}*

Alangari AA, Morris K, Lwaleed BA, Lau L, Jones K, Cooper R, et al. Honey is potentially effective in the treatment of atopic dermatitis: clinical and mechanistic studies. *Immunity, Inflammation and Disease* 2017;**5**(2):190-9. [PUBMED: 28474502]

Ariyoshi 1973 *{published data only}*

Ariyoshi M, Matsumoto T. A clinical trial of amoxycillin in some infectious skin diseases. *Chemotherapy* 1973;**21**(8):1812-6.

Berardesca 2009 *{published data only}*

Berardesca E, Abril E, Serio M, Cameli N. Effects of topical gluco-oligosaccharide and collagen tripeptide F in the treatment of sensitive atopic skin. *International Journal of Cosmetic Science* 2009;**31**(4):271-7. [PUBMED: 19496838]

Bergstrom 2009 *{published data only}*

Bergstrom KG. Tea tree oil: panacea or placebo?. *Journal of Drugs in Dermatology* 2009;**8**(5):494-6. [PUBMED: 19537376]

Bianchi 2014 *{published data only}*

Bianchi P, Villeneuve C, Theunis J, Casas C, Patrizi A, Bacquey A, et al. Evaluation of a novel emollient balm containing Aquaphilus dolomiae extract in atopic dermatitis children: effect on clinical parameters, skin barrier and microflora. *Journal of Investigative Dermatology* 2014;**134**(Suppl 1):S96.

Bjornberg 1975 *{published data only}*

Bjornberg A, Hellgren L, Nygren B. Diproderm with Gentamicin - a new very potent steroid ointment in infected eczema. *Current Therapeutic Research* 1975;**18**(4):556-8. [PUBMED: 810315]

Breneman 1990 *{published data only}*

Breneman DL. Use of mupiricin ointment in the treatment of secondarily infected dermatoses. *Journal of the American Academy of Dermatology* 1990;**22**(5 Pt 1):886-92. [PUBMED: 2112167]

Carpenter 1973 *{published data only}*

Carpenter CL, Jolly HW, McCormick GE, Schneiderman RN, Thompson JG. Combined steroid-antiinfective topical therapy in common dermatoses: a double-blind, multicenter study of iodochlorhydroxyquin-hydrocortisone in 277 patients. *Current Therapeutic Research* 1973;**15**(9):650-9. [PUBMED: 4270829]

Clark 1974 *{published data only}*

* Clark RF. The case for corticosteroid-antibiotic combinations. *Cutis* 1974;**14**(5):737-41. [CENTRAL: CN-00269373]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Craig 2010 *{published data only}*

Craig FE, Smith EV, Williams HC. Bleach baths to reduce severity of atopic dermatitis colonized by Staphylococcus. *Archives of Dermatology* 2010;**146**(5):541-3. [PUBMED: 20479303]

Davis 1968 *{published data only}*

* Davis CM, Fulghum DD, Taplin D. The value of neomycin in a neomycin-steroid cream. *JAMA* 1968;**203**(4):298-300. [CENTRAL: CN-00651515]

Drago 2011 *{published data only}*

Drago L, Iemoli E, Rodighiero V, Nicola L, De Vecchi E, Piconi S. Effects of Lactobacillus salivarius LS01 (DSM 22775) treatment on adult atopic dermatitis: a randomized placebo-controlled study. *International Journal of Immunopathology and Pharmacology* 2011;**24**(4):1037-48. [PUBMED: 22230409]

Drago 2012 *{published data only}*

Drago L, Toscano M, De Vecchi E, Piconi S, Iemoli E. Changing of fecal flora and clinical effect of L. salivarius LS01 in adults with atopic dermatitis. *Journal of Clinical Gastroenterology* 2012;**46 Suppl**:S56-63. [CENTRAL: CN-00967749; PUBMED: 22955359]

Dunstan 2011 *{published data only}*

Dunstan JA, Brothers S, Bauer J, Hodder M, Jaksic MM, Asher MI, et al. The effects of Mycobacteria vaccae derivative on allergen-specific responses in children with atopic dermatitis. *Clinical and Experimental Immunology* 2011;**164**(3):321-9. [CENTRAL: CN-00895034; PUBMED: 21413940]

Eaglstein 1977 *{published data only}*

Eaglstein WH, Feinstein RJ, Halprin KM, Bergstresser PR, Mertz PM. Systemic antibiotic therapy of secondary infected dermatitis. *Archives of Dermatology* 1977;**113**(10):1378-9. [CENTRAL: CN-00016805]

Gauger 2003 *{published data only}*

* Gauger A, Mempel M, Schekatz A, Schafer T, Ring J, Abeck D. Silver-coated textiles reduce Staphylococcus aureus colonization in patients with atopic eczema. *Dermatology* 2003;**207**(1):15-21. [CENTRAL: CN-00438876]

Girolomoni 2016 *{published data only}*

Girolomoni G, Mattina R, Manfredini S, Vertuani S, Fabrizi G. Fusidic acid betamethasone lipid cream. *International Journal of Clinical Practice* 2016;**70**(Suppl 184):4-13. [PUBMED: 27121235]

GP Medical Research 1967 *{published data only}*

* GP Medical Research Unit. Treatment of eczemas and infected eczemas. *British Journal of Clinical Practice* 1967;**21**(10):505-7. [CENTRAL: CN-00001629]

Gratton 1987 *{published data only}*

Gratton D. Topical mupirocin versus oral erythromycin in the treatment of primary and secondary skin infections. *International Journal of Dermatology* 1987;**26**(7):472-3. [CENTRAL: CN-00268360; PUBMED: 3115904]

Gueniche 2008 *{published data only}*

Gueniche A, Knaudt B, Schuck E, Volz T, Bastien P, Martin R, et al. Effects of nonpathogenic gram-negative bacterium Vitreoscilla filiformis lysate on atopic dermatitis: a prospective, randomized, double-blind, placebo-controlled clinical study. *British Journal of Dermatology* 2008;**159**(6):1357-63. [CENTRAL: CN-00665626; PUBMED: 18795916]

Gueniche 2009 *{published data only}*

Gueniche A, Bastien P, Mahe Y, Billoni N, Knaudt B, Piche E, et al. Antimicrobial activity of Vitreoscilla filiformis lysate: results from a randomized, double-blind, vehicle-controlled and in vitro study. *Journal of Investigative Dermatology* 2009;**129**(Suppl 2s):S18. [CENTRAL: CN-00790672]

Hoey 2006 *{published data only}*

Hoey SEH, Catney D, Maguire S, McKenna K. Fixed low dose versus increasing dose of ultraviolet B-TL01 in the treatment of atopic eczema. *British Journal of Dermatology* 2006;**155**(Suppl 1):121-2. [CENTRAL: CN-00602220]

Ishibashi 1993 *{published data only}*

Ishibashi Y, Harada S, Arata J, Niimura M, Takeda K, Shimao S, et al. Clinical utility of DS-2630 ointment on oozing eczema-dermatitis: a double-blind bilateral-paired comparison study with 0.064% betamethasone diproprionate ointment. *Journal of Clinical Therapeutics and Medicines* 1993;**9**(7):1583-601. [CENTRAL: CN-00547143]

Kimata 1998 *{published data only}*

Kimata H. Effect of nadifloxacin on atopic dermatitis with methicillin-resistant Staphylococcus aureus in young children. *European Journal of Pediatrics* 1999;**158**(11):949-54. [CENTRAL: CN-00263884]

Kotrajaras 1971 *{published data only}*

Kotrajaras R. Studies of bacterial infections of skin in Bangkok. *International Journal of Dermatology* 1973;**12**(3):163-5. [CENTRAL: CN-00568720; PUBMED: 4267413]

La Colla 2009 *{published data only}*

La Colla L, Mangano A, Mangano A, Albertin A. Effects of nonpathogenic gram-negative bacterium Vitreoscilla filiformis lysate on atopic dermatitis: a prospective, randomized, double-blind, placebo-controlled clinical study. Does this make a real difference?. *British Journal of Dermatology* 2009;**161**(2):477-9. [PUBMED: 19485997]

Leung 2008 *{published data only}*

Leung TF, Wong KY, Wong CK, Fung KP, Lam CW, Fok TF, et al. In vitro and clinical immunomodulatory effects of a novel Pentaherbs concoction for atopic dermatitis. *British Journal of Dermatology* 2008;**158**(6):1216-23. [PUBMED: 18341655]

Leung 2009 *{published data only}*

Leung DY, Hanifin JM, Pariser DM, Barber KA, Langley RG, Schlievert PM, et al. Effects of pimecrolimus cream 1% in the treatment of patients with atopic dermatitis who demonstrate a clinical insensitivity to topical corticosteroids: a randomized, multicentre vehicle-controlled trial. *British Journal*

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

of Dermatology 2009;**161**(2):435-43. [CENTRAL: CN-00728093; PUBMED: 19416245]

Lloyd 1969 *{published data only}*

* Lloyd KM. The value of neomycin in topical corticosteroid preparations. *Southern Medical Journal* 1969;**62**(1):94-6. [CENTRAL: CN-00307468]

Masako 2005a *{published data only}*

* Katsuyama M, Ichikawa H, Ogawa S, Ikezawa Z. A novel method to control the balance of skin microflora. Part 1. Attack on biofilm of Staphylococcus aureus without antbiotics. *Journal of Dermatological Science* 2005;**38**(3):197-205. [PUBMED: 15927813]

Meenan 1988 *{published data only}*

* Meenan FO. A double-blind comparative study to compare the efficacy of Locoid C with Tri-adcortyl in chldren with infected eczema. *British Journal of Clinical Practice* 1988;**42**(5):200-2. [PUBMED: 2463849]

Mora 2004 *{published data only}*

Mora R, Bellussi L, Passali FM, Crippa B, Mora F, Cordone MP, et al. Efficacy of a topical suspension of bacterial antigens for the management of recurrent eczema in children. *Medical Science Monitor* 2004;**10**(9):PI99-103. [CENTRAL: CN-00501644; PUBMED: 15328495]

Nielsen 1979 *{published data only}*

Nielsen R, Thomsen K. Corticosteroid preparations with and without supplementary antibiotics. Comparison of fluclorolone acetonide (Topilar cream) and betamethasone valerate cream (Betnovat) with neomycin [Kortikosteroidpraeparater med og uden antibiotikumtilsaetning. En sammenligning mellem fluklorolon acetonid (Topilar creme) og cremor betametasonvalerat (Betnovate) med neomycin]. *Ugeskrift For Laeger* 1979;**141**(30):2046-9. [CENTRAL: CN-00022116; PUBMED: 531939]

Parish 1987 *{published data only}*

Parish LC, Parks DB, Layne PP, Uri JV. Ceftizoxime treatment of cutaneous and subcutaneous tissue infections. *Clinical Therapeutics* 1984;**6**(5):613-9. [CENTRAL: CN-00177354; PUBMED: 6090019]

Pratap 2013 *{published and unpublished data}*

Pratap DV, Philip M, Rao NT, Jerajani HR, Kumar SA, Kuruvila M, et al. Evaluation of efficacy, safety, and tolerability of fixed dose combination (FDC) of Halometasone 0.05% and Fusidic Acid 2% W/W topical cream versus FDC of Betamethasone Valerate 0.12% and Neomycin Sulphate 0.5% W/W topical cream in the treatment of infected eczematous dermatosis in Indian subjects: a randomized open-label comparative phase III multi-centric trial. *Indian Journal of Dermatology* 2013;**58**(2):117-23. [CENTRAL: CN-01092632; PUBMED: 23716800]

Prescott 2005 *{published data only}*

Prescott SL, Dunstan JA, Hale J, Breckler L, Lehmann H, Weston S, et al. Clinical effects of probiotics are associated with increased interferon-gamma responses in very young children with atopic dermatitis. *Clinical and Experimental Allergy* 2005;**35**(12):1557-64. [PUBMED: 16393321]

Ravenscroft 2003 *{published data only}*

Ravenscroft JC, Layton AM, Eady EA, Murtagh MS, Coates P, Walker M, et al. Short-term effects of topical fusidic acid or mupirocin on the prevalence of fusidic acid resistant (FusR) Staphylococcus aureus in atopic eczema. *British Journal of Dermatology* 2003;**148**(5):1010-7. [CENTRAL: CN-00558784; PUBMED: 12786834]

Remitz 2001 *{published data only}*

* Remitz A, Kyllonen H, Granlund H, Reitamo S. Tacrolimus ointment reduces staphylococcal colonization of atopic dermatitis lesions. *Journal of Allergy and Clinical Immunology* 2001;**107**(1):196-7. [PUBMED: 11150013]

Rist 2002 *{published data only}*

* Rist T, Parish LC, Capin LR, Sulica V, Bushnell WD, Cupo MA. A comparison of the efficacy and safety of mupirocin cream and cepalexin in the treatment of secondarily infected eczema. *Clinical and Experimental Dermatology* 2002;**27**(1):14-20. [PUBMED: 11952661]

Salo 1988 *{published data only}*

* Salo OP, Gordin A, Brandt H, Antikainen R. Efficacy and tolerability of erythromycin acistrate and erythromycin stearate in acute skin infections of patients with atopic eczema. *Journal of Antimicrobial Chemotherapy* 1988;**21**(Suppl D):101-6. [CENTRAL: CN-00054664]

Sandström Falk 2006 *{published data only}*

Sandstrom Falk MH, Sarnhult T, Hedner T, Faergemann J. Treatment of atopic dermatitis with 1% hydrocortisone and 25% pentane-1,5-diol: effect on Staphylococcus aureus. *Acta Dermato-Venereologica* 2006;**86**(4):372-3. [PUBMED: 16874433]

Sasai-Takedatsu 1997 *{published data only}*

* Sasai-Takedatsu M, Kojima T, Yamamoto A, Hattori K, Yoshijima S, Taniuchi S, et al. Reduction of Staphylococcus aureus in atopic skin lesions with acid electrolytic water - a new therapeutic strategy for atopic dermatitis. *Allergy* 1997;**52**(10):1012-6. [CENTRAL: CN-00145059]

Schempp 2010 *{published data only}*

Schempp C, Wölfle U. Hyperforin - a multi-talent for the skin [Hyperforin - ein multitalent für die haut]. *Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und Verwandte Gebiete* 2010;**21**(4):178-80.

Schultz Larsen 2007 *{published data only}*

Larsen FS, Simonsen L, Melgaard A, Wendicke K, Henriksen AS. An efficient new formulation of fusidic acid and betamethasone 17-valerate (fucicort lipid cream) for treatment of clinically infected atopic dermatitis. *Acta Dermato-Venereologica* 2007;**87**(1):62-8. [CENTRAL: CN-00586553; PUBMED: 17225018]

Senti 2006 *{published data only}*

Senti G, Steinmann LS, Fischer B, Kurman R, Storni T, Johansen P, et al. Antimicrobial silk clothing in the treatment of atopic dermatitis proves comparable to topical corticosteroid

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

treatment. *Dermatology* 2006;**213**(3):228-33. [PUBMED: 17033173]

Stalder 1992 *{published data only}*

* Stalder JF, Fleury M, Sourisse M, Allavoine TH, Chalamet C, Brosset P, et al. Comparative effects of two topical antiseptics (chlorhexidine vs KMnO4) on bacterial skin flora in atopic dermatitis. *Acta Dermato-Venereologica* 1992;**176**(Suppl):132-4. [CENTRAL: CN-00089825]

Takahama 1992 *{published data only}*

Takahama H, Wagatsuma K, Takahashi H, YamIshiada N, Torii H, Ishibashi Y. Clinical trial of ME1207 in the dermatological field. *Chemotherapy* 1992;**40**(Suppl 2):805-8.

Thaci 1999 *{published data only}*

Thaci D, Kokorsch J, Kaufmann R. Fusidic acid/Betamethasone 17-valerate in potentially infected atopic dermatitis. *Journal of the European Academy of Dermatology* 1999;**12**(Suppl 2):S163. [CENTRAL: CN-00478779]

Theodoridis 1979 *{published data only}*

Theodoridis A, Vagena A, Sivenas C, Capetanakis J. Evaluation of a topical steroid antibiotic combination (halcinonide-neomycin-amphotericin) in the treatment of cutaneous candidiasis and inflammatory dermatoses. *Current Medical Research and Opinion* 1979;**5**(10):766-71. [CENTRAL: CN-00020280]

Thum 2013 *{published data only}*

Thum D, Seidl HP, Hein R, Ring J, Andres C, Mempel M. Current resistance patterns of Staphylococcus aureus towards topical antibiotics and relevant antiseptics in patients with atopic dermatitis and impetigo. *Journal der Deutschen Dermatologischen Gesellschaft* 2013;**11**(9):875-8. [PUBMED: 23621472]

Udompataikul 2015 *{published data only}*

Udompataikul M, Huajai S, Chalermchai T, Taweechotipatr M, Kamanamool N. The effects of oral vitamin D supplement on atopic dermatitis: a clinical trial with staphylococcus aureus colonization determination. *Journal of the Medical Association of Thailand* 2015;**98**(Suppl 9):S23-30. [PUBMED: 26817206]

Van der Bijl 1966 *{published data only}*

Van der Bijl WJ. A policlinical study of a new external corticosteroid preparation Locacorten. *Acta Allergologica* 1966;**21**(6):515-21. [PUBMED: 6012554]

Verallo-Rowell 2008 *{published data only}*

Verallo-Rowell VM, Dillague KM, Syah-Tjundawan BS. Novel antibacterial and emollient effects of coconut and virgin olive oils in adult atopic dermatitis. *Dermatitis* 2008;**19**(6):308-15. [CENTRAL: CN-00681044; PUBMED: 19134433]

Weitgasser 1983 *{published data only}*

* Weitgasser H, Schindlery C, Macarol V. A comparative multicentre trial of halometasone/triclosan cream and betamethasone diproprionate/gentamicin sulphate cream in the treatment of infected acute eczematous dermatitis. *Journal of International Medical Research* 1983;**11**(Suppl 1):43-7. [CENTRAL: 6339292]

Whitefield 1998 *{published data only}*

Whitefield M. Effectiveness of a new antimicrobial emollient in the management of eczema/dermatitis. *Journal of Dermatological Treatment* 1998;**9**(2):103-9. [CENTRAL: CN-00261088]

Wilkinson JD 1985 *{published data only}*

* Wilkinson JD, Leigh DA. Comparative efficacy of betamethasone and either fusidic acid or neomycin in infected or potentially infected eczema. *Current Therapeutic Research* 1985;**38**(1):177-82. [CENTRAL: CN-00350766]

Wilkinson RD 1980 *{published data only}*

* Wilkinson RD, Collins JP, Raymond GP, Mailhot R, Perras MA, Ricard P. Therapy of infected dermatitis: comparative response to two corticosteroid antimicrobial creams. *Journal of the American Academy of Dermatology* 1980;**2**(3):207-11. [CENTRAL: CN-00022458]

References to studies awaiting assessment

ACTRN12610000438055 *{published data only}*

ACTRN12610000438055. A randomised, double-blind, placebo-controlled phase I study to determine the safety and efficacy of recombinant human ß defensin 2 (rHuB[beta]D2 cream) in the treatment of staphylococcus aureus and other infections in the skin of patients with atopic dermatitis. www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=335452 (first received 6 May 2010).

EudraCT 2006-004233-15 *{published data only}*

2006-004233-15. Multicentric, randomized, double-blinded, vehicle-controlled, phase III-bilateral comparative study for treatment of staphylococcus superinfection in atopic dermatitis with hydrophobic Triclosan-cream 2% (InfectoDermaSept). www.clinicaltrialsregister.eu/ctr-search/search?query=2006-004233-15 (first received 16 April 2009).

EudraCT 2008-005890-37 *{published data only}*

2008-005890-37. Assessment of the effects on barrier impairment, clinical features and bacterial colonization of topical formulations in patients with atopic eczema; a phase IIa, single-center, randomized, observer-blinded study. www.clinicaltrialsregister.eu/ctr-search/search?query=2008-005890-37 (first received 20 October 2008).

NCT03009734 *{published data only}*

NCT03009734. Evaluation of ATx201 as a topical antibiotic agent. clinicaltrials.gov/ct2/show/NCT03009734 (first received 20 March 2018).

NCT03047954 *{published data only}*

NCT03047954. Broncho-Vaxom (OM 85 BV) in children suffering from atopic dermatitis. clinicaltrials.gov/ct2/show/NCT03047954 (first received 9 February 2017).

Totté 2017 *{published data only}*

NCT02840955. The effect of gladskin on disease severity and the skin microbiome, including Staphylococcus aureus, in

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

patients with atopic dermatitis. clinicaltrials.gov/ct2/show/NCT02840955 (first received 11 July 2016).

* Totté J, De Wit J, Pardo L, Schuren F, Van Doorn M, Pasmans S. Targeted anti-staphylococcal therapy with endolysins in atopic dermatitis and the effect on steroid use, disease severity and the microbiome: study protocol for a randomized controlled trial (MAAS trial). *Trials* 2017;**18**(1):404. [PUBMED: 28859690]

References to ongoing studies

NCT03052348 *{published data only}*

NCT03052348. Efficacy of combining topical antibiotic/steroid/moisturizer therapy compared to active comparator in atopic dermatitis. clinicaltrials.gov/ct2/show/NCT03052348 (first received 10 February 2017).

Additional references

Antonov 2015

Antonov NK, Garzon MC, Morel KD, Whittier S, Planet PJ, Lauren CT. High prevalence of mupirocin resistance in Staphylococcus aureus isolates from a pediatric population. *Antimicrobial Agents and Chemotherapy* 2015;**59**(6):3350-6. [DOI: 10.1128/AAC.00079-15; PUBMED: 25824213]

Barbarot 2016

Barbarot S, Rogers NK, Abuabara K, Aubert H, Chalmers J, Flohr C, et al. Strategies used for measuring long-term control in atopic dermatitis trials: a systematic review. *Journal of the American Academy of Dermatology* 2016;**75**(5):1038-44. [PUBMED: 27522613]

Benetti 2015

Benetti C, Piacentini GL, Capristo C, Boner AL, Peroni DG. Microorganism-induced exacerbations in atopic dermatitis: a possible preventive role for vitamin D?. *Allergy and Asthma Proceedings* 2015;**36**(1):19-25. [DOI: 10.2500/aap.2015.36.3807; PUBMED: 25562552]

BNF 2019

Joint Formulary Committee. British National Formulary. www.bnf.org/products/bnf-online/ (accessed prior to 23 October 2019).

Brown 2002

Brown EM, Thomas P. Fusidic acid resistance in Staphylococcus aureus isolates. *Lancet* 2002;**359**(9308):803. [PUBMED: 11888633]

Chalmers 2014

Chalmers JR, Schmitt J, Apfelbacher C, Dohil M, Eichenfield LF, Simpson EL, et al. Report from the third international consensus meeting to harmonise core outcome measures for atopic eczema/dermatitis clinical trials (HOME). *British Journal of Dermatology* 2014;**171**(6):1318-25. [PUBMED: 24980543]

Chaptini 2015

Chaptini C, Quinn S, Marshman G. Methicillin-resistant Staphylococcus aureus in children with atopic dermatitis from 1999 to 2014: a longitudinal study. *Australasian Journal of Dermatology* 2016;**57**(2):122-7. [DOI: 10.1111/ajd.12371; PUBMED: 26172088]

Charman 2004

Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Archives of Dermatology* 2004;**140**(12):1513-9. [PUBMED: 15611432]

Chopra 2017

Chopra R, Vakharia PP, Sacotte R, Silverberg JI. Efficacy of bleach baths in reducing severity of atopic dermatitis: a systematic review and meta-analysis. *Annals of Allergy, Asthma & Immunology* 2017;**119**(5):435-40. [PUBMED: 29150071]

Costa 1989

Costa C, Rilliet A, Nicolet M, Saurat JH. Scoring atopic dermatitis: the simpler the better?. *Acta Dermato-Venereologica* 1989;**69**(1):41-5. [PUBMED: 2563607]

David 1986

David TJ, Cambridge GC. Bacterial infection and atopic eczema. *Archives of Disease in Childhood* 1986;**61**(1):20-3. [PUBMED: 3954415]

Deckers 2012

Deckers IA, McLean S, Linssen S, Mommers M, Van Schayck CP, Sheikh A. Investigating international time trends in the incidence and prevalence of atopic eczema 1990-2010: a systematic review of epidemiological studies. *PLOS One* 2012;**7**(7):e39803. [PUBMED: 22808063]

Eichenfield 2003

Eichenfield LF, Hanifin JM, Luger TA, Stevens SR, Pride HB. Consensus conference on pediatric atopic dermatitis. *Journal of the American Academy of Dermatology* 2003;**49**(6):1088-95. [PUBMED: 14639390]

European Task Force on Atopic Dermatitis 1993

European Task Force on Atopic Dermatitis. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report. *Dermatology* 1993;**186**(1):23-31. [PUBMED: 8435513]

Finlay 1994

Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) - a simple practical measure for routine clinical use. *Clinical and Experimental Allergy* 1994;**19**(3):210-6. [PUBMED: 8033378]

George 2015

George SM, Makrygeorgou A. 8th Georg Rajka International Symposium on Atopic Dermatitis: meeting report. *British Journal of Dermatology* 2015;**172**(4):916-25. [DOI: 10.1111/bjd.13718]

GRADE Working Group 2004

GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**:1490-4.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hanifin 1980

Hanifin JM, Rajka G. Diagnostic features of atopic eczema. *Acta Dermato-Venerologica* 1980;**92**:44-7.

Hanifin 2001

Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M, EASI Evaluator Group. The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. *Experimental Dermatology* 2001;**10**(1):11-8. [PUBMED: 11168575]

Hann 2007

Hann S, Hughes TM, Stone NM. Flexural allergic contact dermatitis to benzalkonium chloride in antiseptic bath oil. *British Journal of Dermatology* 2007;**157**(4):795-8. [PUBMED: 17714561]

Heng 2013

Heng YK, Tan KT, Sen P, Chow A, Leo YS, Lye DC, et al. Staphylococcus aureus and topical fusidic acid use: results of a clinical audit on antimicrobial resistance. *International Journal of Dermatology* 2013;**52**(7):876-81. [DOI: 10.1111/j.1365-4632.2012.05747.x; PUBMED: 23432159]

Hepburn 2017

Hepburn L, Hijnen DJ, Sellman BR, Mustelin T, Sleeman MA, May RD, et al. The complex biology and contribution of Staphylococcus aureus in atopic dermatitis, current and future therapies. *British Journal of Dermatology* 2017;**177**(1):63-71. [PUBMED: 27779765]

Higgins 2011

Higgins JPT, Green S, (editors). Cochrane Handbook for Systematic Reviews of Interventions. 5.1.0 [updated March 2011]. Chichester (UK): John Wiley & Sons, 2011.

Irvine 2006

Irvine AD, McLean WH. Breaking the (un)sound barrier: filaggrin is a major gene for atopic dermatitis. *Journal of Investigative Dermatology* 2006;**126**(6):1200-2. [PUBMED: 16702964]

Jagadeesan 2014

Jagadeesan S, Kurien G, Divakaran MV, Sadanandan SM, Sobhanakumari K, Sarin A. Methicillin-resistant Staphylococcus aureus colonization and disease severity in atopic dermatitis: a cross-sectional study from South India. *Indian Journal of Dermatology, Venereology and Leprology* 2014;**80**(3):229-34. [DOI: 10.4103/0378-6323.132250; PUBMED: 24823400]

Johansson 2004

Johansson SG, Bieber T, Dahl R, Friedmann PS, Lanier BQ, Lockey RF, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *Journal of Allergy and Clinical Immunology* 2004;**113**(5):832-6. [PUBMED: 15131563]

Koch 2014

Koch A, Wollina U. Chlorhexidine allergy. *Allergo Journal International* 2014;**23**(3):84-6. [PUBMED: 26120519]

Langan 2017

Langan SM, Stuart B, Bradshaw L, Schmitt J, Williams HC, Thomas KS. Measuring long-term disease control in patients with atopic dermatitis: a validation study of well-controlled weeks. *Journal of Allergy and Clinical Immunology* 2017;**140**(6):1580-6. [DOI: 10.1016/j.jaci.2017.02.043; PUBMED: 28456619]

Lee 2014

Lee M, Van Bever H. The role of antiseptic agents in atopic dermatitis. *Asia Pacific Allergy* 2014;**4**(4):230-40. [DOI: 10.5415/apallergy.2014.4.4.230; PUBMED: 25379483]

Lewis-Jones 1995

Lewis-Jones MS, Finlay AY. The Children's Dermatology Life Quality Index (CDLQI): initial validation and practical use. *British Journal of Dermatology* 1995;**132**(6):942-9. [PUBMED: 7662573]

Lewis-Jones 2001

Lewis-Jones MS, Finlay AY, Dykes PJ. The Infants' Dermatitis Quality of Life Index. *British Journal of Dermatology* 2001;**144**(1):104-10. [PUBMED: 11167690]

Lin 2007

Lin YT, Wang CT, Chiang BL. Role of bacterial pathogens in atopic dermatitis. *Clinical Reviews in Allergy & Immunology* 2007;**33**(3):167-77. [PUBMED: 18163223]

Lopes 2013

Lopes C, Silva D, Delgado L, Correia O, Moreira A. Functional textiles for atopic dermatitis: a systematic review and meta-analysis. *Pediatric Allergy and Immunology* 2013;**24**(6):603-13. [PUBMED: 23980847]

Luoma 1983

Luoma R, Koivikko A, Viander M. Development of asthma, allergic rhinitis and atopic dermatitis by the age of five years. A prospective study of 543 newborns. *Allergy* 1983;**38**(5):339-46. [PUBMED: 6614406]

Moka 2015

Moka E, Argyra E, Siafaka I, Vadalouca A. Chlorhexidine: hypersensitivity and anaphylactic reactions in the perioperative setting. *Journal of Anaesthesiology, Clinical Pharmacology* 2015;**31**(2):145-8. [DOI: 10.4103/0970-9185.155138; PUBMED: 25948890]

NICE 2013

National Institute for Health and Care Excellence. NICE support for commissioning for atopic eczema in children. www.nice.org.uk/guidance/qs44/resources/support-for-commissioning-for-atopic-eczema-in-children-pdf-253673821 (accessed prior to 23 October 2019).

Odhiambo 2009

Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI. Global variations in prevalence of eczema symptoms in children from ISAAC phase three. *Journal of Allergy and Clinical Immunology* 2009;**124**(6):1251-8. [DOI: 10.1016/j.jaci.2009.10.009; PUBMED: 20004783]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Ong 2016

Ong PY, Leung DY. Bacterial and viral infections in atopic dermatitis: a comprehensive review. *Clinical Reviews in Allergy & Immunology* 2016;**51**(3):329-37. [PUBMED: 27377298]

Ravenscroft 2000

Ravenscroft JC, Layton A, Barnham M. Observations on high levels of fusidic acid resistant Staphylococcus aureus in Harrogate, North Yorkshire, UK. *Clinical and Experimental Dermatology* 2000;**25**(4):327-30. [PUBMED: 10971497]

Reed 1999

Reed J, Lyons M, Waghorn D, Wilkinson J. Fusidic acid resistance rates in South Buckinghamshire. *British Journal of Dermatology* 1999;**141**(Suppl 55):57.

Reginald 2011

Reginald K, Westritschnig K, Linhart B, Focke-Tejkl M, Jahn-Schmid B, Eckl-Dorna J, et al. Staphylococcus aureus fibronectin-binding protein specifically binds IgE from patients with atopic dermatitis and requires antigen presentation for cellular immune responses. *Journal of Allergy and Clinical Immunology* 2011;**128**(1):82-91. [10.1016/j.jaci.2011.02.034; PUBMED: 21513970]

Schafer 2001

Schafer T, Staudt A, Ring J. German instrument for the assessment of quality of life in skin diseases (DIELH). Internal consistency, reliability, convergent and discriminant validity and responsiveness [Deutsches Instrument zur Erfassung der Lebensqualitat bei Hauterkrankungen (DIELH). Interne Konsistenz, Reliabilitat, konvergente und diskriminante Validitat und Veranderungssensitivitat]. *Der Hautarzt; Zeitschrift fur Dermatologie, Venerologie, und Verwandte Gebiete* 2001;**52**(7):624-8. [PUBMED: 11475643]

Schmitt 2007

Schmitt J, Langan S, Williams HC, European Dermato-Epidemiology Network. What are the best outcome measurements for atopic eczema?- a systematic review. *Journal of Allergy and Clinical Immunology* 2007;**120**(6):1389-98. [PUBMED: 17910890]

Schmitt 2012

Schmitt J, Spuls P, Boers M, Thomas K, Chalmers J, Roekevisch E, et al. Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. *Allergy* 2012;**67**(9):1111-7. [PUBMED: 22844983]

Schmitt 2014

Schmitt J, Spuls PI, Thomas KS, Simpson E, Furue M, Deckert S, et al. The Harmonising Outcome Measures for Eczema (HOME) statement to assess clinical signs of atopic eczema in trials. *Journal of Allergy and Clinical Immunology* 2014;**134**(4):800-7. [PUBMED: 25282560]

Schulz 2010

Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;**340**:c332. [PUBMED: 20332509]

Silverberg 2017

Silverberg JI. Public health burden and epidemiology of atopic dermatitis. *Dermatology Clinics* 2017;**35**(3):283-9. [PUBMED: 28577797]

Simpson-Dent 2000

Simpson-Dent SL, Hunt SJ, Hardman C, Barrett S, Wakelin SH. Rates of fusidic acid resistance in paediatric dermatology patients - a 6-year study. *British Journal of Dermatology* 2000;**143**(Suppl 57):123-30.

Spuls 2017

Spuls PI, Gerbens LAA, Simpson E, Apfelbacher CJ, Chalmers JR, Thomas KS, et al. Patient-Oriented Eczema Measure (POEM), a core instrument to measure symptoms in clinical trials: a Harmonising Outcome Measures for Eczema (HOME) statement. *British Journal of Dermatology* 2017;**176**(4):979-84. [PUBMED: 27858989]

St John's Institute of Dermatology 2016

St John's Institute of Dermatology. The use of Milton® baths in dermatology. www.guysandstthomas.nhs.uk/resources/patient-information/dermatology/milton-baths.pdf (accessed prior to 21 October 2019).

Stalder 1994

Stalder JF, Fleury M, Sourisse M, Rostin M, Pheline F, Litoux P. Local steroid therapy and bacterial skin flora in atopic dermatitis. *British Journal of Dermatology* 1994;**131**(4):536-40. [PUBMED: 7947206]

Staughton 1984

Staughton RCM, Byrom NA, Nagvekar NM, Hobbs JR. Thymostimulin therapy of adult atopic eczema: a phase I clinical trial. In: Byrom NA, Hobbs JR editor(s). Thymic Factor Therapy. New York: Raven Press, 1984:415-24.

Stone 2002

Stone KD. Atopic diseases of childhood. *Current Opinion in Pediatrics* 2002;**14**(5):634-46. [PUBMED: 12352260]

Strange 1996

Strange P, Skov L, Lisby S, Nielson PL, Baadsgaard O. Staphylococcal enterotoxin B applied on intact normal and intact atopic skin induces dermatitis. *Archives of Dermatology* 1996;**132**(1):27-33. [PUBMED: 8546480]

Syed 2015

Syed AK, Reed TJ, Clark KL, Boles BR, Kahlenberg JM. Staphylococcus aureus phenol soluble modulins stimulate the release of pro-inflammatory cytokines from keratinocytes and are required for induction of skin inflammation. *Infection and Immunity* 2015;**83**(9):3428-37. [PUBMED: 26077761]

Thomsen 2015

Thomsen SF. Epidemiology and natural history of atopic diseases. *European Clinical Respiratory Journal* 2015;**2**(1):24642. [DOI: 10.3402/ecrj.v2.24642; PUBMED: 26557262]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Totté 2016

Totté JE, Van der Feltz WT, Hennekam M, Van Belkum A, Van Zuuren EJ, Pasmans SG. Prevalence and odds of Staphylococcus aureus carriage in atopic dermatitis: a systematic review and meta-analysis. *British Journal of Dermatology* 2016;**175**(4):687-95. [PUBMED: 26994362]

Van Zuuren 2017

Van Zuuren EJ, Fedorowicz Z, Christensen R, Lavrijsen A, Arents BWM. Emollients and moisturisers for eczema. *Cochrane Database of Systematic Reviews* 2017, Issue 2. [DOI: 10.1002/14651858.CD012119.pub2]

Williams 1990

Williams REA, Gibson AG, Aitchison TC, Lever R, Mackie RM. Assessment of a contact-plate sampling technique and subsequent quantitative bacterial studies in atopic dermatitis. *British Journal of Dermatology* 1990;**123**(4):493-501. [PUBMED: 2095181]

Williams 1992

Williams HC. Is the prevalence of atopic dermatitis increasing?. *Clinical and Experimental Dermatology* 1992;**17**(6):385-91. [PUBMED: 1486704]

Williams 1994

Williams HC, Burney PG, Hay RJ, Archer CB, Shipley MJ, Hunter JJ, et al. The UK Working Party's diagnostic criteria for atopic dermatitis. I. Derivation of a minimum set of discriminators for atopic dermatitis.. *British Journal of Dermatology* 1994;**131**(3):383-96. [PUBMED: 7918015]

Williams 2008

Williams H, Stewart A, Von Mutius E, Cookson W, Anderson HR, International Study of Asthma and Allergies in Childhood (ISAAC) Phase One and Three Study Groups. Is eczema really on the increase worldwide?. *Journal of Allergy and Clinical Immunology* 2008;**121**(4):947-54.e15. [PUBMED: 18155278]

Wollenberg 2014

Wollenberg A, Seba A, Antal AS. Immunological and molecular targets of atopic dermatitis treatment. *British Journal of Dermatology* 2014;**170**(Suppl 1):7-11. [DOI: 10.1111/bjd.12975; PUBMED: 24720588]

Yueh 2014

Yueh MF, Taniguchi K, Chen S, Evans RM, Hammock BD, Karin M, et al. The commonly used antimicrobial additive triclosan is a liver tumor promoter. *Proceedings of the National Academy of Sciences of the United States of America* 2014;**111**(48):17200-5. [DOI: 10.1073/pnas.1419119111; PUBMED: 25404284]

References to other published versions of this review

Birnie 2008

Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC. Interventions to reduce Staphylococcus aureus in the management of atopic eczema. *Cochrane Database of Systematic Reviews* 2008, Issue 3. [DOI: 10.1002/14651858.CD003871]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Berman 2018

Methods	Design: parallel group Total study duration: not stated
Participants	Setting not specified but conducted in conjunction with Center for Clinical and Cosmetic Research, University of Miami, USA. Incl: atopic dermatitis (Hanifin criteria), score higher than 2 on an itch severity scale (0-4) Excl: not stated Age: not stated Sex: not stated Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Randomised: 30 Evaluable: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Berman 2018 *(Continued)*

Interventions	Application of hypochlorous acid containing solution twice daily or as required for 72 hours versus no treatment Category: topical antiseptic/antibiotic Topical steroids: not stated
Outcomes	1. Participant Global Assessment 2. Investigator Global Assessment 3. Visual Analog Scale itch score 4. Adverse events 5. Incidence of local skin reactions leading to discontinuation Outcomes were assessed at baseline, 24 hours and 72 hours
Funding	Not stated
Notes	Only published as abstract

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided in abstract
Allocation concealment (selection bias)	Unclear risk	No information provided in abstract
Blinding of participants and personnel (performance bias) All outcomes	High risk	Title stated 'investigator blinded', however impossible to blind intervention due to no treatment control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Title stated 'investigator blinded'
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Minimal results reported in abstract. Only 19/20 participants allocated to intervention had results for reduction in itching. Numbers included for other outcomes not reported.
Selective reporting (reporting bias)	High risk	Primary outcomes reported as P values only
Other bias	Unclear risk	Limited information in abstract

Boguniewicz 2001

Methods	Design: cross-over Total study duration: not stated
Participants	Setting: Secondary care, two centres, USA

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Boguniewicz 2001 *(Continued)*

	Incl: moderate to severe atopic dermatitis, *S. aureus* cultured from skin Excl: overt skin infection Age: range 6-58 years Sex: 9 males, 11 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 100% Randomised: 20 Evaluable: 20
Interventions	Cefuroxime axetil orally (dose not stated) twice daily vs placebo orally twice daily given for two weeks each with one week washout in between Category: oral antibiotics Topical steroids: all participants
Outcomes	1. Colony counts from two involved areas and inguinal area at the end of each treatment period
Funding	Glaxo Wellcome, Inc
Notes	Outcomes not clear

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind, placebo-controlled" Comment: considered low risk despite no evidence of success of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All of the patients completed the study protocol" Comment: no attrition
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for colonisation density of *S. aureus* but severity not reported

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Breneman 2000

Methods	Design: parallel group Total study duration: not stated
Participants	Setting not specified but conducted in conjunction with Department of Dermatology in Cincinnati and Portland Incl: atopic dermatitis (Hanifin and Rajka criteria) of moderate severity (Rajka and Langeland criteria), Fitzpatrick skin types I-IV Excl: not stated Age: mean 34.6 years (range 12-74) Sex: 15 males, 35 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 50% Randomised: 50 Evaluable: not stated
Interventions	Bar of soap containing triclocarban 1.5% vs placebo (number in each group not stated) Whole body to be washed at least daily for 42 days Category: antibacterial soap Topical steroids: as needed
Outcomes	1. Change from day 0 to day 14, 28, 42, 49, 56, 63 in self-rating of itching 2. Change from day 0 to day 14, 28, 42, 49, 56, 63 in evaluation scores for extent and severity of dermatitis (3 primary attributes combined, 3 secondary attributes combined, all 6 attributes combined, each attribute individually) 3. Change from day 0 to day 14, 28, 42, 49, 56, 63 in percentage of body surface area (BSA) affected 4. IGA of change from day 0 to day 14, 28, 42, 49, 56, 63 (-5 = severe worsening, 5 = total clearing) 5. Amount of topical steroid used 6. Change from day 0 to day 14, 28, 42, 63 of mean log colony forming units of total organisms and *S. aureus*
Funding	The Procter & Gamble Company
Notes	Participants also used standard moisturiser and 0.025% triamcinolone acetonide cream as required.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "patients were given either a bar soap (Safeguard®) containing 1.5% triclocarban as the active antimicrobial ingredient or a placebo bar soap identical to the antimicrobial bar, but without triclocarban".

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Breneman 2000 *(Continued)*

		Comment: blinding was likely to be effective.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "double-blind" Comment: unclear who was blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcomes presented as means and percentages without sample sizes. One participant withdrew at day 28 because of worsening dermatitis.
Selective reporting (reporting bias)	High risk	Participant rating on itching, % with *S. aureus* isolated and % BSA affected stated as outcomes, but not reported in results.
Other bias	Unclear risk	Reasonably well-balanced at baseline for colonisation density of *S. aureus* but severity not reported

Canpolat 2012

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, Turkey Incl: atopic dermatitis (Hanifin and Rajka criteria), mild to moderate severity, infants age 6 months to 2 years, involving 2%-30% of the body Excl: not stated Age: hydrocortisone group: mean 13.6 months, hydrocortisone plus mupirocin group: mean 13.3 months Sex: not stated Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 40% Randomised: 53 Evaluable: 53
Interventions	Hydrocortisone plus mupirocin (n = 27) vs hydrocortisone (n = 26) applied twice daily (hydrocortisone in the morning and evening and mupirocin at noon and night) by parents to areas affected with atopic dermatitis at least 2 hours before bathing for up to 7 days Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. SCORAD and EASI on day 7 and weeks 2, 4, 8 2. Percentage of BSA affected 3. Treatment success: defined as a > 50% recovery of the lesions or > 50% decrease of EASI or SCORAD indexes
Funding	Not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Canpolat 2012 *(Continued)*

Notes	Additional "control" group consisted of infants whose parents did not want to use pharmacological agents - not included in results of review as not randomised.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Caregivers, investigators, and clinical staff were blinded to treatment except parents. Drugs prescribed by a different investigator". Comment: parents were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "clinical follow up dermatologic assessment made by a different clinician". Comment: outcome assessment was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included for primary outcome.
Selective reporting (reporting bias)	High risk	Follow-up was carried out on day 7 and weeks 2, 4 and 8, but the outcomes were only reported for day 8 and for the end of the study. The outcome of percentage of BSA affected was not reported.
Other bias	Low risk	Well-balanced at baseline for severity (EASI and SCORAD) and presence of *S. aureus*

Daeschlein 2010

Methods	Design: parallel group Total study duration: 7 months
Participants	Setting: secondary care, single centre, Germany Incl: acute atopic dermatitis and written agreement of participants Excl: acute viral infection (herpes zoster, eczema herpeticum), acute dermal staphylococcal or streptococcal infections (impetigo/erysipelas), UV therapy, topical or systemic corticosteroid treatment, severe general disorders (carcinoma, renal insufficiency, autoimmune disease), pregnancy and age <10 years Age: intervention group: mean 32 years (range 13-65); control group: mean 27.3 years (range 20-49) Sex: intervention group: 4 males, 3 females, control group: 5 males, 4 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Daeschlein 2010 *(Continued)*

	Randomised: 16 Evaluable: 16
Interventions	Silver-impregnated long vests and long johns (Juzo Skin Protect Silver ®, Julius Zorn, Aichach, Germany) (n = 7) vs the same textiles without silver (Juzo Skin Protect) (n = 9) "Patients wore the textiles (one pair per patient) for 4 weeks continuously day and night without any special wearing recommendations, with the only request to change and wash the pair every 2 days and to bring used clothes once a week (every Friday) to the dermatological clinic where they were tested." Category: therapeutic textile Topical steroids: not stated
Outcomes	1. Antibacterial reduction during wearing and by washing (weekly) 2. Test for self-reduction by silver textile over 24 hours (from 5 participants from each group) 3. Contamination of conventional underwear by healthy participants 4. Decrease of *S. aureus* and total bacteria after 2 days of wearing the textiles 5. Bacterial load as amount of total CFU and of *S. aureus* of the 8 defined test areas from 1. worn silver textiles and placebo after 2 days of wearing directly after undressing, 2. after washing and 3. separately after 24 hours of storage of the removed unwashed textiles
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Optically and regarding wearing comfort, the two textile types could not be differentiated". "Double-blind" Comment: blinding was likely to be effective.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Results reported for all participants.
Selective reporting (reporting bias)	Unclear risk	Reduction of *S. aureus* from manual washing was reported, as was the complete elimination of *S. aureus*. Neither of these were specified in advance.
Other bias	Unclear risk	Baseline severity and presence of *S. aureus* not reported

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Ewing 1998

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, UK Incl: atopic dermatitis (Hanifin and Rajka criteria) with no sign of bacterial infection, treated with topical steroids, age 1 to 16 years, regular outpatient attendance Excl: systemic steroids (past four weeks), systemic or topical antibiotics (past three weeks) Age: flucloxacillin group: median 7.5 years (range 1.6-15.3), placebo group: median 5.2 years (range 1.1-14.1) Sex: not stated Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 98% Randomised: 50 Evaluable: 46
Interventions	Flucloxacillin 250 mg four times daily (n = 25) vs placebo (n = 25) for 4 weeks (dose halved for < 10 yrs old) Category: oral antibiotic Topical steroids: as needed
Outcomes	1. Daily family assessment of redness, daytime itch and night-time sleep disturbance on a visual analogue scale of 0-10, number of applications of corticosteroid and/or emollient and evening dose of trimeprazine tartrate 2. Amount of corticosteroid used at day 14, 28, 42, 84 3. Extent (% BSA) and severity (1 = mild, 5 = severe) of atopic dermatitis at day 14, 28, 42, 84 4. Patient/family and assessor global degree of improvement (1 = much better, 2 = better, 3 = same, 4 = worse) at day 28, 42, 84 5. Isolation of *S. aureus* from affected and non-affected skin 6. Mean log *S. aureus* counts 7. Emergence of resistant organisms
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Flucloxacillin and placebo capsules were supplied and randomised by SKB Pharmaceuticals (Mundells, Welwyn Garden City UK)". Comment: method not described
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias)	Low risk	Quote: "Double blind", "Placebo was 'taste matched". Comment: blinding was likely to be successful.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Ewing 1998 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Double blind" Comment: low risk for patient-reported outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	Two withdrawals for AEs: one in flucloxacillin and one placebo group; two participants on flucloxacillin had poor compliance and not included; another withdrew because they received erythromycin for a chest infection; By visit 5, 37 subjects were analysed, so in total there were 13 withdrawals.
Selective reporting (reporting bias)	High risk	Data on non-significant differences not shown
Other bias	Low risk	Well-balanced at baseline for severity (surface area and erythema scores) and presence of *S. aureus*

Fattah 1976

Methods	Design: within-patient study (left/right comparison) Total study duration: not stated
Participants	Setting: secondary care, single centre, Egypt Incl: inflammatory dermatoses with bilateral, symmetrical lesions of similar aetiology and severity (results for atopic dermatitis reported separately) Excl: secondary infection Age: not stated Sex: not stated Duration of condition: mean 14.5 weeks Infective status: uninfected *S. aureus* colonisation: not stated Randomised: 4 with atopic dermatitis (of 50 total) Evaluable: 4
Interventions	0.1% halcinonide cream with 0.25% neomycin and 100000u/g nystatin vs 1% hydrocortisone both applied three times daily for not more than 3 weeks Category: topical steroid plus antibiotic and antifungal Topical steroids: all participants
Outcomes	1. Clinician-assessed response to treatment made weekly
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "according to a code of randomisation by which the test drug was applied to the lesions on one side whether left or right, and the control drug to those on the opposite side"

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Fattah 1976 *(Continued)*

		Comment: Method not described
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Reported as "double blind", but the creams were different colours.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "parallel evaluations were made independently by two physicians". Comment: not stated whether either of these two physicians were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete data present for atopic dermatitis participants
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Baseline severity and presence of *S. aureus* not reported

Fluhr 2009

Methods	Design: parallel group Total study duration: 16 months
Participants	Setting: secondary care, Germany Incl: atopic dermatitis with a score of 10 or more according to the Erlangen Atopy Score, mild to moderate eczema on the volar forearm, no other known dermatological disease, age 12-60 years Excl: pregnant or lactating women, patients with a history of malignant diseases, systemic medication for atopic dermatitis 4 weeks prior to the start of the study, any other systemic medication and any known systemic diseases Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 38% Age: intervention group: mean 25.4 years (range 14-47), control group: mean 25.5 years (range 13-51) Sex: intervention group: 11 males, 8 females, control group: 9 males, 9 females Randomised: 37 Evaluable: 37
Interventions	Silver-loaded seaweed-based fibre (SeaCell® Active) as long sleeved t-shirt (n = 19) vs placebo (cotton; n = 18) for 8 weeks Category: therapeutic textile Topical steroids: not stated
Outcomes	1. Skin surface pH on volar forearms at 6 and 12 weeks

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Fluhr 2009 *(Continued)*

	2. TEWL at 6 and 12 weeks 3. Capacity-based skin hydration at 6 and 12 weeks 4. Bacterial colonisation at 8 weeks
Funding	SeaCell GMBH
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Single-blinded" Comment: participants and personnel were not both blinded, although unclear who was blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Paper stated "all data sets were complete" but bacterial colonisation was only reported for 4 and 10 participants in the cotton and silver groups respectively.
Selective reporting (reporting bias)	High risk	Results reported at 4 and 8 weeks and not at 6 and 12 weeks as stated
Other bias	Unclear risk	Baseline severity and presence of *S. aureus* not reported

Foelster Holst 2010

Methods	Design: parallel group Total study duration: 15 weeks
Participants	Setting: secondary care, 13 centres in Germany (9), Bulgaria (3) and Finland (1) Incl: "Dermatologist confirmed diagnosis of atopic dermatitis", mild to moderate atopic dermatitis with IGA of 2-3 at randomisation with affected area(s) of less than or equal to 20% total BSA, current exacerbation requiring "step-up" of standard treatment, over 18 years Excl: not stated Age: intervention group: mean 32.87 years (range 18-61), control group: mean 32.88 years (range 19-59) Sex: intervention group: 14 males, 31 females, control group: 23 males, 25 females Duration of condition: not stated Infective status: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Foelster Holst 2010 *(Continued)*

	S. aureus colonisation: not stated Randomised: 93 Evaluable: 93
Interventions	Study drug SRD441 ointment (mixture of white soft paraffin and Miglyol 812N, a medium chain triglyceride, and 1 mg/g SRD441) (n = 45) vs vehicle ointment (white soft paraffin and Miglyol 812N) (n = 48) Layer of study drug or vehicle applied to all affected areas and commonly affected body areas up to a maximum of 20% BSA for up to 28 days Prohibited medication included systemic and topical steroids, antibiotics, calcineurin inhibitors, phototherapy, skin exfoliation, depilatory cream and moisturisers or emollients containing antibiotics/antiseptics. Washout period one week for topicals, 8 weeks for phototherapy. Inhaled steroids were allowed as long as dose stable and < 800 mcg/day. Unmedicated emollients and moisturisers were allowed during the screening period and on all nontreated skin during the treatment phase. Category: protease inhibitor Topical steroids: rescue medication only
Outcomes	Primary end point: 1. success defined as a score of 0 (clear) or 1 (almost clear) on the 6-point categorical measure IGA (0 = clear, 1 = almost clear, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe) at day 21 Secondary endpoints: 2. Time to resolution of primary (presenting) exacerbation, defined as a score of 0 or 1 in IGA 3. IGA score at day 7, 14, 21, 28 4. Change from baseline SCORAD at day 7, 14, 21, 28 5. Change from baseline total pruritus self-assessment (based on the response none/mild/moderate/severe to the question 'How would you describe your pruritus over the last 24 hours?') at day 7, 14, 21, 28 6. No. of subjects requiring rescue medication 7. Change from baseline DLQI at day 7, 14, 21, 28 8. Monitoring of AEs, physical examination, clinical laboratory measures (haematology and clinical chemistry) and change from baseline in Investigator's Visual Assessment (which records erythema, oedema and asks the subject about additional symptoms) 9. Time to and severity of new exacerbations
Funding	Serentis Ltd
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The random code was generated using a permuted block of size 4, with subjects randomly assigned to either vehicle ointment or SRD441 ointment (1.0 mg/g) in a 1:1 ratio." "A random number seed value was used to generate the treatment order and random code within the permuted block algo-

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Foelster Holst 2010 *(Continued)*

		rithm. Random code identifiers were random 4-digit numbers to avoid the bias associated with sequential numbering of random code." Comment: randomisation method described and unlikely to introduce selection bias
Allocation concealment (selection bias)	Low risk	Quote: "The final random code block size, random code numbering sequence and order of treatments within the blocks was blinded from investigators, study subjects and study staff until the final clinical data base was locked and approved by the sponsor before breaking the blind and applying the random code for analysis." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double blind", "All labelling and packaging for SRD441 and vehicle assignments were identical." Comment: blinding likely to have been successful
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "order of treatments within the blocks was blinded from investigators, study subjects and study staff until the final clinical data base was locked". Comment: investigators and study staff remained blinded until the the clinical data base was locked.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All subjects with missing responses including early dropouts were counted as non-responders in the analysis on response rates. Nine subjects withdrew in the treatment group: three had AEs, three treatment failure, two consent withdrawn, one investigator judgement; 15 subjects in the vehicle group: seven had AEs, five had treatment failure, two consent withdrawn, one investigator judgement
Selective reporting (reporting bias)	Unclear risk	Outcomes specified very vaguely in trial registration
Other bias	Unclear risk	Some imbalance in atopic dermatitis intensity (51% moderate versus 60% moderate), baseline SCORAD and presence of *S. aureus* not reported

Francis 2016

Methods	Design: parallel group Total study duration: 17 months
Participants	Setting: primary and secondary care, 95 centres (91 primary care, 4 secondary care), United Kingdom Incl: children (aged 3 months to < 8 years) who had eczema (UK Working Party definition) that was clinically suspected of being infected Excl: recent use of antibiotics (past week) or potent topical steroids (2 days), suspected eczema herpeticum, significant comorbid illness, severe infection, allergy to study medication Age: oral antibiotic group: mean 2.9 years, topical antibiotic group: mean 3.0 years, control group: mean 3.3 years Sex: oral antibiotic group: 18 males, 18 females, topical antibiotic group: 17 males, 20 females, control group: 17 males, 23 females Duration of condition: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Francis 2016 *(Continued)*

	Infective status: clinically infected *S. aureus* colonisation: 70% Randomised: 113 Evaluable: 101
Interventions	Oral antibiotic (flucloxacillin four times per day for 7 days, 125 mg in 2.5 mL for children aged 3 months to 2 years, 250 mg in 5 mL for children aged > 2 years to < 8 years) and topical placebo (n = 36) vs topical antibiotic (2% fusidic acid cream three times per day for 7 days) and oral placebo (n = 37) vs oral and topical placebo (n = 40). All treatment groups received topical steroids (clobetasone butyrate 0.05% cream or ointment for use on trunk/limbs and/or hydrocortisone 1% cream or ointment for use on face, applied once daily for 14 days) and were encouraged to use emollients (not with antimicrobial agents). Categories: oral antibiotic (flucloxacillin plus topical placebo vs oral and topical placebos) and topical steroid plus antiseptic/antibiotic (fusidic acid plus oral placebo vs oral and topical placebos) Topical steroids: all participants
Outcomes	1. Patient-Orientated Eczema Measure (POEM) at 2 weeks, 4 weeks and 3 months 2. Eczema Area and Severity Index (EASI) at 2 weeks, 4 weeks and 3 months 3. Family impact (Dermatitis Family Impact instrument) at 2 weeks, 4 weeks and 3 months 4. Dermatology-specific quality of life (Infants Dermatology Quality of Life instrument for children aged 3 months to < 4 years/Children's Dermatology Life Quality Index for children aged 4 years to < 8 years) at 2 weeks, 4 weeks and 3 months 5. Heath utility (Atopic Dermatitis Quality of Life instrument) at 2 weeks, 4 weeks and 3 months 6. Daily symptoms for first 4 weeks (parent assessment of overall severity, itch, sleep disturbance, oozing or weeping, bleeding, fever and possible AEs on a scale from 0 = normal to 6 = as worse as it could be) 7. Parental preference for oral or topical treatment at 2 weeks 8. Presence of *S. aureus* and beta-haemolytic streptococci on the skin and in the mouth and nose at 2 weeks and 3 months and resistance in isolates at each time point 9. AEs
Funding	UK National Institute for Health Research
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was conducted by study pharmacists using pre-prepared allocation lists using block randomisation stratified by site and penicillin allergy status. Random allocation lists were prepared by the study statistician and were block-randomised with randomly chosen balanced block sizes of 6 or 9." Comment: randomisation method was described and was unlikely to introduce selection bias.
Allocation concealment (selection bias)	Low risk	Quote: "To ensure allocation concealment, treatment assignment was undertaken by each pharmacy. As patients were recruited they were assigned the

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Francis 2016 *(Continued)*

		next vacant participant identification number. The randomisation list linked each unique participant information number to a treatment group ... The pharmacist selected one or two (for older children) treatment packs for the relevant treatment arm based on the trial pack randomisation list. This was to ensure that trial pack identification numbers could not be used to identify treatment allocation." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Study medication packs were identical (with taste- and colour-matched placebos)." Comment: blinding was likely to have been successful.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No indication that blinding was inadequate
Incomplete outcome data (attrition bias) All outcomes	High risk	12 participants (11%) were withdrawn or lost to follow-up by 2 weeks (primary end point) with a further three participants lost to follow-up by 4 weeks and 24 participants by 3 months. Reasons for withdrawal varied across the study groups.
Selective reporting (reporting bias)	Low risk	All stated outcomes from trial registration reported
Other bias	High risk	Baseline imbalance in severity (mean POEM: oral antibiotic group 14.6, topical antibiotic group 16.9, control group 13.4; mean EASI: oral antibiotic group 7.3, topical antibiotic group 9.5, control group 5.8) and presence of *S. aureus* (oral antibiotic group 83%, topical antibiotic group 60%, control group 67%)

Gauger 2006

Methods	Design: parallel group Total study duration: 10 months
Participants	Setting: secondary care, two centres, Germany Incl: atopic eczema (Hanifin and Rajka criteria), moderate-severe (SCORAD 20 points or more) Excl: systemic/topical antibiotic treatment 4 weeks prior to the study period Age: intervention group: median 17.89 years, control group: median 17.26 years Sex: intervention group: 13 males, 22 females, control group: 6 males, 16 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Infective status: not stated Randomised: 68 Evaluable: 57

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gauger 2006 *(Continued)*

Interventions	Silver-coated textiles as verum (Padycare ®, consisting of micromesh material, 82% polyamide, 18% Lycra, with woven silver filaments with a silver content of 20% in total) as all in one suits for children and long-sleeved and long-legged clothes for adults (n = 37) vs placebo (textiles made of pure cotton of equal size) (n = 31) Participants were instructed to wear the study clothes daily directly on the skin over a two-week period. It was recommended to wear them during the day like underwear and at night like a pyjama. Washing and cleaning behaviours were continued as usual. The textiles could only be washed at 30°C. Category: therapeutic textile Topical steroids: as needed
Outcomes	1. SCORAD at week 1 and 2 2. Functionality and wearing comfort at week 1 and 2 by self-report questionnaire 3. Daily self-reported pruritus intensity during day and night 4. Daily self-reported sleep loss and frequency of waking up 5. Daily self-reported wearing comfort of the study textiles during day and night 6. Symptoms recorded on a 10-point scale 7. Additional topical or systemic treatments (except emollients) 8. Side effects 9. German Instrument for the Assessment of Quality of Life in Skin Diseases at week 1 and 2
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Although stated to be "double blind", the fact that some participants were reported to have dropped out "due to ... assignment to the placebo group" implied that participants knew which study textiles they were wearing.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Participants were not allowed to wear study textiles during their consultation, so investigator didn't recognise them, however it was likely that participants knew which study textiles they were wearing.
Incomplete outcome data (attrition bias) All outcomes	High risk	11 dropouts (16.2%), of which nine were from the placebo group
Selective reporting (reporting bias)	High risk	Functionality and wearing comfort only reported at 7 days; selective reporting of results from the questionnaires; the conclusions and abstract empha-

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gauger 2006 *(Continued)*

		sised the significant (but not randomised) difference within the silver group over time and not the non-significant difference from placebo.
Other bias	Unclear risk	Well-balanced at baseline for severity (SCORAD) but presence of *S. aureus* not reported

Gong 2006

Methods	Design: parallel group Total study duration: 10 months
Participants	Setting: secondary care, four centres, China Incl: atopic dermatitis (Hanifin and Rajka criteria) or eczema (results for atopic dermatitis reported separately) Excl: severe fungal infection, other skin diseases which might disturb the diagnosis and treatment, other severe systemic infection, pregnancy, lactation, diseases affecting immune function e.g. diabetes mellitus, AIDS, autoimmune disease, tumours, and severe heart, liver, kidney, mental diseases, treatment with systemic corticosteroids, immunosuppressive agents last four weeks, allergy to drugs in the study, or in another study in the last four weeks Age (all recruited participants): range 2 to 65 Sex (all recruited participants): 177 males, 150 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 60% Randomised: 337 total Evaluable: 119 with atopic dermatitis (of 327 total)
Interventions	Hydrocortisone butyrate ointment and mupirocin ointment (n = 58) vs hydrocortisone butyrate ointment and vehicle ointment (n = 61) applied once daily (with 2 to 3 hours between products) for 28 days Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. EASI (Eczema Area and Severity Index) score at day 7, 14, 28 2. Bacterial cultures from most severe lesion and non-lesional skin at day 7, 14, 28 3. Assessment of therapeutic effect at day 28 scored as excellent, good, fair, poor 4. Improvement in symptoms and signs at day 7, 14, 28
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gong 2006 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Precautions being taken to preserve the 'blinding' of both patients and observers. All drugs were packaged to maintain randomisation and blinding. Mupirocin ointment and vehicle were identical in appearance and packaging." Comment: blinding was ensured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Precautions being taken to preserve the 'blinding' of both patients and observers. All drugs were packaged to maintain randomisation and blinding. Mupirocin ointment and vehicle were identical in appearance and packaging." Comment: blinding of outcome assessment was achieved.
Incomplete outcome data (attrition bias) All outcomes	High risk	10 dropouts. Reported analyses appearrf to be per protocol only.
Selective reporting (reporting bias)	High risk	Assessment of therapeutic effect only reported at day 28, whereas it was probably measured at day 7 and 14 as well. Positive rates of bacteria only reported at day 7, but measured at day 14 and 28 as well.
Other bias	High risk	Performed subgroup analysis at end of study which were not part of the predetermined outcomes. Well-balanced at baseline for severity (EASI) but presence of *S. aureus* not reported by treatment group

Gonzalez 2016

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, three centres, US Incl: moderate-severe atopic dermatitis (modified Hanifin and Rajka criteria (Eichenfield 2003)), age 3 months to 5 years Excl: concurrent inflammatory skin disorders, currently using or had used systemic/topical antibiotics, corticosteroids or calcineurin inhibitors for atopic dermatitis in the prior 2 weeks, overt infection Age: intervention group: mean 22 months (range 4.5-60), control group: mean 5.4 months (range 3-14) Sex: intervention group: 4 males, 5 females, control group: 7 males, 2 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 57% Randomised: 21 Evaluable: 18
Interventions	Bleach bath (bottle of bleach to be diluted with bath water 2 x /week to achieve a 0.005% sodium hypochlorite concentration) plus topical corticosteroid (n = 10) vs placebo (bottle of water) plus topical corticosteroid (n = 11) Category: antibacterial bath additive Topical steroids: all participants

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gonzalez 2016 *(Continued)*

Outcomes	1. Bacterial densities by high throughput DNA sequencing and quantitative PCR for total bacteria, *Streptococcus*, *Staphylococcus*, *S. aureus*, *Corynebacterium*, *Propionibacterium* (all outcomes reported at week 0 and week 4) Bacterial diversity scores Microbial community composition Relative abundance of major phyla Area under the curve plots of differentiating taxa and differentiating genera with more than 1% abundance All participants with atopic dermatitis had 4 clinical sites swabbed including the worst affected area, i.e. the lesion with the highest local EASI score, a non-lesional site and 2 other representative lesional sites. 2. IGA 3. Total EASI 4. Local EASI at worst lesion 5. Patient-reported treatment use
Funding	"Dr Gonzalez was supported in part by a gift from the Bohnert Foundation"..."Supported in part by UH2 AR057506 and New York University Clinical and Translational Science Awards grant UL1 TR000038 from the National Institutes of Health, and by the Diane Belfer Program in Human Microbial Ecology, and C&D Research Fund."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Treatment randomisation was done by 2 independent nonclinical staff members. One person made 12 sealed envelopes containing the word "bleach" and 12 identical sealed envelopes containing the word "water," which were then shuffled and numbered sequentially. The envelopes were opened in number order and plain white bottles were filled with the corresponding ingredient, bleach or water, and then labelled with the corresponding number." Comment: randomisation method was described and unlikely to introduce selection bias.
Allocation concealment (selection bias)	Low risk	Quote: "Treatment randomisation was done by 2 independent nonclinical staff members. One person made 12 sealed envelopes containing the word "bleach" and 12 identical sealed envelopes containing the word "water," which were then shuffled and numbered sequentially. The envelopes were opened in number order and plain white bottles were filled with the corresponding ingredient, bleach or water, and then labelled with the corresponding number." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Bleach and water were put into plain white sequentially numbered bottles, however it is likely that the participants would have smelled the bleach.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Gonzalez 2016 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Investigators, data analysts, and sequencers were blinded to treatment until unblinding was necessary for comparative data analysis after the experiment ended." Comment: Low risk for objective microbiological assessments; Unclear for IGA and EASI scores as participants would have known which treatment they received.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	3 out of 21 participants with atopic dermatitis didn't complete the study because they moved out of the state or did not return for examination. When contacted, parents of all 3 of these participants reported improvement of their child's eczema.
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	High risk	Groups were well-balanced at baseline for colonisation density of *S. aureus* but there was some imbalance in severity (mean EASI: bleach bath group 18.2, control group 23.6)

Harper 1995

Methods	Design: cross-over Total study duration: not stated
Participants	Setting: secondary care, single centre, UK Incl: atopic eczema displaying features of recurrent infection and/or frequent exacerbations, attending paediatric dermatology clinic, > six months old Excl: systemic or topical antibiotics or systemic steroids within two weeks of study Age: mean 4.5 years (range 1 to 9) Sex: 9 males, 17 females Duration of condition: 19 participants onset at age < 1 year Infective status: mixed *S. aureus* colonisation: not stated Randomised: 30 Evaluable: 26
Interventions	Oilatum Plus vs Oilatum 15 mL in an 8-inch bath of water, soak for 10 to 15 minutes daily for 4 weeks Category: antibacterial bath additive Topical steroids: as needed
Outcomes	1. Area affected, severity of signs and symptoms and total score (based on Costa 1989) at weeks 2 and 4 2. Global Impression Scale (not ill at all, borderline ill, mildly ill, moderately ill, severely ill, extremely ill) at weeks 2 and 4 3. Global Change Scale (much worse, minimally worse, no change, minimally improved, much improved, very much improved) at weeks 2 and 4 4. Daily rating of skin condition by parents on a scale from 0-3 (0 = clear, 3 = severe) 5. AEs
Funding	Not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Harper 1995 *(Continued)*

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The order in which the 2 preparations were used was determined by a computer generated random code." Comment: randomisation method was sufficient.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: but no further information given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: but no further information given
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Four participants dropped out: two for unrelated reasons, one side effect of Oilatum plus and one because of deterioration of eczema while using the Oilatum emollient. Three participants did not adhere to the washout period, so "the data generated during the second treatment phase by the patient with no washout was excluded from the analysis."
Selective reporting (reporting bias)	High risk	Subjective outcomes only reported as 'not significant' and results not shown.
Other bias	High risk	Statistical comparisons only reported as significant differences from baseline and not between groups. Baseline severity and presence of *S. aureus* not reported

Hizawa 1998

Methods	Design: within-patient study (left/right comparison) Total study duration: unknown
Participants	Setting: secondary care, single centre, Japan Incl: mild to moderate atopic dermatitis with similar eczema in bilateral elbow fossae Excl: Skin infection showing pus on exudate Age: 12 to 29 Sex: 3 males, 12 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: Randomised: 15 Evaluable: 15
Interventions	Povidone iodine 10% vs unspecified placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hizawa 1998 *(Continued)*

	Applied twice daily for one week Category: topical antiseptic/antibiotic Topical steroids: not stated
Outcomes	1. Physicians' and patients' assessments of symptoms rated on visual analogue scale (0-100) 2. Patients' assessment of itch rated on visual analogue scale (0-100) 3. Colony counts of *S. aureus* from elbow lesions
Funding	Unknown
Notes	Paper kindly reviewed by Dr Yukihiro Ohya and risk of bias kindly completed by Prof Masaki Futamura

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Drawing lots" Comment: no further information given
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	The intervention treatment was applied on participant's right or left side, and no treatment on the opposite side. Participants would know the intervention side.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All five dermatologists who assessed did not know allocation.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Doctor evaluation was analysed with the data from 15 participants (all participants). However patient evaluation was analysed with data from 13 participants. Authors did not mention it, but was shown on a figure.
Selective reporting (reporting bias)	Unclear risk	Trial not prospectively registered
Other bias	High risk	Statistical comparisons only reported as significant differences from baseline within groups and not between groups. Groups appeared balanced at baseline for severity (VAS) and colonisation density of *S. aureus* on graphical presentation.

Hjorth 1985

Methods	Design: within-patient study (left/right comparison) Total study duration: not stated
Participants	Setting: secondary care, three centres, Denmark Incl: patients presenting to a dermatology clinic with fairly symmetrically located, steroid-responding dermatoses (results for atopic dermatitis reported separately) Excl: age < 2 years, pregnancy Age (all recruited participants): 26 children, median 9 years (range 1-15), and 55 adults, median age 23 years (range 16-78)

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hjorth 1985 *(Continued)*

	Sex (all recruited participants): 26 males, 55 females Duration of condition: not reported Infective status: not stated *S. aureus* colonisation: not stated Randomised: 60 with atopic dermatitis (of 81 total) Evaluable: 60
Interventions	0.1% betamethasone 17-valerate (Betnovate) plus 2% microcrystalline fusidic acid (Fucibet) vs 0.1% betamethasone 17-valerate Applied twice daily for seven days Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Global degree of improvement (cleared, improved, unchanged, worse) at 1 week 2. Change from baseline in symptom score at 1 week 3. Investigator preference for treatment at 1 week 4. AEs 5. Sensitivity to fusidic acid 6. Isolation rate of *S. aureus* Only investigator preference reported separately for atopic dermatitis
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The test preparations were supplied in tubes of identically looking cream containing either 0.1% betamethasone 17-valerate or a combination of this with 2% microcrystalline fusidic acid". Comment: low risk of performance bias
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: unclear who was blinded and how it was achieved
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts
Selective reporting (reporting bias)	High risk	Only P values shown for clinical scores, no details given

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hjorth 1985 *(Continued)*

Other bias	Low risk	Well-balanced at baseline for severity (symptom score) and presence of *S. aureus*

Holland 1995

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, UK Incl: moderate or severe atopic eczema with *S. aureus* present on skin Excl: use of bath emollients, antiseptic bath additives or medicated soaps in past 2 weeks, systemic or topical antibacterials or oral steroids in past month Age: mean 17.3 years (range 4-34) Sex: 6 males, 9 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 100% Randomised: 15 Evaluable: 15
Interventions	Oilatum Plus (containing triclosan and benzalkonium chloride) (n = 7) vs Oilatum (n = 8) 15 mL in 8 inches of water from 10 to15 min soak daily for 4 weeks Category: antibacterial bath additive Topical steroids: not stated
Outcomes	1. Clinical score from summation of symptom score and area of lesions (based on Staughton 1984) 2. Colonisation density of *Micrococcaceae* and *S. aureus* (William & Kligman scrub method) on non-lesional and lesional skin
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: unclear who was blinded and how it was achieved
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: unclear who was blinded and how it was achieved

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Holland 1995 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "those patients receiving Oilatum Emollient decreased from eight to five and eight to three on the third and fourth visits, possibly indicating their dissatisfaction with the treatment. This did not occur with patients receiving the more effective Oilatum Plus treatment." Comment: high attrition rates
Selective reporting (reporting bias)	High risk	Results for clinical score only reported as P values
Other bias	Low risk	Well-balanced at baseline for severity (non-standard clinical score) and colonisation density of *S. aureus*

Hon 2016

Methods	Design: cross-over Total study duration: 24 months
Participants	Setting: secondary care, single centre, Hong Kong Incl: atopic dermatitis (Hanifin and Rajka criteria), moderate-severe (by SCORAD), previous *S. aureus* colonisation Excl: current or recent use (within past 4 weeks) of oral antibiotics, intercurrent illness for two weeks prior to study, coexisting skin diseases Age: mean 12.1 years (range 4-18) Sex: 23 males, 17 females Duration of condition: not stated Infective status: unspecified *S. aureus* colonisation: 90% Randomised: 40 Evaluable: 40
Interventions	Bleach bath (0.005% sodium hypochlorite) vs placebo (water). Participants were instructed to bathe for 10 minutes 2-3 times per week. Four weeks treatment period, four weeks washout, four weeks cross-over treatment Category: antibacterial bath additive Topical steroids: rescue medication only
Outcomes	1. Change from baseline in presence of *S. aureus* at right antecubital fossa and most severely infected or eczematous lesion at end of each treatment period 2. Change from baseline in SCORAD and objective SCORAD at end of each treatment period 3. *S. aureus* antimicrobial resistance patterns 4. Change from baseline in skin hydration and TEWL at end of each treatment period 5. Change from baseline in blood markers (white blood cell, eosinophil, total IgE and specific IgE against staphylococcal enterotoxin A and staphylococcal enterotoxin B) at end of each treatment period 6. Change from baseline in topical steroid usage during each treatment period 7. Change from baseline in Children Dermatology Life Quality Index (CDLQI) at end of each treatment period

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hon 2016 *(Continued)*

	8. Global acceptability of treatment 9. AEs
Funding	The Chinese University of Hong Kong
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were assigned randomly through computerized randomisation (sealed envelope using numbers) generated by a research staff (not involved in the clinical management and patient assessment), to the treatment or placebo study arm". Comment: method was unlikely to introduce selection bias.
Allocation concealment (selection bias)	Low risk	Quote: "Patients were assigned randomly through computerized randomisation (sealed envelope using numbers) generated by a research staff (not involved in the clinical management and patient assessment), to the treatment or placebo study arm". Comment: likely that allocation was concealed
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Bleach and water with patient identification numbers were dispensed in identical opaque bottles with the same brand-name labels. Investigators were blinded to the contents of the bottles. Dispensing of these items sequentially, according to patient identification numbers will be performed by a research assistant in a separate room from the principal investigator who assesses the patients. Neither patients nor clinicians knew the patients' assigned study arm. These bottles were brown plastic bottles and the selected dilution was pretested by the pharmacist so that the colour and odour was similar. However, patients and/or family members might differentiate the pure bleach container from the water container on the basis of odour and were instructed at the beginning not to disclose their suspicions to the investigators. Bathing in the dilute bleach baths was not associated with any odour of bleach, and investigators were not able to distinguish study arms during examinations." Comment: blinding was achieved.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	As above, blinding was achieved.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant did not complete global acceptability of treatment. Blood markers only available for 19/40 participants, but not an outcome of this review
Selective reporting (reporting bias)	High risk	Colony counts and resistance only reported as non-significant. All other outcomes reported in full
Other bias	Low risk	Well-balanced at baseline for severity (SCORAD) and presence of *S. aureus*

Huang 2009

Methods	Design: parallel group

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Huang 2009 *(Continued)*

	Total study duration: 24 months
Participants	Setting: secondary care, single centre, US Incl: moderate-severe atopic dermatitis as determined with the IGA, signs of bacterial skin infection (weeping, crusting and/or pustules) Excl: current/recent use/within the past 8 weeks of topical or oral antibiotic preparations and allergy to cephalosporins or mupirocin Age: intervention group: mean 8.0 years (range 2.1-17.3), control group: mean 6.3 years (range 0.7-15.7) Sex: intervention group: 7 males, 8 females, control group: 8 males, 8 females Duration of condition: not stated Infective status: clinically infected *S. aureus* colonisation: 87% Randomised: 31 Evaluable: 25
Interventions	Bleach and mupirocin (n = 15) vs water and placebo ointment (n = 16). 0.5 cup of 6% bleach (final concentration 0.005%) or water in a full bathtub (40 gallons) of water. Amount of administered bleach solution/water adjusted by the family on the basis of the bath tub size and estimated height of bath tub water. Participants were instructed to bathe in the dilute bleach bath or placebo for 5-10 minutes twice weekly. Participants and their household members were instructed to apply mupirocin ointment (Centany (OrthoNeutrogena, Skillman, NJ)) (treatment group) or petrolatum (control group) intranasally for twice daily for five consecutive days of each month. Continued for 3 months Category: antibacterial bath additive plus antibiotic Topical steroids: as needed
Outcomes	1. EASI at 1 and 3 months 2. Proportion of BSA affected at 1 and 3 months 3. IGA score (clear = 0, almost clear = 1, mild = 2, moderate = 3, severe = 4, very severe = 5) at 1 month and 3 months 4. Before intervention qualitative bacterial cultures of the nares and the worst overtly infected lesions were obtained. At 1-3 months after initiation of treatment, swabs of the nares and the most severely infected eczematous lesions were obtained again. Antibiotic discs tested resistance to amoxicillin, amoxicillin-clavulanate, oxacillin, cephalosporin, trimethoprim-sulphamethoxazole, erythromycin, clarithromycin, mupirocin. 5. AEs
Funding	Society for Pediatric Dermatology; Centany ointment, placebo ointment and partial funding for bacterial cultures were provided by OrthoNeutrogena.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were assigned randomly, through block randomisation generated by the statistician, to the treatment or placebo study arm."

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Huang 2009 *(Continued)*

		Comment: randomisation method unlikely to introduce selection bias.
Allocation concealment (selection bias)	Low risk	Quote: "Investigators were blinded to the contents of the bottles and jars and dispensed these items sequentially, according to patient identification numbers." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Mupirocin and petrolatum ointment were dispensed in identical white jars, labelled with the patient identification numbers... Bleach and water with patient identification numbers were dispensed in identical bleach bottles with the same brand name labels... Neither patients nor clinicians knew the patients' assigned study arm. However, patients and/or family members were able to differentiate the pure bleach container from the water container on the basis of odor and were instructed at the beginning not to disclose their suspicions to the investigators." Comment: unlikely that blinding was achieved
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "patients and/or family members were able to differentiate the pure bleach container from the water container on the basis of odor and were instructed at the beginning not to disclose their suspicions to the investigators. Bathing in the dilute bleach baths was not associated with an odor of bleach, and investigators were not able to distinguish study arms during examinations." Comment: unclear if blinding of outcome assessment was achieved
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT analysis, but six participants in treatment group and three in placebo group either lost to follow-up or withdrew consent
Selective reporting (reporting bias)	High risk	Primary outcome measures in trial registration changed following completion of the trial.
Other bias	High risk	Groups were well-balanced at baseline for presence of *S. aureus* but there was some imbalance in severity (mean EASI: intervention group 22.1, control group 16.6).

Hung 2007

Methods	Design: parallel group (2 x 2 factorial) Total study duration: 1 year
Participants	Setting: secondary care, single centre, Taiwan Incl: atopic dermatitis (Hanifin and Rajka criteria), moderate to severe at the time of entry (Rajka and Langeland criteria) Excl: systemic or topical antibiotics, systemic or topical steroid use within 4 weeks, overt secondary infection requiring oral antibiotic treatment Age: steroid group: mean 17.4 years, steroid + fusidic acid group: mean 12.9 years, tacrolimus group: mean 15.4 years, tacrolimus + fusidic acid: mean 16.9 years Sex: steroid group: 4 males, 11 females, steroid + fusidic acid group: 8 males, 7 females, tacrolimus group: 8 males, 7 females, tacrolimus + fusidic acid group: 6 males, 9 females

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hung 2007 *(Continued)*

	Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 75% Randomised: 60 Evaluable: 54
Interventions	0.05% fluticasone propionate cream (Cutivate) (n = 15) vs 0.05% fluticasone propionate cream with 2% fusidic acid cream (Fucidin) (n = 15) vs 0.03% tacrolimus ointment (Protopic) (n = 15) vs 0.03% tacrolimus ointment with 2% fusidic acid cream (n = 15) applied twice daily for 8 weeks. Fusidic acid cream was applied first followed by fluticasone or tacrolimus 20 minutes later without occlusive dressings. Oral antihistamine was given to all participants. Categories: topical steroid plus antibiotic (steroid plus fusidic acid vs steroid) and topical calcineurin inhibitor plus antibiotic (tacrolimus plus fusidic acid vs tacrolimus) Topical steroids: all participants (steroid plus fusidic acid vs steroid)/none (tacrolimus plus fusidic acid vs tacrolimus)
Outcomes	1. SCORAD at 2 and 8 weeks 2. Local clinical severity of atopic dermatitis at 2 and 8 weeks, evaluated using modified local SCORAD of 6 intensity items (1. erythema/darkening, 2. oedema/papulation, 3. oozing/crusts, 4. excoriation, 5. lichenification/prurigo and 6. local dryness) graded on a 4 point scale (0 = absent, 1 = mild, 2 = moderate, 3 = severe) to give a total score from 0-18 3. Proportion of BSA affected at 2 and 8 weeks 4. Pruritus and sleep loss score at 2 and 8 weeks 5. *S. aureus* colonisation from most severe lesion at enrolment at 2 and 8 weeks (presence/absence and colonisation density) 6. Antibiotic resistance
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Clinical assessment not blinded so high risk, but bacteriology studies blinded so low risk - hence unclear overall

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hung 2007 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	54/60 participants completed the study; two participants receiving tacrolimus with fusidic acid dropped out of the treatment protocol because of intolerance to a burning sensation. Two participants receiving tacrolimus only and another two receiving fluticasone only dropped out of the treatment protocol because of poor compliance, but we did not know the reason for poor compliance.
Selective reporting (reporting bias)	High risk	Local SCORAD only reported at baseline
Other bias	Low risk	Well-balanced at baseline for severity (SCORAD) and presence and colonisation density of *S. aureus*

Juenger 2006

Methods	Design: parallel group Total study duration: 8 months
Participants	Setting: single centre, Germany Incl: "acute" atopic dermatitis, age > 2 years Excl: acute viral infection, acute "staphyloderma", other skin disease that could influence evaluation, UV treatment, topical or systemic immunosuppressive or immunomodulating treatment, topical or systemic antibiotics, severe generalised disease, pregnancy, female not on contraception, allergy to silver Age: silver textile group: median 21 years, silver-free textile group: median 25.5 years Sex: silver textile group: 6 males, 4 females, silver-free textile group: 3 males, 7 females Duration of condition: silver textile group: 20.5 years, silver-free textile group: 25.5 years Infective status: uninfected *S. aureus* colonisation: not stated Randomised: 30 Evaluable: 30
Interventions	Long-sleeved undershirt and long underpants with silver thread (n = 10) vs identical garment with polyester thread (n = 10) vs prednicarbate 0.25% ointment (n = 10) for 14 days (only comparison of silver textile versus silver-free textile eligible for this review) Category: therapeutic textile Topical steroids: as needed
Outcomes	1. Patient/carer global rating of "overall disease control" at day 14 on scale from 0 (controlled) to 3 (not controlled) 2. Change from baseline SCORAD at day 3, 7, 14 3. Patient/carer rating of severity of pruritus at day 3, 7, 14 on scale from 0 (no itching/scratching) to 3 (bothersome itching/scratching that interfered with sleep) 3. Colonisation density of bacteria at day 14 4. AEs (patient/carer-reported)
Funding	Julius Zorn GmbH
Notes	Participants were allowed to use as much prednicarbate ointment as they wished; those in the silver textile group used almost as much as those in the prednicarbate group whereas those in the non-silver group barely used any.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Juenger 2006 *(Continued)*

	Did not provide adequate data for primary outcomes for this review. Outcomes beyond 14 days not included as participants in all three groups wore silver textile garments from day 15-28

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The 30 study patients were assigned to one of three groups on the basis of a randomisation list...generated by an independent biometrician before recruiting". Comment: low risk of selection bias
Allocation concealment (selection bias)	Unclear risk	Closed envelopes, but not stated to be sequentially numbered or opaque
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Silver and silver-free garments (each set consisting of one long-armed undershirt and one pair of long underpants) were identical with respect to appearance and wearing comfort." Comment: Silver and silver-free garments were similar, however the steroid group had no garment and there was no indication that clinicians were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Patient-reported - high, microbiological - low, SCORAD (primary) - unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "All patients randomised and enrolled in the study completed the entire course of the study; there were no drop outs." Comment: low risk of attrition bias due to no dropouts
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	High risk	Large baseline imbalance in severity (mean SCORAD: silver textile group 72.7, silver-free textile group 54.5), presence of *S. aureus* not reported

Koller 2007

Methods	Design: within-patient study (left/right comparison) Total study duration: 3 months
Participants	Design: secondary care, single centre, Austria Incl: children with mild to moderate atopic dermatitis (Hanifin and Rajka criteria) Excl: topical or systemic anti-inflammatory agents Age: mean 8.1 years (range 5-12) Sex: 11 males, 11 females Duration of condition: not stated Infective status: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Koller 2007 *(Continued)*

	S. aureus colonisation: not stated Randomised: 22 Evaluable: 22
Interventions	Dermasilk® (sericin-free silk treated with AEGIS AEM5772/5) for 12 weeks vs simple silk fabric (sericin-free silk without AEGIS AEM5772/5) for 2 weeks followed by cotton for 10 weeks Participants received 3 different 'arm tubes'. "For the first 2 wk of the study, parents were advised to dress one arm of their children with simple silk fabric and the other one with the Dermasilk® fabric. After 2 wk - throughout the rest of the study - one arm had to be covered with the cotton and the other with the Dermasilk® tube." Category: therapeutic textile Topical steroids: none
Outcomes	1. Intensity score and subjective symptom score from SCORAD at week 2, 4, 8, 12
Funding	Menzl GesmbH provided cotton, silk and Dermasilk®.
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomised by age group and by disease severity." Comment: randomisation method was not described.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	No indication that parents or investigators were blinded, other than for outcome assessment
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "The investigator performing the clinical examination did not know which arm had been covered by Dermasilk®. Clinical evaluations were carried out by the same medical blinded doctor." Comment: Intensity score was at low risk but subjective symptom score was at high risk.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for severity (SCORAD intensity and subjective scores) but presence of *S. aureus* not reported

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Korting 1994

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, six centres, Germany Incl: atopic eczema suggestive of heavy *S. aureus* colonisation with > 10^6 CFU/cm^2 Excl: age < 12 (though < 18 subsequently excluded from analysis), infection requiring antibiotics, other severe disease, pregnant, antibiotics last 48 h Age: not stated Sex: 54 males, 89 females (not reported for final 117 eligible participants) Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 100% Randomised: unclear (180 "enrolled and diagnosed as cases of atopic eczema" but implied not all of these met inclusion criteria and 143 "recruited") Evaluable: unclear (numbers included varied from 81 to 114 across outcome measures; 26 randomised participants appeared to have been excluded - 18 that did not meet the microbiological inclusion criterion and eight aged less than 18 years)
Interventions	Prednicarbate 0.25% cream plus didecyldimethylammonium chloride 0.25% vs prednicarbate 0.25% cream applied twice daily for 5 days Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Clinician assessments of efficacy, aesthetic acceptability and tolerability at day 6 (ratings were made on a scale from 1 = excellent to 4 = poor, but results reported only as % "efficacious" with no indication of cut-point used) 2. Clinical score (10 clinical parameters rated from 1 = none to 5 = very severe) at day 6, 20, 34 3. Colonisation density of *S. aureus* at day 6 and 34 and number exceeding 10^6 CFU/cm^2 4. Presence of *S. aureus* at initially lesional site at day 6 and 34 (Williamson & Kligman method) 5. AEs
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind" identical preparation. "The preparations were supplied in a blind coded fashion." Comment: blinding was likely to have been successful.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Korting 1994 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	High risk	Very large number of post-randomisation exclusions/loss to follow-up. Reasons not reported by treatment group
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	High risk	Inclusion criteria changed after recruitment to exclude participants aged < 18 years. Well-balanced at baseline for severity (non-standard clinical score) and presence of *S. aureus*.

Leins 2013

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, Australia Incl: Patients aged between 6 months and 18 years with moderate to severe atopic eczema (SCORAD > 25) at time of randomisation Excl: not stated Age: not stated Sex: not stated Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Randomised: 19 Evaluable: 19
Interventions	Bleach bath (sodium hypochlorite 0.005%) three times per week vs bath emollient (bath oil containing liquid paraffin 95% volume per volume). All participants received a course of oral antibiotics. Category: antibacterial bath additive Topical steroids: not stated
Outcomes	1. SCORAD at 4 and 12 weeks 2. eradication of *S. aureus* at 4 and 12 weeks 3. use of systemic antibiotics at 4 and 12 weeks 4. tolerability of bleach baths at 4 and 12 weeks
Funding	Royal Children's Hospital, Melbourne

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Leins 2013 *(Continued)*

Notes	Only published as abstract. Copy of conference poster obtained from corresponding author

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No information provided in conference poster
Allocation concealment (selection bias)	Low risk	Sequentially numbers, sealed, opaque envelopes (trial registration)
Blinding of participants and personnel (performance bias) All outcomes	High risk	'Single blinded'
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Eczema severity was measured using the SCORAD index by a dermatology nurse blinded to the participant's treatment". No patient-reported outcomes were included.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Conference poster was based on 19 participants that completed follow-up. It was unclear whether these were all the participants randomised. The trial registration indicated a total sample size of 74 participants. Correspondence with the author indicated that the conference poster reported 'pilot data'.
Selective reporting (reporting bias)	Unclear risk	Only results from the 12-week follow-up were reported. The trial registration indicated additional follow-up at 24 weeks.
Other bias	High risk	Baseline imbalance in severity (mean SCORAD 39 vs 47)

Lembo 2011

Methods	Design: cross-over Total study duration: not stated
Participants	Setting: secondary care, single centre, Italy Incl: children with atopic dermatitis (Hanifin and Rajka criteria) Excl: systemic treatment in the previous 2 weeks, presence of malignancy, presence or recurrence of skin infection or other dermatoses/inability to cooperate Age: mean 4.2 years (range 6 months-14 years) Sex: 24 males, 14 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 100% Randomised: 38 Evaluable: 19

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Lembo 2011 *(Continued)*

Interventions	During the first week: no use of topical or systemic drug; then from day 8 onwards: intervention 1% erythromycin (Sigma-Aldrich S.r.l., Milano) in white Vaseline on whole skin surface twice daily from day 8 to day 21 and Vaseline from day 22 to 35 vs Vaseline from day 8 to 21 on whole skin surface twice daily and erythromycin from day 22 to 35 Category: topical antiseptic/antibiotic Topical steroids: none
Outcomes	1. SCORAD at day 8, 21, 35 2. Bacterial colonisation of lesional/non-lesional skin by culture at day 35 3. Safety and tolerability: all participants patch tested at the beginning and end
Funding	Not stated
Notes	Dr Nadia Terrazzini assisted with data extraction.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Correspondence with authors: "This is the method we used to generate the two groups stratified for sex and age: 1. Age and sex of patients were recorded in a word excel sheet in which patients were anonymized 2. Patients were ordered by age 3. Four classes were identified by age range: I: 0.5 to 3 years II: 4 to 7 years III: 8 to 11 years IV: 12 to 14 years. 1. Two subclasses were identified by sex in each age class: male and female 2. Each subject in the sex subclass was sequentially enumerated (1…2…3…4…) 3. Pare [even] numbers were assigned to group B and spare [odd] numbers were assigned to group A." Further correspondence clarified: "I confirm that subjects were randomly distributed before enumeration." Comment: The patients were randomised into two groups stratified by sex and age: the method was unlikely to introduce selection bias.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Correspondence with authors: "Patients and SCORAD evaluator were blind." Comment: blinding was done.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Lembo 2011 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Correspondence with authors: "Patients and SCORAD evaluator were blind." Comment: blinding was done.
Incomplete outcome data (attrition bias) All outcomes	High risk	Only 50% of participants completed the study.
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for severity (SCORAD) but presence of *S. aureus* not reported by group

Lever 1988

Methods	Design: cross-over Total study duration: not stated
Participants	Setting: secondary care, single centre, UK Incl: atopic dermatitis, age > 2 years Excl: potent topical steroids, topical or systemic antibiotics during past 4 weeks Age: mupirocin/placebo group: mean 22.4 years (range 2-52), placebo/mupirocin group: mean 20.4 years (range 2 -56) Sex: mupirocin/placebo group: 12 males, 12 females, placebo/mupirocin group: 12 males, 9 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 89% Randomised: 49 Evaluable: 45
Interventions	2% mupirocin ointment followed by placebo (polyethylene glycol ointment) or vice-versa applied once daily for two weeks. All participants received 0.05% clobetasol butyrate ointment applied twice daily during the two-week pre-trial period and once daily while using mupirocin/placebo. Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Clinical severity score (six features assessed at 16 body sites on a scale of 0-3) at end of each 2-week treatment 2. Percentage BSA affected at end of each 2-week treatment period 3. Participants' subjective assessment of itch, sleep disturbance and appearance of skin on a 5-point scale (much better, better, same, worse, much worse) during each 2-week treatment period 3. Isolation rates of *S. aureus* at worst affected site and control site at end of each 2-week treatment period 4. Emergence of resistant organisms 5. AEs
Funding	Beecham Pharmaceutical Co supplied mupirocin and placebo and assisted with statistical analysis.
Notes	-

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Lever 1988 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients were randomly allocated to receive placebo first or mupirocin first". Comment: randomisation method was not described.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No mention of appearance of formulations
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Observers were blind as to the topical preparation used and the bacteriological findings". "Bacteriological results were scored blind by the same bacteriologist". Comment: blinding was done.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Four participants dropped out.
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	High risk	No washout period between treatments. Well-balanced at baseline for presence of *S. aureus* but some imbalance in severity (non-standard clinical score 69.9 versus 59.5).

Leyden 1977

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, USA Incl: unclear ("typical but rather severe atopic dermatitis") Excl: use of antibacterial soaps or receipt of antibiotic therapy in previous month Age: not stated ("mainly children") Sex: not stated Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 100% Randomised: 36 Evaluable: 36
Interventions	Fluocinolone acetonide plus 0.5% neomycin sulphate (Neo-Synalar) cream (n = 15) vs fluocinolone acetonide (Synalar) cream (n = 21) applied twice daily for one week Category: topical steroid plus antiseptic/antibiotic

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Leyden 1977 *(Continued)*

	Topical steroids: all participants
Outcomes	1. Improvement in pruritus, erythema, lichenification, oozing and crusting, scaling (scored 0-3, then graded % reduction in total score from baseline as 75% or greater = excellent, 50-75% = good, 25-50% = fair, 0-25% = poor) at 1 week 2. Change in isolation rate of *S. aureus* at 1 week 3. Change in bacterial counts of *S. aureus* at 1 week
Funding	Not stated
Notes	Two studies were reported in this paper. Only study I was included as study II did not have proper controls.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "36 patients were randomly assigned". Comment: randomisation method was not described.
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: but method not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: but method not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for
Selective reporting (reporting bias)	Unclear risk	Not all information for the different clinical parameters reported but not clear as to what extent this biased the results. No trial registration provided
Other bias	High risk	Baseline imbalance in colonisation density of *S. aureus* (mean 420,000/cm^2 versus 200,000/cm^2). Baseline severity not reported

Lopes 2015

Methods	Design: parallel group Total study duration: 7 months
Participants	Setting: secondary care, single centre, Portugal Incl: atopic dermatitis; age older than 12 years Excl: severe skin disease other than atopic dermatitis; secondary infections; major systemic diseases; women who were pregnant; subjects unable to comply with study and follow-up procedures Age: intervention group: median 23 years, control group: median 26 years Sex: intervention group: 20 males, 23 females, control group: 14 males, 21 females Duration of condition: intervention group: median 18 years, control group: median 12 years

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Lopes 2015 *(Continued)*

	Infective status: uninfected *S. aureus* colonisation: 61% Randomised: 78 Evaluable: 69
Interventions	Cotton pyjamas coated with chitosan (ChitoClear CG-800) (n = 43) vs uncoated cotton pyjamas (n = 35). Pyjamas consisted of long-sleeved top and long pants to be worn at night for the duration of the study (2-week run-in period and 8-week intervention period) Category: therapeutic textile Topical steroids: rescue medication only
Outcomes	1. Mean relative and absolute change in SCORAD at 8 weeks 2. Number of participants with a minimal clinically important difference in SCORAD at 8 weeks 3. Mean change in DLQI (or CDLQI if aged less than 16 years) at 8 weeks 4. Changes in daily pruritus and sleep loss scores at 8 weeks 5. Need for rescue medication 6. Number of flares 7. Number of totally controlled weeks and well controlled weeks 8. Number and severity of AEs 9. Mean change in CFU of total staphylococci and *S. aureus* at 8 weeks
Funding	None
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Subjects were randomly assigned ... through computer-generated random numbers." Comment: randomisation method unlikely to introduce selection bias
Allocation concealment (selection bias)	Low risk	Quote: "The randomisation was performed by an independent researcher; the randomisation table and intervention codes were kept by the independent researcher in an opaque sealed envelope up to completion of data analysis. A study nurse established phone contact with the independent researcher, who informed the nurse which treatment package was to be assigned to which patient." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Both pyjamas were made of 100% organic cotton, without dyes or preservatives and were visually indistinguishable from each other." Comment: blinding likely achieved
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No indication that blinding was inadequate

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Lopes 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Approx 10% were lost to follow-up, reasons were unclear.
Selective reporting (reporting bias)	High risk	The trial registration listed a number of immunological serum markers that were not reported. Quality of life was a co-primary outcome in the trial registration but listed as a secondary outcome in the paper. Additional outcomes of totally controlled weeks and well-controlled weeks were included in the paper but not in the trial registration.
Other bias	Low risk	Reasonably well-balanced at baseline for severity (SCORAD) and presence of *S. aureus*

Masako 2005b

Methods	Design: within-patient study (left/right comparison) Total study duration: not stated
Participants	Setting: single centre, Japan Incl: volunteers with atopic dermatitis of mild to moderate severity on their arms Excl: none stated Age: mean 29.8 years Sex: 7 males, 10 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Randomised: 17 Evaluable: 17
Interventions	FX cream (0.2% farnesol + 5% xylitol) vs placebo cream (identical in appearance) for 7 days. Frequency not stated Category: topical antiseptic/antibiotic Topical steroids: not stated
Outcomes	1. Scores of dryness, scaling, excoriation, redness and papules at day 7 (scoring system not described) 2. Colonisation density of *S. aureus* (stamp bottle method) and ratio of *S. aureus* to total number of aerobic skin microflora at day 7 3. TEWL and skin conductance at day 7
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Masako 2005b *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "no difference between [FX cream and placebo cream] in colour or texture" Comment: blinding likely achieved
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Evaluation of skin microflora was performed by a single biologist who was blinded to care allocation". Comment: outcome assessment was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for
Selective reporting (reporting bias)	High risk	Incomplete reporting of clinical outcomes (dryness and scaling reported as significance only; excoriation, redness and papules not reported)
Other bias	Unclear risk	Well-balanced at baseline for colonisation density of *S. aureus*, but baseline severity not reported

Nilsson 1992

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, Sweden Incl: moderate-severe atopic dermatitis (Hanifin and Rajka criteria) Excl: topical or oral antibiotics or topical corticosteroids in previous 2 weeks, skin infection requiring oral antibiotics Age (for all participants, including 40 with mild-moderate atopic dermatitis): median 13 years (range 2-58) Sex (for all participants): 30 males, 40 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 93% Randomised: 30 Evaluable: 28
Interventions	Betamethasone plus neomycin cream applied to all affected areas except face twice daily for one week then once daily for one week (n = 15 evaluable) vs clobetasol cream applied twice daily on days 1, 2, 3, 4, 8, 9, 12 and 14 (n = 13 evaluable) Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Patients' daily subjective assessment of total severity of symptoms (0 = no symptoms to 8 = very severe symptoms)

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Nilsson 1992 *(Continued)*

	2. Severity score for most severe lesion (7 clinical features graded 0 = none, 1 = mild, 2 = moderate, 3 = severe) at 1 and 2 weeks 3. Isolation of *S. aureus* from most severe lesion at 1 and 2 weeks 4. Density of *S. aureus* from most severe lesion at 1 and 2 weeks
Funding	Not stated
Notes	A second study was also reported (clobetasone butyrate 0.05% vs alclometasone dipropionate 0.05% cream for mild-moderate atopic dermatitis), which was not eligible for the review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Allocated at random" Comment: method not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Different regimens used for steroid alone/steroid plus antibiotic combination
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated. Low for bacteriology - "all specimens... were coded and processed blindly".
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information on why four participants were "not evaluable"
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Low risk	Well-balanced at baseline for severity (non-standard clinical score) and presence and colonisation density of *S. aureus*

Polano 1960

Methods	Design: cross-over (four arms, four periods) Total study duration: not stated
Participants	Setting: secondary care, single centre, The Netherlands Incl: atopic dermatitis ("neurodermatitis") of long standing without apparent secondary infection, having failed to respond to standard treatments Excl: none stated Age: not stated Sex: not stated Duration: "long standing" Infective status: uninfected *S. aureus* colonisation: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Polano 1960 *(Continued)*

	Randomised: 24 Evaluable: 14
Interventions	Metiderm (0.5% prednisolone plus 0.5% neomycin) vs 0.5% prednisolone vs 1% hydrocortisone vs petrolatum base (used in all other ointments). Applied for one week (or until ointment was used up). Frequency not stated Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Severity score (lichenification, redness, weeping, crusting, apparent secondary infection scored from 0 = absent to 5 = maximum development) at end of each treatment
Funding	Hydrocortisone and prednisolone supplied by N.V. Organon; Metiderm was supplied by Pharbil (agent of Schering Corp).
Notes	Outcomes were pooled without giving primary data, thus not fulfilling outcome measures.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each of the 24 possible sequences was written down on a filing card. For any patient to be treated for the first time, the junior author chose a card at random." Comment: unclear if this method would introduce selection bias
Allocation concealment (selection bias)	High risk	Quote: "Each of the 24 possible sequences was written down on a filing card. For any patient to be treated for the first time, the junior author chose a card at random." Comment: method described could easily have been manipulated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Ointments dispensed in identical tubes, labels removed by junior author. No information on similarity of ointments
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Senior author was blinded to treatment and did assessments.
Incomplete outcome data (attrition bias) All outcomes	High risk	Only 14 participants completed
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	High risk	No washout between treatments. Impossible to assess balance as more combinations of treatment order than participants. Unclear whether statistical transformation to normalise data (inverse sin square root) was preplanned

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Portela Araujo 2013

Methods	Design: parallel group Total study duration: 27 months
Participants	Setting: secondary care, single centre, Portugal Incl: atopic dermatitis (Hanifin and Rajka criteria), age < 16 years, presence of active lesions Excl: presence of other skin diseases, history of hypersensitivity to silver, use of antibiotics and/or anti-inflammatories in the 2 weeks prior to, or during, the study Age: mean 7 years Sex: 11 males, 7 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Randomised: 19 Evaluable: 18
Interventions	Skintoskin textiles® (70% cotton, 20% cellulose with algae extracts, 10% silver activated algal cellulose; 6000 ppm, 0.6% silver (n = 12) vs 100% cotton (woven similarly to the trial textile (n = 7) as babygrows for babies around one year old and pyjamas and socks for older participants worn continuously for 7 days, after that only at night (until day 90) Category: therapeutic textile Topical steroids: rescue medication only
Outcomes	1. SCORAD at day 7, 90 2. Intensity of itching (0-10 on a visual analogue scale) at day 7, 90 3. Sleep disturbance (0-10 on a visual analogue scale) at day 7, 90
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The clothes were indistinguishable by look and feel". Comment: likely that blinding was achieved
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Clothes made with the fiber under study and the placebo were provided by the manufacturer and randomly distributed by a different element from that who made the clinical assessment".

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Portela Araujo 2013 *(Continued)*

		Comment: outcome assessment was blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	One participant in the treatment group didn't complete the study.
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for severity (SCORAD) but presence of *S. aureus* not reported

Ramsay 1996

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, number of centres unclear, Canada Incl: mild - moderate atopic dermatitis, amenable to treatment with topical steroid, age > 3 years Excl: systemic steroids or antibiotics, topical antibiotics or "other effective topical therapy" during past seven days Age: not stated Sex: not stated Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 36%-53% across groups Randomised: 186 Evaluable: 174 (154 completed study)
Interventions	Fusidic acid 2% plus 1% hydrocortisone cream (n = 91 evaluable) vs 1% hydrocortisone cream (n = 83 evaluable) for 2 weeks. Frequency not stated Category: topical steroids plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Severity score (erythema, scaling, oedema, discharge, crusting graded 0 = absent, 1 = mild, 2 = moderate, 3 = severe) in all participants and those with pathogens at 1 and 2 weeks 2. Extent of lesions (localised, limited or generalised) at 1 and 2 weeks 3. Patients' and investigators' assessments of overall severity (0 = nil, 1 = minimal, 2 = mild, 3 = moderately severe) at 1 and 2 weeks 4. Overall clinical response (excellent = reduction in severity score by 75% or more, good = reduction by 50-74%, fair = reduction by 25-49%, poor = reduction by < 25%) at 1 and 2 weeks 5. Treatment failure, defined as < 50% reduction in severity score by end of treatment or withdrawal due to inadequate response before 2 weeks or persistence of baseline pathogen at end of treatment 6. Sensitivity testing 7. AEs
Funding	Leo Laboratories

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Ramsay 1996 *(Continued)*

Notes	Reported two studies. Study II (comparing topical 2% fusidic acid vs 2% fusidic acid plus 1% hydrocortisone) excluded. Unclear if pathogens were *S. aureus*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double-blind" Comment: but no details given
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	High risk	174/186 participants analysed and 154 completed study. More dropouts in steroid only group
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Baseline severity and presence of *S. aureus* not reported

Schempp 2003

Methods	Design: within-patient study (left/right comparison) Total study duration: not stated
Participants	Setting: secondary care, single centre, Germany Incl: symmetrical subacute atopic dermatitis, SCORAD < 80, age 12-59 years Excl: infectious disease, severe underlying clinical disease, cancer, poor health, dependence on alcohol/drugs, pregnancy, breast feeding, other study within 4 weeks, use of oral steroids in past 2 weeks or topical steroids in past 1 week, hypersensitivity to hypericum or any of the cream ingredients, current treatment with psychotropic, anti-inflammatory, antibiotic, immunomodulatory drugs. Age: mean 30.4 years (SD 12.9) Sex: 10 males, 8 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: 94% Randomised: 21 Evaluable: 18
Interventions	Hyperforin 1.5% cream vs placebo (identical vehicle with added chromogenic substances to colour the vehicle for the purpose of blinding). Applied twice daily for four weeks Category: topical antiseptic/antibiotics

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Schempp 2003 *(Continued)*

	Topical steroids: none
Outcomes	1. Modified SCORAD (excluding subjective score) at day 7, 14, 28 2. Colonisation with *S. aureus* (number of CFU) at day 28 3. Patient-assessed tolerance and cosmetic acceptability at day 7, 14, 28 4. AEs
Funding	Lichtwer Pharma AG
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "Double blind" Comment: Low risk for participants as identical vehicle in placebo coloured to blind treatment; unclear risk for personnel
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "Double blind" Comment: but no details given
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	3/21 not included in analysis as they withdrew - in all cases there was acute episode of atopic dermatitis which led to withdrawal from the study.
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Low risk	Well-balanced at baseline for severity (SCORAD) and presence and colonisation density of *S. aureus*

Schuttelaar 2005

Methods	Design: parallel groups Total study duration: not stated
Participants	Setting: secondary care, single centre, The Netherlands Incl: atopic eczema (modified Hanifin and Rajka criteria), SCORAD 25 or more, > 18 years old Excl: clinical infection, visible pustular lesions, investigational drugs, nonsteroidal immunosuppressants, phototherapy, systemic steroids or topical/systemic antibiotics past four weeks, topical ultrapotent steroids or tar past seven days, known hypersensitivity to drug, pregnant, breast feeding Age: tetracycline + triamcinolone: mean 36.8 years, triamcinolone: mean 31.1 years Sex: tetracycline + triamcinolone: 8 males, 14 females, triamcinolone: 5 males, 17 females Duration of condition: not stated

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Schuttelaar 2005 *(Continued)*

	Infective status: uninfected *S. aureus* colonisation: 91% Randomised: 44 Evaluable: 44
Interventions	3% tetracycline + 0.1% triamcinolone acetonide in oculentum simplex FNA (n = 22) vs 0.1% triamcinolone acetonide in oculentum simplex FNA (n = 22). Applied all over body twice daily for two weeks Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Modified SCORAD (excluding subjective score) and Six Area, Six Sign Atopic Dermatitis (SASSAD) score at weeks 2, 4, 8 2. Bacteriological efficacy, defined as eradication of the pretreatment pathogen, at week 2 3. AEs
Funding	Not stated
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "computer generated in blocks of four. The list was produced and stored by the clinical trials pharmacist." Comment: randomisation method unlikely to introduce selection bias.
Allocation concealment (selection bias)	Low risk	Quote: "The list was produced and stored by the clinical trials pharmacist." Comment: allocation was concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants and assessor were blinded to group assignment during collection of data." "Colorant chinoline yellow CI 47005 (0.2%) and AZO rubine red E122 (0.000375%) were used to achieve adequate blinding by making the two ointments exactly similar in appearance." Comment: blinding was likely to have been successful.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No indication that blinding was inadequate
Incomplete outcome data (attrition bias) All outcomes	Low risk	No dropouts for primary outcome (week 2)
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Low risk	Well-balanced at baseline for severity (SCORAD and SASSAD) and presence of *S. aureus*

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Shi 2016

Methods	Design: within-patient study (left/right comparison) Total study duration: 2 years
Participants	Setting: secondary care, single centre, US Incl: atopic dermatitis Excl: none specified Age: mean 26.3 years (range 12-45) Sex: 5 males, 5 females Duration of condition: not stated Infective status: not stated *S. aureus* colonisation: not stated Randomised: 10 Evaluable: 10
Interventions	Bleach bath (sodium hypochlorite 0.005%) vs placebo (tap water). Each arm was immersed for 10 minutes. Category: antibacterial bath additive Topical steroids: none
Outcomes	1. Skin hydration at 0, 15, 30 and 60 minutes post-immersion 2. TEWL at 0, 15, 30 and 60 minutes post-immersion 3. pH at 0, 15, 30 and 60 minutes post-immersion 4. Skin discomfort including itching and burning or pain during the 10-minute immersion and throughout the post-immersion period
Funding	None
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not stated
Allocation concealment (selection bias)	Low risk	Quote: "The randomisation was performed prior to recruitment by the study coordinator, and stored in sealed envelopes that were not opened until the patient was recruited by the investigators." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Participants remained blinded to the water or dilute hypochlorite immersion." Comment: participants and investigators are likely to have been able to distinguish bleach from water by smell.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Skin hydration, TEWL and pH are objective measures.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Shi 2016 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for
Selective reporting (reporting bias)	Unclear risk	All outcomes reported but trial registration indicated a second intervention (multiple moisturisers) not reported in the paper
Other bias	Unclear risk	No comparison of severity or presence of *S. aureus* for left/right sides

Stinco 2008

Methods	Design: within-patient study (left/right comparison) Total study duration: 8 months
Participants	Setting: secondary care, single centre, Italy Incl: atopic dermatitis (Hanifin and Rajka criteria), patients presenting with eczematous lesions located on the arms and without any signs of infection Excl: acute infections, neurological or psychiatric disorders, autoimmune disease and immune defects Age: mean 14.2 years (range 3-31) Sex: 15 males, 15 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: not stated Randomised: 30 Evaluable: 26
Interventions	Tubular sleeves made from knitted fibrin silk bonded with AEGIS AEM 5772/5 (DermaSilk®) vs an identical product without the bonded AEGIS AEM 5772/5 Each participant was given 4 pairs of tubular sleeves (with seams of different colours) and parents/participants were asked to dress their arms with the sleeves all night and day, changing them once a day and washing them with a mild detergent. The parents/participants were asked to use the same colour sleeve always on the same arm and not to cross them over. Only moisturising treatment with an assigned emollient was permitted. A gentle, non-irritating skin cleanser without antiseptics/antimicrobial products was provided. Washout phases for current treatment were 1 week for topical corticosteroids/antibiotics on the body areas to be treated with the silk, 2 weeks for systemic corticosteroids/antibiotics, 1 week for topical antimycotics, 4 weeks for topical calcineurin inhibitors and 8 weeks for systemic immunosuppressant treatment other than corticosteroids, investigational agents, UV light treatment or systemic antimycotics. Category: therapeutic textile Topical steroids; none
Outcomes	1. Local SCORAD (adapted for arm only) at days 7, 14, 21, 28 2. Parent/participant assessment of pruritus measured with a VAS (between 0 and 10) at days 7, 14, 21, 28

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Stinco 2008 *(Continued)*

	3. AEs
Funding	Garments were provided by Alpretec
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The choice of which arm to dress with the red- or green-coded sleeve was randomised and labeled on the basis of a computer-generated randomization schedule". Comment: randomisation method unlikely to introduce selection bias
Allocation concealment (selection bias)	Low risk	Quote: "Each pair consisted of a sleeve with a red seam and one with a green seam. One of these colours indicated that the sleeve had been treated with AEGIS AEM 5772/5 but neither the authors, parents nor participants knew which one hade been coated. This information was known only to the manufacturer and sealed in an envelope." Comment: allocation was likely concealed.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	As above, blinding was likely to have been successful.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	As above, blinding was likely to have been successful.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Four participants withdrew from the study due to the excessive distance/other personal reasons
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for severity (local SCORAD) but presence of *S. aureus* not reported

Tan 2009

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: Secondary care, single centre, Singapore Incl: atopic dermatitis (Hanifin and Rajka criteria), mild to moderate severity (SCORAD) Excl: severe atopic dermatitis, recent hospitalisation, recent/current use of systemic antibiotics, systemic steroids, potent or very potent topical steroids or phototherapy in the past 1 month, known contact allergy to any of the ingredients, uncooperative patients and pregnant women Age: intervention group: mean 17.8 years, control group: mean 18.1 years

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Tan 2009 *(Continued)*

	Sex: intervention group: 19 males, 11 females, control group: 20 males, 10 females Duration of condition: intervention group: median 12 years, control group: median 9 years Infective status: not stated *S. aureus* colonisation: not stated Randomised: 60 Evaluable: 60
Interventions	Emollient containing 1% triclosan (n = 30) vs vehicle alone (n = 30) applied twice daily to whole body for 27 days. Washout period of one week. All participants were provided with 0.0025% betamethasone valerate cream for the first 27 days and asked to apply a thin layer of the corticosteroid cream over the eczematous areas for the first 27 days followed by either study cream or vehicle on the whole body. Following this, participants who still had persistent eczema were allowed to continue use of the steroid if necessary. Participants were provided with emulsifying ointment as cleansers and instructed not to use any systemics or topical antibiotics, antibacterial soap or antibacterial shampoo. Category: topical steroid plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. SCORAD at days 14, 27 and 41 2. Amount of topical steroid used to day 41 3. AEs
Funding	Hygieia Healthcare Ltd
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were assigned to one of two treatment groups using a computer-generated randomisation list, stratified according to disease severity". Comment: randomisation method unlikely to introduce selection bias
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote "All study personnel and physicians remained blinded to allocation of treatment until completion of the data analysis. Both the study cream and vehicle were odourless, of the same appearance and consistency and provided in identical bottles." Comment: blinding was likely to have been successful.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote "All study personnel and physicians remained blinded to allocation of treatment until completion of the data analysis. Both the study cream and vehicle were odourless, of the same appearance and consistency and provided in identical bottles." Comment: blinding was maintained until analysis.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Tan 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	None
Selective reporting (reporting bias)	Unclear risk	No trial registration provided
Other bias	Unclear risk	Well-balanced at baseline for severity (SCORAD) but presence of *S. aureus* not reported. Results for amount of steroid used disagree between text and table.

Wachs 1976

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: Secondary care, single centre, USA Incl: clinically infected, moderate to severe atopic dermatitis Excl: pregnant, age < 1 year, renal disease, symptoms requiring oral antibiotics or steroids Age: not stated Sex: not stated Duration of condition: not stated Infective status: clinically infected *S. aureus* colonisation: 79% Randomised: 83 Evaluable: 79
Interventions	Betamethasone valerate (Betnovate) plus gentamicin cream (n = 25 evaluable) vs betamethasone valerate cream (n = 27 evaluable) vs gentamicin cream (n = 27). Applied three times daily for 22 days. Only the comparison of betamethasone valerate plus gentamicin vs betamethasone valerate was eligible for the review. Category: topical steroids plus antiseptic/antibiotic Topical steroids: all participants
Outcomes	1. Physician graded global assessment of severity (from 0 = complete absence to 10 = very severe - worst case ever seen) at days 4, 8, 15, 22 2. Degree of inflammation and infection (graded 0-10) at days 4, 8, 15, 22 3. Severity of individual signs and symptoms (erythema, pustules, crusting, exudate, vesiculation, lichenification; graded 0-10) at days 4, 8, 15, 22 4. Results of treatment and overall evaluation rated Poor (< 25% improvement, or worsening), Fair (25-49% improvement), Good (50-74% improvement) or Excellent (75% or greater improvement) at days 4, 8, 15, 22 5. Bacterial cultures (species and sensitivity) at days 8, 22
Funding	Not stated
Notes	-
Risk of bias	

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Wachs 1976 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Patients under the care of an individual investigator were randomly assigned so that five were to receive [each treatment]". Comment: randomisation method not fully described
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "precautions being observed to preserve the 'blinding' of both patients and therapists" Comment: unclear if blinding was achieved
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "precautions being observed to preserve the 'blinding' of both patients and therapists" Comment: unclear if blinding was achieved
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Four dropouts, treatment groups not stated
Selective reporting (reporting bias)	High risk	Results for individual signs and symptoms not reported; all results only reported at the beginning and end of treatment and not intermediate assessments
Other bias	Low risk	Well-balanced at baseline for severity (nonstandard clinical score) and presence of *S. aureus*

Weinberg 1992

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, South Africa Incl: *S. aureus* super-infected atopic dermatitis (Hanifin and Rajka criteria) Excl: cefadroxil resistant organisms, "concomitant medications that could have affected the variables being measured" Age: cefadroxil: mean 4.1 years, placebo: mean 4.4 years Sex: cefadroxil: 7 males, 6 females, placebo: 7 males, 10 females Duration of condition: cefadroxil: mean 3.2 years, placebo: mean 2.6 years Infective status: mixed (28/30 clinically infected) *S. aureus* colonisation: 100% Randomised: 33 Evaluable: 30
Interventions	Cefadroxil 50 mg/kg/day in 2 equal doses (n = 16) vs placebo (n = 17) for 2 weeks Category: oral antibiotic Topical steroids: not stated
Outcomes	1. Patient- and physician-rated global evaluations of improvement at 2 weeks 2. Hanifin/Rajka activity scale at 2 weeks

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Weinberg 1992 *(Continued)*

	3. Severity of individual signs and symptom (pruritus, erythema, peeling, lichenification, induration, ulceration) at 2 weeks 4. Positive bacterial cultures, sensitivity and clinical superinfection at 2 weeks 5. Total serum IgE, IgA, IgG, IgM at 2 weeks 6. AEs
Funding	Not stated (one author was an employee of Bristol-Myers Squibb (Pty) Ltd)
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomised". Comment: unclear if randomisation method was adequate
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "double-blind", "placebo-controlled" Comment: unclear if blinding was achieved and what method was used
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	High risk	Three withdrawn from cefadroxil group because of side effects, severe non-compliance and presence of a resistant organism
Selective reporting (reporting bias)	High risk	Results not shown for lichenification, induration or ulceration (reported as "not significant"). Within-group improvements reported in clinical parameters, not between groups.
Other bias	Low risk	Well-balanced at baseline for severity (pruritus and erythema), all participants had *S. aureus*

Wong 2013

Methods	Design: parallel group Total study duration: not stated
Participants	Setting: secondary care, single centre, Malaysia Incl: atopic dermatitis (Hanifin and Rajka criteria), moderate to severe (Rajka and Langeland criteria) Excl: known sensitivity to sodium hypochlorite (bleach), eczema herpeticum or other cutaneous infections, systemic antibiotics or systemic steroids at the time of recruitment, those on other antiseptic baths, pregnant/lactating

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Wong 2013 *(Continued)*

	Age: 2-30 years Sex: bleach bath group: 4 males, 14 females, placebo group: 7 males, 11 females Duration of condition: not stated Infective status: uninfected *S. aureus* colonisation: 94% Randomised: 42 Evaluable: 36
Interventions	Bleach bath (100 mL of sodium hypochlorite (bleach) in 100 L of water, equivalent to approximately half a bathtub full, diluting the sodium hypochlorite to concentration of 0.005%) (n = 21) vs placebo (100 mL of distilled water in 100 L of water) (n = 21). For children < 12 years old 50 mL was added to a quarter tub of water. Instructed to soak from the neck down in the diluted baths for 10 minutes twice a week for 2 months. After each bath, participants rinsed off with normal tap water. Maintained on a stable regimen of topical anti-inflammatory and emollient therapy. No new topical/systemic treatment was introduced before and during the study period. Aqueous cream as soap substitute. Category: antibacterial bath additive Topical steroids: as needed
Outcomes	1. EASI score (overall and for each body region) at weeks 2, 4 and 8 2. Physicians' assessment of severity of specific signs and symptoms (erythema, oedema/induration/papulation, excoriation, lichenification) on a 4-point scale (from "absent" to "severe") at weeks 2, 4 and 8 3. Participants' assessment of overall response (from "much worse" to "much better") and intensity of itch (visual analogue scale from 1 to 10) at weeks 2, 4 and 8 4. Quantitative bacterial cultures and *S. aureus* density at weeks 4 and 8 5. AEs
Funding	Dermatological Society of Malaysia
Notes	Correspondence with author confirmed additional details about the study and risk of bias.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Correspondence with author: "Patients were randomly assigned through computer generated simple randomised numbers to the treatment or placebo study arms". Comment: randomisation method unlikely to introduce selection bias
Allocation concealment (selection bias)	Low risk	Correspondence with author: "[Dr S Wong] had no access to the allocation sequence. The study pharmacist dispensed either bleach or placebo (distilled water) according to the computer generated numbers. [Dr S Wong] did not know which treatment the patient received either at the start or on follow-up." Comment: allocation was concealed.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Wong 2013 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Although double-blind, it is possible that the participant could smell the bleach and identify which treatment group he or she was in.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	As above
Incomplete outcome data (attrition bias) All outcomes	Low risk	Three participants withdrew in treatment arm - one lost to follow-up, one non-compliant, one withdrew consent and three participants withdrew in placebo arm - one lost to follow-up, one non-compliant, one worsening itch
Selective reporting (reporting bias)	Unclear risk	No trial registration provided. In paper nothing reported for week 2 or total numbers positive and negative for *S. aureus*. Authors have provided this information via email.
Other bias	High risk	Well-balanced at baseline for severity (EASI) but imbalance in colonisation density of *S. aureus* (mean log CFU/cm^2: bleach bath group 16.8 SD 15.7, placebo group 7.5, SD 13.6 - data supplied by author)

AE: adverse event
AIDS: acquired immune deficiency syndrome
BSA: body surface area
CDLQI: Children's Dermatology Life Quality Index
CFU: colony forming units
DLQI: Dermatology Life Quality Index
DNA: deoxyribonucleic acid
EASI: Eczema Area & Severity Index
Excl: exclusion criteria
IGA: Investigator Global Assessment
IgE: immunoglobulin E
IgG: immunoglobulin G
IgM: immunoglobulin M
Incl: inclusion criteria
ITT: intention-to-treat
PCR: polymerase chain reaction
POEM: Patient Oriented Eczema Measure
SASSAD: Six Area, Six Sign Atopic Dermatitis
SCORAD: SCORing Atopic Dermatitis
TEWL: transepidermal water loss
UV: ultra-violet
VAS: visual analogue scale
Vs: versus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Alangari 2017	Not randomised
Ariyoshi 1973	Not atopic dermatitis
Berardesca 2009	Topical gluco-oligosaccharide and collagen tripeptide F, not an anti-staphylococcal intervention

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Study	Reason for exclusion
Bergstrom 2009	Review article, not a randomised controlled trial
Bianchi 2014	Emollient containing bacterial extract, not an anti-staphylococcal intervention
Bjornberg 1975	Not randomised or controlled
Breneman 1990	No separate results for atopic dermatitis
Carpenter 1973	Studied "common dermatoses", no separate results for atopic dermatitis
Clark 1974	Not specifically atopic dermatitis. Not randomised
Craig 2010	Commentary on another paper, not a randomised controlled trial
Davis 1968	Studied "inflammatory and infective dermatoses", no separate results for atopic dermatitis
Drago 2011	Probiotic, not an anti-staphylococcal intervention
Drago 2012	Probiotic, not an anti-staphylococcal intervention
Dunstan 2011	Studied *Mycobacteria vaccae*, not an antistaphylococcal intervention
Eaglstein 1977	Studied "secondarily infected dermatitis" with no further description of atopic dermatitis
Gauger 2003	Open-label, controlled left/right comparison. Not randomised
Girolomoni 2016	Review article, not a randomised controlled trial
GP Medical Research 1967	Compared anti-staphylococcal - steroid combination with addition of antifungal, no appropriate control
Gratton 1987	Not atopic dermatitis
Gueniche 2008	Study involving *Vitreoscilla filiformis*, not an anti-staphylococcal intervention
Gueniche 2009	Study involving *Vitreoscilla filiformis*, not an anti-staphylococcal intervention
Hoey 2006	Phototherapy, not an anti-staphylococcal intervention
Ishibashi 1993	No separate results for atopic dermatitis
Kimata 1998	Not randomised
Kotrajaras 1971	Not atopic dermatitis. Not randomised
La Colla 2009	Correspondence relating to another study using *Vitreoscilla filiformis*, not an anti-staphylococcal intervention
Leung 2008	Chinese herbal medicine, not an anti-staphylococcal intervention. Not randomised
Leung 2009	Pimecrolimus cream, not an anti-staphylococcal intervention
Lloyd 1969	No separate results for atopic dermatitis
Masako 2005a	In vitro study

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Study	Reason for exclusion
Meenan 1988	Compared two anti-staphylococcal - steroid combinations, no appropriate control
Mora 2004	Topical suspension of bacterial antigens, not an anti-staphylococcal intervention
Nielsen 1979	No separate results for atopic dermatitis. Not randomised
Parish 1987	Not atopic dermatitis
Pratap 2013	Not specifically atopic dermatitis. Correspondence with Dr Mariam Philip on 30 December 2014 confirmed this: "The study was on infected eczema. In our study there were only very few cases of atopic dermatitis."
Prescott 2005	Probiotics, not an anti-staphylococcal intervention
Ravenscroft 2003	Compared two anti-staphylococcal agents, no appropriate control
Remitz 2001	No control, and not randomised
Rist 2002	Compared two anti-staphylococcal agents, no appropriate control
Salo 1988	Compared two preparations of the same anti-staphylococcal agent, no appropriate control
Sandström Falk 2006	Not randomised
Sasai-Takedatsu 1997	Treatment arbitrarily divided by a referee physician, not appropriately randomised
Schempp 2010	Review article, not a randomised controlled trial
Schultz Larsen 2007	Compared two anti-staphylococcal agents, no appropriate control
Senti 2006	Not randomised
Stalder 1992	Compared two anti-staphylococcal agents, no appropriate control
Takahama 1992	Not specifically atopic dermatitis
Thaci 1999	Compared two anti-staphylococcal agents, no appropriate control
Theodoridis 1979	Studied "eczematous dermatitis" with no further description of atopic dermatitis
Thum 2013	Study on resistance patterns, not a randomised controlled trial
Udompataikul 2015	Compared vitamin D against placebo - not primarily an anti-staphylococcal intervention
Van der Bijl 1966	Not atopic dermatitis. Not randomised
Verallo-Rowell 2008	Compared coconut and virgin olive oils, both interventions suggested to have anti-staphylococcal properties, no appropriate control
Weitgasser 1983	Compared two different anti-staphylococcal - steroid combinations, no appropriate control. No separate results for atopic dermatitis
Whitefield 1998	In vitro study and case series using antimicrobial lotion, not a randomised controlled trial

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Study	Reason for exclusion
Wilkinson JD 1985	Compared two different steroid - antibiotic combinations, no appropriate control. No separate results for atopic dermatitis
Wilkinson RD 1980	Compared three steroid - antibiotic combinations, no appropriate control. No separate results for atopic dermatitis

Characteristics of studies awaiting assessment *[ordered by study ID]*

ACTRN12610000438055

Methods	Parallel groups RCT
Participants	Patients aged 18 to 50 years, currently suffering from atopic dermatitis with a primary diagnosis of atopic dermatitis at least 12 weeks prior to inclusion into the study, with a SCORAD between 20 and 50 (i.e. mild to moderate atopic dermatitis), diagnosed with disseminated symmetric dermatitis and with colonisation of lesional skin with *S. aureus*
Interventions	rHuB[beta]D2 cream versus placebo cream
Outcomes	Safety and tolerability, change in local SCORAD) at end of treatment (day 14), change in *S. aureus* colonization rate at end of treatment, change in the colonization rate of any bacteria at end of treatment, symptomatic relief using a Likert scale
Notes	Recruitment completed (reported September 2011). No response to queries.

EudraCT 2006-004233-15

Methods	Within patient (left/right) RCT
Participants	Patients aged 6 month to 50 years, first atopic dermatitis diagnosis at least 4 weeks prior to study entry, actual clinically manifested atopic dermatitis, disseminated symmetric eczemas of the limbs, ESCORAD (SCORAD of extremities) between 5 and 12, Staphylococcus superinfection
Interventions	Triclosan cream versus placebo
Outcomes	Changes in ESCORAD from baseline to day 14, changes in logarithm of staphylococcus-bacteria count from baseline to day 7 and 14, changes in ESCORAD from baseline to day 7, changes in single-ESCORAD of erythema, oedema/papulation, oozing/crusting, excoriation, lichenification from baseline to day 7 and 14, clinical and microbiological response rates for day 7 and 14, evaluation of skin parameters on a numeric scale by the investigator and the subject, side effects, tolerance and efficacy evaluation on a numeric scale from 1-6 by the investigator and the patient, compliance.
Notes	Recruitment completed (19 May 2009). No response to queries.

EudraCT 2008-005890-37

Methods	Within patient RCT
Participants	Patients aged 18 years or older, manifest atopic eczema (Hanifin and Rajka criteria), two comparable lesional areas of 20 - 50 cm^2 with a distance of at least 5 cm, clinical condition of atopic eczema

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

EudraCT 2008-005890-37 *(Continued)*

	mild to moderate (meeting Hanifin and Rajka's criteria), TEWL in the lesional areas at least 12 g/m^{2}h, TEWL value differences ≤ 30 % are allowed between both lesional areas
Interventions	K201 cream [Lactic acid (5 %), Propylene glycol (20 %), Urea (5 %)] versus placebo
Outcomes	Barrier impairment (TEWL measurements), clinical skin condition (corneometric measurements and clinical assessments) and bacterial colonization of *S. aureus* over a four-week treatment period.
Notes	Recruitment completed (15 April 2009). No response to queries.

NCT03009734

Methods	Parallel groups RCT
Participants	Adults aged 18 to 70 years with localised atopic dermatitis (e.g. flexural eczema in a more or less symmetrical distribution on arms) where two individual lesions each covering an area between 10-200 cm^2 and where each individual lesion has an investigators global assessment score between 1-3, additional localised lesion of area between 10-200 cm^2 and where the individual lesion has an investigators global assessment score between 1-3, total localised disease not exceeding 20% body surface area, and colonisation of lesions with *S. aureus*
Interventions	ATx201 (topical antibiotic) versus placebo
Outcomes	Treatment related adverse events, investigators global assessment score, treatment success (100-fold reduction in *S. aureus* colony count), local dermal tolerability
Notes	Recruitment completed (March 2018)

NCT03047954

Methods	Parallel groups RCT
Participants	Children aged 6 months to 7 years with atopic dermatitis (Hanifin and Rajka or Williams 1994 criteria) with affected BSA 15-70% and SCORAD 25-70
Interventions	Broncho-Vaxom 1 capsule (3.5 mg) per day versus placebo
Outcomes	Number of atopic dermatitis flares over 9 months of treatment, changes in SCORAD over 9 months of treatment, area of eczema involvement, amount of corticosteroids used
Notes	Recruitment completed (December 2006)

Totté 2017

Methods	Parallel groups RCT
Participants	Patients aged 18 years or older, atopic dermatitis of moderate and severe severity (EASI score of 7.1 to 50), topical corticosteroid use
Interventions	Staphefekt SA.100 cream (Gladskin) versus placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Totté 2017 *(Continued)*

Outcomes	Number of days/week corticosteroid use over 12 weeks, mean grams/week topical corticosteroid use at 12 and 20 weeks, proportion of patients with atopic dermatitis who indicate to have used less corticosteroids at week 2 and 12 as compared to baseline and at week 20 as compared to the 12 week treatment period, change in EASI from baseline to week 2, 6, 12 and 20, change in POEM from baseline to week 2, 6, 12 and 20, change in IGA from baseline to week 2, 6 and 12 and week 20, change in Pruritus Numerical Rating Scale from baseline to week 2, 6, 12 and week 20, mean time to flare from baseline through week 12 and from week 12 through week 20, number of flares through week 12, change in Skindex-29 score from baseline to week 12 and week 20, proportion of patients with a reduction of *S. aureus* from baseline to measurement 1 (0.5 hour after baseline) as determined by semi quantitative culture, proportion of patients with a > 1 log reduction of *S. aureus* from the lowest measurement (visit 1 or visit 2a) to week 2 and week 12 as determined by qPCR, change in relative abundance of bacteria from baseline to weeks 2, 12 and 20, incidence of (serious) adverse device events
Notes	Recruitment completed (February 2018)

BSA: body surface area
EASI: Eczema Area & Severity Index
ESCORAD: SCORing Atopic Dermatitis of the Extremities
IGA: Investigator Global Assessment
POEM: Patient Oriented Eczema Measure
qPCR: quantitative polymerase chain reaction
RCT: randomised clinical trial
SCORAD: SCORing Atopic Dermatitis
TEWL: transepidermal water loss

Characteristics of ongoing studies *[ordered by study ID]*

NCT03052348

Trial name or title	A multicentre study evaluating the efficacy of combining topical antibiotic/steroid/moisturizer therapy compared to an active comparator in the treatment of severe atopic dermatitis: a randomized, clinical trial
Methods	Parallel group RCT
Participants	Children aged 2-9 years with atopic dermatitis (UK Working Party Criteria), baseline SCORAD score of 50 or above (severe atopic dermatitis), not on systemic antibiotics, qualifying for second-line treatment agents for atopic dermatitis (systemic or phototherapy)
Interventions	Antibiotic and steroid combination (Supiroban 2% cream and fluocinolone acetonide) versus steroid alone
Outcomes	Change in SCORAD from baseline to weeks 4, 8 and 12, frequency of atopic dermatitis relapse episodes, change in IDQoL index from baseline to weeks 4, 8 and 12
Starting date	March 2017 (anticipated)
Contact information	Dr Carol Hlela, Red Cross War Memorial Childrens Hospital carol.hlela@uct.ac.za
Notes	-

IDQoL: Infants' Dermatitis Quality of Life
RCT: randomised clinical trial

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

SCORAD: SCORing Atopic Dermatitis

DATA AND ANALYSES

Comparison 1. Oral antibiotic vs placebo

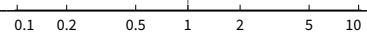
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global outcome (good or excellent) at end of treatment	2	75	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.18, 3.50]
2 Change from baseline in IDQoL at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
3 Change from baseline in CDLQI at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
4 Adverse events requiring withdrawal from treatment	4	199	Risk Ratio (M-H, Random, 95% CI)	1.43 [0.28, 7.36]
5 Change from baseline in POEM at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
6 Change from baseline in EASI at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
7 Mean erythema scores as assessed by a physician at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8 Number of people with erythema at end of treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
9 Presence of clinically apparent infection at end of treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10 Number of patients in whom *S. aureus* was isolated at end of treatment	3	144	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.46, 1.26]
11 Change from baseline in isolation rate of *S. aureus* at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
12 Mean log of *S. aureus* counts from lesional skin at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
13 Change from baseline in IDQoL at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
14 Change from baseline in CDLQI at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
15 Change from baseline in POEM at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
16 Change from baseline in isolation rate of *S. aureus* at 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
17 Mean erythema scores as assessed by physician 56 days post-treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Oral antibiotic vs placebo, Outcome 1 Global outcome (good or excellent) at end of treatment.

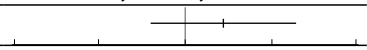
Study or subgroup	Oral antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ewing 1998	6/22	17/24		48.49%	0.39[0.19,0.8]
Weinberg 1992	10/12	9/17		51.51%	1.57[0.94,2.63]
Total (95% CI)	**34**	**41**		**100%**	**0.8[0.18,3.5]**
Total events: 16 (Oral antibiotic), 26 (Placebo)					
Heterogeneity: Tau^2=1.04; Chi^2=11.05, df=1(P=0); I^2=90.95%					
Test for overall effect: Z=0.3(P=0.76)					



Favours placebo — Favours oral antibiotic

Analysis 1.2. Comparison 1 Oral antibiotic vs placebo, Outcome 2 Change from baseline in IDQoL at end of treatment.

Study or subgroup	Flucloxacillin N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	25	20	0.1 (0.107)		0.11[-0.1,0.32]



Favours flucloxacillin — Favours placebo

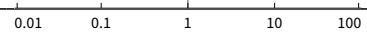
Analysis 1.3. Comparison 1 Oral antibiotic vs placebo, Outcome 3 Change from baseline in CDLQI at end of treatment.

Study or subgroup	Flucloxacillin N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	9	14	0.4 (0.301)		0.43[-0.16,1.02]

Favours flucloxacillin — Favours placebo

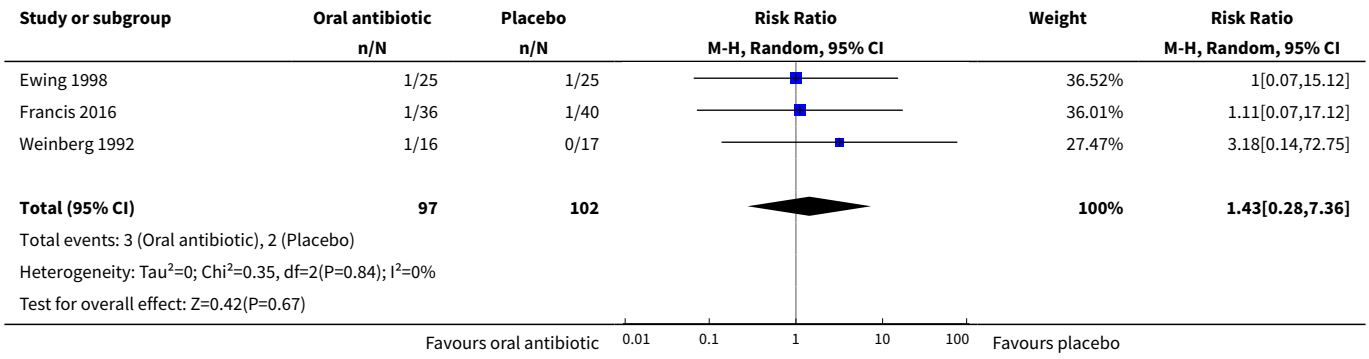
Analysis 1.4. Comparison 1 Oral antibiotic vs placebo, Outcome 4 Adverse events requiring withdrawal from treatment.

Study or subgroup	Oral antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Boguniewicz 2001	0/20	0/20			Not estimable

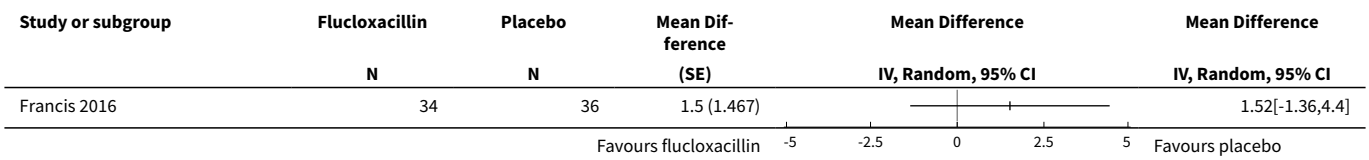


Favours oral antibiotic — Favours placebo

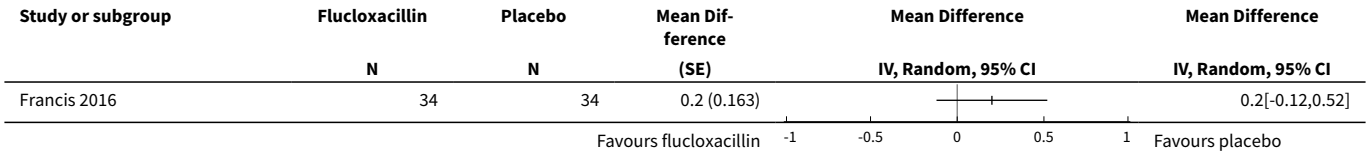
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.



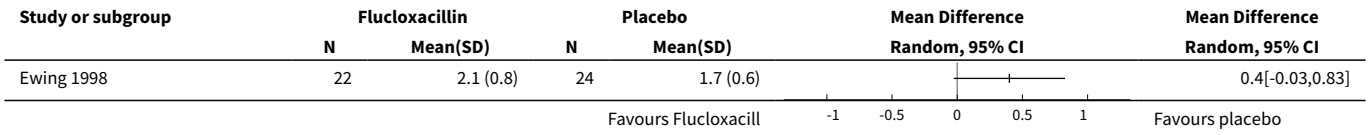
Analysis 1.5. Comparison 1 Oral antibiotic vs placebo, Outcome 5 Change from baseline in POEM at end of treatment.



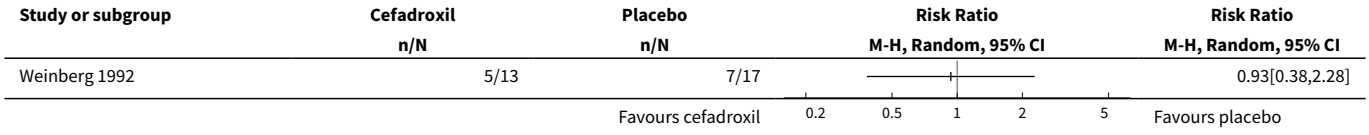
Analysis 1.6. Comparison 1 Oral antibiotic vs placebo, Outcome 6 Change from baseline in EASI at end of treatment.



Analysis 1.7. Comparison 1 Oral antibiotic vs placebo, Outcome 7 Mean erythema scores as assessed by a physician at end of treatment.



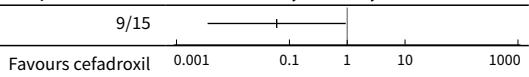
Analysis 1.8. Comparison 1 Oral antibiotic vs placebo, Outcome 8 Number of people with erythema at end of treatment.



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

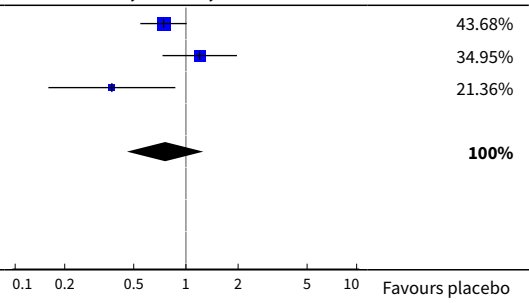
Analysis 1.9. Comparison 1 Oral antibiotic vs placebo, Outcome 9 Presence of clinically apparent infection at end of treatment.

Study or subgroup	Cefadroxil n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Weinberg 1992	0/13	9/15		0.06[0,0.94]



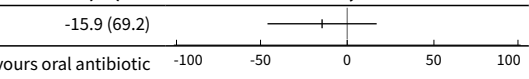
Analysis 1.10. Comparison 1 Oral antibiotic vs placebo, Outcome 10 Number of patients in whom *S. aureus* was isolated at end of treatment.

Study or subgroup	Oral antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ewing 1998	15/22	22/24		43.68%	0.74[0.55,1.01]
Francis 2016	18/34	15/34		34.95%	1.2[0.73,1.97]
Weinberg 1992	4/13	14/17		21.36%	0.37[0.16,0.87]
Total (95% CI)	**69**	**75**		**100%**	**0.76[0.46,1.26]**
Total events: 37 (Oral antibiotic), 51 (Placebo)					
Heterogeneity: Tau^2=0.13; Chi^2=5.92, df=2(P=0.05); I^2=66.22%					
Test for overall effect: Z=1.06(P=0.29)					



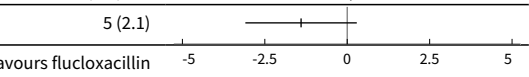
Analysis 1.11. Comparison 1 Oral antibiotic vs placebo, Outcome 11 Change from baseline in isolation rate of *S. aureus* at end of treatment.

Study or subgroup	Oral antibiotic N	Oral antibiotic Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Francis 2016	34	-30.4 (63.1)	34	-15.9 (69.2)		-14.5[-45.98,16.98]



Analysis 1.12. Comparison 1 Oral antibiotic vs placebo, Outcome 12 Mean log of *S. aureus* counts from lesional skin at end of treatment.

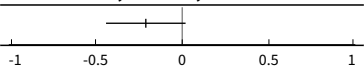
Study or subgroup	Flucloxacillin N	Flucloxacillin Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Ewing 1998	21	3.6 (3.3)	19	5 (2.1)		-1.4[-3.09,0.29]



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

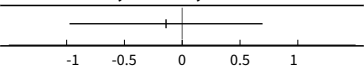
Analysis 1.13. Comparison 1 Oral antibiotic vs placebo, Outcome 13 Change from baseline in IDQoL at 3 months.

Study or subgroup	Fluxcloxacillin N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	18	16	-0.2 (0.117)		-0.21[-0.44,0.02]



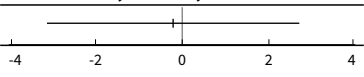
Analysis 1.14. Comparison 1 Oral antibiotic vs placebo, Outcome 14 Change from baseline in CDLQI at 3 months.

Study or subgroup	Flucloxacillin N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	6	8	-0.1 (0.426)		-0.14[-0.97,0.69]



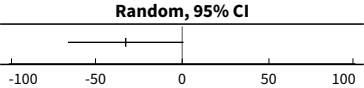
Analysis 1.15. Comparison 1 Oral antibiotic vs placebo, Outcome 15 Change from baseline in POEM at 3 months.

Study or subgroup	Flucloxacllin N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	28	25	-0.2 (1.485)		-0.21[-3.12,2.7]



Analysis 1.16. Comparison 1 Oral antibiotic vs placebo, Outcome 16 Change from baseline in isolation rate of *S. aureus* at 3 months.

Study or subgroup	Oral antibiotic N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Francis 2016	26	-52.6 (56.1)	25	-20 (64.8)		-32.6[-65.92,0.72]



Analysis 1.17. Comparison 1 Oral antibiotic vs placebo, Outcome 17 Mean erythema scores as assessed by physician 56 days post-treatment.

Study or subgroup	Flucloxacillin N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Ewing 1998	19	1.9 (0.9)	18	2 (0.6)		-0.1[-0.59,0.39]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Comparison 2. Topical steroid plus topical antibiotic vs topical steroid

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global outcome (good or excellent) at end of treatment	3	224	Risk Ratio (M-H, Random, 95% CI)	1.10 [1.00, 1.21]
2 Global outcome (mean self-assessment score) at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Change from baseline in IDQoL at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
4 Change from baseline in CDLQI at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
5 Adverse events requiring withdrawal from treatment	4	325	Risk Ratio (M-H, Random, 95% CI)	1.24 [0.21, 7.25]
6 Minor adverse events not requiring withdrawal from treatment	2	218	Risk Ratio (M-H, Random, 95% CI)	0.30 [0.12, 0.78]
7 Change from baseline in EASI at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
8 Change from baseline in POEM at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
9 Mean value of composite rating scale at end of treatment	4	256	Std. Mean Difference (IV, Random, 95% CI)	-0.00 [-0.33, 0.33]
10 No of patients in whom *S. aureus* was isolated at end of treatment	7	298	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.27, 0.84]
11 Change from baseline in isolation rate of *S. aureus* at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
12 Change from baseline in IDQoL at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
13 Change from baseline in CDLQI at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
14 Change from baseline in POEM at 3 months	1		Mean Difference (Random, 95% CI)	Totals not selected
15 Change from baseline in isolation rate of *S. aureus* at 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 2.1. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 1 Global outcome (good or excellent) at end of treatment.

Study or subgroup	Steroid +antibiotic n/N	Steroid alone n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Canpolat 2012	20/27	17/26		7.2%	1.13[0.79,1.62]
Gong 2006	55/58	54/61		78.22%	1.07[0.96,1.19]
Wachs 1976	23/25	20/27		14.58%	1.24[0.97,1.6]
Total (95% CI)	**110**	**114**		**100%**	**1.1[1,1.21]**
Total events: 98 (Steroid+antibiotic), 91 (Steroid alone)					
Heterogeneity: Tau^2=0; Chi^2=1.3, df=2(P=0.52); I^2=0%					
Test for overall effect: Z=1.93(P=0.05)					

Favours steroid alone — Favours combination

Analysis 2.2. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 2 Global outcome (mean self-assessment score) at end of treatment.

Study or subgroup	Steroid+antibiotic N	Steroid+antibiotic Mean(SD)	Steroid alone N	Steroid alone Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Nilsson 1992	15	1.7 (1.6)	13	0.5 (0.9)		1.2[0.25,2.15]

Favours combination — Favours steroid

Analysis 2.3. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 3 Change from baseline in IDQoL at end of treatment.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	22	20	0.2 (0.11)		0.18[-0.04,0.4]

Favours antibiotic — Favours placebo

Analysis 2.4. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 4 Change from baseline in CDLQI at end of treatment.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	9	14	0.7 (0.296)		0.7[0.12,1.28]

Favours antibiotic — Favours placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 2.5. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 5 Adverse events requiring withdrawal from treatment.

Study or subgroup	Steroid +antibiotic n/N	Steroid alone n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Francis 2016	5/37	1/40		37.46%	5.41[0.66,44.14]
Hung 2007	0/15	0/15			Not estimable
Ramsay 1996	1/91	3/83		34.84%	0.3[0.03,2.87]
Schuttelaar 2005	1/22	1/22		27.7%	1[0.07,15]
Total (95% CI)	**165**	**160**		**100%**	**1.24[0.21,7.25]**
Total events: 7 (Steroid+antibiotic), 5 (Steroid alone)					
Heterogeneity: Tau^2=1.01; Chi^2=3.43, df=2(P=0.18); I^2=41.68%					
Test for overall effect: Z=0.24(P=0.81)					

Analysis 2.6. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 6 Minor adverse events not requiring withdrawal from treatment.

Study or subgroup	Steroid +antibiotic n/N	Steroid alone n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Ramsay 1996	2/91	3/83		28.27%	0.61[0.1,3.55]
Schuttelaar 2005	3/22	13/22		71.73%	0.23[0.08,0.7]
Total (95% CI)	**113**	**105**		**100%**	**0.3[0.12,0.78]**
Total events: 5 (Steroid+antibiotic), 16 (Steroid alone)					
Heterogeneity: Tau^2=0; Chi^2=0.83, df=1(P=0.36); I^2=0%					
Test for overall effect: Z=2.49(P=0.01)					

Analysis 2.7. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 7 Change from baseline in EASI at end of treatment.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	31	34	0.4 (0.168)		0.42[0.09,0.75]

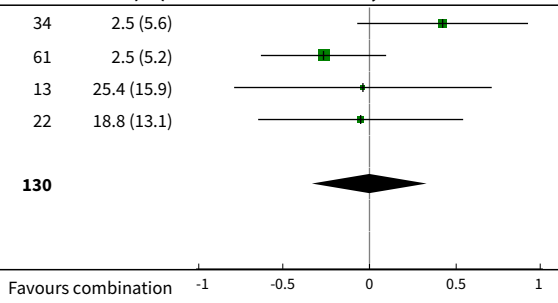
Analysis 2.8. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 8 Change from baseline in POEM at end of treatment.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	31	36	1.5 (1.551)		1.49[-1.55,4.53]

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

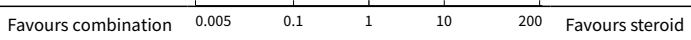
Analysis 2.9. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 9 Mean value of composite rating scale at end of treatment.

Study or subgroup	Steroid+antibiotic N	Steroid+antibiotic Mean(SD)	Steroid alone N	Steroid alone Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Francis 2016	31	4.9 (5.7)	34	2.5 (5.6)		26.74%	0.42[-0.07,0.91]
Gong 2006	58	1.4 (2.3)	61	2.5 (5.2)		36.81%	-0.27[-0.63,0.1]
Hung 2007	15	24.7 (16.5)	13	25.4 (15.9)		15.24%	-0.04[-0.78,0.7]
Schuttelaar 2005	22	18.1 (13.9)	22	18.8 (13.1)		21.21%	-0.05[-0.64,0.54]
Total ***	**126**		**130**			**100%**	**-0[-0.33,0.33]**
Heterogeneity: Tau^2=0.04; Chi^2=4.87, df=3(P=0.18); I^2=38.37%							
Test for overall effect: Z=0.01(P=0.99)							



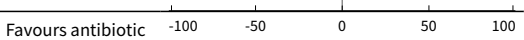
Analysis 2.10. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 10 No of patients in whom *S. aureus* was isolated at end of treatment.

Study or subgroup	Steroid +antibiotic n/N	Steroid alone n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Francis 2016	11/31	16/34		26.99%	0.75[0.42,1.37]
Hung 2007	3/15	5/13		13.7%	0.52[0.15,1.77]
Lever 1988	1/24	14/21		6.92%	0.06[0.01,0.44]
Leyden 1977	3/15	13/21		16.22%	0.32[0.11,0.94]
Nilsson 1992	0/15	0/13			Not estimable
Schuttelaar 2005	6/22	15/22		23.17%	0.4[0.19,0.84]
Wachs 1976	4/25	4/27		12.99%	1.08[0.3,3.86]
Total (95% CI)	**147**	**151**		**100%**	**0.48[0.27,0.84]**
Total events: 28 (Steroid+antibiotic), 67 (Steroid alone)					
Heterogeneity: Tau^2=0.22; Chi^2=9.35, df=5(P=0.1); I^2=46.51%					
Test for overall effect: Z=2.58(P=0.01)					



Analysis 2.11. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 11 Change from baseline in isolation rate of *S. aureus* at end of treatment.

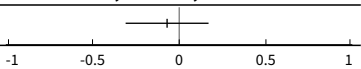
Study or subgroup	Topical antibiotic N	Topical antibiotic Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Francis 2016	31	-31.2 (67)	34	-15.9 (69.2)		-15.3[-48.43,17.83]



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

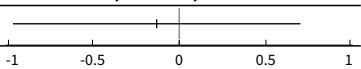
Analysis 2.12. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 12 Change from baseline in IDQoL at 3 months.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	15	16	-0.1 (0.122)		-0.07[-0.31,0.17]



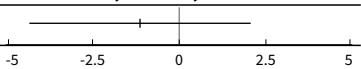
Analysis 2.13. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 13 Change from baseline in CDLQI at 3 months.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	6	8	-0.1 (0.423)		-0.13[-0.96,0.7]



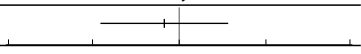
Analysis 2.14. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 14 Change from baseline in POEM at 3 months.

Study or subgroup	Topical antibiotic N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Francis 2016	21	25	-1.1 (1.628)		-1.13[-4.32,2.06]



Analysis 2.15. Comparison 2 Topical steroid plus topical antibiotic vs topical steroid, Outcome 15 Change from baseline in isolation rate of *S. aureus* at 3 months.

Study or subgroup	Topical antibiotic N	Topical antibiotic Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Francis 2016	21	-28.6 (62.4)	25	-20 (64.8)		-8.6[-45.44,28.24]



Comparison 3. Topical calcineurin inhibitor plus antibiotic vs topical calcineurin inhibitor

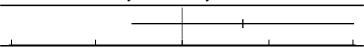
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Adverse events requiring withdrawal from treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Mean SCORAD at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3 No of patients in whom *S. aureus* was isolated at end of treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 3.1. Comparison 3 Topical calcineurin inhibitor plus antibiotic vs topical calcineurin inhibitor, Outcome 1 Adverse events requiring withdrawal from treatment.

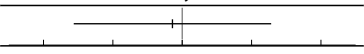
Study or subgroup	Tacrolimus+antibiotic n/N	Tacrolimus alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Hung 2007	2/15	0/15		5[0.26,96.13]



Favours combination — Favours tacrolimus

Analysis 3.2. Comparison 3 Topical calcineurin inhibitor plus antibiotic vs topical calcineurin inhibitor, Outcome 2 Mean SCORAD at end of treatment.

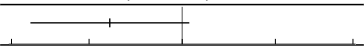
Study or subgroup	Tacrolimus+antibiotic N	Mean(SD)	Tacrolimus alone N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Hung 2007	13	31.5 (17.6)	13	32.9 (19.4)		-1.41[-15.64,12.82]



Favours combination — Favours tacrolimus

Analysis 3.3. Comparison 3 Topical calcineurin inhibitor plus antibiotic vs topical calcineurin inhibitor, Outcome 3 No of patients in whom *S. aureus* was isolated at end of treatment.

Study or subgroup	Tacrolimus+antibiotic n/N	Tacrolimus alone n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Hung 2007	2/13	7/13		0.29[0.07,1.13]



Favours combination — Favours tacrolimus

Comparison 4. Bleach bath vs placebo or bath emollient

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Global outcome (good or excellent) at 1 month	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Global outcome (mean IGA score) at 4 weeks	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Change from baseline in CDLQI at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Adverse events requiring withdrawal from treatment	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Minor adverse events not requiring withdrawal from treatment	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Mean EASI score at 1 month	2	54	Mean Difference (IV, Random, 95% CI)	-2.48 [-7.36, 2.40]
7 Change from baseline in objective SCORAD at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
8 Mean *S. aureus* counts from lesional skin at 1 month	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9 Global outcome (not good or excellent) at 2 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
10 Mean value of composite rating scale at 2-3 months	2	55	Std. Mean Difference (IV, Random, 95% CI)	-1.11 [-1.68, -0.53]
11 Mean *S. aureus* counts from lesional skin at 2 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 4.1. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 1 Global outcome (good or excellent) at 1 month.

Study or subgroup	Bleach bath n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wong 2013	7/18	9/18		0.78[0.37,1.63]

Favours placebo 0.2 0.5 1 2 5 Favours bleach bath

Analysis 4.2. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 2 Global outcome (mean IGA score) at 4 weeks.

Study or subgroup	Bleach bath N	Bleach bath Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Gonzalez 2016	9	0.5 (1.6)	9	1.1 (1)		-0.54[-1.79,0.71]

Favours bleach bath -2 -1 0 1 2 Favours placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

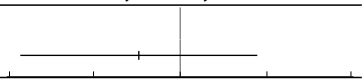
Analysis 4.3. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 3 Change from baseline in CDLQI at end of treatment.

Study or subgroup	Bleach bath N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Hon 2016	40	40	0.9 (1.133)		0.9[-1.32,3.12]

Favours bleach bath — Favours placebo

Analysis 4.4. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 4 Adverse events requiring withdrawal from treatment.

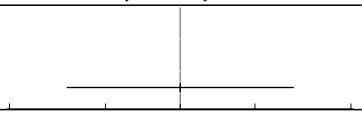
Study or subgroup	Bleach bath n/N	Placebo/emollient n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Leins 2013	0/8	0/11		Not estimable
Wong 2013	0/21	1/21		0.33[0.01,7.74]



Favours bleach bath — Favours placebo/emollient

Analysis 4.5. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 5 Minor adverse events not requiring withdrawal from treatment.

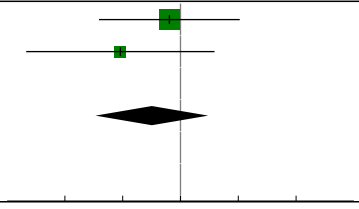
Study or subgroup	Bleach bath n/N	Placebo/emollient n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Leins 2013	0/8	0/11		Not estimable
Shi 2016	0/10	0/10		Not estimable
Wong 2013	5/18	5/18		1[0.35,2.87]



Favours bleach bath — Favours placebo/emollient

Analysis 4.6. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 6 Mean EASI score at 1 month.

Study or subgroup	Bleach bath N	Bleach bath Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Gonzalez 2016	9	1.4 (6.3)	9	2.3 (6.9)		64.17%	-0.96[-7.05,5.13]
Wong 2013	18	20.2 (11.8)	18	25.4 (13.1)		35.83%	-5.2[-13.34,2.94]
Total ***	**27**		**27**			**100%**	**-2.48[-7.36,2.4]**
Heterogeneity: Tau²=0; Chi²=0.67, df=1(P=0.41); I²=0%							
Test for overall effect: Z=1(P=0.32)							

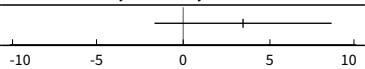


Favours bleach bath — Favours placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 4.7. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 7 Change from baseline in objective SCORAD at end of treatment.

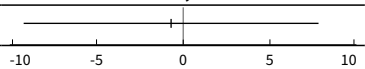
Study or subgroup	Bleach bath N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Hon 2016	40	40	3.5 (2.605)		3.45[-1.66,8.56]



Favours bleach bath — Favours placebo

Analysis 4.8. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 8 Mean *S. aureus* counts from lesional skin at 1 month.

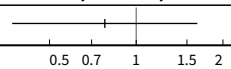
Study or subgroup	Bleach bath N	Bleach bath Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Wong 2013	18	9.7 (12.4)	18	10.4 (13.6)		-0.7[-9.2,7.8]



Favours bleach bath — Favours placebo

Analysis 4.9. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 9 Global outcome (not good or excellent) at 2 months.

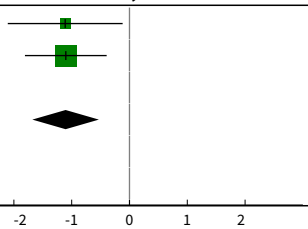
Study or subgroup	Bleach bath n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Wong 2013	7/18	9/18		0.78[0.37,1.63]



Favours bleach bath — Favours placebo

Analysis 4.10. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 10 Mean value of composite rating scale at 2-3 months.

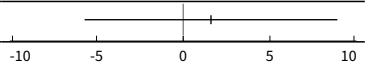
Study or subgroup	Bleach bath N	Bleach bath Mean(SD)	Placebo/emollient N	Placebo/emollient Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Leins 2013	8	15 (13.7)	11	32 (15.2)		33.6%	-1.11[-2.11,-0.12]
Wong 2013	18	13.1 (7.8)	18	25.8 (13.9)		66.4%	-1.1[-1.81,-0.39]
Total ***	**26**		**29**			**100%**	**-1.11[-1.68,-0.53]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.99); I²=0%							
Test for overall effect: Z=3.76(P=0)							



Favours bleach bath — Favours placebo/emollient

Analysis 4.11. Comparison 4 Bleach bath vs placebo or bath emollient, Outcome 11 Mean *S. aureus* counts from lesional skin at 2 months.

Study or subgroup	Bleach bath N	Bleach bath Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Wong 2013	18	7.8 (11.6)	18	6.2 (10.7)		1.6[-5.69,8.89]



Favours bleach bath — Favours placebo

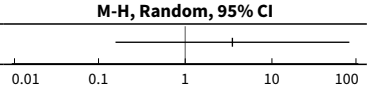
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Comparison 5. Bleach bath plus antibiotic vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients in whom MRSA was isolated at 1 month	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Change from baseline in EASI at 1 month	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3 Number of patients in whom *S. aureus* was isolated at 1 month	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Number of patients with a reduction in IGA at 3 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
5 Number of patients in whom MRSA was isolated at 3 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
6 Change from baseline in EASI at 3 months	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Number of patients in whom *S. aureus* was isolated at 3 months	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

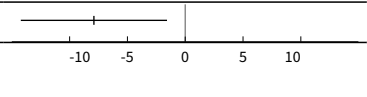
Analysis 5.1. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 1 Number of patients in whom MRSA was isolated at 1 month.

Study or subgroup	Bleach bath + antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Huang 2009	1/11	0/13		3.5[0.16,78.19]



Analysis 5.2. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 2 Change from baseline in EASI at 1 month.

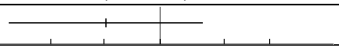
Study or subgroup	Bleach bath + antibiotic N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Huang 2009	11	-10.4 (9.3)	14	-2.5 (6)		-7.9[-14.22,-1.58]



Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

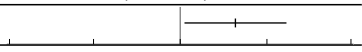
Analysis 5.3. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 3 Number of patients in whom *S. aureus* was isolated at 1 month.

Study or subgroup	Bleach bath + antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Huang 2009	6/11	10/13		0.71[0.38,1.31]



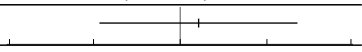
Analysis 5.4. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 4 Number of patients with a reduction in IGA at 3 months.

Study or subgroup	Bleach bath + antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Huang 2009	6/9	2/13		4.33[1.12,16.82]



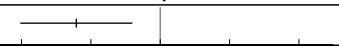
Analysis 5.5. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 5 Number of patients in whom MRSA was isolated at 3 months.

Study or subgroup	Bleach bath + antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Huang 2009	1/8	1/13		1.63[0.12,22.5]



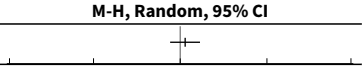
Analysis 5.6. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 6 Change from baseline in EASI at 3 months.

Study or subgroup	Bleach bath + antibiotic N	Mean(SD)	Placebo N	Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Huang 2009	9	-15.3 (11.4)	13	-3.2 (5.8)		-12.1[-20.18,-4.02]



Analysis 5.7. Comparison 5 Bleach bath plus antibiotic vs placebo, Outcome 7 Number of patients in whom *S. aureus* was isolated at 3 months.

Study or subgroup	Bleach bath + antibiotic n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Huang 2009	7/8	10/13		1.14[0.77,1.69]

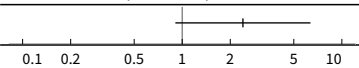


Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Comparison 6. Therapeutic textile vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Number of patients in complete remission or well under control at end of study	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Adverse events requiring withdrawal from treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Minor adverse events not requiring withdrawal from treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
4 Mean SCORAD at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5 Change from baseline in local SCORAD at end of treatment	1		Mean Difference (Random, 95% CI)	Totals not selected
6 Mean log of *S. aureus* counts from lesional skin at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
7 Mean *S. aureus* counts (thousands) from lesional skin at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
8 Mean DLQI at 8 weeks	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9 Mean SCORAD at 8 weeks	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
10 Mean SCORAD at 90 days	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
11 No of patients in whom *S. aureus* was isolated at 8 weeks	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
12 Mean log of *S. aureus* counts at 8 weeks	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Therapeutic textile vs placebo, Outcome 1 Number of patients in complete remission or well under control at end of study.

Study or subgroup	Silver textile n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Juenger 2006	8/10	3/9		2.4[0.91,6.36]
		Favours placebo	0.1 0.2 0.5 1 2 5 10	Favours silver textile

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 6.2. Comparison 6 Therapeutic textile vs placebo, Outcome 2 Adverse events requiring withdrawal from treatment.

Study or subgroup	Chitosan-coated textile n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Lopes 2015	1/43	0/35		2.45[0.1,58.45]

Favours chitosan 0.02 0.1 1 10 50 Favours placebo

Analysis 6.3. Comparison 6 Therapeutic textile vs placebo, Outcome 3 Minor adverse events not requiring withdrawal from treatment.

Study or subgroup	Silver textile n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Juenger 2006	2/10	2/10		1[0.17,5.77]

Favours silver textile 0.1 0.2 0.5 1 2 5 10 Favours placebo

Analysis 6.4. Comparison 6 Therapeutic textile vs placebo, Outcome 4 Mean SCORAD at end of treatment.

Study or subgroup	Silver textile N	Silver textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Juenger 2006	10	36.1 (21.1)	10	45.9 (18.7)		-9.8[-27.27,7.67]

Favours silver textile -20 -10 0 10 20 Favours placebo

Analysis 6.5. Comparison 6 Therapeutic textile vs placebo, Outcome 5 Change from baseline in local SCORAD at end of treatment.

Study or subgroup	Dermasilk N	Placebo N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Stinco 2008	26	26	-10 (1.81)		-10.05[-13.6,-6.5]

Favours Dermasilk -20 -10 0 10 20 Favours placebo

Analysis 6.6. Comparison 6 Therapeutic textile vs placebo, Outcome 6 Mean log of *S. aureus* counts from lesional skin at end of treatment.

Study or subgroup	Silver textile N	Silver textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Juenger 2006	10	2.1 (0.9)	10	2.1 (1.2)		0[-0.93,0.93]

Favours silver textile -1 -0.5 0 0.5 1 Favours placebo

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Analysis 6.7. Comparison 6 Therapeutic textile vs placebo, Outcome 7 Mean *S. aureus* counts (thousands) from lesional skin at end of treatment.

Study or subgroup	Silver textile N	Silver textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Daeschlein 2010	11	13.7 (6.9)	8	23.6 (45.7)		-9.9[-41.83,22.03]

Favours silver textile -50 -25 0 25 50 Favours placebo

Analysis 6.8. Comparison 6 Therapeutic textile vs placebo, Outcome 8 Mean DLQI at 8 weeks.

Study or subgroup	Chitosan-coated textile N	Chitosan-coated textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Lopes 2015	37	4.8 (4.3)	32	5.6 (6.1)		-0.8[-3.32,1.72]

Favours chitosan -5 -2.5 0 2.5 5 Favours placebo

Analysis 6.9. Comparison 6 Therapeutic textile vs placebo, Outcome 9 Mean SCORAD at 8 weeks.

Study or subgroup	Chitosan-coated textile N	Chitosan-coated textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Lopes 2015	37	29.4 (24.8)	32	25.7 (21.4)		3.7[-7.2,14.6]

Favours chitosan -10 -5 0 5 10 Favours placebo

Analysis 6.10. Comparison 6 Therapeutic textile vs placebo, Outcome 10 Mean SCORAD at 90 days.

Study or subgroup	Silver/seaweed textile N	Silver/seaweed textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Portela Araujo 2013	11	24 (12.5)	7	24.2 (12.5)		-0.2[-12.05,11.65]

Favours silver/seaweed -20 -10 0 10 20 Favours placebo

Analysis 6.11. Comparison 6 Therapeutic textile vs placebo, Outcome 11 No of patients in whom *S. aureus* was isolated at 8 weeks.

Study or subgroup	Chitosan-coated textile n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Lopes 2015	22/34	18/28		1.01[0.69,1.46]

Favours chitosan 0.5 0.7 1 1.5 2 Favours placebo

Analysis 6.12. Comparison 6 Therapeutic textile vs placebo, Outcome 12 Mean log of *S. aureus* counts at 8 weeks.

Study or subgroup	Chitosan-coated textile N	Chitosan-coated textile Mean(SD)	Placebo N	Placebo Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
Lopes 2015	34	4 (1.8)	28	3.8 (1.6)		0.2[-0.65,1.05]

Favours chitosan -2 -1 0 1 2 Favours placebo

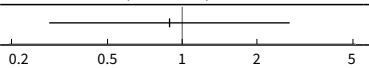
Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Comparison 7. Protease inhibitor vs placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global outcome (good or excellent)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
2 Adverse events requiring withdrawal from treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3 Adverse events not requiring withdrawal from treatment	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 7.1. Comparison 7 Protease inhibitor vs placebo, Outcome 1 Global outcome (good or excellent).

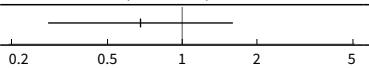
Study or subgroup	Protease inhibitor n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Foelster Holst 2010	5/45	6/48		0.89[0.29,2.71]



Favours placebo | Favours protease inhibito

Analysis 7.2. Comparison 7 Protease inhibitor vs placebo, Outcome 2 Adverse events requiring withdrawal from treatment.

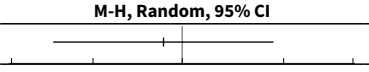
Study or subgroup	Protease inhibitor n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Foelster Holst 2010	7/45	11/48		0.68[0.29,1.6]



Favours protease inhibito | Favours placebo

Analysis 7.3. Comparison 7 Protease inhibitor vs placebo, Outcome 3 Adverse events not requiring withdrawal from treatment.

Study or subgroup	Protease inhibitor n/N	Placebo n/N	Risk Ratio M-H, Random, 95% CI	Risk Ratio M-H, Random, 95% CI
Foelster Holst 2010	20/45	23/48		0.93[0.6,1.44]



Favours protease inhibito | Favours placebo

ADDITIONAL TABLES

Table 1. Correspondence with authors

Study ID	Information requested	Response
Canpolat 2012	10th April 2015	No response

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	Dear Professor Canpolat We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your recent article 'Hydrocortisone acetate alone or combined with mupirocin for atopic dermatitis in infants under two years of age – a randomized double blind pilot trial' (Eur Rev Med Pharmacol Sci 2012; 16:1989-93) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence in the trial? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. The abstract indicates that efficacy evaluation was made at 'day 7 and weeks 2, 4 and 8' however the results are only reported for 'day 8'. Could you please clarify and provide any outcome data for additional time points that are available? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	
Fluhr 2009	11th April 2015 Dear Dr Fluhr We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your article 'Silver-loaded seaweed-based cellulosic fiber improves epidermal skin physiology in atopic dermatitis: safety assessment, mode of action and controlled, randomized single-blinded exploratory in vivo study' (Exp Dermatol 2009; 19:e9-15) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the randomised in vivo study? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. You have indicated that the study was single-blinded. Could you clarify who was and was not blinded (the participants, investigators, wider study team, those assessing the outcomes)? 4. Could you clarify how and when the outcomes were assessed and who made the assessment? 5. Did you record any clinical assessment of the severity of atopic dermatitis or of quality of life? 6. Could you provide the values for the mean and standard error of the mean for the S. aureus colonisation changes reported in Figure 2a? I look forward to hearing from you.	No response

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	
Gauger 2006	11th April 2015 Dear Dr Gauger We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your article 'Efficacy and functionality of silver-coated textiles in patients with atopic eczema' (JEADV 2006; 18:534-41) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the trial? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. You have indicated that the study was double-blind. However, the Results state that 'Nine of the 11 dropouts were from the placebo group, due to either systemic antibiotics or assignment to the placebo group by the patient.' This appears to imply that patients in the placebo group were aware of their assignment. Could you clarify who was and was not blinded (the participants, investigators, wider study team, those assessing the outcomes) and how long this was maintained? 4. Could you supply the full results for the responses to the questionnaire (Table 2) at 1 week and at the end of the study in terms of the number of participants in each group giving each response? 5. Could you supply the standard deviations at each time point for the general SCORAD (fig. 1), eczema extent in the SCORAD (fig. 2), subjective symptoms in SCORAD (fig. 3) and impairment of quality of life (fig. 4)? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	No response
Hung 2007	18th April 2015 Dear Dr Chiang We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your article by Hung et al, 'Staphylococcus colonization in atopic dermatitis treated with fluticasone or tacrolimus with or without antibiotics' (Ann Allergy Asthma Immunol 2007; 98:51-6) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the trial?	No response

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	2. Could you describe the method used, if any, to conceal the allocation sequence? 3. Could you supply the full results for the outcomes reported in Figure 1 and Figure 2 (e.g. means and standard deviations or standard errors at each time point)? 4. Could you supply the full results for each group at each time point for the other outcomes not reported in the paper – modified local SCORAD, colonisation density of S. aureus, antibiotic resistance? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	
Koller 2007	18th April 2015 Dear Dr Koller We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your article 'Action of a silk fabric treated with AEGIS™ in children with atopic dermatitis: a 3-month trial' (Pediatr Allergy Immunol 2009; 18:335-8) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the trial? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. Did you give any instructions on washing and drying the tubes? 4. Did you calculate a total for the modified SCORAD? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	No response
Leins 2013	13th October 2015 Dear Liz Leins, We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Our searches identified your trial on Bleach Baths for Eczema as possibly relevant for the Cochrane Systematic Review and we would be very grateful if you could send us further details of the study and any results. Many thanks for your help. Kind regards, Susannah George Specialty Registrar in Dermatology	18th October 2015 Hi Susannah, The final results are unpublished so I can't send you those, however our poster was presented at the Australasian College of Dermatologist's annual conference and reported pilot data (although our final results are the same).

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	Eastbourne District General Hospital	Best, Liz [Conference poster attached]
Lembo 2011	10th April 2015 Dear Dr Lembo We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your recent article 'L'eritromicina topica nella terapia della dermatite atopica' (Ann Ital Dermatol Allergol 2011; 65:3) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. You have indicated that the patients were randomised into the two groups stratified by age and sex. Could you describe the method used to generate the allocation sequence within each stratum? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. You have indicated that the study was double-blind. Could you clarify who was and was not blinded (the participants, investigators, wider study team, those assessing the outcomes)? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	30th April 2015 Dear Dr. George. Sorry for writing you so late but it has been a very busy period. We are happy about your intention to include our paper in your updated review. This is the method we used to generate the two groups stratified for sex and age: 1. Age and sex of patients were recorded in a word excel sheet in which patients were anonymised 2. Patients were ordered by age 3. Four classes were identified by age range: I: 0.5 to 3 years II: 4 to 7 years III: 8 to 11 years IV: 12 to 14 years. 1. Two subclasses were identified by sex in each age class: male and female 2. Each subject in the sex subclass was sequentially enumerated (1…2…3…4…) 3. Pare numbers were assigned to group B and spare numbers were assigned to group A. Patients and SCORAD evaluator were blind. Best regards Claudio Lembo
Leyden 1977	15th February 2017 Dear Professor Leyden	16th February 2017

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	I am a consultant dermatologist in the UK and I am currently updating the Cochrane systematic review on antistaphylococcal interventions in atopic dermatitis. Your paper on steroid-antibiotic combinations from 1977 is included in the review and I am having some difficulty interpreting the detail of the results to include them in the review. For the comparison of Synalar vs Neo-Synalar, you reported clinical responses of 30% excellent, 40% good and 30% fair for Synalar and 70% excellent, 20% good and 10% fair for Neo-Synalar. However, these exact percentages do not seem possible based on the reported sample sizes of 21 and 15, respectively. I realise this study was a long time ago, however I wondered if you would be able to clarify whether the percentages reported were based on a smaller subset of patients, or whether they have been approximated/rounded off to multiples of 10%. Many thanks for your help. Kind regards Susannah Dr Susannah George Consultant Dermatologist Brighton and Sussex University Hospitals NHS Trust	I assume the % were rounded off
Portela Araujo 2013	13th October 2015 Dear Dr Araujo We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your recent article 'A proposal for the use of new silver-seaweed-cotton fibers in the treatment of atopic dermatitis' (Cutan Ocul Toxicol 2013; 32:268-74) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the trial? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. Could you describe the reason why one patient in the intervention group did not complete the study? At what point did they drop out? 4. In your study, were patients given only one set of clothes to wear continuously for the first seven days? How often were they expected to wash the clothing? Do you have any data as to whether the patients did or did not wear the clothing as instructed? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	No response
Wong 2013	12th April 2015	13th April 2015

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

Dear Dr Wong We are currently updating the Cochrane systematic review of Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Your recent article 'Efficacy and safety of sodium hypochlorite (bleach) baths in patients with moderate to severe atopic dermatitis in Malaysia' (J Dermatol 2013; 40:874-80) will be included in the updated review. We would be grateful if you could answer a few questions for clarification: 1. Could you describe the method used to generate the allocation sequence for the trial? 2. Could you describe the method used, if any, to conceal the allocation sequence? 3. You have indicated that the study was double-blind. However, previous studies of bleach baths have reported that the intervention was obvious due to the smell of bleach. Did you make any attempt to address this in your study, and did you have any evidence that the participants were genuinely blinded to their treatment allocation? More generally, could you clarify who was and was not blinded (the participants, investigators, wider study team, those assessing the outcomes) and how long this was maintained? 4. Could you supply the full results for the bacteriological assessments (means and standard deviations in CFU/cm2 at baseline and follow-up)? 5. Could you supply the mean and standard deviation for each group at each time point for EASI (Figure 3), BSA affected (Figure 5) and itch scores (Figure 7)? I look forward to hearing from you. Kind regards Dr Susannah George Specialty Registrar in Dermatology Eastbourne District General Hospital	Dear Dr George, Thank you for your email. I will try and answer all your questions as accurately as possible. 1.Could you describe the method used to generate the allocation sequence for the trial? Patients were assigned randomly through computer generated simple randomised numbers to the treatment or placebo study arms. 2. Could you describe the method used, if any, to conceal the allocation sequence? I had no access to the allocation sequence. the pharmacist helping in this study, dispensed either bleach or placebo (distilled water) according to the computer generated numbers. So I didn't know which the patient got, and on all the subsequent follow-up, the patient was assessed by me without knowledge of what treatment they were given. 3. You have indicated that the study was double-blind. However, previous studies of bleach baths have reported that the intervention was obvious due to the smell of bleach. Did you make any attempt to address this in your study, and did you have any evidence that the participants were genuinely blinded to their treatment allocation? More generally, could you clarify who was and was not blinded (the participants, investigators, wider study team, those assessing the outcomes) and how long this was maintained?

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Table 1. Correspondence with authors *(Continued)*

	Both treatment and placebo were placed in identical bottles. yes, the patient may have been able to smell the bleach. but nothing else was done to mask the smell. The investigator (also assessed outcomes) was blinded, pharmacist dispensing the medication was not. This was maintained throughout the study period. 4. Could you supply the full results for the bacteriological assessments (means and standard deviations in CFU/cm^2 at baseline and follow-up)? - see excel sheet attached 5. Could you supply the mean and standard deviation for each group at each time point for EASI (Figure 3), BSA affected (Figure 5) and itch scores (Figure 7)? - see excel sheet attached I hope the above answers your questions. Please do not hesitate to contact me if you need further clarification. Thank you. Regards, Dr Wong S

APPENDICES

Appendix 1. CENTRAL (Cochrane Library) search strategy

#1 MeSH descriptor: [Staphylococcus aureus] explode all trees
#2 MeSH descriptor: [Staphylococcal Skin Infections] explode all trees
#3 MeSH descriptor: [Staphylococcus] explode all trees
#4 staphylococc*:ti,ab,kw
#5 {or #1-#4}
#6 MeSH descriptor: [Eczema] explode all trees
#7 MeSH descriptor: [Dermatitis, Atopic] explode all trees
#8 MeSH descriptor: [Neurodermatitis] explode all trees
#9 MeSH descriptor: [Dermatitis] explode all trees
#10 eczema or dermatitis or neurodermatitis:ti,ab,kw
#11 besnier$ prurigo:ti,ab,kw

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

#12 {or #6-#11}
#13 #5 and #12

Appendix 2. MEDLINE (Ovid) search strategy

1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. randomized.ab.
4. placebo.ab.
5. clinical trials as topic.sh.
6. randomly.ab.
7. trial.ti.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp animals/ not humans.sh.
10. 8 not 9
11. exp Eczema/ or eczema.mp.
12. exp Dermatitis, Atopic/
13. neurodermatitis.mp. or exp Neurodermatitis/
14. exp Dermatitis/ or dermatitis.mp.
15. Besnier$ Prurigo.mp.
16. or/11-15
17. exp staphylococcus/ or exp staphylococcus aureus/
18. staphylococc$.ti,ab.
19. exp Staphylococcal Skin Infections/
20. or/17-19
21. 10 and 16 and 20

[Lines 1-10: Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE: sensitivity- and precision-maximizing version (2008 revision)]

Appendix 3. Embase (Ovid) search strategy

1. exp staphylococcal skin infection/
2. exp Staphylococcus aureus/
3. exp Staphylococcus/
4. staphylococc$.ti,ab.
5. or/1-4
6. eczema.mp. or exp ECZEMA/
7. exp DERMATITIS/ or dermatitis.mp.
8. exp atopic dermatitis/
9. neurodermatitis.mp. or exp NEURODERMATITIS/
10. Besnier$ Prurigo.mp.
11. or/6-10
12. crossover procedure.sh.
13. double-blind procedure.sh.
14. single-blind procedure.sh.
15. (crossover$ or cross over$).tw.
16. placebo$.tw.
17. (doubl$ adj blind$).tw.
18. allocat$.tw.
19. trial.ti.
20. randomized controlled trial.sh.
21. random$.tw.
22. or/12-21
23. exp animal/ or exp invertebrate/ or animal experiment/ or animal model/ or animal tissue/ or animal cell/ or nonhuman/
24. human/ or normal human/
25. 23 and 24
26. 23 not 25
27. 22 not 26
28. 5 and 11 and 27

Appendix 4. LILACS search strategy

In LILACS we searched using the Controlled clinical trials topic-specific query filter and the following terms:

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

(dermatitis or eczema or neurodermatitis or besnier$ or eccema) and (staphylococc$ or estafilococo)

WHAT'S NEW

Date	Event	Description
15 October 2019	New search has been performed	A new search led to the addition of 20 new included studies, and we updated the review in line with MECIR standards.
15 October 2019	New citation required but conclusions have not changed	Update completed. We incorporated GRADE into this update of the review.

HISTORY

Protocol first published: Issue 1, 2002
Review first published: Issue 3, 2008

Date	Event	Description
14 March 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

SG was the contact person with the editorial base, SG co-ordinated contributions from the co-authors, and wrote the final draft of the review.
SG, SK, DH screened papers against eligibility criteria.
SG obtained data on ongoing and unpublished studies.
SG, SK, DH appraised the quality of papers.
SG, SK, DH extracted data for the review and sought additional information about papers.
SG, DH entered data into RevMan.
SG, DH analysed and interpreted data.
SG, DH worked on the methods sections.
SG drafted the clinical sections of the background and responded to the clinical comments of the referees.
DH responded to the methodology and statistics comments of the referees.
AR was the consumer co-author and checked the review for readability and clarity, as well as ensuring outcomes were relevant to consumers.
AB, FBH, JR, HW performed the original review and provided advice on inclusion of studies and interpretation of data.
SG is the guarantor of the update.

Disclaimer

This project was supported by the National Institute for Health Research, via Cochrane Infrastructure funding to the Cochrane Skin Group. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, NHS or the Department of Health.

DECLARATIONS OF INTEREST

Susannah MC George: none known.
Sanja Karanovic: none known.
David A Harrison: none known.
Anjna Rani: none known.
Andrew J Birnie has received payment from Leo Pharma and Almirall for delivering lectures on skin cancer and sun damage. Almirall has covered meeting registration fee, plus travel and accommodation, for the American Academy of Dermatology meeting in March 2017.
Fiona J Bath-Hextall: none known.
Jane C Ravenscroft: none known.

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Hywel C Williams: I am director of the NIHR HTA Programme. HTA is part of the NIHR which also supports the NIHR systematic reviews programme from which this work is funded. I was also a co-applicant on a relevant clinical trial (SCIN trial) that is not yet published that sought to prevent hand eczema in nurses, funded by the National Institute of Health Research Health Technology Assessment Programme

SOURCES OF SUPPORT

Internal sources

- Queens Medical Centre NHS Trust, UK.

External sources

- The National Institute for Health Research (NIHR), UK.

  The NIHR, UK, is the largest single funder of the Cochrane Skin Group

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have changed the title of this review to 'Interventions to reduce *Staphylococcus aureus* in the management of eczema'. In the original protocol, it was 'Interventions to reduce *Staphylococcus aureus* for atopic eczema'. The wording 'in the management of' was added in response to a comment from an external referee. The word 'atopic' was removed in the subsequent update to meet current terminology.

Under 'Objectives' we changed the text from 'To assess the efficacy and possible adverse effects of interventions to reduce *S. aureus* for treating atopic eczema' to 'To assess the effects of interventions to reduce *S. aureus* for treating eczema', in line with updated guidance from the *Cochrane Handbook for Systematic Reviews of Interventions*.

Under 'Types of interventions' in the review text, we adjusted the categories of types of interventions to cover all relevant interventions identified by the searches. We also clarified the rationale (as originally intended) for which comparators were considered valid for each intervention and included placebo and untreated textiles in the list of potential comparators.

Under 'Types of outcome measures', we have omitted the secondary outcome listed in the protocol: 'we will report on skin irritation separately as it is a common occurrence' from the review. We have explained this in the Methods section under 'Data extraction and management'. We have also explained the definitions of short-term benefit and long-term benefit.

Also under 'Measures of treatment effects', we have analysed the results as risk ratios rather than odds ratios as was planned in the protocol; this is in line with Cochrane Skin Group policy and has been explained in the text. We also added that for continuous outcomes we would use standardised mean differences (SMD) when different instruments were used.

To align with the current Cochrane methodology, we assessed risk of bias in the update using the Cochrane 'Risk of bias' tool (Higgins 2011). We also assessed heterogeneity using the I^2 statistic and planned to create funnel plots to explore reporting bias (however, we could not do this as the meta-analyses did not include 10 or more studies). We planned to perform subgroup analysis according to infection status and to perform sensitivity analyses examining the effects of excluding study subgroups, e.g. those studies with low methodological quality, but there were insufficient studies to do so. For the meta-analyses, we used a random-effects model as studies were considered to be clinically heterogeneous. We also included a 'Summary of findings' table to summarise our most important comparisons, and used the GRADE methodology to assess the certainty of evidence for important outcomes within these comparisons.

INDEX TERMS

Medical Subject Headings (MeSH)

*Staphylococcus aureus; Anti-Bacterial Agents [adverse effects] [therapeutic use]; Anti-Infective Agents, Local [therapeutic use]; Antifungal Agents [therapeutic use]; Clothing; Dermatitis, Atopic [*drug therapy] [microbiology]; Drug Resistance, Bacterial; Randomized Controlled Trials as Topic; Silver Compounds [therapeutic use]; Soaps [adverse effects] [therapeutic use]; Staphylococcal Skin Infections [*drug therapy]

MeSH check words

Humans

Copyright © 2019 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.