I. Appendix I: Search strategy

The search strategy retrieved 6,300 hits for antiviral and 9,784 hits for antifungal. To identify the most relevant literature, filters for systematic reviews, randomized control trials, and observational studies were applied.

PubMed:
*(*dermatitis, atopic[MeSH Terms] OR eczema [MeSH Terms] OR neurodermatitis[MeSH Terms] OR eczema OR dermatitis OR neurodermatitis) AND *(*virus[MeSH Terms] OR viral infection[MeSH Terms] OR viral infect* OR virus) (dermatitis, atopic[MeSH Terms] OR eczema [MeSH Terms] OR neurodermatitis[MeSH Terms] OR eczema OR dermatitis OR neurodermatitis) AND (antifungal[MeSH Terms] OR fungus[MeSH Terms] OR antifungal OR malassezia OR fungus)

II. Appendix III: Summary of findings

III. **Table 1: Oral antibiotic compared with placebo for eczema (adapted from George et al)[1]**

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Placebo	Oral antibiotic				
Global outcome (good or excellent improvement in symptoms or signs, or both) Follow-up: 14-28 days	Low risk population 619 per 1000[a]	495 per 1000 (111 to 1000)	RR 0.80 (0.18 to 3.50)	75 (2)	⊕⊕⊖⊖ low[b]	-
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: 4-28 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 microorganisms 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, objective SCORAD ranges from 0 to 83 and SCORAD ranges from 0 to 108, with higher values indicating greater severity. Follow-up: 14 days	The mean EASI score in the control group at the end of treatment decreased by 3.29 from the baseline value.	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.
No of participants in whom *S. aureus* was isolated Follow-up: 14-28 days	High risk population 824 per 1000[a]	626 per 1000 (379 to 1000)	RR 0.76 (0.46 to 1.26)	144 (3)	⊕⊕⊖⊖ low*b*	-

*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). Abbreviations: 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

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)

Table 2: Topical steroid plus topical antibiotic compared with topical steroid for eczema (adapted from George et al)[1]

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of Participants (studies)	Quality of the evidence (GRADE)	Comments
	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 741 per 1000[a]	815 per 1000 (741 to 897)	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.
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 31 per 1000[a]	11 per 1000 (7 to 225	RR 1.24 (0.21 to 7.25)	325 (4)	⊕⊖⊖⊖ very low[d]	Rates of adverse events were very low (zero in one study and consequently the result is very uncertain.
Minor adverse events not requiring withdrawal from treatment Follow-up: 14 days	Low risk population 36 per 1000[e]	11 per 1000 (4 to 28)	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.
	High risk population 636 per 1000[e]	191 per 1000 (76 to 496)				
Emergence of antibiotic-resistant microorganisms 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 471 per 1000[a]	226 per 1000 (127 to 396)	RR 0.48 (0.27 to 0.84)	298 (7)	⨁⨁⨁⊖ moderate[i]	-

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

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 (attritio n 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)

Table 3: Bleach bath compared with placebo or bath emollient for eczema (adapted from George et al)[1]

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of Participants (studies)	Quality of the evidence (GRADE)	Comments
	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 500 per 1000[a]	390 per 1000 (185 to 815)	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.
Change from baseline in quality of life IDQoL 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 result could not be combined due to differing study designs.
Minor adverse events not requiring withdrawal from treatment Follow-up: 2 months	Medium risk population 278 per 1000[e]	278 per 1000 (97 to 798)	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.

Emergence of antibiotic-resistant microorganisms Follow-up: 4 months	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, objective SCORAD ranges from 0 to 83 and SCORAD ranges from 0 to 108, with higher values indicating greater severity. Follow-up: 1 month	The mean EASI score in the control group at the end of treatment was 13.87f.	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 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). Abbreviations: 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.

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

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