Effects of oral and topical antibiotics in children with infected eczema in primary care: The **CREAM** Study

Eczema Evidence Based Update:
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NHS
National Institute for Health Research

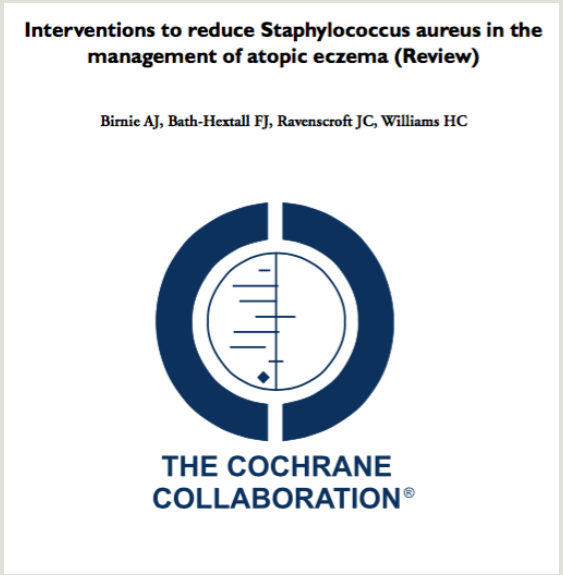
Conflicts of interest

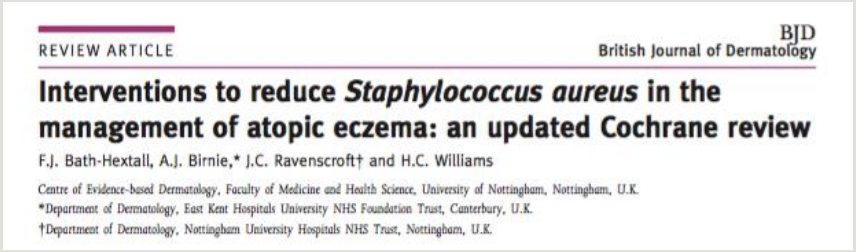
None

Antibiotics for infected eczema

- What constitutes ‘infection’?
- When should children with eczema by treated with anti-staphylococcal treatments?

Systematic Reviews





- "We failed to find clear evidence of benefit for antimicrobial interventions for people with atopic eczema, despite their widespread use."
- "Further large studies with long-term outcomes and clearly defined participants are urgently required."

Aim

To determine the effectiveness of oral and topical antibiotics, in addition to standard treatment with emollients and topical corticosteroids, in children with clinically infected eczema in primary care.

Participants

Inclusion

Children (aged 3 months to less than eight years) with atopic eczema (UK working party) who presented with **clinically suspected infected eczema**.

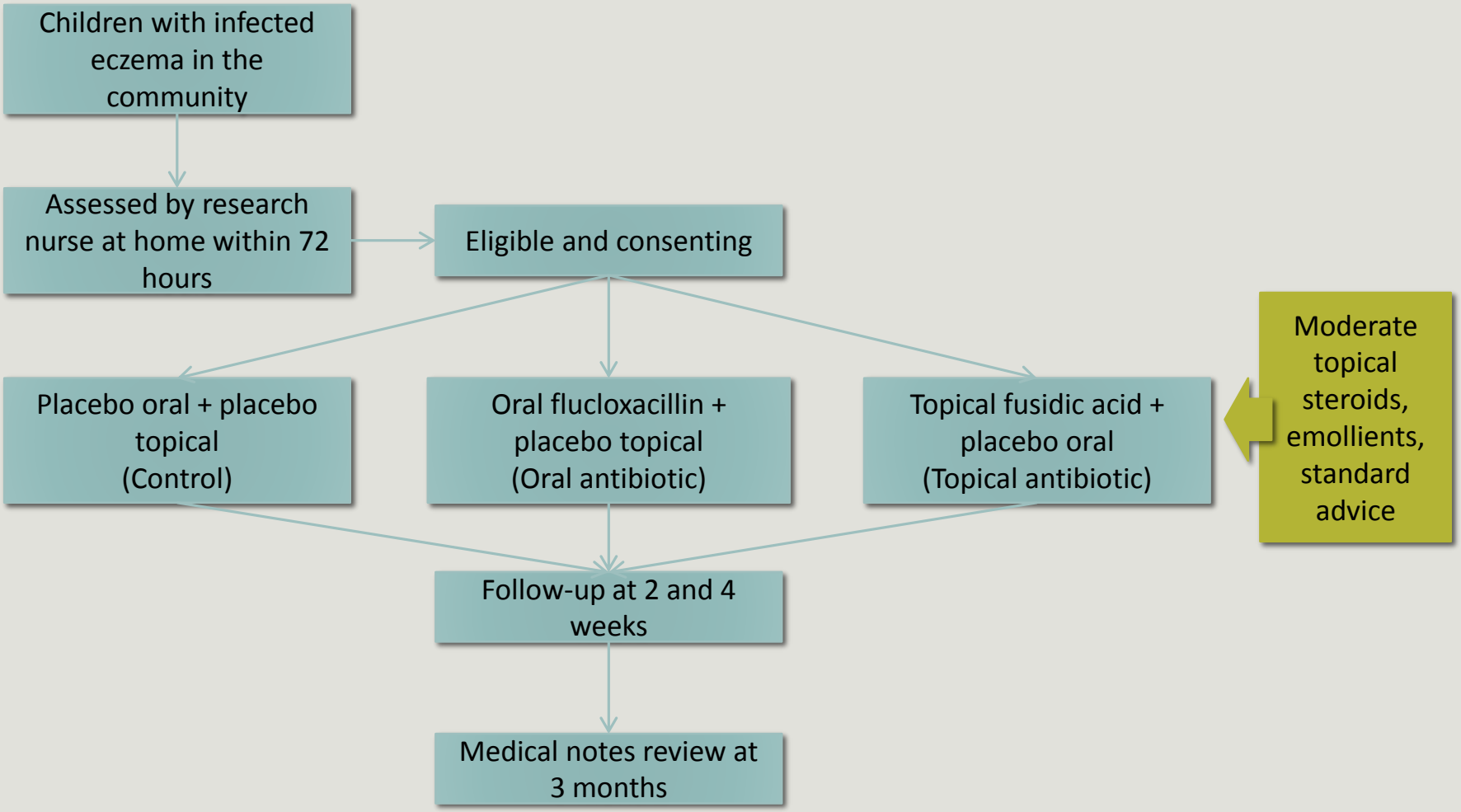
Exclusion

Used antibiotics to treat a skin infection within the past week.

Used potent or very potent topical corticosteroids within the past two days.

Severe infection requiring immediate antibiotics or was arranging immediate hospitalisation

Design


Children with infected eczema in the community
Assessed by research nurse at home within 72 hours
Eligible and consenting
Placebo oral + placebo topical (Control)
Oral flucloxacillin + placebo topical (Oral antibiotic)
Topical fusidic acid + placebo oral (Topical antibiotic)
Moderate topical steroids, emollients, standard advice
Follow-up at 2 and 4 weeks
Medical notes review at 3 months

Outcome Measures

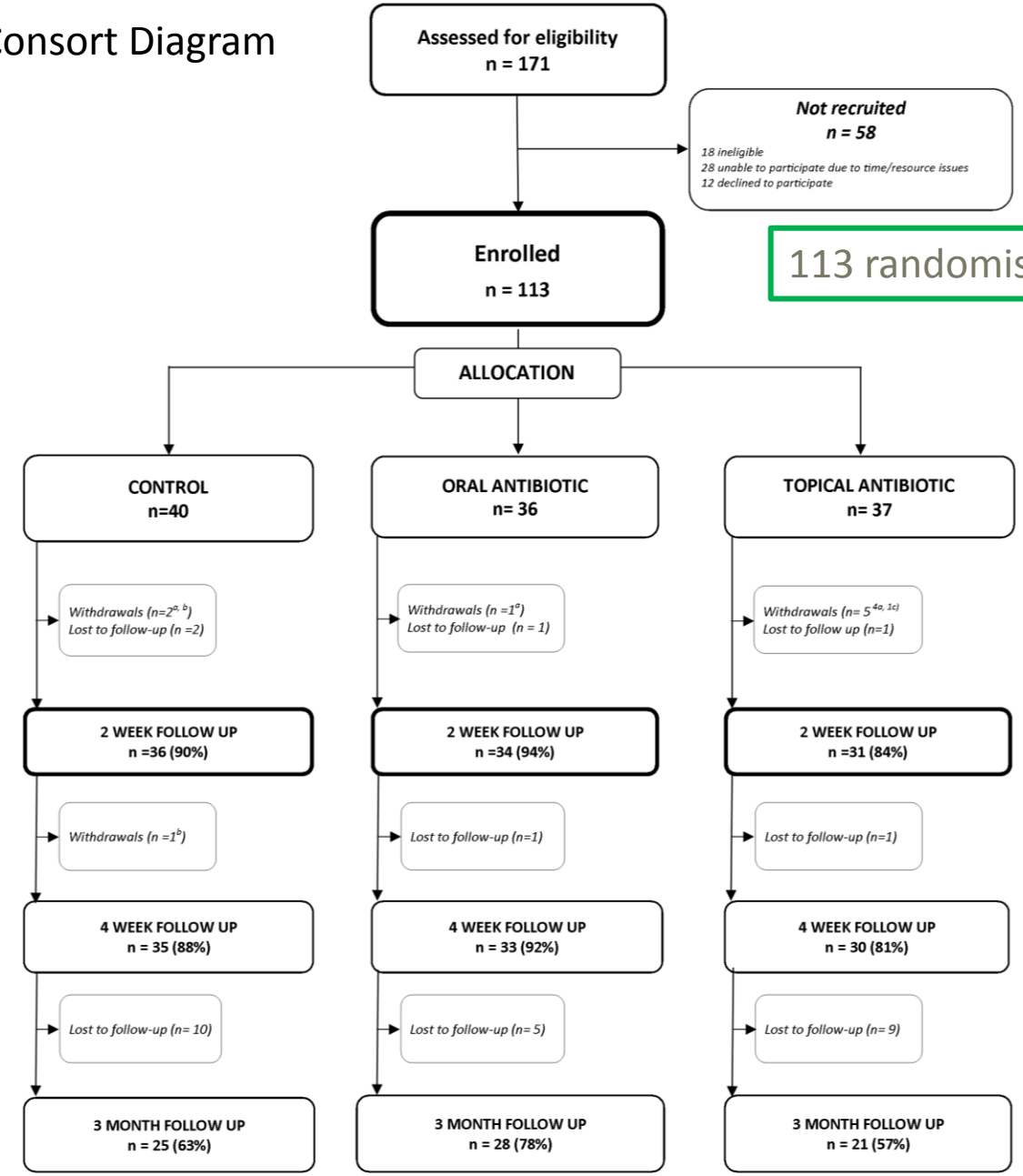
- **Patient-Oriented Eczema Measure (POEM) at 2 weeks**
- Eczema Area and Severity Index (EASI)
- Infants Dermatitis Quality of Life (IDQoL)
- Children's Dermatology Life Quality Index (CDLQI)
- Dermatitis Family Impact (DFI)
- Atopic Dermatitis Quality of Life (ADQoL)
- Adverse effects (nausea, vomiting, diarrhoea, abdominal pain, joint pains, and new rash)
- Skin, mouth and nose swabs
- Consultations and prescribing

Daily Symptom Score

- Carer's assessment of overall severity
- Itch
- Sleep disturbance
- Oozing or weeping
- Bleeding
- Fever

Each rated from 0 (normal / not affected) to 6 (as bad as it could be)

Consort Diagram



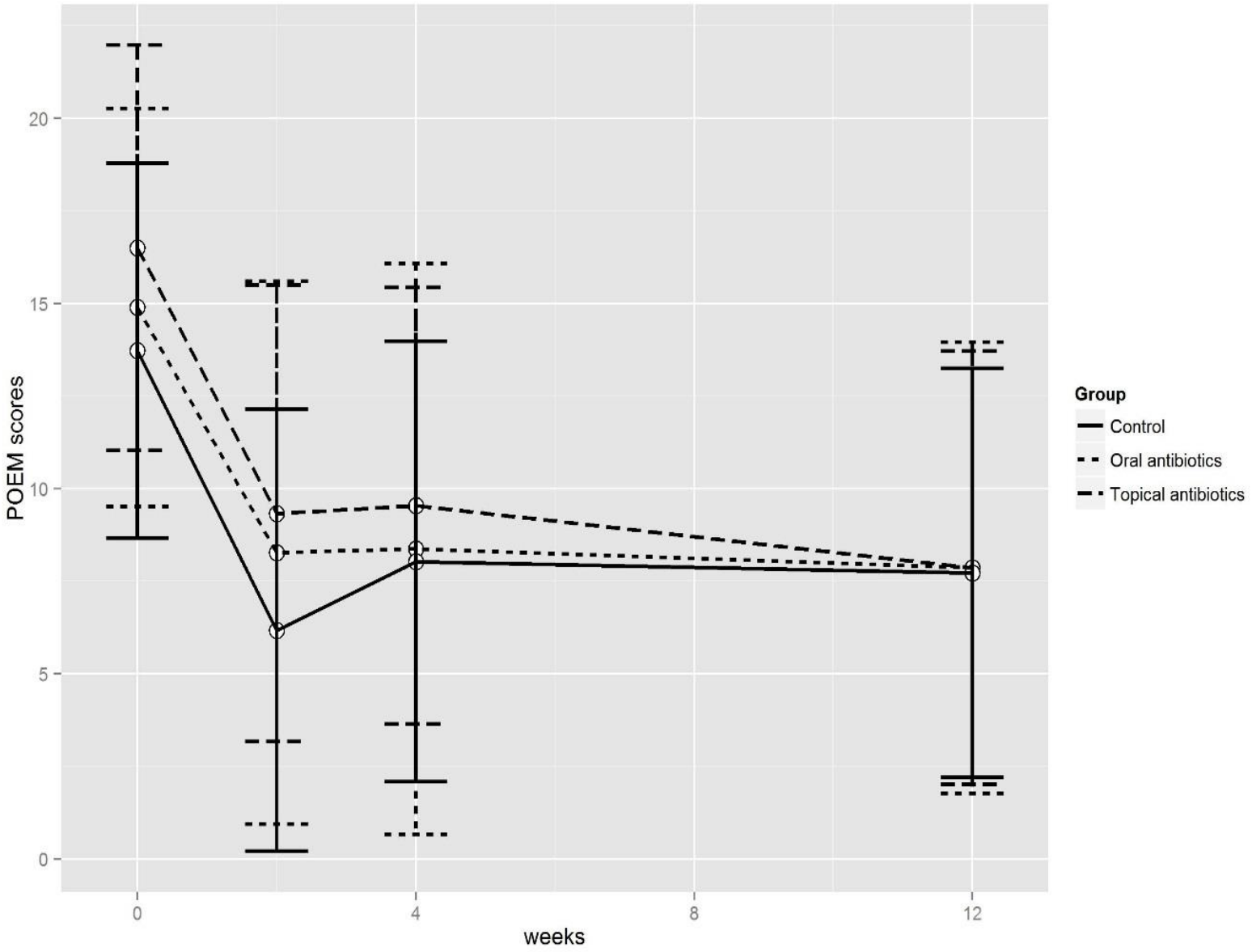
113 randomised

101 (89%) primary outcome data

Baseline characteristics

	Control (n=40)	Oral antibiotic (n=36)	Topical antibiotic (n=37)	Overall (n=113)
Age – mean (SD)	3.3 (2.2)	2.9 (2.2)	3.0 (2.1)	3.1 (2.1)
Gender – n (%)				
Male	17 (42.5)	18 (50.0)	17 (45.9)	52 (46.0)
Female	23 (57.5)	18 (50.0)	20 (54.1)	61 (54.0)
Ethnicity – n (%)				
White	33 (82.5)	31 (86.1)	27 (73.0)	91 (80.5)
Mixed	4 (10.0)	1 (2.8)	3 (8.1)	8 (7.1)
Asian, Chinese or other	1 (2.5)	3 (8.3)	3 (8.1)	7 (6.2)
Black	2 (5.0)	0 (0.0)	3 (8.1)	5 (4.4)
Prefer not to answer	0 (0.0)	1 (2.8)	1 (2.7)	2 (1.8)
Duration of eczema flare – n (%)				
1-3 days	3 (12.5)	3 (13.0)	2 (10.0)	8 (11.9)
4-7 days	10 (41.7)	9 (39.1)	4 (20.0)	23 (34.3)
8-14 days	7 (29.2)	7 (30.4)	5 (25.0)	19 (28.4)
15-28 days	4 (16.7)	4 (17.4)	9 (45.0)	17 (25.4)
Indicators or infection – n (%)				
One or more of weeping, crusting, pustules or painful skin	35 (89.7)	33 (91.7)	35 (94.6)	103 (92.0)
Temperature (38ºC or higher)	1 (2.6)	2 (6.1)	2 (5.7)	5 (4.7)
Growth of *S. aureus* from skin swab	16 (60.0)	30 (83.3)	24 (66.7)	78 (69.6)
Bath/shower frequency – n (%)				
Daily	23 (59.0)	14 (38.9)	18 (48.6)	55 (49.1)
Less than daily	16 (41.0)	22 (61.1)	19 (51.4)	57 (50.9)

POEM Scores over time



Primary Outcome

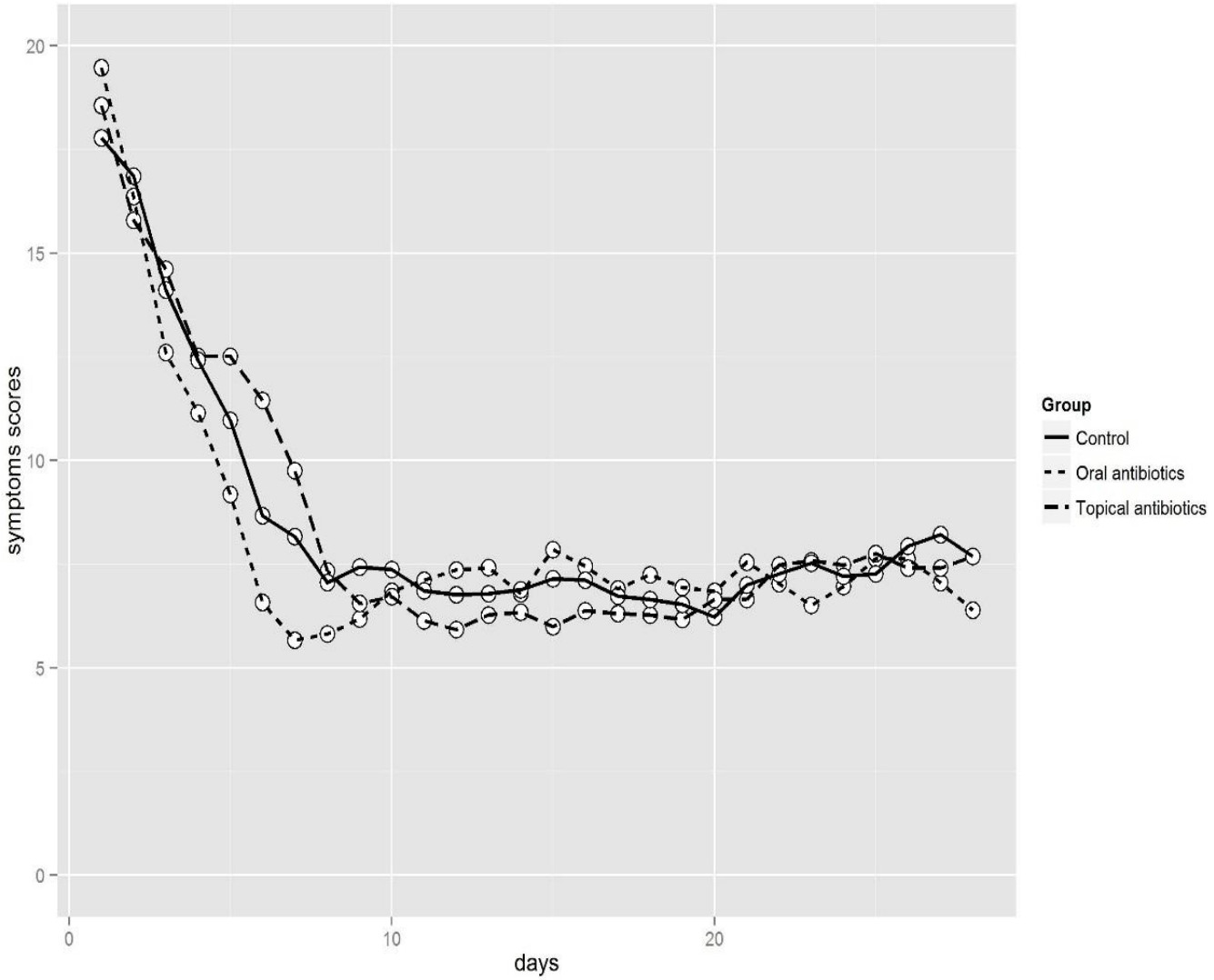
	n	Baseline POEM – mean (SD)	Week 2 POEM – mean (SD)	Intervention Effect (95% CI)*
Control	36	13.42 (5.06)	6.17 (5.97)	
Oral antibiotic	34	14.62 (5.34)	8.27 (7.33)	1.52 (-1.35, 4.40)
Topical antibiotic	31	16.90 (5.54)	9.32 (6.17)	1.49 (-1.55, 4.53)

**Difference in POEM score between control and intervention group, controlling for baseline. A positive intervention effect means the intervention is associated with an increase in POEM score, which equates to more severe subjective eczema.*

Minimal clinically important difference = 3.4

		Oral antibiotics - Effect size (95% CI)	Topical antibiotics - Effect size (95% CI)
POEM	– 4 weeks	-0.18 (-3.10, 2.75)	0.00 (-3.07, 3.07)
EASI	– 2 weeks	0.20 (-0.12, 0.52)	0.42 (0.09, 0.75)
	– 4 weeks	-0.13 (-0.47, 0.22)	0.02 (-0.34, 0.38)
IDQoL	– 2 weeks	0.11 (-0.10, 0.32)	0.18 (-0.03, 0.40)
	– 4 weeks	-0.04 (-0.28, 0.21)	0.05 (-0.20, 0.30)
CDLQI	– 2 weeks	0.43 (-0.16, 1.02)	0.70 (0.12, 1.28)
	– 4 weeks	-0.15 (-0.84, 0.54)	-0.17 (-0.87, 0.53)
DFI	– 2 weeks	0.17 (-0.18, 0.53)	0.21 (-0.15, 0.58)
	– 4 weeks	-0.02 (-0.43, 0.39)	-0.00 (-0.43, 0.42)

Total Daily Symptom Score



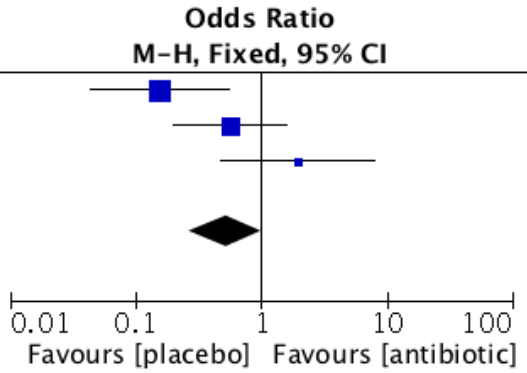
Oral antibiotics

1.1 Clinical improvement

Study or Subgroup	Antibiotic Events	Antibiotic Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ewing 1998	6	22	17	24	49.7%	0.15 [0.04, 0.56]
Francis 2016	25	36	32	40	38.9%	0.57 [0.20, 1.62]
Weinberg 1992	11	16	9	17	11.5%	1.96 [0.47, 8.11]
Total (95% CI)		**74**		**81**	**100.0%**	**0.52 [0.27, 1.02]**
Total events	42		58			

Heterogeneity: $Chi^2 = 6.78$, $df = 2$ ($P = 0.03$); $I^2 = 70\%$

Test for overall effect: $Z = 1.91$ ($P = 0.06$)



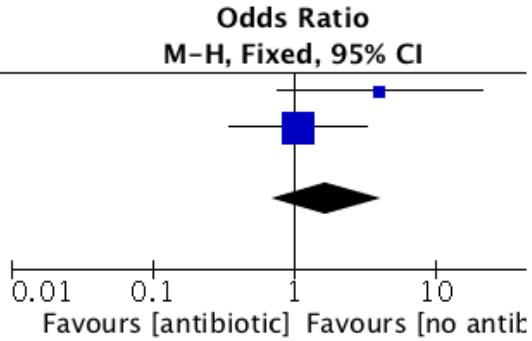
Topical antibiotics

2.1 Global improvement

Study or Subgroup	Topical AB + TCS Events	Total	TCS alone Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Wachs 1976	23	25	20	27	20.9%	4.03 [0.75, 21.64]	1976
Francis 2016	30	37	32	40	79.1%	1.07 [0.35, 3.32]	2016
Total (95% CI)		**62**		**67**	**100.0%**	**1.69 [0.68, 4.18]**	
Total events	53		52				

Heterogeneity: $Chi^2 = 1.65$, $df = 1$ ($P = 0.20$); $I^2 = 39\%$

Test for overall effect: $Z = 1.13$ ($P = 0.26$)



Interpretation

- Sample size – statistical power
- Internal validity
- External validity
  - More severe infection not included
  - Baseline POEM higher than other PC studies

Conclusions

Many children with clinically infected eczema in the community do not benefit from oral or topical antibiotics

- Respond rapidly to standard care with TCS / emollients.

What are the features that do predict benefit?

Oral and Topical Antibiotics for Clinically Infected Eczema in Children: A Pragmatic Randomized Controlled Trial in Ambulatory Care

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ABSTRACT

PURPOSE Eczema may flare because of bacterial infection, but evidence supporting antibiotic treatment is of low quality. We aimed to determine the effect of oral and topical antibiotics in addition to topical emollient and corticosteroids in children with clinically infected eczema.

METHODS We employed a 3-arm, blinded, randomized controlled trial in UK ambulatory care. Children with clinical, non-severely infected eczema were randomized to receive oral and topical placebos (control), oral antibiotic (flucloxacillin) and topical placebo, or topical antibiotic (fusidic acid) and oral placebo, for 1 week. We compared Patient Oriented Eczema Measure (POEM) scores at 2 weeks using analysis of covariance (ANCOVA).

RESULTS We randomized 113 children (40 to control, 36 to oral antibiotic, and

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Study Team

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Department of Health Disclaimer:

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