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Randomised controlled trial of silk therapeutic clothing for the long-term management of atopic eczema in children

The CLOTHES Trial

Thomas et al (2017) Silk garments plus standard care compared with standard care for treating eczema in children: A randomised, controlled, observer-blind, pragmatic trial (CLOTHES Trial) PLOS Medicine 14(4): e1002280.

https://doi.org/10.1371/journal.pmed.1002280

- Disclaimer

- Trial was funded by UK National Institute for Health Research Health Technology Assessment Programme

- Garments were provided free for use in the trial:

Dermasilk™ (Espere Healthcare Ltd, UK and AIPre Tec, Italy)

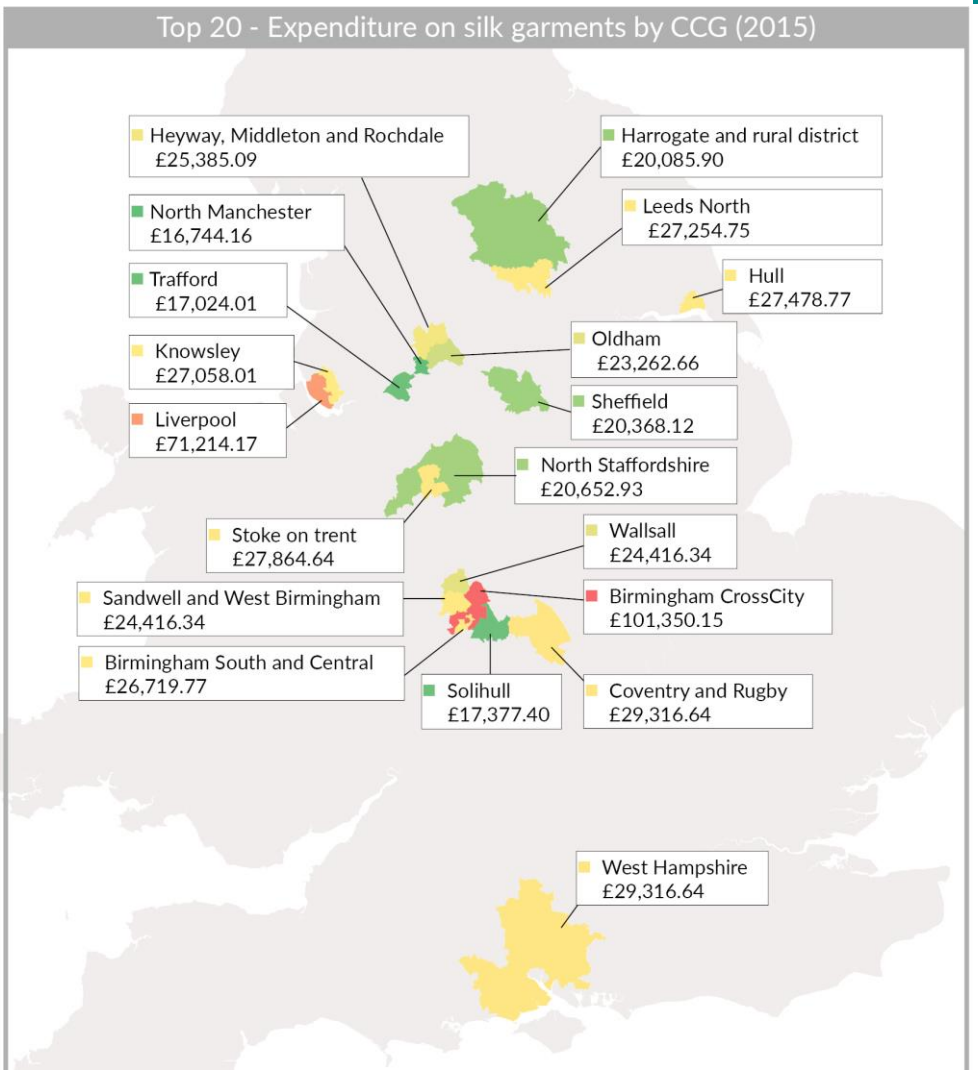
Dreamskin™ (Dreamskin Health Ltd, UK)

- No other conflicts of interest

Rationale

- Silk clothing (CE approved medical device) available on prescription in the UK
- Currently NHS spends approx. £2 million per year (cost of single set £66 to £155 depending on the size of the child).
- Increasingly popular with patients
- Limited evidence of effectiveness
  (3 small RCTs: 79 participants in total)

Mechanism of action:
Soft, smooth fibres next to the skin, temperature regulation, possibly antimicrobial effects


Top 20 - Expenditure on silk garments by CCG (2015)
Heyway, Middleton and Rochdale £25,385.09
Harrogate and rural district £20,085.90
North Manchester £16,744.16
Leeds North £27,254.75
Trafford £17,024.01
Hull £27,478.77
Knowsley £27,058.01
Oldham £23,262.66
Liverpool £71,214.17
Sheffield £20,368.12
North Staffordshire £20,652.93
Stoke on trent £27,864.64
Wallsall £24,416.34
Sandwell and West Birmingham £24,416.34
Birmingham CrossCity £101,350.15
Birmingham South and Central £26,719.77
Solihull £17,377.40
Coventry and Rugby £29,316.64
West Hampshire £29,316.64

Objective:

To assess whether silk therapeutic clothing, when used in addition to standard eczema care, reduces atopic eczema severity in children over six months.

Participants

- 300 children (1 to 15 years)
- Eczema (UK Diagnostic Criteria for Atopic Eczema)
- Moderate to severe (Nottingham Eczema Severity Scale[1])
- Secondary and primary care, plus self-referral

[1] Emerson RM *et al Br J Dermatol.* 2000 Feb;142(2):288-97

Trial design

Trial design: Observer-blind, parallel group, pragmatic RCT (6 months)

Intervention: Standard care plus 100% sericin-free knitted silk garments (x3 sets per participant) [DermaSilk & DreamSkin]

Control: standard care

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Multicentre Study

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- Nottingham (lead site),
  Royal Free London, Cambridge,
  Portsmouth,
  Isle of Wight

Outcomes

Primary outcome:

Eczema severity: Eczema Area and Severity Index (EASI): Baseline 2, 4 and 6 months (blinded).

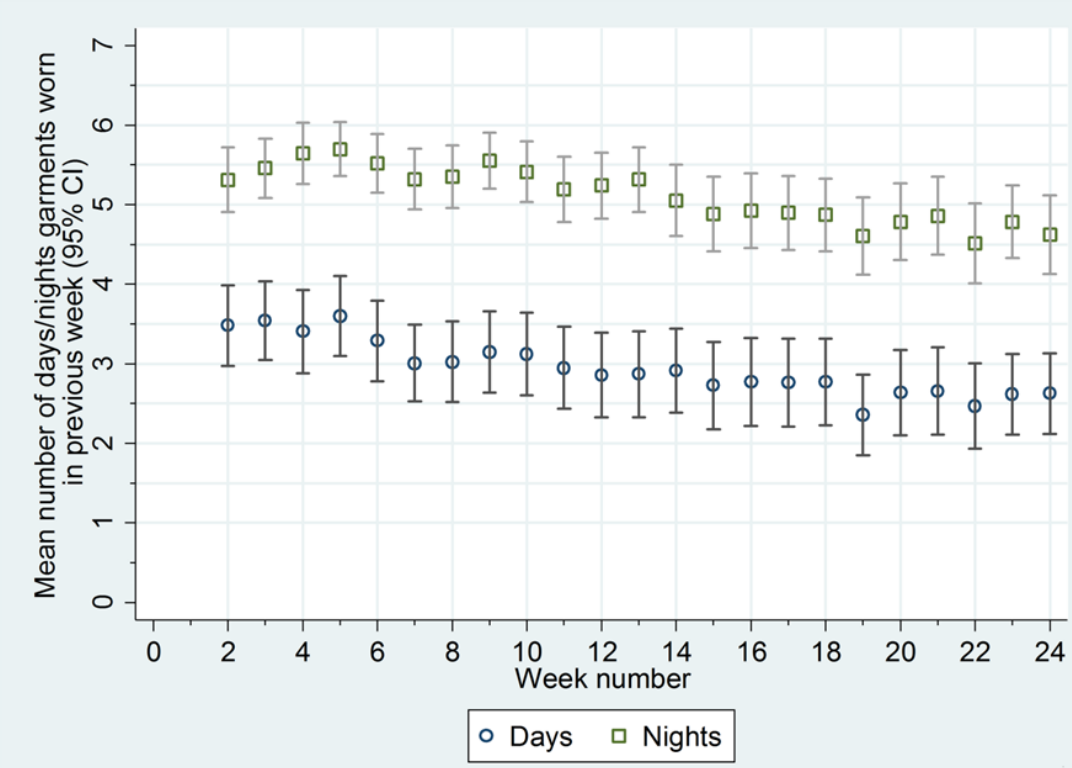
Secondary outcomes:

- Investigator and Patient Global Assessment
- Three Item Severity scale (TIS)
- Use of topical treatments for eczema
- POEM – patient-reported symptoms
- Quality of Life
- Adverse events: skin infections, hospitalisation for eczema
- Cost-effectiveness

Baseline characteristics

- Mean age: 5.1 years, 58% boys, 79% white European
- Eczema severity in last 12 months (NESS): moderate (19%); severe (81%)
- Eczema severity at baseline visit (IGA): mild (28%); moderate (48%); severe (24%)
- Follow-up: 5% loss-to follow-up over 6 months.

Adherence


Mean number of days/nights garments worn in previous week (95% CI)
0
1
2
3
4
5
6
7
0
2
4
6
8
10
12
14
16
18
20
22
24
Week number
Days
Nights

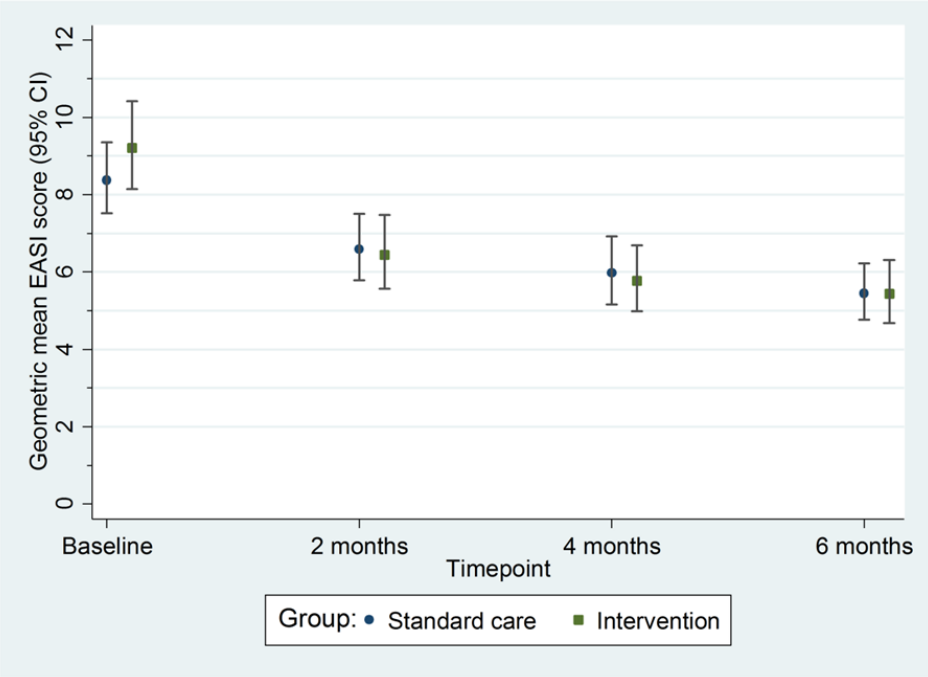

Clothing for the relief
of Eczema Symptoms

Remember:

- Children and parents new their treatment allocation
- Expectation of benefit from the silk clothing was high
- Risk of bias – for participant-reported outcomes

Primary outcome

EASI over time



- Ratio of geometric means: 0.95, 95% (95% CI 0.85 to 1.07).

EASI score was log transformed, analysis adjusted for baseline EASI score, age and recruiting site

Primary outcome

- No difference between the groups
- 95% confident that the true difference lies between -1.5 points (favouring silk) and 0.5 points (favouring standard care) in the original EASI scale
- Sensitivity analysis (adherence, missing data), and sub-group analysis (*filaggrin status, eczema severity*) were all supportive of the primary result

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Secondary outcomes – topical steroid use

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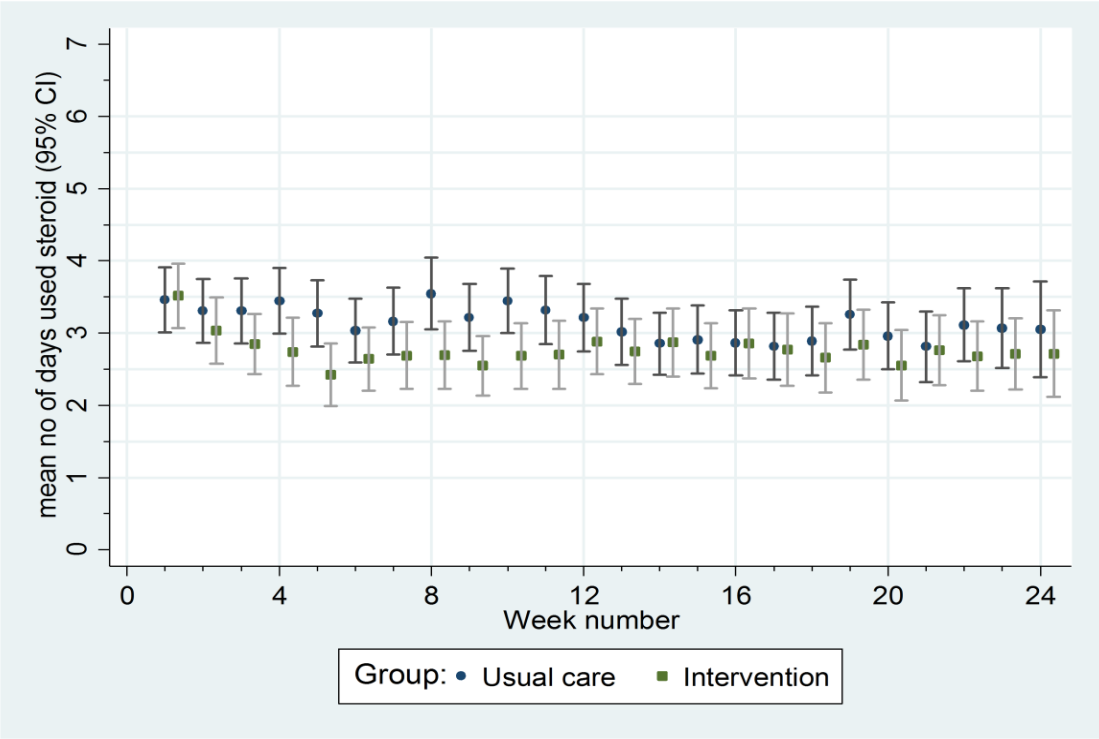
Difference in means -3.7 % days topical steroid used (95% CI -9.6, 2.3)

Equivalent to a difference of 6 days over the 24 weeks (16 days less to 4 days more)



Objective secondary outcomes

Measure	Difference between 2 groups
Investigator Global Assessment	x
Three Item Severity scale (TIS)	x
Use of topical treatments for eczema (including topical steroids)	x
Safety (skin infections, hospitalisations for eczema)	x
Other healthcare resource use	x

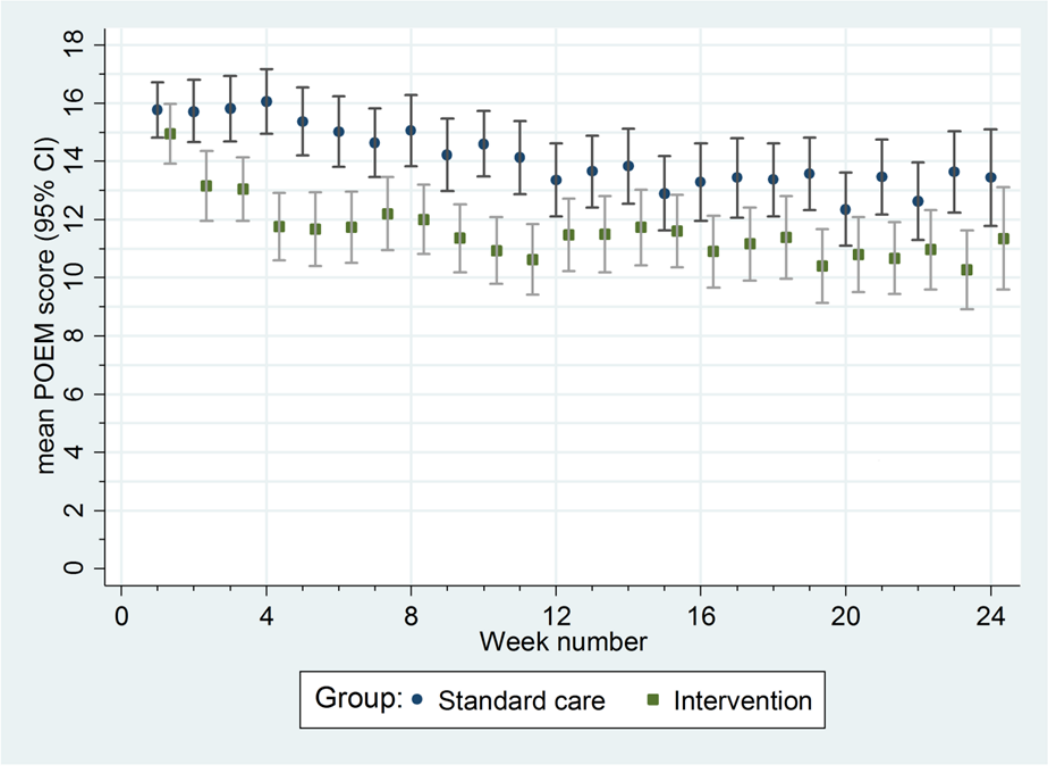
Subjective secondary outcomes

Measure	Difference between 2 groups
Patient Global Assessment	✓.
POEM – patient reported symptoms	✓.
Quality of Life: Patient (ADQoL)	x
Quality of Life: Parent (EQ-5D-3L)	x
Quality of Life: Family (DFI)	x

Secondary outcome

Weekly POEM scores

Difference in means -2.8
(95% CI -3.9, -1.8)



Cost-effectiveness

- NHS perspective (n = 273, 91%)
- Mean set of garments per participant = 4.15
- Mean cost £318.52
- No reduction in other healthcare costs (healthcare visits, prescriptions)
- Incremental cost per quality-adjusted life year was £56,811

- At a willingness to pay of £30,000 per QALY, the probability of silk garments being cost-effective was 12%

External validity

- Pragmatic design, reflects normal practice
  - Adherence in wearing the silk garments
  - Recruited children with moderate to severe eczema, but trial participants may have had milder disease than patients for whom silk garments are currently prescribed in the NHS
- Not able to comment on effectiveness if worn 100% of the time or in more severe patients
- Not able to comment on other forms of clothing / garments e.g tubifast, viscose garments

Conclusions

- This is the first independent RCT of silk clothing
- It was adequately powered with high follow-up rates and good adherence with the intervention
- CLOTHES trial found no evidence of clinical or economic benefit from silk clothing

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www.nottingham.ac.uk/CLOTHES

Team:
•The CLOTHES trial team
•Recruiting centres (Nottingham, Royal Free London, Cambridge, Portsmouth, and Isle of Wight)
•The parents and children who took part
•Nottingham Clinical Trials Unit
•UK Dermatology Clinical Trials Network
•UK Clinical Research Network
•University of Nottingham, University of East Anglia, University of Portsmouth, University of Dundee
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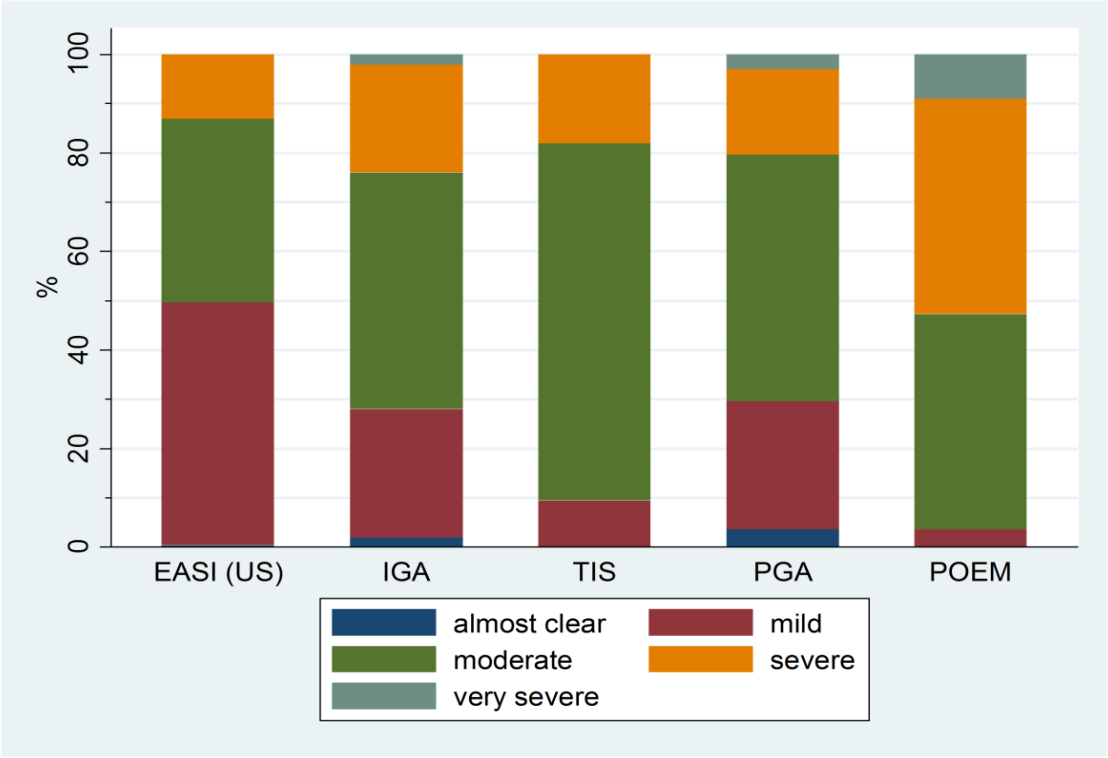
- @cebdnottm

Baseline severity



- *FLG* status: 32% had at least one null mutation