



Fig. 1. Article inclusion. RCT: randomized control trials.

Appendix S1.

Search strategy for the systematic literature search

For observational studies

- # 1 Dermatitis, Atopic/
- # 2 atopic dermatitis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 3 Eczema/
- # 4 eczema.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 5 1 or 2 or 3 or 4
- # 6 epidemiologic studies/ or exp case-control studies/ or exp cohort studies/ or exp seroepidemiologic studies/ (epidem: adj stud:).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 7 6 or 7
- # 8 5 and 8
- # 9 exp Hypersensitivity, Immediate/
- # 10 Allergens/
- # 11 Skin Tests/
- # 12 Hypersensitivity/
- # 13 prick.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 14 exp Immunoglobulin E/
- # 15 immunoglobulin E.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 16 IgE.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 17 Genotype/
- # 18 Genetic Heterogeneity/
- # 19 Hygiene Hypothesis/
- # 20 Animals, Domestic/
- # 21 Cats/
- # 22 Dogs/
- # 23 Avoidance Learning/
- # 24 Administration, Topical/
- # 25 Intermediate Filament Proteins/df, ge [Deficiency, Genetics]

- # 27 Therapeutics/mt, ut [Methods, Utilization]
- # 28 Pharmaceutical Preparations/ad, de [Administration & Dosage, Drug Effects]
- # 29 Adrenal Cortex Hormones/dt, tu [Drug Therapy, Therapeutic Use]
- # 30 Androstadienes/tu [Therapeutic Use]
- # 31 Calcineurin/ai [Antagonists & Inhibitors]
- # 32 Dermatologic Agents/tu [Therapeutic Use]
- # 33 Immunosuppressive Agents/tu [Therapeutic Use]
- # 34 Methylprednisolone/aa, tu [Analogues & Derivatives, Therapeutic Use]
- # 35 Tacrolimus/tu [Therapeutic Use]
- # 36 allerg:.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier] (142303)
- # 37 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36
- # 38 9 and 37
- # 39 limit 38 to humans
- # 40 limit 39 to (english or german)
- # 41 limit 41 to abstracts

For RCT

- # 1 randomized controlled trial.pt.
- # 2 controlled clinical trial.pt.
- # 3 randomized.ab.
- # 4 randomly.ab.
- # 5 placebo.ab.
- # 6 trial.ti.
- # 7 clinical trials as topic.sh.
- # 8 1 or 2 or 3 or 4 or 5 or 6 or 7
- # 9 humans.sh.
- # 10 exp Animals/
- # 11 10 not 9
- # 12 8 not 11
- # 13 Dermatitis, Atopic/
- # 14 atopic dermatitis.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 15 13 or 14
- # 16 Eczema/
- # 17 eczema.mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- # 18 16 or 17
- # 19 15 or 18
- # 20 12 and 19

Table SI. Methodological quality of included studies based on the Newcastle-Ottawa Scale

| Authors | Selection score | | | | Outcome | | | | Total score |
|------------------------|--|-----------------------------------|---------------------------|--|---|-----------------------|--|----------------------------------|-------------|
| | Representativeness of the exposed cohort | Selection of the unexposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was not present at the start of the study | Comparability of cohorts on the basis of the design or analysis | Assessment of outcome | Was follow-up long enough for outcomes to occur? | Adequacy of follow-up of cohorts | |
| Illi et al. (5) | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 |
| Ballardini et al. (25) | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |

Total score ranges from 0 to 9 points.

Table SII. Crude and adjusted associations of predefined factors with remission of atopic dermatitis – results of the 2 included birth cohorts

| Authors | Total no. of remissions (%) | Exposure | Main outcome | No remission exposed | No remission unexposed | OR | 95% CI | p-value | aOR ^a | 95% CI |
|------------------|---|--|--------------|--|------------------------|------|------------|---------|------------------|------------|
| Illi et al. (5) | 21.5% (241/1,123) had infant AD 192/241 children with infant AD had complete data on the course of AD and were further analysed. Of the 192 children, 83 (43%) were in complete remission after 2 years old | Age of onset of AD (first vs. second year of life) | Remission | n.r. | n.r. | n.r. | n.r. | n.s. | n.r. | n.r. |
| | | Severity score at 2 years old (mean ± SD) | Persistence | 17,89±14.04 | CR 1.62±5.57 | 1.10 | 1.07–1.13 | n.r. | 1.10 | 1.07–1.14 |
| | | Frequent scratching with early AD | | 26/36 | CR 12/83 | 6.44 | 3.45–12.02 | n.r. | 5.86 | 3.04–11.29 |
| | | ≥ Two atopic family members | | 18/36 | 16/83 | 2.73 | 1.51–4.92 | n.r. | 2.40 | 1.29–4.48 |
| | | Increased cord blood IgE levels (≥0.9 kU/l) | | 2/34 | 11/80 | 0.83 | 0.38–1.82 | n.r. | 1.29 | 0.52–3.19 |
| | | Increased total IgE levels (≥3.0 kU/l) at 2 years old | | 11/22 | 20/53 | 1.63 | 0.83–3.22 | n.r. | 1.54 | 0.75–3.17 |
| | | Any atopic sensitization at 2 years old | | 13/22 | 13/52 | 3.08 | 1.50–6.32 | n.r. | 2.76 | 1.29–5.91 |
| | | Any food sensitization | | 8/22 | 7/52 | 2.72 | 1.24–5.93 | n.r. | 2.87 | 1.27–6.48 |
| | | Any inhalant sensitization | | 9/22 | 8/52 | 2.68 | 1.23–5.84 | n.r. | 1.68 | 0.70–4.01 |
| | | Sensitization to wheat | | n.r. | n.r. | n.r. | n.r. | n.r. | 7.43 | 2.21–25.02 |
| | | Sensitization to soy beans | | n.r. | n.r. | n.r. | n.r. | n.r. | 4.46 | 1.34–14.87 |
| | | Early wheeze | | 17/32 | 24/77 | 1.91 | 1.08–3.39 | n.r. | 1.80 | 1.01–3.23 |
| | | A cat in the home in early childhood | | n.r. | n.r. | n.r. | n.r. | n.r. | 2.33 | 0.85–6.38 |
| | | Corticosteroid treatment | | n.r. | n.r. | 2.20 | 1.10–3.71 | n.r. | n.r. | n.r. |
| | | Sex, older siblings, breast-feeding, age at introduction of solid foods, dog ownership, level of mite allergen exposure, parental smoking, maternal smoking during pregnancy, parental level of education, and number of infectious diseases | | No significant association, and no further details were reported | | n.r. | n.r. | n.r. | n.r. | n.r. |
| Sex | | | Remission | n.r. | n.r. | n.r. | n.r. | n.s. | n.r. | |
| Parental allergy | | | Remission | n.r. | n.r. | n.r. | n.r. | n.s. | n.r. | |
| Parental allergy | | | Persistence | n.r. | n.r. | n.r. | n.r. | <0.001 | n.r. | |

^aIn Illi et al. adjustments were made for 2 or more atopic family members and early wheeze (excluding the respective risk factor of interest). n.r.: not reported; n.s.: not significant; CR: complete remission; AD: atopic dermatitis; OR: odds ratio; 95% CI: 95% confidence interval; SD: standard deviation; IgE: immunoglobulin E.

Table SIII. Factors that have been assessed for remission of eczema

| Study | Loss-of-function mutations within <i>FLG</i> ^a | Exposure to pets (cats, dogs) during early childhood | Avoidance behaviour of pets | Sensitization/atopy (spec. IgE) ^a | Topical anti-inflammatory treatment of eczema during infancy ^a | Severity of eczema in infancy ^a | Family history of allergic disease | Sex | Number of siblings | Socioeconomic status ^b | Lifestyle and home environment ^c |
|------------------------|---|--|-----------------------------|--|---|--|------------------------------------|-----|--------------------|-----------------------------------|---|
| Illi et al. (5) | | × | | × | | × | × | × | × | × | × |
| Ballardini et al. (25) | | | | | | | × | × | | | |

^aPrimary exposures were defined as described in the Methods section. ^bIndicated by education, occupation, (household) income, or economic problems. ^cSuch as breast-feeding, house location (rural/urban), and day-care attendance.

IgE: immunoglobulin E; spec.: specific.

Table SIV. Calculated crude odds ratios of factors and remission of atopic dermatitis (AD) based on data in Illi et al. (5)

| Factors | Complete remission | Intermittent AD | Persistent AD | OR (95% CI) |
|--|--------------------|-----------------|---------------|---------------------------|
| Frequent scratching with early AD | 12/83 | 26/73 | 26/36 | 0.12 (0.059–0.259) |
| ≥ Two atopic family members | 16/83 | 23/72 | 18/36 | 0.39 (0.200–0.762) |
| Parental AD | 9/81 | 13/71 | 69/36 | 0.48 (0.209–1.115) |
| Parental hay fever | 38/83 | 41/72 | 20/3 | 0.65 (0.366–1.157) |
| Parental asthma | 19/83 | 14/72 | 12/36 | 0.81 (0.414–1.582) |
| Increased cord blood IgE levels (≥ 0.9 kU/l) | 11/80 | 13/68 | 2/34 | 0.92 (0.399–2.141) |
| Increased total IgE levels (≥ 30 kU/l) | 20/53 | 24/44 | 11/22 | 0.54 (0.257–1.120) |
| Any sensitization | 13/52 | 21/42 | 13/22 | 0.31 (0.142–0.693) |
| Any food sensitization | 7/52 | 16/43 | 8/22 | 0.28 (0.109–0.714) |
| Any inhalant sensitization | 8/52 | 14/43 | 9/22 | 0.35 (0.141–0.861) |
| Early wheeze | 24/77 | 28/66 | 17/32 | 0.53 (0.286–0.996) |

Statistically significant correlations are highlighted in bold. OR: odds ratio; 95% CI: 95% confidence interval; IgE: immunoglobulin E.