

## **[PROTOCOL]**

# **Psychological and educational interventions for atopic dermatitis in adults. A Systematic Review and Meta-Analysis**

Kayoko Hashimoto

## **BACKGROUND**

Atopic dermatitis (Atopic eczema) is a chronic relapsing skin disorder characterized by inflammation and intensive itching. The prevalence of atopic dermatitis ranged from 1.4% in China to 22.3% in Sweden among children. [ISAAC2006] Its prevalence was estimated at 9.98% in a Japanese hospital-based study [Furue2011], and at 10.2% in a US population-based study among adults [Silverberg2013]. Prevalence has shown a 2- to 3-fold increase over the last three decades in industrialized countries [Leung2003].

AD is not only highly prevalent but also causes significant morbidity, impairs quality of life, increases health care costs and represents a major public health problem. AD causes psychological burden including sleep disturbance, anxiety [Linnet2001, Hashiro1997], depression, [Hashiro1997], feeling of unattractiveness and financial strain [Carrol2005]. Intensive itching causes sleep disturbance associated with daytime tiredness, lack of concentrations and impaired quality of life. Sleep disturbance of family, time required to take care of atopic dermatitis and financial costs lead to family stress. In short AD is a disorder with considerable social and financial costs. Management of AD is therefore a matter of clinical and social urgency.

AD commonly presents before age 5 and 70% of these patients achieve remission before adolescence, However, AD may persist until adulthood in severe cases and it may also begin in adults. Adult-onset type of AD has chronic course with atypical morphologic variants and disposition of eruption which are different from early age onset type of AD [Carmhausen2013, Kulthanan2007, Bannister2000].

Topically-applied corticosteroids and emollient are standard treatment at present. However the effectiveness of standard treatments for AD is limited and unpleasant sensation of greasy ointment, steroid phobia due to the fear of adverse effects [Charman2000] and requirement of repeated treatment with often unsatisfactory effect lead to frustration, disappointment and poor adherence with standard treatment.

Given the close association of psychosocial factors with AD, we postulate that successful management of AD would involve psychological and educational interventions as well as standard treatment. Two previous meta-analyses [Chida2007, Erssr2014] of psychological and educational interventions for AD were reported. However, one systematic review [Ersser2014] focused only on children and another [Chida2007] focused on both adults and children but it included only 5 RCTs for adult AD published before 2006. Several important RCTs on this topic have been conducted since then. Thus the effectiveness of psychological and educational intervention have not been fully evaluated, especially with regard to management of adult AD.

The objective of this study is therefore to systematize evidence on the effectiveness and acceptability of psychological and educational interventions for AD in adults.

## **OBJECTIVES**

To evaluate the effectiveness and acceptability of psychological and educational interventions for AD in adults.

## **METHODS**

### **Criteria considering studied for this review**

#### **Types of studies**

##### **Inclusion criteria**

All relevant randomized controlled trials (RCTs) will be included. For cross-over trials only the first phase will be included due to uncertainty regarding the period to allow for a washout for psychological/educational treatment. Cluster-randomized trials will be included if they are correctly analyzed.

##### **Exclusion criteria**

Quasi-randomized trials, in which treatment assignment is decided through methods such as alternative days of the week, will be excluded. There will be no restriction in terms of sample size, language or publication status.

#### **Types of participants**

##### **Participant characteristics**

##### **Inclusion criteria**

Adults aged 16 or older who have been clinically diagnosed as atopic dermatitis will be included. Participants of any gender, ethnicity and who are treated in any setting will be included.

##### **Exclusion criteria**

We will exclude patients with severe physical or psychiatric co-morbidity that will be likely to interfere with the psychological/educational intervention.

#### **Types of interventions**

Conventional treatment alone versus conventional plus psychological/educational approaches with more than one session.

##### **a) Psychological interventions**

###### **1. Behavioural interventions**

Behavioural management therapy is the application of behavioural theory such as conditioning and/or reinforcement to modify undesired behaviours.

###### **2. Cognitive interventions**

Cognitive behavioural therapy involves cognitive skills such as cognitive restructuring and problem solving to enhance the patients' coping abilities. It can be supplemented by behavioural interventions above.

###### **3. Psychodynamic interventions**

Psychodynamic therapies focuses on revealing and resolving intrapsychic or unconscious conflicts.

#### 4. Relaxation interventions

These are relaxation therapies including progressive muscle relaxation, biofeedback, aromatherapy and yoga.

#### b) Educational interventions

Educational interventions may include tools such as lectures, audiotapes, books, leaflets, handouts, videotapes, demonstrations, and question and answer sessions. It includes information on the disease, treatment options, management strategies, and prevention strategies. When educational interventions is followed by a psychological interventions, study arm will be classified accordingly to the latter and educational interventions will be regarded as a component of that intervention.

### **Types of outcome measures**

#### **Primary outcomes**

(1) Global severity of atopic dermatitis at short-term (less than 6 months). Measured by the validated scales such as Eczema Area and Severity Index (EASI), Severity Scoring of Atopic Dermatitis (SCORAD), patient oriented eczema measure (POEM) and others which includes the total affected body area and signs of skin severity of erythema, induration, population, excoriation and lichenification for patients with atopic dermatitis.

(2) Global severity of atopic dermatitis at long-term (6-18 months, the time point closest to 12 months will be given preference). Measured by the validated scales such as Eczema Area and Severity Index (EASI), Severity Scoring of Atopic Dermatitis (SCORAD), patient oriented eczema measure (POEM) and others which includes the total affected body area and signs of skin severity of erythema, induration, population, excoriation and lichenification for patients with atopic dermatitis.

(3) Dropouts for any reasons as a proxy measure of acceptability of treatment. The proportion of patients who could not complete the required psychoeducation program for any reasons.

#### **Secondary outcomes**

(1) Quality of life of patients. Measured by the validated scales such as Skindex-16, Dermatology Life Quality Index (DLQI).

(2) Improvement of sleep.

(3) Severity of anxiety. Measured by the validated scales such as State-Trait Anxiety Index (STAI).

(4) Severity of depression. Measured by self-rated scales such as the Beck Depression Inventory (BDI) or by clinician-rated scales such as the Hamilton Rating Scale for Depression (HDSR).

(5) Use of medication and cost.

## **Search methods for identification of studies**

### **Electronic searches**

We will conduct a literature search to identify relevant randomized trials. We will impose no language restrictions when searching for the literature, and translations will be sought where necessary. We will search the following electronic databases to identify potential studies: MEDLINE (1950 to 13 Feb 2014), Cochrane Central Register of Controlled Trials (CENTRAL) (1950 to 13 Feb 2014), CINAHL, Scopus and PsycINFO. The respective search terms are listed in Appendix 1, 2, 3 4 and 5.

### **Searching other resources**

We will handsearch the references of all included studies. We will also search the U.S. National Institute of Health trials register [clinicaltrials.gov](http://clinicaltrials.gov), the WHO International Clinical Trial Registry Platform and International Standard Randomised Controlled Trial Number Register (ISRCTN). The respective search terms are listed in Appendix 6, 7 and 8.

## **Data collection and analysis**

### **Selection of studies**

Only randomised controlled trials (RCTs) will be considered. Two review authors will independently check titles and abstracts identified from the searches and studies that do not refer to an RCT on atopic dermatitis will be excluded. Two review authors will independently assess the full texts of studies to decide which trials fulfill the inclusion criteria. All discrepancies will be discussed and a consensus will be achieved and a third author will be involved if necessary. Agreement between the two review authors in determining study eligibility will be reported as percentage agreement and kappa. Where randomisation procedures or any other relevant information are unclear correspondence will be undertaken with the relevant trial authors in an attempt to clarify the missing information.

### **Data extraction and management**

Data extraction will be performed independently by two review authors who enter data onto a data extraction form. All discrepancies will be discussed and a consensus will be achieved for each paper and a third author will be involved if necessary. Agreement between the two review authors in the data extraction will be reported as percentage agreement and weighted kappa. Where necessary, the authors of the studies will be contacted for further information.

### **Assessment of risk of bias in included studies**

Risk of bias will be assessed for each included study using The Cochrane Collaboration's 'Risk of bias' tool ([Higgins 2011](#)). This tool encourages consideration of the following six domains.

1. Sequence generation: Was the allocation sequence adequately generated?
2. Allocation concealment: Was allocation adequately concealed?
3. Blinding of participants and personnel for each main outcome or class of outcomes: Was knowledge of the allocated treatment be adequately prevented during the study?
4. Blinding of outcome assessment:
5. Incomplete outcome data for each main outcome or class of outcomes: Are incomplete outcome data adequately addressed?
6. Selective outcome reporting: Are reports of the study free of any suggestion of selective outcome reporting? Searching protocols of studies, we will assess as unclear risk of bias in case we will not identify the protocols of studies, we will assess as unclear risk of bias in case we will not identify the protocols of studies.
7. Other sources of bias: Was the study apparently free of other problems that could put it at high risk of bias? Additional items to be included here are blinding of data analysts, baseline imbalance, cointervention, deviation from the study protocol in a way that does not reflect clinical practice, therapist qualifications, treatment fidelity and researcher allegiance/conflict of interest.

A description of what is reported to have happened in each study will be provided, and a judgement on the risk of bias will be made for each domain within and across studies, based on the following three categories.

1. Low risk of bias.
2. Unclear risk of bias.
3. High risk of bias.

Two review authors will independently assess the risk of bias in selected studies. Any disagreement will be discussed with a third review author. Agreement between the two review authors with regard to the risk of bias will be reported as percentage agreement and weighted kappa. When necessary, study authors will be contacted for further information. We will summarize the risk of bias judgements across different studies for each of domains listed. All risks of bias data will be presented graphically.

## **Statistical analyses**

### **Measures of treatment effect**

#### **1) Continuous outcomes**

Where studies use the same outcome measure for comparison, data will be pooled by calculating the mean difference (MD). When different measures are used to assess the same outcome, data will be pooled with standardised mean difference (SMD) and 95% confidence intervals (95% CIs) will be calculated.

#### **2) Dichotomous outcomes**

These outcomes will be analysed by calculating a pooled odds ratio(OR) and 95% CIs for each comparison. Because ORs can be difficult to interpret, these pooled ORs will be converted to risk ratios (RRs) using the formula provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2008a) and will be presented in this form for ease of interpretation.

### **Unit of analysis issues**

1) The unit of analysis will be individuals in most studies.

#### **2) Cluster-randomised trials**

Cluster-randomised trials will be included as long as proper adjustment for the intracluster correlation could be conducted in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2012, Section 16.3). We will use the effective sample sizes as below:

$(\text{number of the events or number of the denominators}) / \{1 + (M - 1) \text{ICC}\}$

(M: average cluster size, ICC: intracluster correlation coefficient)

#### **3) Cross-over trials**

For trials employing a cross-over design only the first phase will be included due to uncertainty regarding the period to allow for a washout for psychological/educational treatment.

#### **4) Studies with multiple treatment groups**

Where multiple trial arms are reported in a single trial, we will include only the relevant arms. Data will be managed in this review as follows. For continuous data, means, SDs and numbers of participants for all active treatment groups will be pooled across treatment arms as a function of the number of participants in each arm to be compared against the control group (Law 2003; Higgins 2008; Higgins 2008a). For dichotomous data, data from relevant active intervention arms will be collapsed into a single arm for comparison, or data from relevant active intervention arms will be split equally between comparator arms.

#### **5) Repeated observations**

When outcomes are measured repeatedly at different times, we will classify them as short-term (less than 6 months) data and as long-term (6-18 months, the time point closest to 12 months will be given preference) data respectively.

### **Dealing with missing data**

#### 1) Missing participants

##### 1. Dichotomous data

All data will be analyzed on the basis of the intention-to-treat (ITT) principle: dropouts will always be included in this analysis. Where participants were withdrawn from the trial before the endpoint and the original authors did not impute it appropriately, it will be assumed that their condition remained unchanged if they had stayed in the trial. Any assumptions and imputations to handle missing data will be clearly described and the effect of imputation will be explored by sensitivity analyses.

##### 2. Continuous data

The Cochrane Handbook recommends avoiding imputations of continuous data and suggests rather that the data must be used in the form presented by the original authors. Whenever ITT data are presented by the authors, they will be preferred to “per protocol or completer” data sets.

#### 2) Missing data

We will contact the trial author of a study for more information if there is any missing data in the trial.

#### 3) Missing statistics

When only the standard error (SE) or *P* values were reported, standard deviations (SDs) will be calculated according to Altman (Altman 1996). In the absence of supplemental data after requests to the authors, the SDs will be calculated from CIs, *t* values or *P* values as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011); or they will be imputed from other studies in the meta-analysis according to a validated method (Furukawa 2006). We will examine the validity of these imputations in a sensitivity analysis.

### **Assessment of heterogeneity**

We will first assess heterogeneity by visual inspection of forest plots. Statistical heterogeneity will be formally tested using the Chi squared test, which provides evidence of variation in effect estimates beyond that of chance. Because the Chi squared test has low power to assess heterogeneity when a small number of participants or trials are included, the *P* value will be conservatively set at 0.1. Heterogeneity will also be quantified using the  $I^2$  statistic, which calculates the percentage of variability due to heterogeneity rather than to chance. We will expect, a priori, that considerable clinical heterogeneity would be noted between studies, and so  $I^2$  values in the range of 50% to 90% will be considered to represent substantial statistical heterogeneity and will be explored further. However, the importance of

the observed  $I^2$  depends on the magnitude and direction of treatment effects and the strength of evidence for heterogeneity (Higgins 2003; Deeks 2008). Forest plots generated in RevMan5 provide an estimate of tau squared, the between-study variance in a random-effects meta-analysis. To provide an indication of the spread of true intervention effects, we will also use the tau squared estimate to determine an approximate range of intervention effects using the method outlined in Section 9.5.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2008). This will be done only for the primary outcomes.

### **Assessment of reporting biases**

As far as possible, the impact of reporting biases will be minimized by undertaking comprehensive searches of multiple sources (including trial registries), increasing efforts to identify unpublished material and including non-English language publications. We will also try to identify outcome reporting bias in trials by recording all trial outcomes, planned and reported, and noting where outcomes are missing. When we find evidence of missing outcomes, we will attempt to obtain any available data directly from the authors. When ten or more trials allow for a meaningful analysis, funnel plots will be constructed and tests for funnel plot asymmetry will be used to investigate the potential influence of reporting biases and small-study effects.

### **Data synthesis**

Given the potential heterogeneity of psychological therapy approaches for inclusion, together with the likelihood of differing secondary comorbid allergic disorders in the population of interest, a random-effects model will be used in all analyses.

### **Subgroup analysis and investigation of heterogeneity**

We plan to conduct the following subgroup analyses, when there is enough data.

1. Baseline eczema severity: The severity of eczema on entry into the trial is expected to have an impact on outcomes. We plan to categorize baseline severity as mild, moderate or severe. Had enough studies used SCORAD (SCORing Atopic Dermatitis), we will split eczema severity into mild, moderate, and severe (where mild is 0 to 15, moderate is 15 to 40, and severe is > 40).
2. Age of participants: Many cases develop AD in their childhood or adolescence. AD appears to be less responsive to treatments as the age of the patients or the length of their suffering grow [Patel 1997]. Meta-regression will be applied to the relationship between intervention effect and the average age of the participants if ten or more studies are available in a meta-analysis because meta-regression has low power to detect genuine relationship in including few studies. If there are less than 10 studies, we will perform subgroup analyses by subdividing the studies at the median of the participants' mean ages.
3. Number of sessions: Differences in the numbers of therapy sessions received are likely, and this is expected to affect treatment outcomes. Meta-regression will be applied to the



relationship between intervention effect and number of sessions if ten or more studies are available in a meta-analysis.

4. Types of interventions: Types of interventions is expected to have an impact on outcomes. We plan to categorise interventions as education, cognitive behavioural treatment, dynamic psychotherapy and relaxation. We plan to categorize them as individual or group intervention.

### **Sensitivity analysis**

We will perform sensitivity analyses defined a priori to assess the robustness of our conclusions. This will involve:

1. Fidelity to treatment: Studies that do assess fidelity to the psychological therapy model(s) under evaluation through assessment of audiotapes or videotapes of therapy sessions will be excluded.
2. Study quality: Allocation concealment is to be used as a marker of trial quality. We plan to conduct sensitivity analysis excluding studies that do not use allocation concealment.
3. Trials for which missing data are imputed will be excluded.

### Summary of findings' tables

We will use the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the body of evidence associated with the following main outcomes:

1. Global severity of AD at short-term (less than 6 months) as measured by EASI, SCORAD and POEM.
2. Global severity of AD at long-term (6-18 months, the time point closest to 12 months will be given preference) as measured by EASI, SCORAD and POEM.
3. Dropouts for any reason.
4. Quality of life of patients. Measured by the validated scales such as Skindex-16, Dermatology Life Quality Index (DLQI).
5. Improvement of sleep.
6. Severity of anxiety. Measured by the validated scales such as State-Trait Anxiety Index (STAI).
7. Severity of depression. Measured by self-rated scales such as the Beck Depression Inventory (BDI) or by clinician-rated scales such as the Hamilton Rating Scale for Depression (HDSR).

We will construct a 'Summary of findings' (SoF) table using the GRADE profiler software (Higgins 2011).

The SoF will provide key information concerning the quality of evidence, the magnitude of effect of the interventions examined and the sum of available data for all main outcomes for a given comparison. For each main outcome, we will also carry out quality assessment of the results using the GRADE approach. Randomised trials start as high-quality evidence, but may be down-graded due to risk of bias (methodological quality), indirectness of evidence, unexplained heterogeneity, imprecision (sparse data) and publication bias. We will determine the overall quality of the evidence for each outcome after considering each of these factors.

We will express the results as one of four levels of quality (high, moderate, low or very low).

## REFERENCES

- 1) The ISAAC Phase Three Study Group: World time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood : ISAAC phase one and three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733-743.
- 2) Furue M et al: Prevalence of dermatological disorders in Japan: A nationwide, cross-sectional, seasonal, multicenter, hospital-based study. *J Dermatol* 2011;38:310-320.
- 3) Silverberg JI, Hanifin JM: Adults eczema prevalence and associations with asthma and other health and dermatographic factors: A US population-based study. *J Allergy Clin Immunol* 2013;132:1132-1138.
- 4) Leung DYM, Bieber T: Atopic dermatitis. *Lancet* 2003;361:151-160.
- 5) Charman CR, Morris AD, Williams HC: Topical corticosteroids phobia in patients with atopic eczema. *Br J Dermatol* 2000;142(5):931-6.
- 6) Linnet J et al: Anxiety level and severity of skin condition predicts outcome of psychotherapy in atopic dermatitis patients. *Inter J of Dermatol* 2001;40:632-636.
- 7) Hashiro M, Okumura M: Anxiety, depression and psychosomatic symptoms in patients with atopic dermatitis: comparison with normal controls and among groups of different degrees of severity. *J Dermatol Science* 1997;14:63-67.
- 8) Carrol CL, Balkrishnan R: The burden of atopic dermatitis: impact on the patients, family and society. *Pediatr Dermatol* 2005; 22:192-199.
- 9) Garmhausen D, Hagemann T et al: Aharacterization of different courses of atopic dermatitis in adolescent and adult patients. *Allergy* 2013; 68:498-506.
- 10) Kulthanan K et al: Adult-onset atipic dermatitis: A cross-sectional study of natural history and clinical manifestation. *Asian Pacific J Allergy* 2007; 25:207-214.
- 11) Bannister M et al: Adult-onset atopic dermatitis. *Australasian J Dermatol* 2000; 41:225-228.
- 12) Chida Y et al: The effects of psychological intervention on atopic dermatitis. A systematic review and meta-analysis. *Int Arch Allergy Immunol* 2007; 144:1-9.
- 13) Esser SJ et al: Psychological and educational interventions for atopic eczema in children (Review). *Cochrane Database of Systematic Review*.
- 14) Patel L et al: Adult height in patients with childhood onset atopic dermatitis. *Archives of Disease in childhood*. 1997; 76:505-508.

### **Appendix 1. 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. (animals not (human and animals)).sh.
10. 8 not 9
11. exp Dermatitis/ or dermatitis.mp.
12. exp Eczema\$/ or eczema\$.mp.
13. exp Neurodermatitis/ or neurodermatitis.mp.
14. Besniers prurigo.mp.
15. 11 or 12 or 13 or 14
16. 10 and 15
17. Psychotherapy.mp.
18. behavior\$ therapy.mp.
19. exp Behavior Therapy/
20. psychodynamic therapy.mp.
21. exp Autogenic training/
22. exp Cognitive therapy/ or cognitive therapy.mp.
23. counsel\$.mp.
24. behavior\$ manag\$.mp.
25. exp Hypnosis/ or hypno\$.mp.
26. exp Biofeedback/ or biofeedback.mp.
27. exp Family therapy/ or famil\$ therap\$.mp.
28. exp Relaxation/ or relaxation.mp.
29. exp Aromatherapy/
30. exp Patient education/ or patient education.mp.
31. patient teaching.mp.
32. exp Skin care/ or skin care.mp.
33. exp Health promotion/ or health promot\$.mp.
34. exp Education/
35. exp Psychiatry
36. or/17-35
37. 16 and 36

## Appendix 2. CENTRAL search strategy

#1 eczema\*or neurodermatitis or (besnier\* prurigo)

#2 MeSH descriptor Dermatitis explode all trees

#3 MeSH descriptor Eczema explode all trees

#4 MeSH descriptor Dermatitis, Atopic explode all trees

#5 MeSH descriptor Neurodermatitis explode all trees

#6 (#1 OR #2 OR #3 OR #4 OR #5)

#7 psycho\* or behavior\* or behaviour\* or psychodynamic or cognitive\* or psychia\*

#8 (autogenic train\*) or biofeedback or mindfulness or (family therap\*)

#9 (hypnosis or hypnotherapy)\* or relaxation\* or aroma\* or (muscle\* therapy) or (skin care)

#10 (education\* program) or (behavior\* management) or counsel\* or teaching\* or training\* or session

#11 (health promot\*) or (health educa\*)

#12 MeSH descriptor psychology explode all trees

#13 MeSH descriptor psychotherapy explode all trees

#14 MeSH descriptor behavior therapy explode all trees

#15 MeSH descriptor behaviour explode all trees

#16 MeSH descriptor cognitive therapy explode all trees

#17 MeSH descriptor autogenic training explode all trees

#18 MeSH descriptor relaxation explode all trees

#19 MeSH descriptor hypnosis explode all trees

#20 MeSH descriptor aromatherapy explode all trees

#21 MeSH descriptor skin care all trees

#22 MeSH descriptor program explode all trees

#23 MeSH descriptor education explode all trees

#24 MeSH descriptor counseling explode all trees

#25 MeSH descriptor health promotion explode all trees

#26 MeSH descriptor Education explode all trees

#27 MeSH descriptor Self-Help Groups explode all trees

#28 (#7 OR #8 OR #9 OR #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)

#29 (#6 AND #28)

**Appendix 3. CINAHL search strategy** (Cumulative Index to Nursing and Allied Health Literature) was searched as follows:

1. (MH "Clinical Trials+")
2. TI (clinic\* N1 trial\*) or AB (clinic\* N1 trial\*)
3. TI ((singl\* or doubl\* ) and (blind\* or dummy or mask)) or AB ((singl\* or doubl\*) and (blind\* or dummy or mask))
4. TI ( randomi?ed or randomly) or AB (randomi?ed or randomly)
5. AB (random\* N3 allocat\*) or AB (random\* N3 assign\*)
6. (MH "Random Assignment")
7. PT clinical trial
8. (MH "Placebos")
9. TI placebo\* or AB placebo\*
10. AB (control N3 trial\*) or AB (control N3 study) or AB (control N3 studies)
11. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
12. (MH "Eczema")
13. (MH "Dermatitis, Atopic")
14. (MH "Dermatitis")
15. (MH "Neurodermatitis")
16. 12 or 13 or 14 or 15
17. (MH "Psychotherapy+")
18. (MH "Education+")
19. (MH "Psychology+")
20. (MH "Behavior Therapy+")
21. (MH "Cognitive Therapy")
22. (MH "Autogenic Training ")
23. (MH "Hypnosis")
24. (MH "Counseling+")
25. (MH "Relaxation")
26. (MH "Biofeedback")
27. (MH "Family Therapy")
28. (MH "Health Promotion+")
29. (MH "Skin Care+")
30. (MH "Support Groups+")
31. (psychodynamic therap\*) OR (behavio\* therapy) OR (autogenic training) OR counsel\* OR psychotherapy OR suggestion OR hypnosis OR hypnotherapy OR (cognitive therap\*) OR relaxation OR "self help" OR support OR mindfulness OR imagery OR biofeedback OR (family therap\*) OR (health promotion) OR (patient teaching) OR (patient training)
32. 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
33. 11 and 16 and 32

#### **Appendix 4. SCORPUS**

TITLE-ABS-KEY ((atopic dermatitis) OR (atopic eczema) OR eczema\* OR neurodermatitis OR (besnier\* prurigo))

AND ((behavio\* therapy) OR psychodynamic OR (cognitive therapy)

OR (autogenic training) OR biofeedback OR hypnotherapy OR relaxation\* OR (aroma therapy) OR (muscle therapy) OR (skin care) OR (education\* program) OR counsel\* OR teaching OR training OR (health education\*))

AND (((clinical W/1 trial\*) OR "randomi?ed controlled trial" OR randomization OR ret OR "random allocation" OR "randomly allocated" OR (allocated W/2 random\*) OR ((singl\* or doubl\* or treb\* or tripl\*) W/1 (blind\$3 or mask\$3)) OR "crossover procedure" OR placebo\*) AND NOT ("case study" OR "case report" OR "abstract report" OR letter OR "historical article"))

#### **Appendix 5. PsycINFO search strategy**

1. xp Dermatitis/ or exp Neurodermatitis/ or atopic dermatitis.mp. or dermatitis.mp. or neurodermatitis.mp.
2. eczema.mp. or exp ECZEMA/
3. or/1-2
4. (trial\$ or random\$ or placebo\$ or doube-blind or control).mp. [mp=title, abstract, subject headings, table of contents, key concepts]
5. 3 and 4

#### **Appendix 6. clinicaltrials.gov search strategy**

(“atopic dermatitis” OR “atopic eczema” OR neurodermatitis) AND (behavior\* OR behaviour\* OR “cognitive therapy” OR training OR counsel\* OR relaxation\* OR program OR aromatherapy OR education)

#### **Appendix 7. WHO International Clinical Trial Registry Platform search strategy**

Condition = “atopic dermatitis” OR eczema OR neurodermatitis

Intervention = psychotherapy\* OR behavior\* OR behaviour\* OR cognitive OR training OR counsel\* OR relaxation\* OR program OR aromatherapy OR education

**Appendix 8. International Standard Randomised Controlled Trial Number Register (ISRCTN) search strategy.**

("atopic dermatitis" OR eczema OR neurodermatitis ) AND (psychotherapy\* OR behavior\* OR behaviour\* OR cognitive OR training OR counsel\* OR relaxation\* OR program OR aromatherapy OR education )