

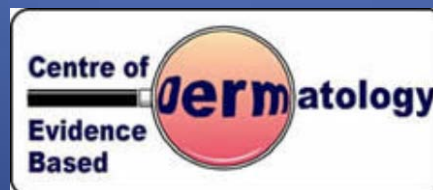


I The International
S Study of
A Asthma and
A Allergies in
C Childhood



News on **eczema** from the Centre of Evidence-Based Dermatology

Hywel Williams
University of Nottingham



Greetings from Nottingham





Making connections....



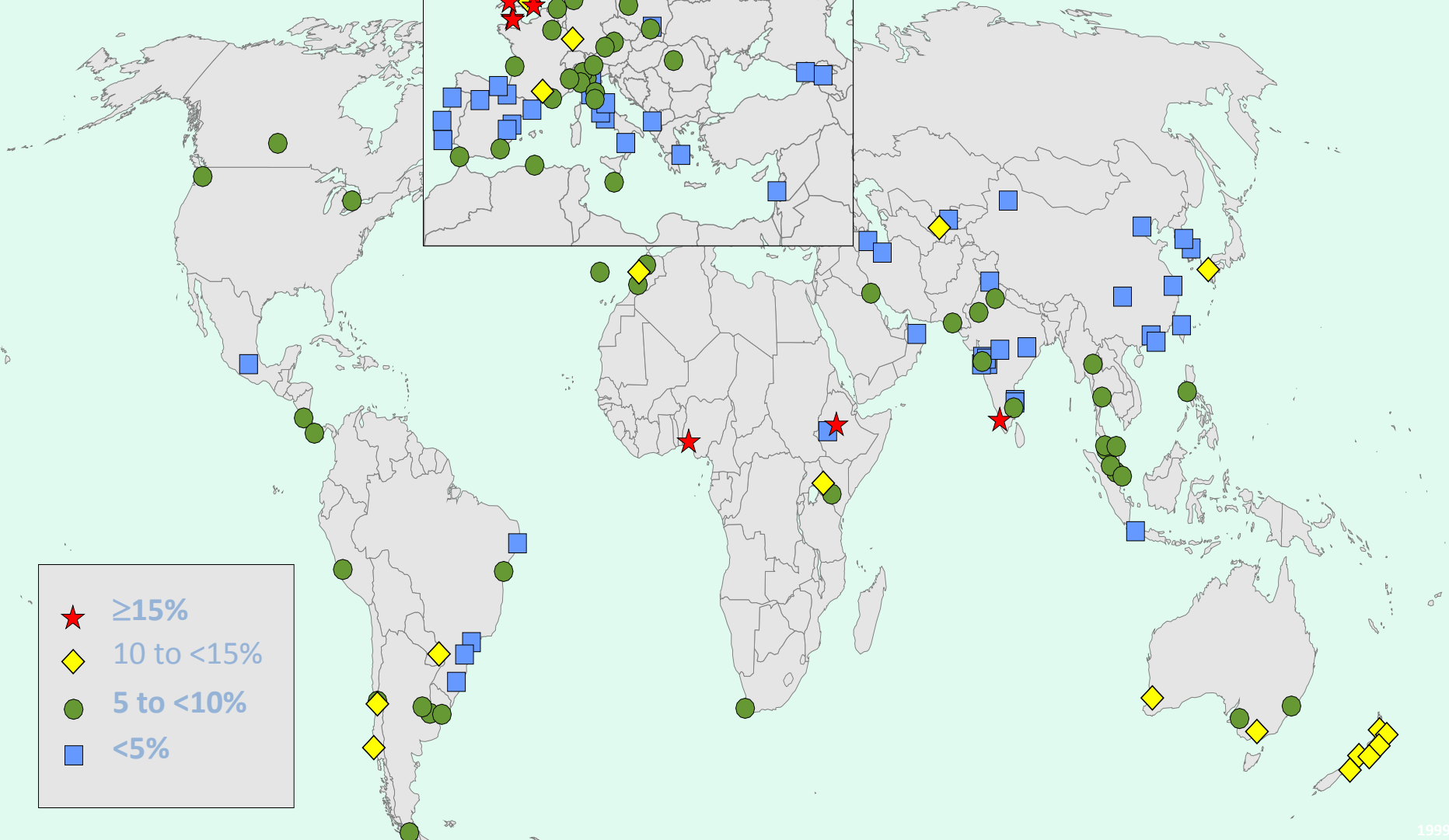
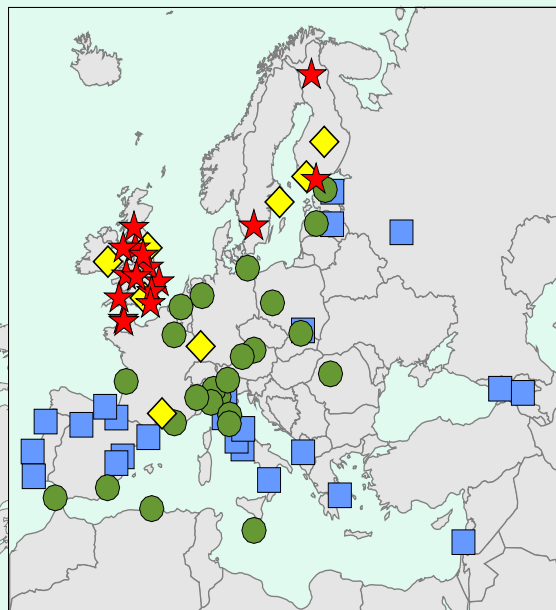






ISAAC Phase One

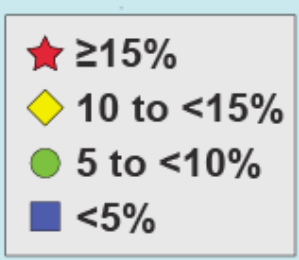
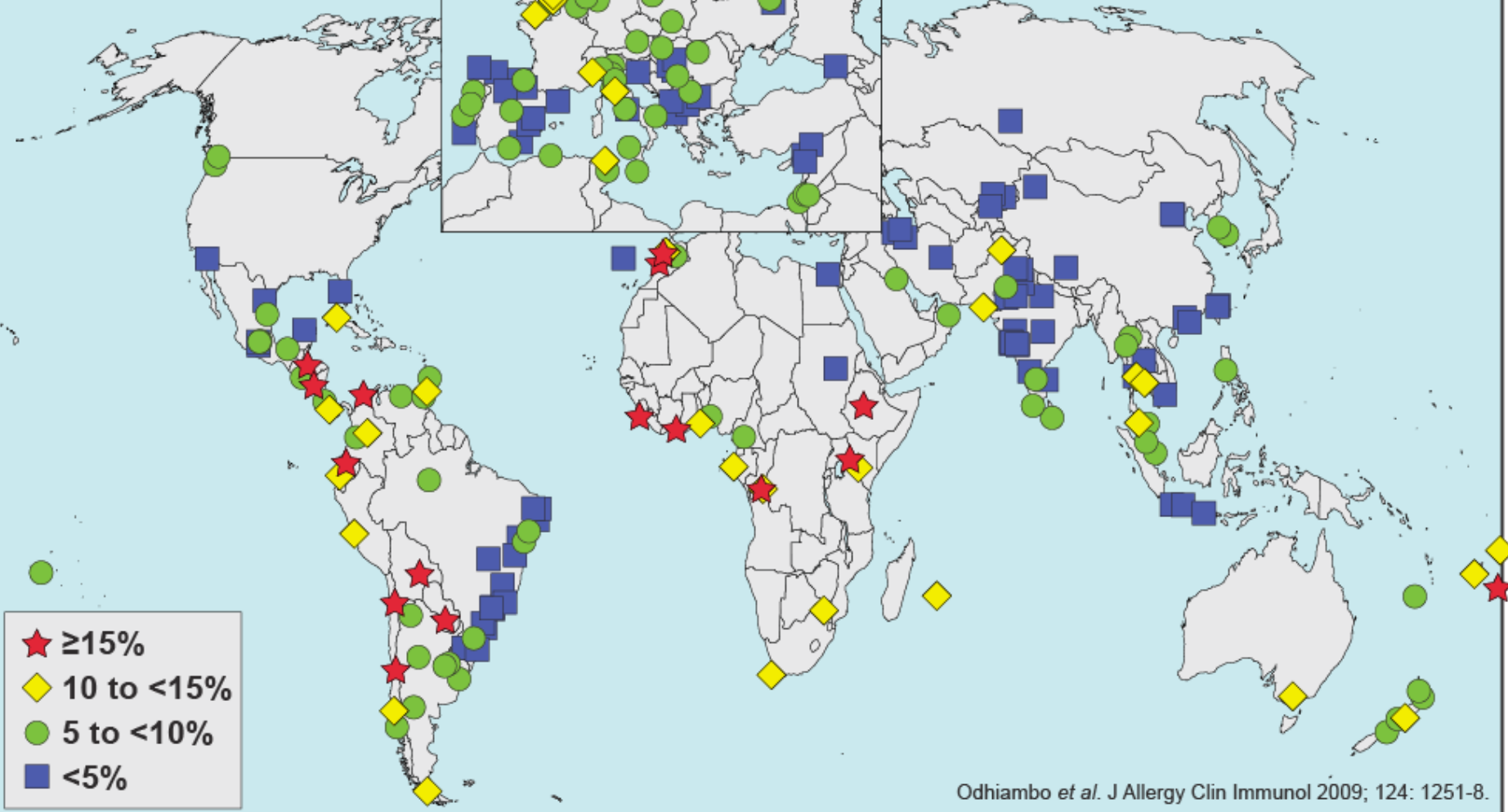
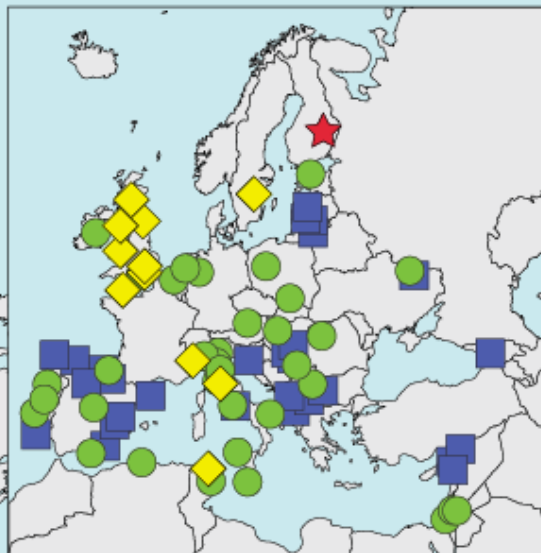
Symptoms of Eczema in the Last 12 Months, 13-14 Year Age Group





ISAAC Phase Three

Symptoms of Eczema 13-14 Year Age Group

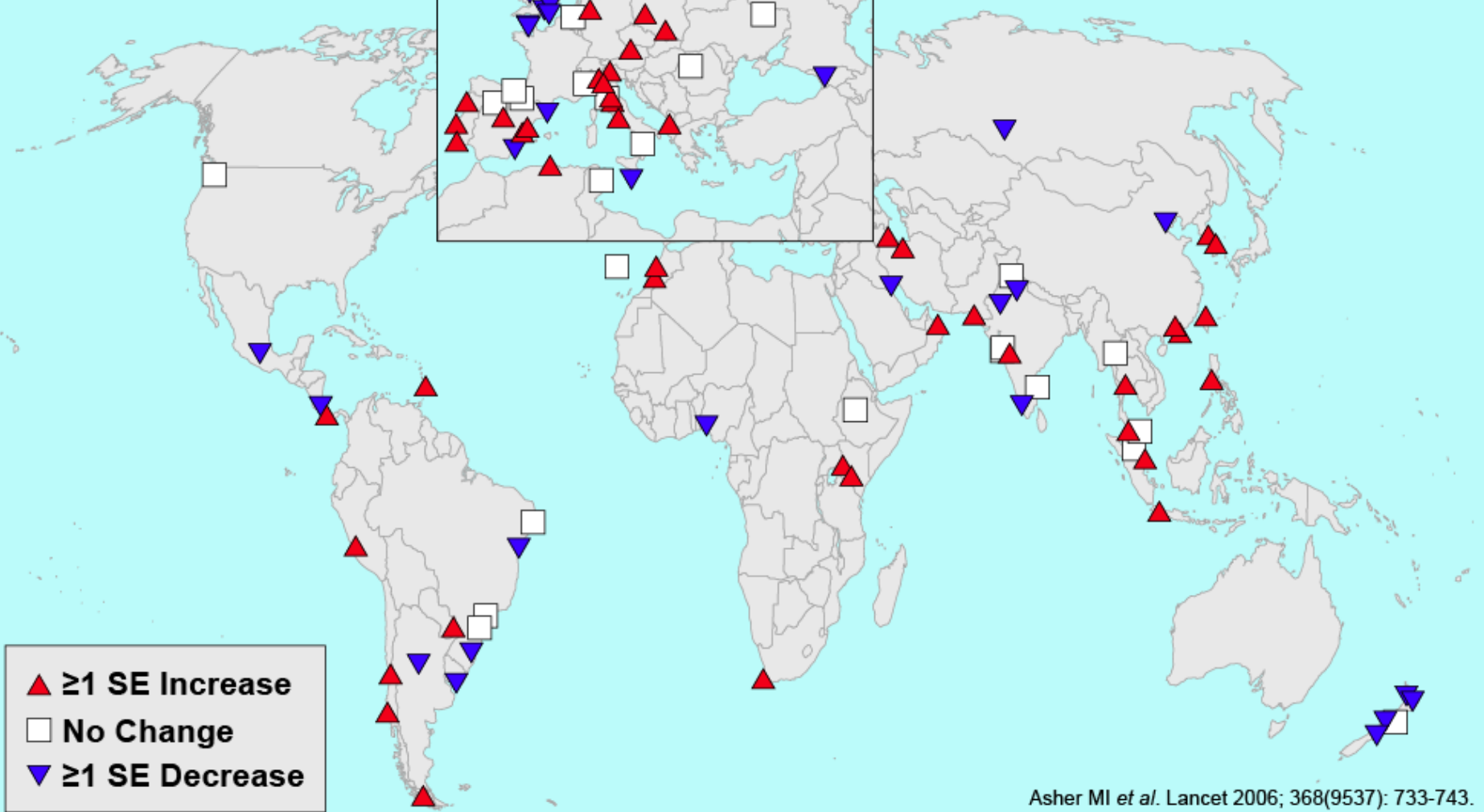
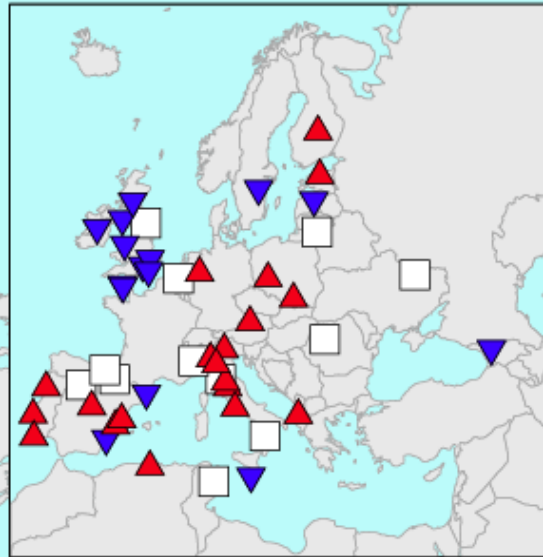


Odhiambo *et al.* J Allergy Clin Immunol 2009; 124: 1251-8.



ISAAC Phase Three Time Trends

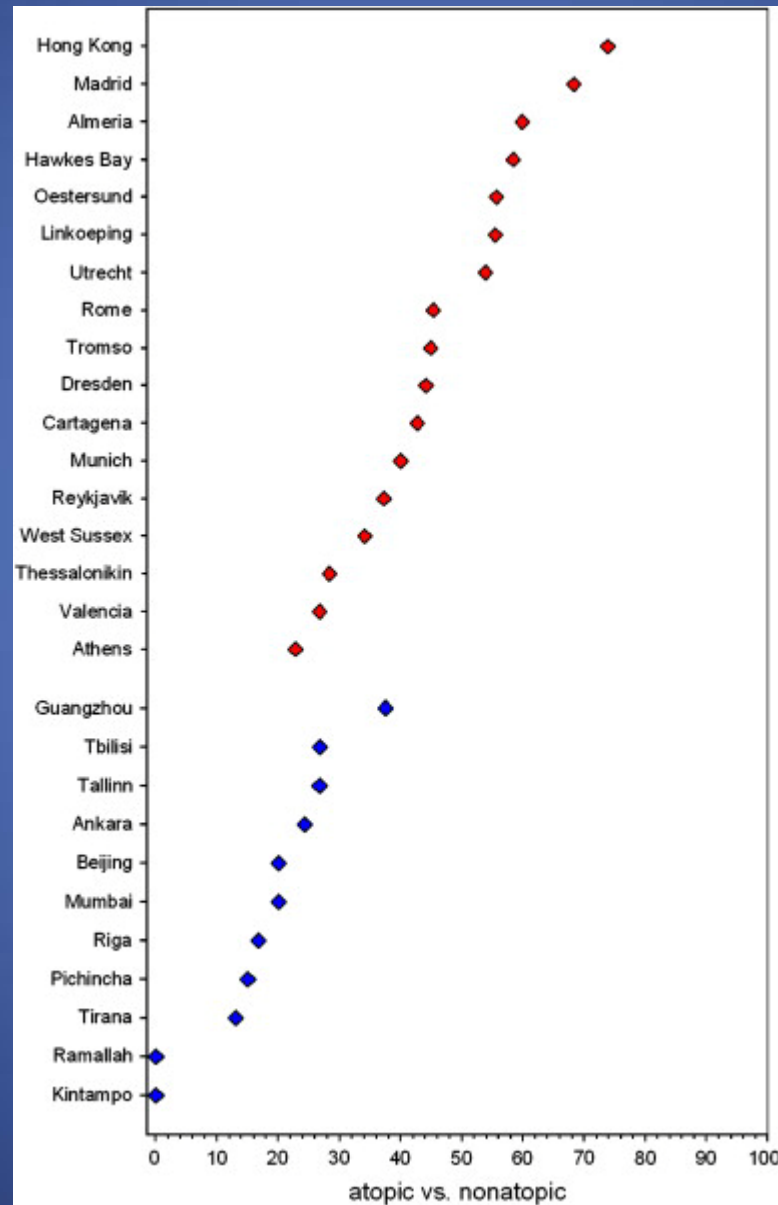
Change in Symptoms of Eczema 13-14 Year Age Group



- ▲ ≥1 SE Increase
- No Change
- ▼ ≥1 SE Decrease

Asher MI *et al.* Lancet 2006; 368(9537): 733-743.

ISAAC Phase Two



The Koru of eczema



What I am going to cover

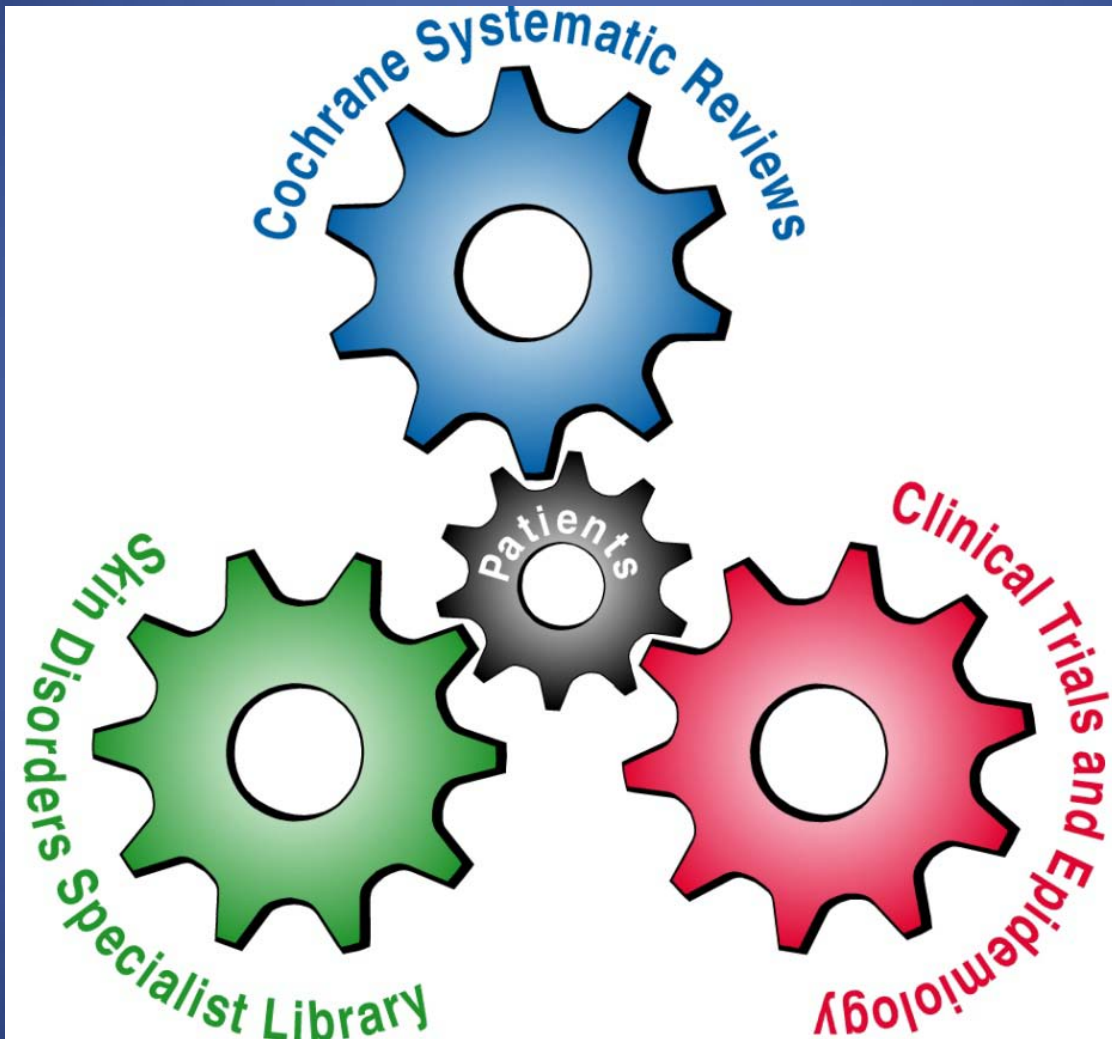
- Introduce the Centre of Evidence-Based Dermatology
- Our global collection of randomized controlled trials
- The water softener study
- The Harmonising Outcome Measures for Eczema project
- Our mapping of eczema systematic reviews
- Five ways my practice has changed

Conflicts of interest

- I work for the UK National Health Service
- I have no financial or research associations with pharmaceutical or for-profit companies
- I have previously accepted some emollient samples from a pharmaceutical exhibition

Williams HC, Naldi L, Paul C, et al Conflicts of interest in dermatology. *Acta Derm Venereol.* 2006;86(6):485-97.

The Centre of Evidence-Based Dermatology



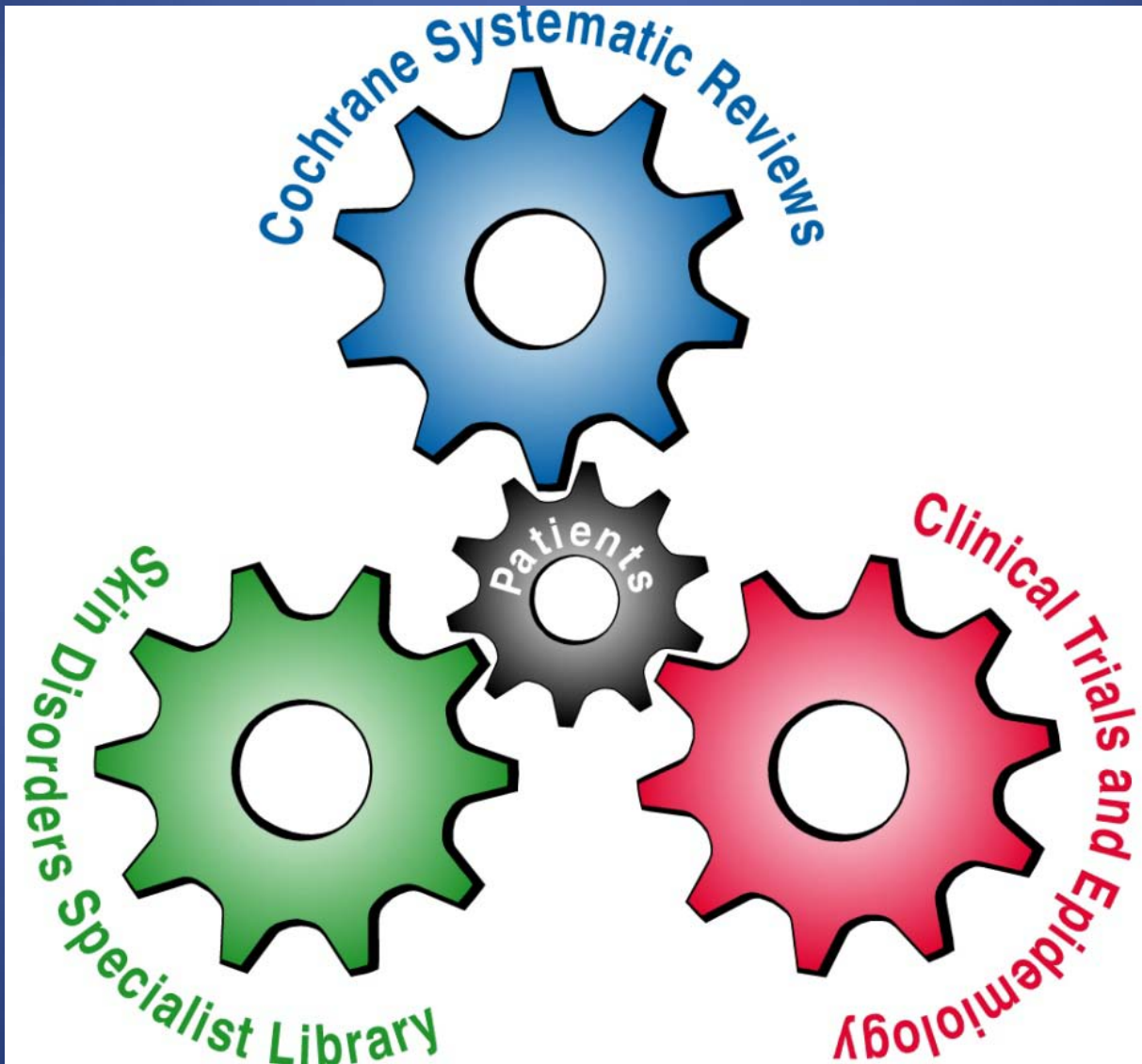
www.nottingham.ac.uk/dermatology

Recently published reviews:

- Probiotics for treating atopic dermatitis
- Anti-staphylococcal interventions for atopic dermatitis
- Topical treatments for chronic plaque psoriasis
- Safety for topical corticosteroids in pregnancy
- Excision margins for melanoma
- Interventions for erythema nodosum leprosum
- Interventions for Old World Cutan Leishmaniasis
- Interventions for pemphigus vulgaris

www.thecochranelibrary.com

The UK Dermatology Clinical Trials Network



Trials portfolio- funded studies



Prophylactic Antibiotics for the Treatment of Cellulitis at Home: investigating whether prophylactic antibiotics can prevent further episodes of cellulitis of the leg (320K).



Study of Treatments for Pyoderma Gangrenosum Patients: first trial of its kind to formally evaluate the most commonly used treatments for pyoderma gangrenosum (800K) .



RCT to compare the safety and effectiveness of doxycycline with prednisolone for the treatment of bullous pemphigoid (830K).

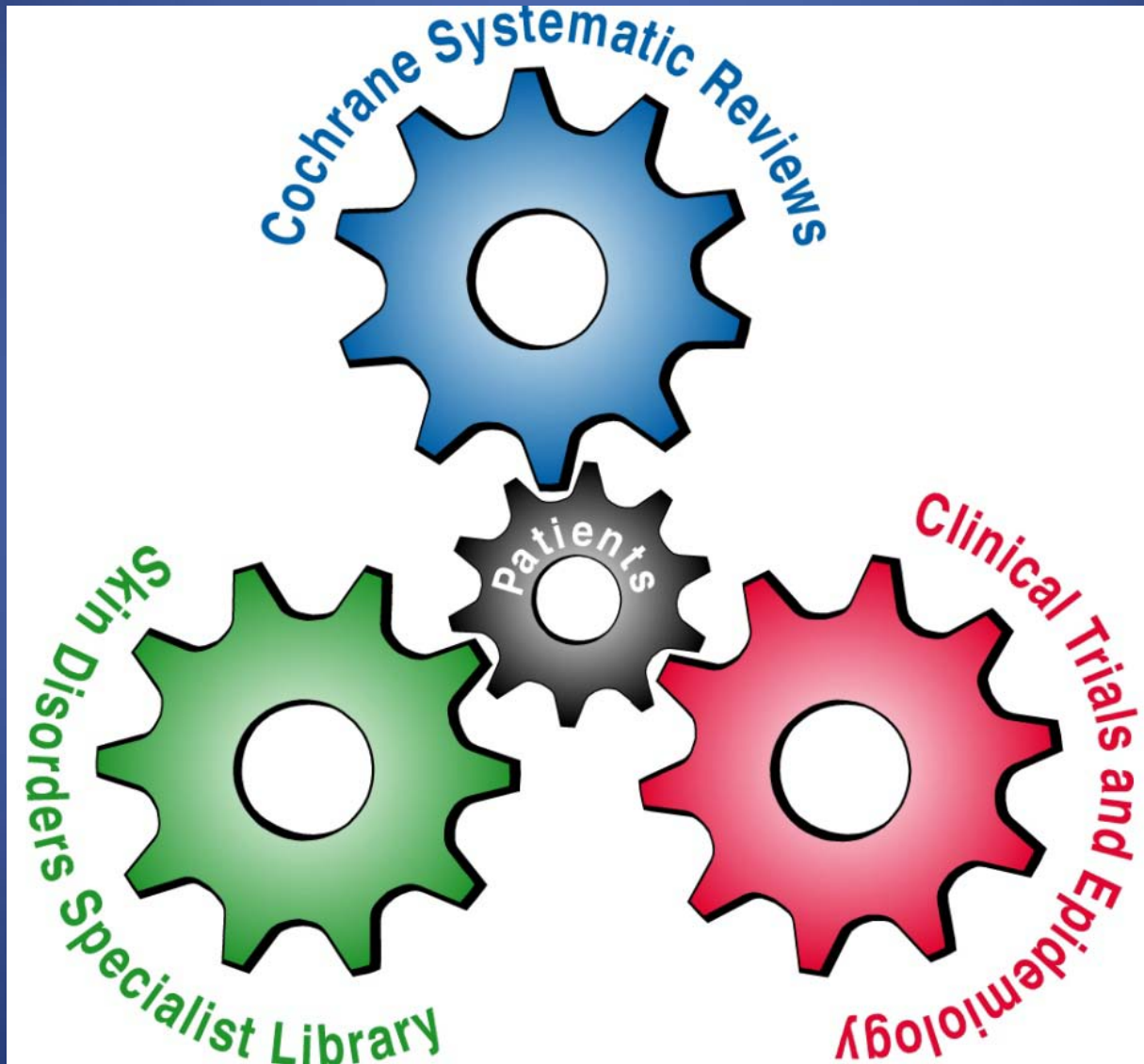


Softened Water Eczema Trial: investigating whether water softeners help reduce the severity of eczema in children (930K).



LIMIT-1 Phase II study investigating the use of imiquimod in the treatment of lentigo maligna (250K)

NHS Evidence - skin disorders



National electronic library



www.library.nhs.uk/skin

- Disorders
 - General skin disease
 - Acne, rosacea & related
 - Benign tumours, moles & cysts
 - Birthmarks, naevi & disfigurements
 - Connective tissue
 - Dermal & subcutaneous
 - Drug & treatment complications
 - Eczema & dermatitis

Disorders > Eczema & dermatitis > Atopic eczema

2010 Annual Evidence Update on Atopic Eczema - Commentary

"What's new?" — a tour of the 2010 Annual Evidence Update on Atopic Eczema with the busy clinician in mind

Professor Hywel Williams, Clinical Lead for NHS Evidence - skin disorders and Co-ordinating Editor of the Cochrane Skin Group, and Dr Kave Shams, Dermatology Registrar, Southern General Hospital, Glasgow



Hywel (left) and Kave (right)

GUIDELINE

Diagnosis and management of food allergy

In last year's Annual Evidence Update, we included German guidelines on the investigation and management of food allergy which failed to connect recommendations with the evidence sufficiently [1]. This year, guidelines on the diagnosis and management of food allergies in general have been published in draft form by the National Institute of Allergy and Infectious Diseases (NIAID) in the USA ([Link to full text](#)). Due to the increasing public health concerns and reports of increased prevalence of food allergies, these guidelines set out to provide advice to healthcare workers on how to approach food allergies in a clinical setting. The methodology is fairly well described, and the quality of evidence behind the various recommendations stated.

One of the great challenges of the new US guidelines is the lack of a consistent definition of food allergy in the

Email to a colleague

Colleague's email:

Your email:

Message:

GO

What I am going to cover

- Introduce the Centre of Evidence-Based Dermatology
- Our global collection of randomized controlled trials
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- The Harmonising Outcome Measures for Eczema project
- Our mapping of eczema systematic reviews
- Five ways my practice has changed as a result

Mapping the evidence on atopic eczema treatments:



....An update of all randomized controlled trials on atopic eczema since the 2000 HTA review

www.greatdatabase.org.uk

Potential users

- Clinicians who want to see if their treatments have been tested properly
- Those writing treatment guidelines eg JDS
- Those doing systematic reviews
- Those writing funding applications

Background

This database has been created as part of a larger National Institute for Health Research funded programme investigating ways to set priorities and reduce uncertainties for people with skin disease. The database contains information on randomised controlled trials on treatments for [eczema](#). The database will be periodically updated.

This database represents independent research commissioned by the National Institute for Health Research (NIHR) Programme Grants for Applied Research (RP-PG-0407-10177). The views expressed in this resource are those of the author(s) or the trial authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Aim

To provide a comprehensive, easy to use and access resource which contains pertinent information about randomised controlled trials of eczema treatments, in order to facilitate and speed up future eczema research projects.

Future research collaboration

The data contained within this database is just part of a much larger data set being collected. We are keen to hear from anyone who is interested in collaborating with us to use this information, which includes detailed results data on efficacy outcomes. Please contact us at great@nottingham.ac.uk

TREATMENT CATEGORIES

Antihistamines and Mast Cell

Antimicrobial and Antiseptic Agents

Complementary therapies

Dietary interventions

Non-pharmacological treatments

Other interventions

Other topical agents

Systemic immunomodulatory agents

Topical corticosteroids

Topical immunomodulatory agents

TREATMENTS

Cetirizine

Chlorpheniramine

Fexofenadine

Fexofenadine

Ketotifen

Loratidine

Sodium cromoglycate

Topical doxepin

Background

This data set is part of a programme to set up randomised controlled trials of eczema treatments.

This data set is part of a programme of NIHR Grants for Health Research funded programme investigating ways to set up randomised controlled trials of eczema treatments. The database contains information on randomised controlled trials of eczema treatments, which are periodically updated.

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Nankervis, H, Samuels, HJ, Delamere F, Thomas, K, Williams HC. The Global Resource of Eczema Trials. Centre of Evidence Based Dermatology. Accessed at www.greatdatabase.org.uk on

2000 - 2009



HOME	TREATMENT CATEGORIES	TREATMENTS	TRIALS	FEEDBACK	GLOSSARY	SEARCH
------	----------------------	------------	--------	----------	----------	--------

TREATMENT CATEGORIES

- Antihistamines and Mast Cell Stabilisers
- Antimicrobial and Antiseptic Agents
- Complementary therapies
- Dietary interventions
- Non-pharmacological treatments
- Other interventions
- Other topical agents
- Systemic immunomodulatory agents
- Topical corticosteroids
- Topical immunomodulatory agents

- TREATMENTS
- Cetirizine
 - Chlorpheniramine
 - Fexofenadine
 - Fexofenadine
 - Ketotifen
 - Loratidine
 - Sodium cromoglycate
 - Topical doxepin

TRIALS

<p>Capella-2001-European Journal of Dermatology-A randomized trial of leukotriene receptor antagonist montelukast in moderate-to-severe atopic dermatitis of adults</p> <p>Trial 35</p>
<p>Diepgen-2002-Pediatric Allergy and Immunology-Long-term treatment with cetirizine of infants with atopic dermatitis: A multi-country, double-blind, randomized, placebo-controlled trial (the ETAC trial) over 18 months</p>

Background

This data set provides information to set up controlled trials of eczema treatments.

This data set provides information on Grants from the National Institute for Health Research (NIHR) Programme for Applied Research in Health Care (PARCHC) (reference number 10407-10177). The views expressed in this resource are those of the author(s) or the trial sponsor and do not necessarily represent those of the Department of Health.

Aim

To provide a comprehensive, easy to use and access resource which lists eczema treatments, in order to facilitate and speed up future eczema trials.

Future research collaboration

The data contained within this database is just part of a much larger data set being collected. We are keen to hear from anyone who is interested in collaborating with us to use this information, which includes detailed results data on efficacy outcomes. Please contact us at great@nottingham.ac.uk

Author	Title	Year	Journal
Capella	A randomized trial of leukotriene receptor antagonist montelukast in moderate-to-severe atopic dermatitis of adults	2001	European Journal of Dermatology

Intervention A	Oral montelukast and placebo tablets and pharmacologically inert, non-moisturising, non-greasy gel
Intervention A schedule	Montelukast = Once a day, Placebo tablet = Three times a day, Placebo cream = twice a day on atopic eczema lesions and xerotic skin
Intervention A dose	10mg montelukast
Intervention B	Cetirizine and clarythromycin and topical mometasone furoate 0.1% or topical methylprednisolone aceponate 0.1% and topical emulsions containing urea or ammonium lactate
Intervention B schedule	Cetirizine = twice a day for 6 weeks. Clarythromycin = twice a day for 10 days. Topical preparations = 6 weeks.
Intervention B dose	10mg cetirizine, 250mg clarythromycin, topical cream on atopic eczema lesions (except face and external genitalia), topical emulsions on xerotic skin.
Comments on Interventions	Oral and topical steroids were given to the montelukast group to minimise outward differences between groups and to avoid the introduction of placebo effect bias. Ethical considerations forbade the use of a true placebo.
Is the trial randomised?	Yes
Is the trial blinded?	Yes
Country	Not stated
Single or multicentre trial	Not stated
Type of trial	Not stated
Number of participants randomised	32 participants. 16 in each group.
Follow up	Baseline and 6 weeks
Inclusion criteria	Adult (18 years or over). Moderate to severe atopic eczema (SCORAD 30 or over). Eczema to fulfil Hanifin and Rajka criteria. Consulted due to a flare up and/or intolerance to and/or ineffectiveness or previous treatments.
Exclusion criteria	No drug active on atopic manifestations except inhaled or intranasal drugs or eye drops (corticosteroids, short and long acting beta-2- agonists, cromones, spaglumic acid, anticholinergics alpha-1-angonists in the event of coexisting allergic asthma, rhinitis or keratoconjunctivitis) for 10 days before the study.
Description of	

Please use it.....



www.greatdatabase.org.uk

What I am going to cover

- Introduce the Centre of Evidence-Based Dermatology
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- Five ways my practice has changed as a result

Hard water and eczema

- Ecological link between hard water and eczema prevalence in UK, Spain and Japan
- Anecdote that eczema improves with soft water
- Link plausible since increased soap needed in hard water irritates the skin



www.swet-trial.co.uk

Softened Water Eczema Trial

A multi-centre randomised controlled trial of ion-exchange water softeners for the treatment of eczema in children



Funded by the HTA (Health Technology Assessment programme)

Chief Investigator: Professor Hywel Williams

Centre of Evidence Based Dermatology, University of Nottingham

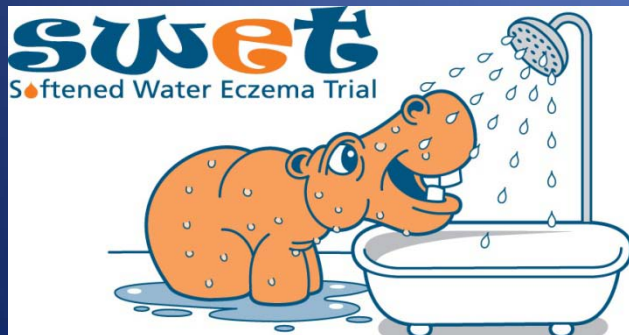
Study design

STUDY PERIOD = 16 weeks			
0 to 12 weeks		12 to 16 weeks	
Group A	Usual eczema care + water softener installed (n = 155)	Unit removed	Option to purchase unit at reduced cost
Group B	Usual eczema care + delayed installation (n = 155)	Unit installed	

Parallel group, single-blind, randomised controlled trial

SWET Study now completed

- 330 children recruited = moderate/severe eczema
- Primary outcome = change in eczema severity at 12 weeks
- Huge interest and high follow-up
- Results out PLoS Med Feb.15th!



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The problem – how to measure eczema severity



Outcome measures – a real mess

- Too many – at least 20 named scales
- Many not tested at all (Charman C et al *JID* 2003; **120:932–941**)
- Some are only partly tested (validity, repeatability, sensitivity change, consistency, interpretability)
- Some that are tested do not pass the tests

Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? A systematic review *JACI* 2007;120:1389-98.



What's all the FSSS about?

Take it EASI

TIS a right mess

Me too!

Meet my SIS

My name is ADAM

SCORAD scores again

SASSAD rules OK

Give me a POEM

ADASI tonight?

IGADA bad headache

Engraving for "Patriarchs and Prophets."

THE TOWER OF BABEL.

Copyrighted 1859

Why core outcomes?

- Easier to compare, contrast and synthesise results
- Reduces risk of inappropriate outcomes
- Reduces risk of selective reporting outcome bias



New Trends
in Allergy VII

& 6th Georg Rajka Symposium

International Symposium on Atopic Dermatitis

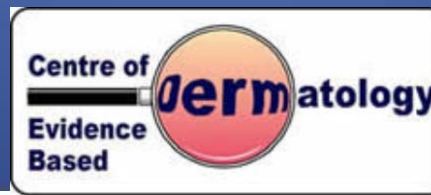
Munich, 22 - 24 July 2010

HOME I

Harmonising Outcome Measures for Eczema

Hywel Williams and Jochen Schmitt

Universities of Nottingham and Dresden



What I am going to cover

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- Five ways my practice has changed as a result

General skin disease

+ Acne, rosacea & related

+ Benign tumours, moles & cysts

+ Birthmarks, naevi & disfigurements

+ Connective tissue

+ Dermal & subcutaneous

+ Drug & treatment complications

- Eczema & dermatitis

Atopic eczema

Eczema in infants

Seborrhoeic dermatitis

Nappy rash (napkin dermatitis)

Discoid eczema (nummular dermatitis)

Hand & foot eczema

Lichen simplex & prurigo

+ Contact dermatitis

Venous eczema

Other eczematous disorders

Occupational

2010 Annual Evidence Update on Atopic Eczema - Home Page

Published: 13 September 2010



Atopic eczema, used with kind permission of Dr Amanda Oakley, New Zealand Dermatological Society. © DermNet NZ.

Welcome to the fourth Annual Evidence Update on Atopic Eczema produced by NHS Evidence - skin disorders, with the results of a search for new guidelines and systematic reviews published or indexed since the last Annual Evidence Update in September 2009. There is also a "what's new" analysis, discussing the new evidence and its implications for clinical practice.

Contents

1. [Introduction](#)
2. [Results of 2010 Annual Evidence Update on Atopic Eczema](#)
3. [Commentary and analysis - "What's new?"](#)
4. [Summary points and implications for practice](#)
5. [UK DUETs uncertainties update](#)
6. [Systematic reviews on atopic eczema from 2000—mapping by topic](#) ←
7. [Link to National Eczema Week \(National Eczema Society\)](#)
8. [Methodology](#)

Publication Date: 13 Sep 2010

Publication Type: [Annual Evidence Update](#)

Publisher: [NHS Evidence - skin disorders](#)

Creator: NHS Evidence - skin disorders

Next Review Date: 03 Sep 2011

Topics

Colleague's email:

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Disorders

General skin disease

Acne, rosacea & related

Benign tumours, moles & cysts

Birthmarks, naevi & disfigurements

Connective tissue

Dermal & subcutaneous

Drug & treatment complications

Eczema & dermatitis

Atopic eczema

Eczema in infants

Seborrhoeic dermatitis

Nappy rash (napkin dermatitis)

Discoid eczema (nummular dermatitis)

Hand & foot eczema

Lichen simplex & prurigo


Disorders > Eczema & dermatitis > Atopic eczema

Systematic reviews on atopic eczema - INDEX PAGE

This is the index page for a **mapping by topic of systematic reviews on atopic eczema** published from 2000 onwards (the date of the HTA monograph [Systematic review of treatments for atopic eczema](#)).

The systematic reviews are those found in the searches for the Skin Disorders Specialist Library's Annual Evidence Updates on Atopic eczema for [2007](#), [2008](#) and [2009](#).

Index of main topic headings:

- [Epidemiology](#) 
- [Prevention](#)
- [Topical treatments](#)
- [Systemic treatments](#)
- [Phototherapy](#)
- [Dietary treatments for established eczema](#)
- [Psychological and educational interventions](#)
- [Complementary and alternative therapies](#)
- [Other interventions for established eczema](#)

[Link to homepage of Annual Evidence Update on Atopic Eczema](#)

Publication Date: 14 Sep 2009

Publication Type: [Systematic Review](#)

Publisher: [NHS Evidence - skin disorders](#)

Creator: Grindlay D

Systematic reviews on atopic eczema - Epidemiology

This is a mapping by topic of **systematic reviews on the epidemiology of atopic eczema** that have been published from 2000 onwards. The systematic reviews were found in the searches for the Skin Disorders Specialist Library's Annual Evidence Updates on Atopic Eczema. The links given are to the PubMed abstract or free full text where available.

Please see also the full version of the 2007 NICE Clinical Guideline "[Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years](#)". This includes a systematic review of the diagnosis (Chapter 3), assessment of severity, psychological and psychosocial wellbeing and quality of life (Chapter 4), epidemiology (Chapter 5) and identification and management of trigger factors (Chapter 6) in atopic eczema in this age group.

Aetiology	2009	Filaggrin gene defects and risk of developing allergic sensitisation and allergic disorders: systematic review and meta-analysis
	2009	Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disease
	2007	Toward a major risk factor for atopic eczema: meta-analysis of filaggrin polymorphism data
	2005	Atopic dermatitis and the 'hygiene hypothesis': too clean to be true?
	2004	How atopic is atopic dermatitis?
Risk factors	2008	Caesarean delivery and risk of atopy and allergic disease: meta-analyses
	2008	A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis
	2006	What causes worsening of eczema? A systematic review
	2004	No epidemiological evidence for infant vaccinations to cause allergic disease
Co-morbidities	2008	Alexithymia and dermatology: the state of the art
	2007	Atopy and risk of brain tumors: a meta-analysis
	2007	Risk of developing asthma in young children with atopic eczema: A systematic review
Diagnosis	2008	Diagnostic criteria for atopic dermatitis: a systematic review
	2006	What is meant by a "flare" in atopic dermatitis? A systematic review and proposal
Severity & outcome measures	2007	What are the best outcome measurements for atopic eczema? A systematic review
	2003	Measuring atopic dermatitis severity in randomized controlled clinical trials: what exactly are we measuring?
	2000	Outcome measures of disease severity in atopic eczema
Disease impact	2008	The socioeconomic impact of atopic dermatitis in the United States: a systematic review
	2008	Sleep disruptions in parents of children and adolescents with chronic illnesses: prevalence, causes, and consequences
	2008	A bidirectional relationship between psychosocial factors and atopic disorders: a systematic review and meta-analysis
	2003	Treatment of atopic dermatitis and impact on quality of life: a review with emphasis on topical non-corticosteroids



Search: PubMed

[Limits](#) [Advanced search](#) [Help](#)

[Display Settings:](#) Abstract

[Send to:](#)



J Allergy Clin Immunol. 2009 Jun;123(6):1361-70.e7.

Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors in atopic disease.

Rodríguez E, Baurecht H, Herberich E, Wagenpfeil S, Brown SJ, Cordell HJ, Irvine AD, Weidinger S.

Division of Environmental Dermatology and Allergy, Helmholtz Zentrum Munich and ZAUM-Center for Allergy and Environment, Technische Universität München, Munich, Germany.

Abstract

BACKGROUND: The discovery of filaggrin (FLG) null mutations as a major risk factor for eczema represents a milestone toward the understanding of an important mechanism in this complex disease. However, published studies demonstrate differences concerning design and effect size, and conflicting results for asthma have been reported. **OBJECTIVES:** We sought to provide a more accurate estimate of FLG effect sizes and to better refine FLG risk profiles within the broad and inclusive eczema diagnosis. We also sought to provide a more detailed and conclusive estimate of the risk for asthma associated with FLG null alleles. **METHODS:** We performed a meta-analysis of 24 studies on FLG mutations and eczema involving 5,791 cases, 26,454 control subjects, and 1,951 families as well as 17 studies on asthma involving 3,138 cases, 17,164 control subjects, and 1,511 offspring. **RESULTS:** Both case-control and family studies showed strong associations with eczema. Case-control studies were heterogeneous, whereas family studies yielded more homogeneous results. Combined analysis showed that FLG haploinsufficiency strongly increases the eczema risk (odds ratio [OR], 3.12; 95% CI, 2.57-3.79) and is associated with more severe and dermatologist-diagnosed disease. FLG mutations are also significantly associated with asthma (OR, 1.48; 95% CI, 1.32-1.66). However, although strong effects for the compound phenotype asthma plus eczema (OR, 3.29; 95% CI, 2.84-3.82) were observed, there appears to be no association with asthma in the absence of eczema. **CONCLUSIONS:** This meta-analysis summarizes the strong evidence for a high eczema risk conferred by FLG mutations and refines their risk profiles, suggesting an association with more severe and secondary care disease. FLG mutations are also a robust risk factor for asthma and might help define the asthma endophenotype linked with eczema.

PMID: 19501237 [PubMed - indexed for MEDLINE]

[+](#) Publication Types, MeSH Terms, Substances

[+](#) LinkOut - more resources

Related citations

The burden of disease associated with filaggrin mutations: a population-based study [J Allergy Clin Immunol. 2008]

Filaggrin mutations, atopic eczema, hay fever, and asthma in children [J Allergy Clin Immunol. 2008]

Filaggrin null mutations and childhood atopic eczema: a population-based study [J Allergy Clin Immunol. 2008]

Review Filaggrin gene defects and risk of developing allergic sensitisation and asthma [BMJ. 2009]

Review Atopic eczema and the filaggrin story. [Semin Cutan Med Surg. 2008]

[See reviews...](#)

[See all...](#)

All links from this record

- [Related Citations](#)
- [Gene](#)
- [Gene \(GeneRIF\)](#)
- [HomoloGene](#)
- [Nucleotide \(RefSeq\)](#)
- [Nucleotide \(Weighted\)](#)
- [Protein \(RefSeq\)](#)
- [Protein \(Weighted\)](#)
- [Taxonomy via GenBank](#)
- [UniGene](#)
- [GEO Profiles](#)

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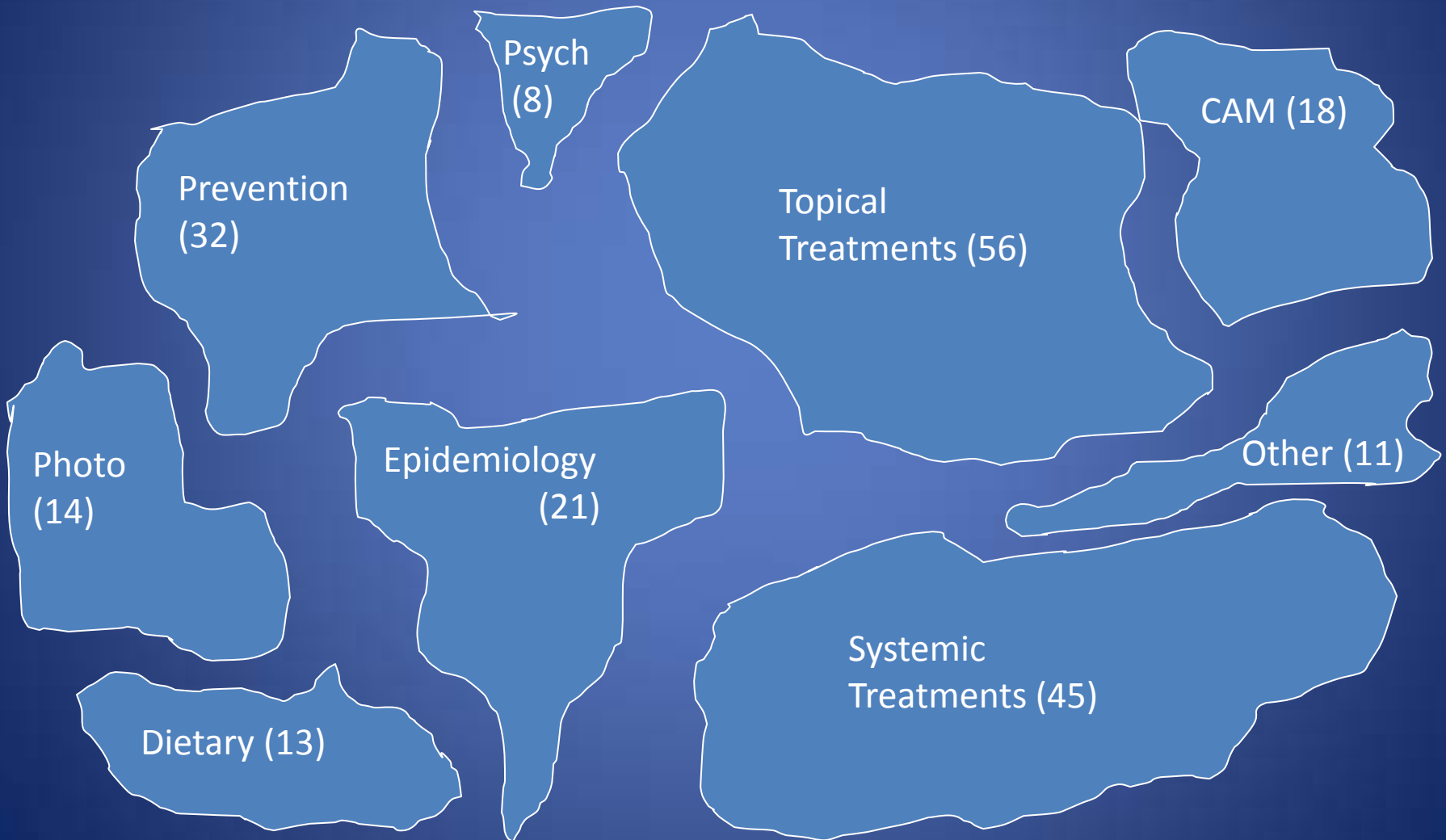
Meta-analysis of filaggrin polymorphisms in eczema and asthma: robust risk factors [PubMed]

Preatrophy: covert sign of thinned skin. [PubMed]

covert AND dermatology (6) [PubMed]

Allergic and non-allergic rhinitis in swimmers: clinical and cytological aspects [PubMed]

The 2010 “map” of atopic eczema systematic reviews



What I am going to cover

- Introduce the Centre of Evidence-Based Dermatology
- Our global collection of randomized controlled trials
- The water softener study
- The Harmonising Outcome Measures for Eczema project
- Our mapping of eczema systematic reviews
- Five ways my practice has changed



Question: All this evidence is all very well, but has it made any difference to your clinical practice for people like me with eczema?

Five things that I have changed

1. I now only prescribe topical corticosteroids once a day
2. I do not prescribe bath emollients
3. I use weekend therapy with TCS for maintaining eczema remission
4. I use topical tacrolimus and TCS concurrently at different body sites and times of the week
5. I am more likely to explore dietary factors in the first year of life

What I have covered

- Introduced the Centre of Evidence-Based Dermatology
- Our global collection of randomized controlled trials – the GREAT database
- The water softener study - SWET
- The Harmonising Outcome Measures for Eczema project - HOME
- Our mapping of eczema systematic reviews
- Five ways my practice has changed

