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Acupuncture for allergic rhinitis

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Acupuncture for Allergic Rhinitis

A WEST MIDLANDS HEALTH TECHNOLOGY ASSESSMENT COLLABORATION REPORT

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WEST MIDLANDS HEALTH TECHNOLOGY ASSESSMENT COLLABORATION (WMHTAC)

The West Midlands Health Technology Assessment Collaboration (WMHTAC) produce rapid systematic reviews about the effectiveness of healthcare interventions and technologies, in response to requests from West Midlands Health Authorities or the HTA programme. Reviews usually take 3-6 months and aim to give a timely and accurate analysis of the quality, strength and direction of the available evidence, generating an economic analysis (where possible a cost-utility analysis) of the intervention.

CONTRIBUTIONS OF AUTHORS:

Jonathon Roberts undertook the research and production of the report.

CONFLICTS OF INTEREST:

None

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West Midlands Regional Evaluation Panel

Recommendation

Evidence level IV – Not Proven.

Further research needs to be undertaken into costs/effectiveness

Anticipated expiry date:

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EXECUTIVE SUMMARY

Background

Allergies cause a considerable burden to both sufferers and the National Health Service (NHS). Allergic rhinitis (hay fever) is a common allergy that can cause persistent symptoms during the pollen season, which lasts for around four months. Current treatment options aim to alleviate symptoms. Acupuncture is growing in popularity and is thought to modulate the immune system. Acupuncture may therefore be a useful treatment for allergic rhinitis sufferers.

Aim

To investigate the evidence base behind the clinical effectiveness and cost effectiveness of using acupuncture in patients with allergic rhinitis.

Methods

Searches were conducted in the MEDLINE, EMBASE and Cochrane databases as well as specialist acupuncture databases to identify studies evaluating the clinical and cost effectiveness of acupuncture in the treatment of allergic rhinitis.

Results

After inclusion and exclusion criteria were applied, seven relevant randomised controlled trials (RCTs) were identified. The majority of studies compared acupuncture to a sham or inactive acupuncture treatment. A wide variety of outcomes were measured in these studies. The trials were generally of poor quality and results inconclusive. Interestingly, an improvement in symptoms for both an active and inactive acupuncture group were often seen, raising the question as to whether the placebo or hawthorn effect is being seen in these trials. Acupuncture was not associated with any additional adverse events.

Economic analysis

No published studies evaluating the cost effectiveness of acupuncture for allergic rhinitis were identified. Two models were constructed using a simple

decision tree approach and costs from a recently published acupuncture trial for low back pain. The results showed providing an acupuncture service would be highly likely to be cost-effective

Conclusions

Although acupuncture treatment appears to be safe and is associated with low costs, making it highly likely to be cost-effective, there is currently insufficient evidence on the clinical effectiveness to support or refute its use in patients with allergic rhinitis. A large well conducted RCT is needed and it is hoped the cost-effectiveness model in this review would help to form the basis of a power calculation.

LIST OF ABBREVIATIONS

AACP	Association of chartered physiotherapists
ACTH	Adrenocorticotrophic Hormone
AMED	Allied and complementary medicines database
APC	Antigen presenting cell
ARIA	Allergic Rhinitis and its impact on Asthma
BMA	British Medical Association
BMAS	British Medical Acupuncture Society
CAM	Complementary and Alternative Medicine
CASP	Critical appraisal skills program
CI	Confidence Interval
DOH	Department of Health
ECF-A	Eosinophil chemotactic factor-A
EED	Economic Evaluations Database
ELISA	Enzyme linked immunoabsorbent assay
ENT	Ear, Nose and Throat
FEV1	Forced expiratory volume
GP	General Practitioner
HTA	Health Technology Assessment
ICER	Incremental cost effectiveness ratio
IgE	Immunoglobulin E
IL	Interleukin

NCF-A	Neutrophil chemotactic factor-A
NHS	National Health Service
QALY	Quality added life year
QoL	Quality of life
RCT	Randomised Controlled Trial
SD	Standard Deviation
TENS	Transcutaneous Electrical Nerve Stimulation
VAS	Visual analogue scale
WHO	World Health Organisation

CONTENTS

TABLES

FIGURES

1 AIM OF THE REVIEW

To systematically review the evidence of the effectiveness and cost effectiveness of acupuncture for individuals with allergic rhinitis.

2 BACKGROUND

2.1 Allergies

Allergies are responsible for an estimated annual expenditure of £1 billion in the National Health Service (NHS),[1] with an estimated 0.8% of all hospital admissions being for allergy. It is also estimated that 6% of GP consultations and 10% of the total costs resulting from primary care consultations are for allergies.[1,2] Part of the reason for this is that allergies often coexist, so conditions such as allergic rhinitis, asthma and eczema are commonly found together in patients, hence creating a combined cost.[3]

2.2 What causes allergy?

2.2.1 Type I hypersensitivity

Hypersensitivity reactions were first classified by Gell and Coombs in 1963.[4] There are four main types of hypersensitivity reactions. The differences between types are essentially due to the type of immune system cell involved in the response. Types I-III are antibody mediated responses and type IV is T-cell and macrophage mediated response.[5] In reality there is interaction between types and one reaction type is unlikely to occur in isolation. Type I hypersensitivity is classically associated with allergic reactions and is associated with immunoglobulin E (IgE). IgE in the circulation has a short half life, but IgE has a high affinity with mast cells via the binding of the Fc fragment of IgE with the receptor for IgE on mast cells known as Fc εRI. Once bound to its receptor IgE is protected from the serum proteases that would normally break it down. Therefore, IgE bound to mast cells in the mucosal surfaces are primed for contact with allergens. IgE is produced by B-cells after an antigen has been presented to it by a professional antigen presenting cell

(APC) which can either directly activate B-cells, or activate a T-helper cell which in turn will release cytokines such as Interleukin (IL) -4 and IL-13 that stimulate the B-cell to release IgE. Once an allergen has bound to IgE it stimulates the immediate release of primary mediators such as histamine that are stored within the mast cells (degranulation) the activated mast cell will then synthesise secondary mediators such as bradykin. The downstream consequences of the release of these mediators is the increased permeability of blood vessels, smooth muscle contraction and inflammation.[5]

2.2.2 Allergic Rhinitis

Traditionally allergic rhinitis has been grouped into two forms, seasonal and perennial. Seasonal allergic rhinitis (also known as hay fever) is a complex of symptoms associated with type 1 hypersensitivity to grass, tree or weed pollen. Allergy to other seasonal antigens such as fungal spores may also give rise to similar symptoms. Perennial allergic rhinitis is most commonly caused by sensitivity to allergens such as dust mites, animal danders and insects and is present for a longer period of time commonly throughout the year. However, there is some overlap between these as some patients may have symptoms all year long, but have seasonal exacerbations and studies have shown up to 80% of patients seen in clinic have a mixed aetiology for their rhinitis.[6] The classic symptoms of allergic rhinitis include sneezing, nasal itching, nasal blockage and watery secretions. Other symptoms can include general tiredness, fever, sore eyes, cough, wheezing and shortness of breath.[7] Non-allergic rhinitis is caused by irritants such as small molecular weight compounds like aldehydes and chlorine.

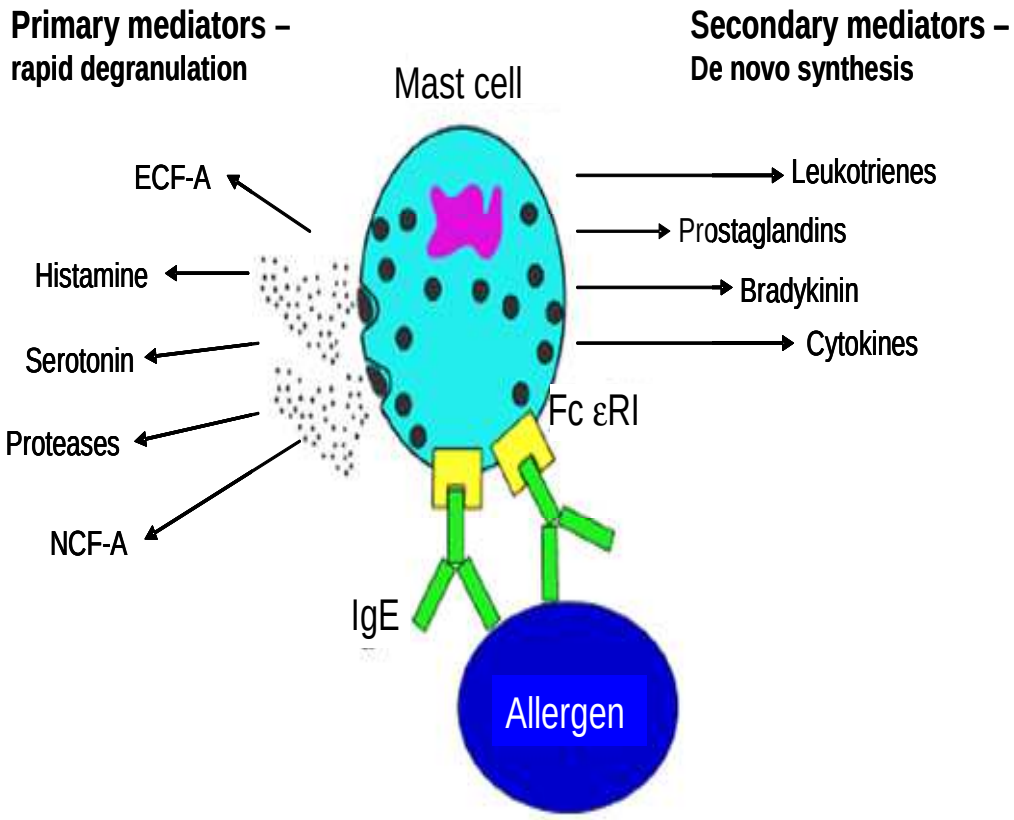
*A new classification was put forward by the UCB Institute of Allergy in 1994 suggesting the adoption of the terms intermittent and persistent to replace seasonal and perennial.[8]

2.2.3 Prevalence

The prevalence of allergic rhinitis is highest in developed countries.[9] In Western Europe, allergic rhinitis is estimated to affect 23% of the population.[2,9,10] The higher prevalence in developed countries is thought to be due to lower rates of childhood infections that may cause a deviation of T-helper cells and the innate immune response, thus modulating its ability to control the adaptive arm of the immune response in later life. This was originally termed the 'hygiene hypothesis'.[11] Subsequently the likely role of genetics and gene-environment interactions in forming the immune response, along with higher rates of immunization and breast feeding, have been included as other differences in Western populations that may affect immune responses and allergy rates, leading to calls for term 'hygiene' to be removed.[12]

2.3 Diagnosis and treatment

Diagnosis of allergic rhinitis is confirmed by a skin prick test and measurement of serum specific IgE antibodies. Current treatment options include the use of antihistamines with or without a pseudoephedrine (decongestant). Intranasal antihistamines can be used as can oral leukotriene receptor antagonists with or without oral anti-histamines.[13] Treatments aim to reduce symptoms and to optimise quality of life, but can rarely eliminate symptoms.[14] These treatments are commonly associated with some side-effects that range in severity. Mild symptoms may include drowsiness, sedation and somnolence (sleepiness), whilst in the extreme case, anti-histamine use has been associated with ventricular arrhythmias and the long-term use of corticosteroids is thought to be related to the suppression of adrenocortical function.[15]



ECF-A (Eosinophil chemotactic factor-A), NCF-A (Neutrophil chemotactic factor-A)

Figure 1. A basic overview of the type I hypersensitivity reaction.

Adapted with permission from;

http://www.immuno.path.cam.ac.uk/~immuno/part1/lec13/lec13_97.html

2.4 Acupuncture

Acupuncture developed from the traditional Chinese medicine techniques that can trace recorded origins back to the 2nd century BC.[16] Acupuncture involves the stimulation of acupoints that are located at lines of meridians that correspond to the flow of energy (known as qi) through the body. Traditionally solid needles are inserted into acupoints in order to restore the flow of qi.[17] However, modern acupuncture has evolved other methods of stimulating acupoints including the use of electrical signals known as transcutaneous electrical nerve stimulation (TENS) or by applying pressure to the acupoint (acupressure) or using a low intensity laser. Modern Western 'medical acupuncture' is therefore an integration of traditional practices with the concepts of anatomy, physiology and pathology.

2.4.1 Rationale for the use of acupuncture in allergic rhinitis

Complementary and alternative medicine (CAM) treatments are becoming increasingly popular in the UK.[18] It is estimated the UK spends an average of £1.6 billion per year on CAM with acupuncture the fourth most common treatment behind aromatherapy, homeopathy and herbal medicines.[18]

There is a biological plausibility to the use of acupuncture for allergies. Acupuncture has been shown to have an effect on modulating the immune response in particular to have an effect on inducing an anti-inflammatory response.[19,20] [17,21] Acupuncture can stimulate the release of beta endorphin (β endorphin) which is coupled to the release of adrenocorticotrophic hormone (ACTH). ACTH acts on the adrenal cortex to stimulate the release of cortisol. It is thought that some of the anti-inflammatory effects of acupuncture may be related to the effects of both β endorphin and cortisol.[19,22] Synthetic cortisol (hydrocortisone) for example is used as a drug in the treatment of allergies and inflammation.

Previous studies have shown that no additional side effects would be likely to be associated with acupuncture as side effects are rare in acupuncture

studies and generally only minor, such as irritation at the needle site.[23-26] Acupuncture treatment if successful, may also last for the whole hay fever season which is generally 4 months long, so would lead to a reduced cost in terms of medication use over the spring and summer months.

2.5 Existing Evidence

The World Health Organisation (WHO) along with key UK acupuncture bodies the British Medical Acupuncture Society (BMAS) and the Acupuncture Association of Chartered Physiotherapists (AACP) list on their websites conditions and indications that acupuncture is a suitable treatment for. Allergic rhinitis is listed by all three of these bodies.[27-29] The WHO produced a review of clinical trial evidence in 2003 [30] and stated that allergic rhinitis was an indication 'for which acupuncture has been proved through clinical trials to be an effective treatment'.[30] It is unclear from this document which trials were included in the analysis or what the clinical effectiveness of acupuncture is. It is also unclear as to whether the UK acupuncture bodies evaluate the evidence behind the conditions they list on their websites.

The Cochrane database, Medline and Embase were searched for previous systematic reviews that have addressed the use of acupuncture for allergic rhinitis. One previous systematic review was identified.[31] The systematic review was published by the international board of the Allergic Rhinitis and its Impact on Asthma (ARIA) collaboration in 2006.[31] The review was critically appraised using the CASP 10 point checklist for systematic reviews.[32] The review has looked at a number of CAM treatments for both allergic rhinitis and asthma. It has included studies on acupuncture, herbal medicines, homeopathy and physical techniques (including yoga, chiropractic and educational programs). This review is attempting answer a very broad question. It is limited in the fact that it only included studies published in the English language and the searches were only conducted in MEDLINE and the Cochrane library. Further, probably due to space limitations in publishing a review of this size, the inclusion and exclusion criteria for studies has not been described. There is also no information on the number of trials identified by

the searches before inclusion and exclusion was applied, which makes it difficult to assess the validity of their results. There is no economic evaluation of the treatment options. The conclusion of this review is that the studies identified have inadequate methodology (using the Jadad scoring system) to make strong recommendations on the use of acupuncture for allergic rhinitis.

It is thought that this review will add further to this evidence by employing a more rigorous systematic review methodology. This will include a comprehensive search strategy covering a number of databases and will included studies in any languages. A separate search will also be conducted for studies evaluating the cost-effectiveness of acupuncture. This is an area which has not been addressed by the current reviews.

3 METHODS

3.1 Search strategy

The details of the search strategy can be found in appendix 1.

A number of bibliographic databases were searched to identify relevant studies.

- MEDLINE (1966-August 2006)
- EMBASE (1988-August 2006)
- Cochrane library (including CRD, DARE, HTA, CENTRAL)

Specialist databases were also searched including

- The national library for health - complementary and alternative medicines library
- The allied and complementary medicines database of the British library
- Bandolier
- Acubriefs specialist acupuncture website.
- The Chinese literature was searched using the sina website.

The bibliographies of retrieved references were searched and hand searching of the journal 'acupuncture in medicine' was conducted (2000-2002). Ongoing trials were searched for in the National Research Register and websites including Clinical trials.gov. Studies in any language were considered for the review.

3.2 Inclusion/exclusion Criteria

- **Population.** Patients or subjects with allergic rhinitis with or without other allergies such as asthma. Studies looking at patients with non-allergic rhinitis were excluded. Patients of any age were included.

- **Intervention**. Any form of acupuncture treatment that stimulates an acupoint. This will include solid needles, TENS (or electro-acupuncture)

and acupressure. Acupuncture needles with burning mugwort (moxibustion) will be included, but separated in the analysis as the effects of burning the mugwort herb cannot be distinguished from the stimulation of the acupuncture point. Studies will be sub-grouped into different types of acupuncture to see if different methods of stimulating acupoints affects outcome. If studies have used different acupoints, they may be sub-grouped into common acupoints to see if there is differing effects with the acupoint used or duration of insertion of needle.

- **The comparison group.** Sham or fake acupuncture treatment with or without standard care. Studies using a control group who are not receiving acupuncture will be included providing standard care has been given. Comparisons will be made between studies using different methods of sham acupuncture and controls.

- **Outcome measures**. Any outcome measure relating to the effectiveness of treatment, quality of life (QoL) including days off work/school, rhinitis symptom scores, medication usage score and adverse effects. There is a specific Rhinoconjuctivitis quality of life questionnaire, which is a 28 question (in seven domains) questionnaire covering activity problems, sleep problems, nasal/eye symptoms and emotional function.

- **Study designs.** The search will be for randomised controlled trials. Participants in studies must be randomised to acupuncture treatment or control group.

The inclusion and exclusion criteria were applied by two reviewers where possible, studies in non-English languages were reviewed by one reviewer only. Any discrepancies were resolved through discussion. Details of the included and excluded studies can be seen in appendix 2.

3.3 Data extraction and quality assessment

The data from the identified studies was extracted independently by two reviewers using the data extraction sheet shown in appendix 3. Any discrepancies were discussed. A modification of the Jadad scoring system[33] was applied to the included trials to asses the quality of the evidence found. The scoring system enabled a maximum score of 20 for each study and addressed issues of quality such as blinding, allocation concealment, intention to treat analysis and comparability of treatments between groups. Details can be seen in appendix 4.

3.4 Data synthesis

The trials identified have been described in table 1. The table contains a summary of the extracted data including trial characteristics, the study population, outcomes measured and review of the results. Where possible the results have been combined into a meta-analysis using the Revman software package (Version 4.2, Cochrane Collaboration, Oxford). The trials included in the first meta-analysis had an outcome measure recorded on different VAS so a standardised mean difference measure was used to compensate for the different scales used. A random effects model was used to compensate for the heterogeneity seen between studies. In the second meta-analysis the outcome measure found in two studies was serum IgE levels. These were combined again using a standardised mean difference but there was no heterogeneity so a fixed effects model was used.

4 RESULTS

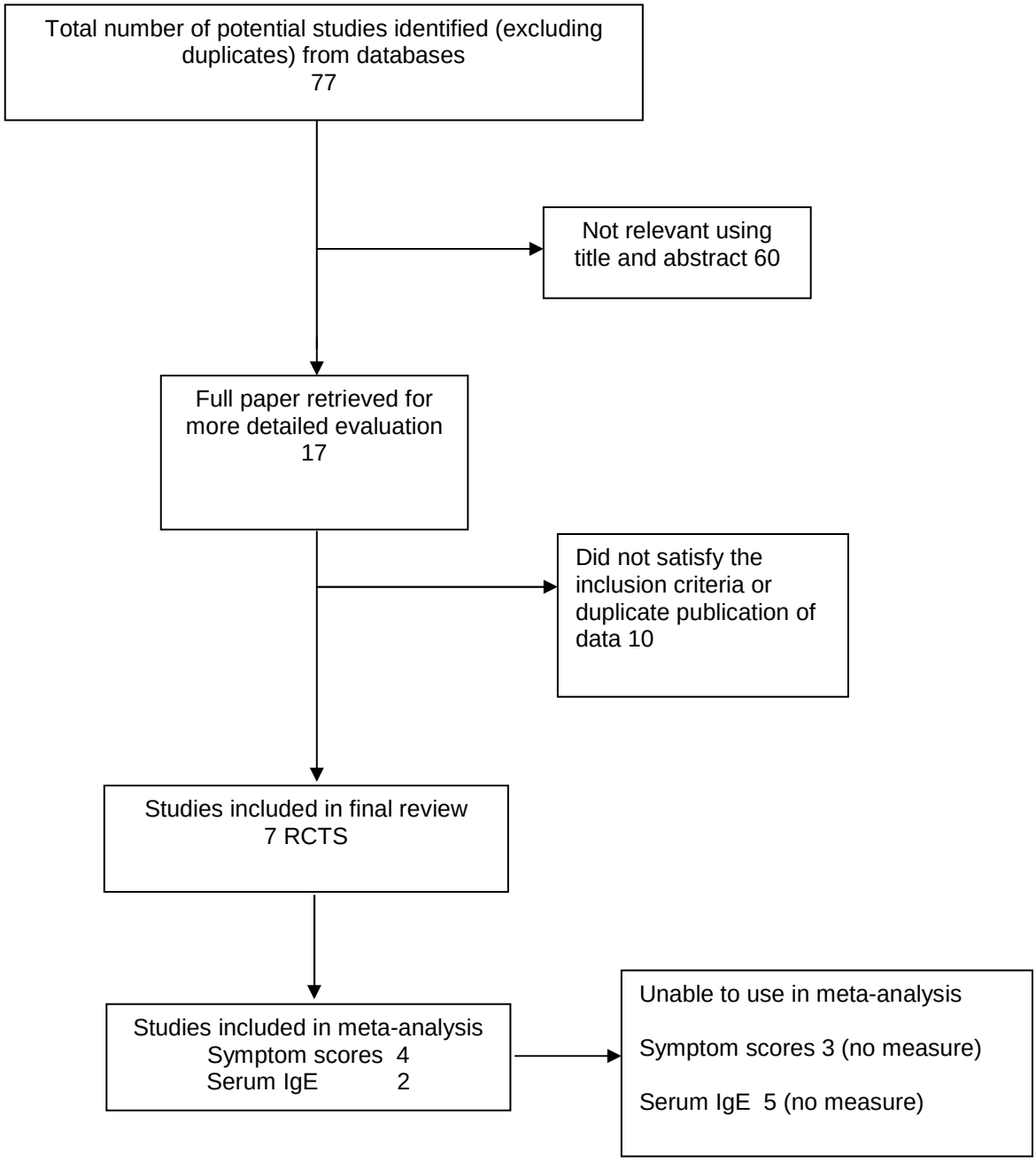


Figure 2. Breakdown of the steps to finding the 7 RCTS included in the review.

4.1 Summary of included studies

Seven trials met the inclusion criteria after 17 were selected for further analysis. This included 14 trials, with one trial reported in duplicate and one in triplicate. The trials included 5 in German, 1 in Czech, 1 in Chinese and 7 in English (details of excluded studies can be found in appendix 3). Of the included trials 5 were in English language, and 2 were in German.

There are some differences in the designs of the studies. Most of the studies compared an active with inactive or placebo acupuncture group. Only the study by Petti[34] included a standard care group who did not have any additional treatment. The studies by Wolkenstein[35-37] were conducted in a chamber with a regulated flow of pollen, so patients were exposed to pollen before and after acupuncture treatment and outcomes measured during the exposure to pollen and 24 hours after. The study by Xue[38] used a cross-over RCT design, where participants were exposed to both the inactive and active acupuncture treatments.

Individuals in the studies were recruited either via advertisements in GP practices or in the local media. This volunteer population may not be a true representation of the general hay fever suffering population as people who are keen to enter a trial may have an interest in acupuncture or have more severe symptoms. In the majority of studies patients had their allergy confirmed by a skin prick test or measurement of serum IgE reactivity to allergen. In the study by Xue[38] allergy was confirmed by a patient questionnaire only. Only the study by Langer & Hauswald[39] included participants with allergic rhinitis confirmed by an ENT specialist.

The studies generally recruited individuals within the age range 18-65 with the exception of the study by Ng[40], which was set in a paediatric respiratory clinic. However, despite the average age being 11 years in this study it included a range of ages from 6-19 in the intervention group and 6-20 in the control group so was really a mixture of children with some adults.

The intervention varied considerably across the trials with the number and duration of sessions. Outcomes ranged from symptom severity scores measured on a visual analogue scale (VAS) and medication use to biochemical markers such as serum cytokine levels, blood eosinophil counts and serum IgE.

4.1.1 Quality of included studies

Using an adapted version of the Jadad quality assessment tool[33] (see appendix 4) the included studies were given a quality score out of a maximum of 20. The scores ranged from 6-14 (average score 10). All of the trials were described as randomised but only 4 (57%) gave details of the method used. Only 2 of the trials (28.5%) included information on allocation concealment and blinding was adequately described in 4 (57%). In all of the studies it was difficult to tell if the intervention was distinguishable from the control treatment or not. None of the studies reported on the patient's ability to guess if they had received active or inactive acupuncture treatments. Petti[34] excluded patients after two treatments if there was what they termed 'anomalies to propagation of sensation along meridians' suggesting some degree of patient selection bias in the intervention group. Blinding of patients and/or outcome assessors was mentioned in 4 (57%) of the trials but was only adequately described in 1 trial. An intention to treat (ITT) analysis was described in 1 trial with no details given in the others, but even in this trial it was difficult to assess if this had really been carried out. Losses to follow-up were described in all trials and minimal. The main quality issue that arises from the trials are the differences in baseline characteristics between groups. Four (57%) of the trials have been scored with a 'no' or 'can't tell' on the quality checklist by two independent reviewers for comparability of baseline characteristics. This maybe due to the low numbers of participants in some trials, but raises quality concerns.

Comments on specific issues with individual trials can be found in Table 2.

Table 1. Details of included studies

Study	Study Design/Setting	Population (N (m/f) age, medication use)	Intervention/Comparator	Outcomes	Result summary
Wolkenstein & Horak 1993[37] Wolkenstein 1996[35] Wolkenstein & Horak 1998[36]	RCT (see comments) Hospital setting, Germany	Patients with grass pollen allergy 18-65 yrs with allergic rhinitis for at least 2 yrs and confirmed allergy with skin prick test, nasal provocation and serum IgE measures. Excluded if severe co-morbidity existed N=30 randomised (unclear on numbers in each group). Mean age 41 yrs, (10/14) 6 drop-outs.	Needle acupuncture according to patient needs (criteria of the Vienna School of Acupuncture) Placebo needle was placed 2.5cm away from defined acupoint. 1 session per week for a total of 9 sessions.	1) Nasal secretions measured every 30 mins 2) Subjective well-being (VAS 0-10cm) every 15 mins 3) subjective symptom score (0-21) every 15 mins 4) FEV1 every 30mins 5) Change in the nasal flow every 15 mins 6) Daily symptom diary for two months including general and specific symptoms (0-3 score)	1 + 5)There was no difference in the sum of nasal flows between the groups 2) There was no difference in subjective well being 3 + 6) No difference for symptom score measures or the daily symptom diary scores 4) No difference reported
Langer & Hauswald 1989[39]	RCT comparing needle and laser acupuncture groups	Diagnosis of allergic rhinitis confirmed by an ENT specialist	Acupoints used DI20, NP12, B1, B2, PAM3, PAM10, E17, DI4, DU3	1) Nasal swelling 2) Flow of watery	Results are expressed as a percentage. The results have been compared for before and after values

Study	Study Design/Setting	Population (N (m/f) age, medication use)	Intervention/Comparator	Outcomes	Result summary
	with control. Hospital internal medicine and rheumatology clinic, Germany.	Needle Intervention group n=22 mean age 33 m/f ratio not stated Laser intervention n=26 no further details Control group n=17 no further details	Needle acupuncture: 3 sessions per week total 9 sessions. Laser acupuncture: 15 sessions, 5 times per week, 3 weeks Control: as laser but with laser inactive.	secretions 3) Conjunctivitis 4) Medication use 5) Sneezing 6) Subjective patient report of breathing through the nose 7) Patient judgment	with a group, but not between groups. Placebo, acupuncture and laser acupuncture significantly reduced nasal swelling, flow of watery secretions and conjunctivitis at the 2% significance level unless stated. 1) Nasal swelling – acupuncture 374% - 121% Laser acupuncture 314% - 136% Placebo 235% -127% 2) Flow of watery secretions - acupuncture 492%-231% (N/S) Laser acupuncture 266%-144% Placebo 344% - 156% (N/S) 3) Conjunctivitis acupuncture 471%-192% Laser acupuncture 382%-91% Placebo 433% - 275% 4) Medication use acupuncture 550%-75% Laser acupuncture 283%-150% Placebo 263% - 88% (N/S) 5-6) No results were reported for subjective patient measure of breathing through the nose or sneezing.

Study	Study Design/Setting	Population (N (m/f) age, medication use)	Intervention/Comparator	Outcomes	Result summary
Ng 2004[40]	RCT Paediatric respiratory outpatient clinic, Hong Kong.	>6 yrs old with symptoms for more than 4 weeks and other allergies at two sites. Confirmed allergy by skin prick test, blood eosinophil and total blood IgE measures. Excluded if they have had previous experience of acupuncture, serious co-morbidity or are on corticosteroids. Intervention group n=35 ave age 11.7 ± 3.1 yrs (22/13) Control group n=37 ave age 11± 3.8 (25/12)	Needle acupuncture Acupoints used EX-HN3, EX-NH8, ST36 Control needling at less depth 2 sessions per week for 8 weeks (16 sessions) Follow-up 12 weeks	1) Daily rhinitis score 2) symptom free days 3) Daily relief medication score 4) Blood eosinophil count 5) Serum IgE levels 6) Adverse events/preference	1) There was a significant reduction in daily symptom score in the intervention group from baseline 6.5 to 5.4 ± 3.9 in the intervention group and 7.1 ± 3.9 in the control group p=0.03 2) This corresponded with an increase in symptom free days in the intervention group from baseline 3.2 to 12.7 p=0.0001 whereas control group remained unchanged from baseline 1.38 to 2.4 at follow-up 3-6) There was no change in symptom relief scores between the groups or the serum markers measured.
Magnusson 2004[41]	RCT Primary care setting in South West Sweden	Patients with seasonal allergic rhinitis aged between 18-50 with a positive skin prick test for allergy and serum IgE measurement. Intervention n=20 M/F unclear (numbers don't add up) Ave age 35.3 ± 9.5 Control n=20 M/F unclear ave age 35.3 ± 9.5	Needle acupuncture Intervention acupoints used LI4, LI20, LIV3, LU7, ST36 Yintang Control acupuncture 1-2cm away from intervention acupoints and shallow needling used 12 sessions of 3 needling events in 30 mins.	1) Allergic symptoms (VAS) 2) mediation use 3) Allergic symptom due to pollen (VAS) 4) Tiredness during pollen season 5) Depression during pollen	1-6) There were no significant findings between intervention and control groups for any of the outcome measures. 7) Serum IgE levels were found to be reduced in the intervention group for the mugwort allergen, but there were differences in baseline characteristics between the groups (see comments)

Study	Study Design/Setting	Population (N (m/f) age, medication use)	Intervention/Comparator	Outcomes	Result summary
			Follow-up 12 months	season 6) Impaired ability to work (VAS) 7) Serum IgE	
Williamson 1996[42]	RCT GP practices across Oxford, Lincolnshire, Peterborough, Cambridgeshire UK.	Recruited individuals Aged over 16 yrs with moderate or severe symptoms and who were taking continuous therapy for allergic rhinitis. Intervention n=51 ave age 31.9 ± 10.2 (19/32) Control n=51 ave age 29.9 ± 7.5 (23/28) Baseline characteristics were similar and individuals were allowed to continue any medication.	Needle acupuncture Intervention points –BL2, LI20, LI4 Control group – needling on the patella 5 minute sessions 3/4 times per week	1) Patients in remission (weekly symptom score less then 14) 2) Mean weekly symptom score 3) Units of medication 4) Perceived effect of acupuncture	1) There were no changes in remission of symptoms over the course of the study 2) Mean symptom score was similar between the two groups. Intervention 18.4 ± 11.2 control 17.6 ± 11.2 p=ns 3) There was no difference between medication use score 4) There was no difference between perceived effect with 37% in the intervention group and 32% in the control group rating the effect as v.good and 25% in the intervention group and 30% in the control group rating as no effect p=ns for both.
Petti 2002[34]	RCT University of Rome, Italy	Volunteers 22-45 yrs with >2 yrs symptoms from allergic rhinitis Group A: Plasma reference control. Healthy individuals n=30 22-42 yrs (14/16)	Needle acupuncture with electrostimulation of the needle once in place. Acupoints in intervention (B1) LI4, ST36, EX-HN3, LI20 Control (B2) EX-HN3, LI20,	1) Symptom score (5-point scoring system) 2) Serum cytokine measurements for IL-2, IL-6 and IL-10 Measures were	1) Groups B1 and B2 showed an improvement in symptom scores after acupuncture ($p<0.05$) despite B2 receiving sham acupuncture. 2) Serum IL-2 cytokine levels were increased after 24 hours in the reference control group ($p<0.05$) and group B1 ($p<0.05$). However all

Study	Study Design/Setting	Population (N (m/f) age, medication use)	Intervention/Comparator	Outcomes	Result summary
		Group B1: Intervention. n=30 22-45 yrs (12/18) Group B2: Sham Intervention n=30 24-45 yrs (13/17) Group B3: patient control no intervention. n=30 age not clear (12/18) Excluded if taking drugs that may inhibit acupuncture (Naxolone).	CI4, ST36. In the intervention group the needles in points ST36 and LI4 were electrostimulated with pulsating waves for 15 mins. All sessions lasted ~20 mins	taken 2hrs and 24hrs after treatment (24 hrs only for symptom scores).	values were still within the normal range Serum IL-6 levels did not change in any groups over the 24hrs. Serum IL-10 levels were significantly reduced in the active intervention group (B1) only ($p<0.05$) Levels were reduced from 130.12ng/ml $\pm$ 28.58ng/ml to 74.92ng/ml $\pm$ 21.47ng/ml $p<0.05$
Xue 2002[38]	Cross-over RCT (Cross-over after 4 weeks) University Clinic Bundoora, Australia	Recruited via the media. n= 30 seasonal allergic rhinitis subjects (>2 years duration) Subjects had no previous acupuncture experience or co-morbidities. Age range 18-70 years Group A: n=17 subjects , age 44 $\pm$ 15.8 (6/11) Group B: n=13 subjects, age 44 $\pm$10.8 (8/5)	Needle acupuncture at points LI20, GB20, Yintang $\pm$ symptom specific points at BL13, LU9, BL20, ST36, BL23,CV6. Administered 3 times a week for 4 weeks, sessions lasted 25 minutes. Sham group received shorter needles.	1) Severity symptom score 2) Relief medication score 3) Side effects	1) Subjects baseline symptom scores were similar. There was a significant improvement in post treatment symptom severity scores between intervention and control groups 1.04 (0.77) vrs 1.67 (0.97) p=0.012, Symptom scores - nasal symptoms 0.65 (0.59) vrs 1.28 (0.89) p=0.003 and non-nasal symptoms 0.39 (0.66) vrs 0.91 (0.99) p=0.032 2) One patient in each group required relief medication – no analysis was performed. 3) no side effects

Table 2. Comments and issues on included studies

Study	Quality assessment score (Max 20)	Comments
Langer & Hauswald	5	Percentage change is significant at the 2% level for changes in the placebo group as well as the intervention groups for reduction in nasal swelling, conjunctivitis, flow of watery secretions and drug usage. The control group received inactive laser treatment but this was also used to compare with needle treatment.
Wolkenstein & Horak	7	Data extracted from 3 papers reporting the same study. Patients were placed in a provocation chamber for 180 minutes and exposed to pollen allergens at baseline and 3 months after treatment. Measures were taken whilst patients were in the chamber. Authors state that baseline VAS scores were different in intervention and placebo groups.
Petti	7	Follow-up time is only 24 hours which is short for symptom score measures. Symptom scores were reduced in both the active and sham acupuncture groups – patients were blinded to the intervention. Cytokine levels for IL-2 and IL-6 were within the normal range. Patients were excluded after 2 treatments if anomalies to propagation of sensation along meridians (no propagation or excessively fast propagation) was observed.
Xue	10	Patients in the sham arm of the trial also dropped from baseline. There was no statistical test of the difference between baseline and post-treatment scores in the groups, only between final values between arms. There appears to be a drop in the control arm. Subjects were given acupuncture specific to their symptoms so intervention varied between subjects. Subjects allergy was confirmed by questionnaire not a laboratory or skin prick measure
Magnusson	12	28% in the intervention group and 18% in the control group had previously had an acupuncture treatment. There was a higher number of individuals in the intervention group with sensitivity to mugwort p=0.01 allergen at baseline, which was subsequently found to improve compared to control.
Ng	13	Although the trial was described as being in children the range of ages in the intervention group was 6-19 and in the control group 6-20. Symptom scores were completed with help from parents or carers where needed.
Williamson	14	-

4.1.2 Summary of positive trial findings

The study by Ng[40] showed two positive findings. The study was small in size with 35 in the intervention arm and 30 in the control arm. Baseline rhinitis scores were similar between the two groups and patients in this study seem well classified with blood eosinophil, serum IgE or skin prick test confirmation of allergy. A slight improvement in daily rhinitis score was seen, with a baseline value 6.58 in the intervention group being reduced to 5.4 whereas baseline 6.51 in the control group was raised at follow-up to 7.19 (p=0.03). However, this corresponded to a highly significant increase in the number of symptom free days from baseline 3.2 to 12.7 after follow-up in the acupuncture group compared to baseline 1.38 to 2.4 in the control group (p=0.0001). The baseline values although similar for rhinitis score were different for symptom free days. The patients in this study were children and parents or carers' helped fill in symptom scores in some cases. This trial was one of the higher quality scoring with 13 points.

The study by Magnusson[41] found a reduced level of serum IgE sensitivity for the mugwort allergen in the acupuncture intervention group. The serum IgE level in the intervention group was reduced by -2.78 (+/ 6.4) SU/ml at 12 month follow-up compared with an increase of +0.43 (+/2.2) Su/ml in the control group (p=0.03). However baseline sensitivity to mugwort allergen confirmed by a skin prick test was higher in the intervention group compared to the control group after randomisation (p=0.01). This trial had a quality score of 12.

The study by Petti[34] showed an improvement in symptom scores and reduction in plasma IL-10 levels. The study had 30 participants in each group and included a sham treatment group and control (no treatment) group. The follow-up was only 24 hours after treatment. Symptom scores were reduced in the active intervention group from baseline 19.3 +/ 2.6 to 8.5 +/ 1.6 after 24 hours ($p<0.05$) in the active intervention group, but also in the inactive intervention group from baseline 19.5 +/ 2.3 to 16.3 +/ 2.0 ($p<0.05$). Plasma

IL-10 levels were shown to be significantly reduced in the intervention group from baseline 138.1 +/ 28.5ng/ml to 74.9 +/ 21.4ng/ml ($p<0.05$). However this trial had a low score of 7 mainly due to the lack of blinding and fact that individuals were excluded from the intervention group if they did not respond to acupuncture after 2 sessions.

The study by Xue[38] showed a significant improvement in symptom score in a small cross-over RCT study with only 26 participants in total. Symptom severity scores were reduced from baseline 2.5 +/ 0.7 to 1.0 +/ 0.7 in the intervention phase, compared to baseline 2.2 +/ 0.8 to 1.6 +/0.9 during the control phase ($p=0.012$). This was then broken down into nasal and non-nasal symptoms which were both significant. This cross-over trial scored 10 points in the quality checklist, but did not have a wash out phase between the cross-over of treatments. The authors did not comment on possible carry-over of treatment effect between phases. This was however the only trial to address the issue of power and was powered to 80% to detect a treatment effect of 70%.[38]

The study by Langer & Hauswald[39] quotes percentage changes from a pre-season level set to 100%. They then measure symptoms during the hay fever season and after treatment. The study was again small with 22 in the acupuncture group, 26 in the laser acupuncture group and 17 in the placebo group. The study reports before and after levels, not between group levels and finds a significant (at the 2% level) change in nose swelling and conjunctivitis for both acupuncture groups and the placebo group. They report a reduction in drug usage in the acupuncture group from 550% to 75% but this is higher at the start than the placebo group which ends with a similar value 263% to 88%. This trial scored 7 due to differences in baseline scores and a lack of blinding.

4.1.3 Summary of trials finding no difference

Wolkenstein & Horak[35-37] found no differences between groups in sum of nasal flow, subjective well- being, symptom scores or symptom diary scores.

Ng[40] showed no change between groups in daily relief of symptoms scores or biochemical measures of blood eosinophil levels and serum IgE. Magnusson[41] showed no differences between intervention and control groups in allergic symptoms, medication use, symptoms due to pollen, and tiredness during the pollen season. There was no difference in depression during the pollen season or ability to work. There was also no difference between intervention and control groups in the measurement of plasma IgE reactivity to common allergens such as birch, Timothy grass, household dust and animal dander. Williamson[42] showed no change in symptom severity over the course of the trial or mean weekly symptom score. There was also no difference in the unit use of medication between the groups. Petti[34] showed no change in plasma IL-2 or plasma IL-6 levels between the intervention and control groups. Langer & Hauswald[39] found no difference in the flow of nasal secretions and did not report on sneezing and patient reported breathing although they were stated as outcomes measures in the study.

4.1.4 Adverse events

There were no adverse events reported in any of the trials. This is in keeping with previous work that has shown acupuncture to be a safe treatment[24,26,43]

4.1.5 Meta-analysis

A wide variety of outcome measures were found in the trials included, the most consistently used outcome measured across the trials was a change in symptom severity score, measured on a VAS. Four studies by Petti[34], Williamson[42], Xue[38] and Ng[40] were included in this analysis. Only the study by Langer and Hauswald[39] did not report a symptom severity score. The study by Magnusson[41] did not report the VAS data in a way that could be used in the meta-analysis. The study reports baseline VAS scores for symptoms, but reports outcomes in terms of number of patients improving and does not give a final value VAS score. The authors' were contacted to see if this information was available, but no response was received. The study by Wolkenstein[35-37] could not be used as it reports baseline VAS scores as means with SD and

medians, but only reports the outcome as medians. There was a high degree of heterogeneity between the studies when combined in a meta-analysis (Figure 3) (Chi^2 5.77 p<0.00001 I^2 95.7%) with 142 in the intervention arm and 144 patients in the control arm. The overall effect estimate was -1.25 in favour of treatment, but this was not statistically significant (95% CI -2.54 to 0.04). The sources of heterogeneity are discussed in detail in the next section of this report. The Petti[34] study has shown a strong treatment effect in favour of the intervention, however in this study there was also an improvement in symptom scores for the sham treatment group. Further, this study is questionable due to the fact that patients were excluded from the intervention group after two acupuncture sessions if they didn't respond to treatment. This study was removed as a sensitivity analysis and the degree of heterogeneity dropped (Chi^2 5.77 p=0.06 I^2 65.3%) with 112 in the intervention arm and 114 in the control arm. The overall effect estimate was -0.33 in favour of the treatment but was not significant (95% CI -0.78 to 0.13).

Two of the studies included measurement of serum IgE levels. These were included in a meta-analysis. The studies were by Magnusson[41] and Ng[40] and included a total of 55 patients in the intervention arm and 57 in the control arm. There was very little heterogeneity between these studies (Chi^2 0.61 p=0.43 I^2 0%) and the effect estimate was in favour of treatment -0.19 but was not significant (95% CI -0.56 to 0.18).

It was not possible to combine any studies in a further meta-analysis due to a lack of common outcome measures.

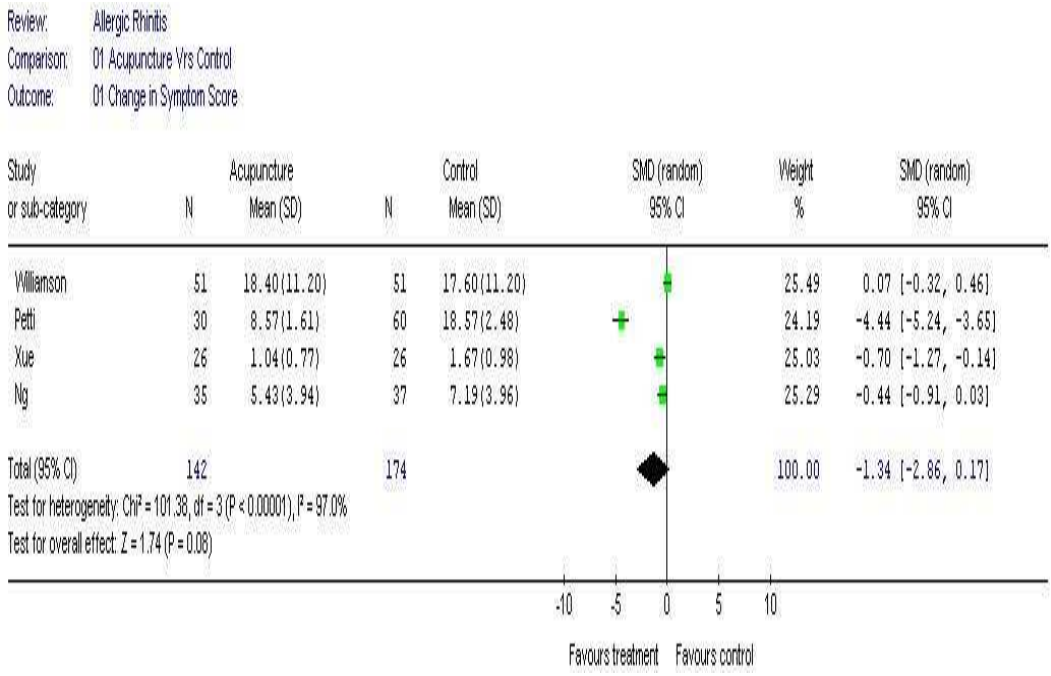


Figure 3. Symptom severity scores for acupuncture versus control in 4 trials reporting symptom severity on a VAS scale.

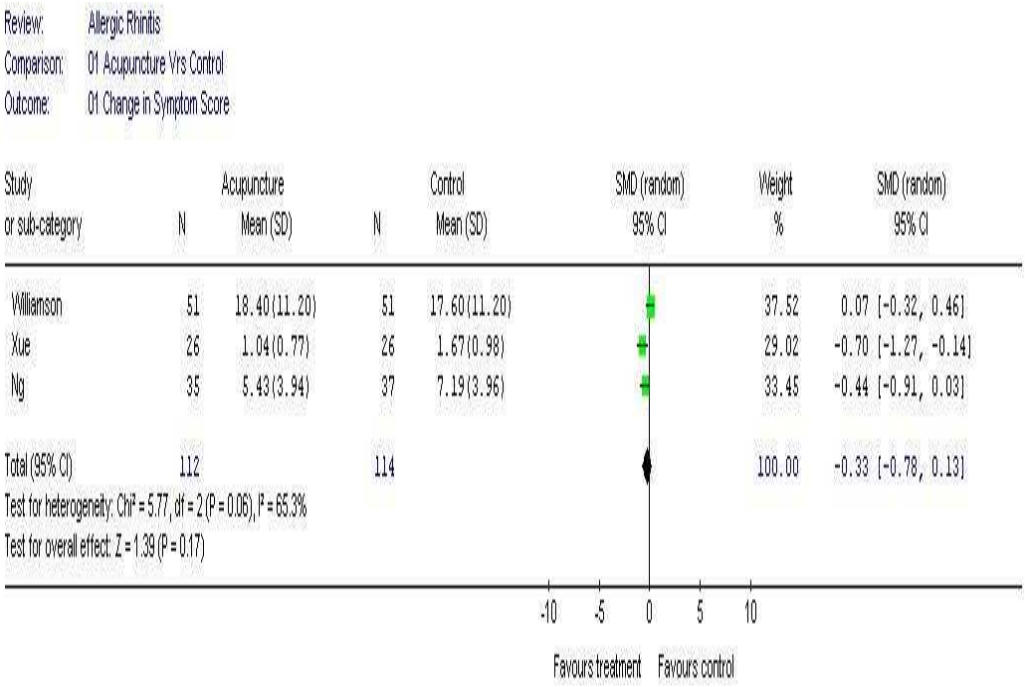


Figure 4. Sensitivity analysis of symptom severity scores for acupuncture versus control in 3 trials reporting symptom severity on a VAS scale.

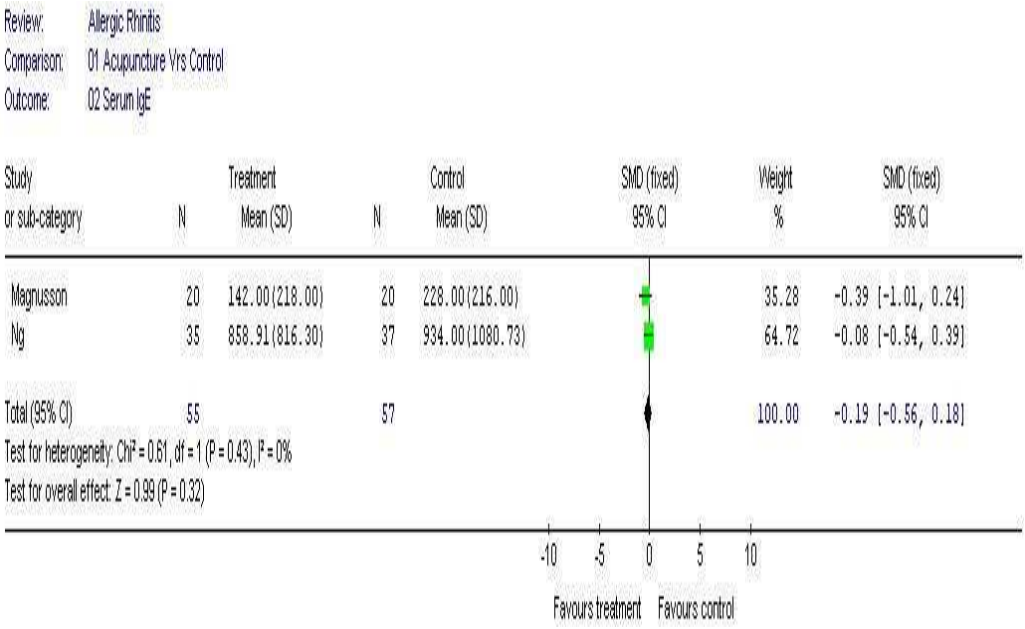


Figure 5. Change in serum IgE levels for acupuncture versus control in 2 trials.

4.2 Differences between studies and sources of heterogeneity

The intervention varied considerable in the studies with the type of acupuncture being applied. Figure 6 shows the different acupoints which were detailed in 4 of the studies. There were a total of 24 different acupoints used with only 2 acupoints (ST-36 and LI-20) being used in all 4 studies. The number of acupoints used varied from 3-9 in the studies. Acupoint LI-4 was used in 3 of the 4 studies. The intervention also varied in the number of sessions and the length of time the acupuncture was applied for. There was a range in number of sessions from 1 session to 5 sessions per week with repeats varying from 2 to 16 sessions overall. The duration of the sessions also varied ranging from 5 minutes to 20 minutes where details were given.

Control groups were treated differently, with some inserting smaller needles whilst other studies used different acupoints away from the study acupoint. One study using laser acupuncture had a control group with an inactive laser treatment, but this was also the comparison group for the needle acupuncture group. The follow-up times ranged from 24 hours immediately after treatment to 12 months.

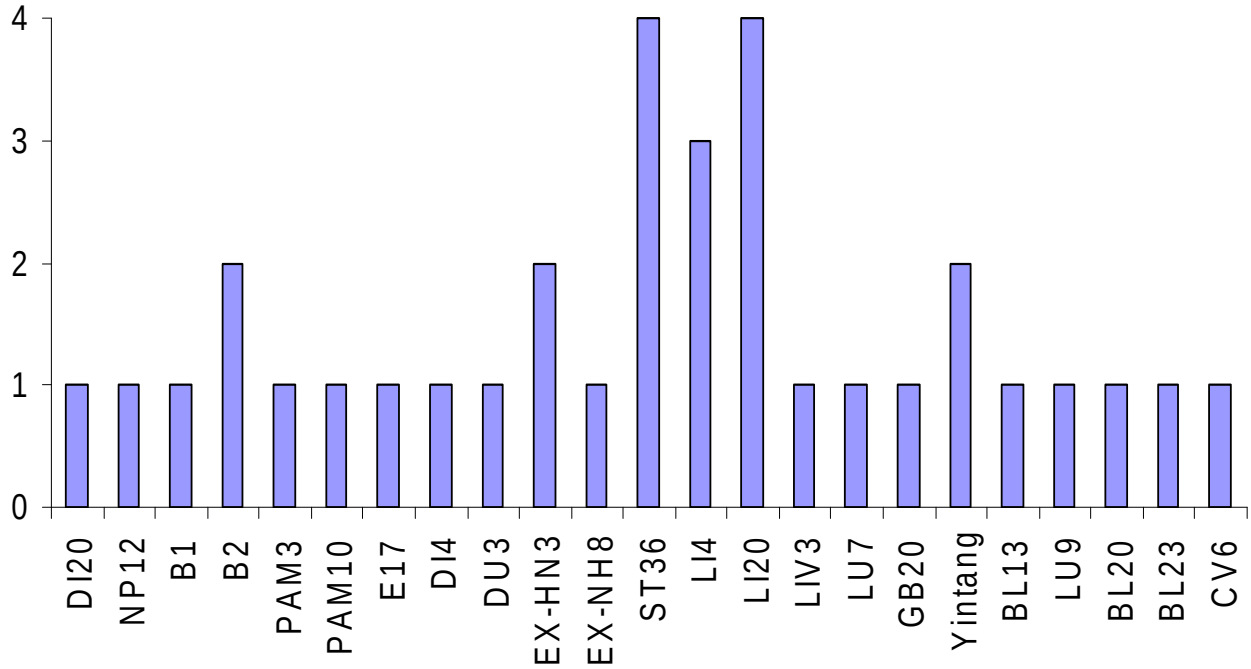


Figure 6. Different acupoints used in 4 included studies which gave detail.

NB. ST-36 (Zusanli) is a major general point on the antereolateral side of the leg linked to the stomach meridian and point LI-20 (yingxiang) is located on the outer side of the left nostril corresponding to the large intestine meridian.

5 COST EFFECTIVENESS AND ECONOMIC ANALYSIS

A separate literature search was conducted to identify published cost-effectiveness and economic evaluations of the use of acupuncture for allergic rhinitis from the NHS perspective. The search terms were kept open to include further information on the wider costs such as running clinics, specialist practitioner time, and acupuncture equipment.

5.1 Method

The search terms used were ‘cost’ ‘cost effectiveness’ and ‘economic analysis’ in combination with elements of the previously used terms including ‘acupuncture’.

The following databases were searched

- EconLIT (OVID) 1969-August 2006
- Cochrane Library (NHS EED)
- MEDLINE (1966-August 2006)
- EMBASE (1988-August 2006)

5.2 Results

There are currently no cost effectiveness or economic analysis models of the use of acupuncture for allergic rhinitis. There was one report of the setting up and running of a Nurse-led acupuncture clinic in a primary care setting.[44] This report detailed a program for providing an acupuncture service (appendix 5) and provided minimal cost information. The author was contacted to see if further costs could be calculated and for comment on the success of the program, but no response was received.

It was estimated in this report that the cost of monthly medication for allergic rhinitis is £18.[44] Assuming this clinic was successful the costs of running it would be minimal.

The British Medical acupuncture society (BMAS) has information on its website relating to the cost of training programs for health professionals who would like to perform acupuncture on patients. The cost of the training program to the standard required to treat patients is approximately £600. This would be a one-off training cost. The cost of acupuncture needles ranges from £4-£10 for sets of 100 needles depending on type (BMAS website). The unit cost of Nurse time is currently evaluated at £24/hour.[45]

A recent clinical trial was identified that evaluated acupuncture in the treatment of low back pain. This trial included an economic evaluation of the treatment and provided the following information on costs associated with providing acupuncture.[46]

Table 3. Estimated NHS costs of providing an acupuncture service.

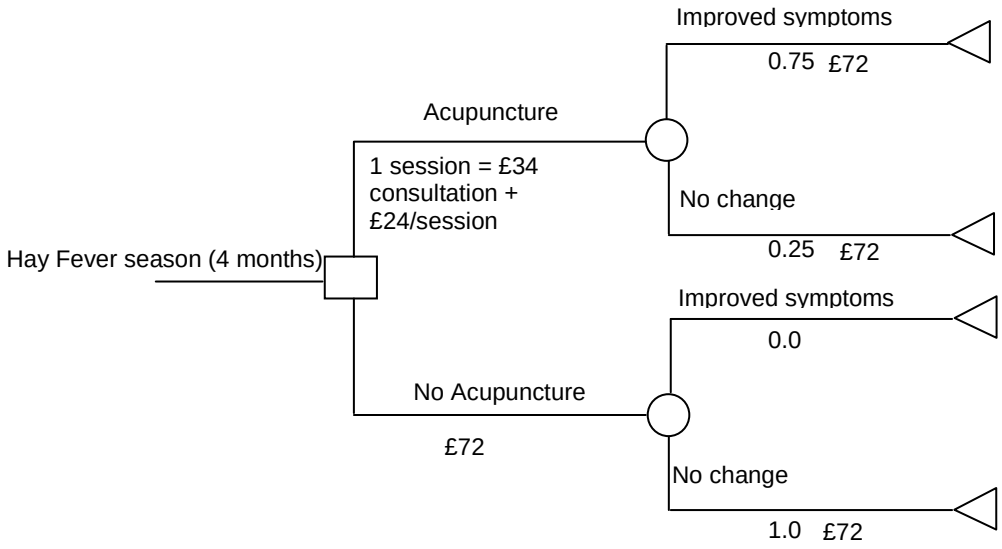
Healthcare resource	Unit	Cost per unit (£)	Details
Acupuncture:			
Initial consultation	Visit (60 minutes)	34.00	Treatment costs met by NHS authority in study
Subsequent treatment	Visit (45 minutes)	24.00	
Non-study acupuncture	Visit	24.00	Cost assumed to be similar to study cost
Private visit	Visit	24.00	Additional treatment after study
NHS visits			
Hospital outpatient	Visit	82.00	Mean cost of outpatient visit (generic)
GP consultation	Visit	20.00	Assumes consultation lasts 9.36 minutes
Nurse consultation	Visit	25.00	Cost per hour of time
Other Costs			
Private health care	Visit	Various	Patient reported costs in trial
Over the counter drugs	Item	Estimated £18/month	From Cochrane 2001
Prescription drugs	Item		
Time off work	Day	88.86	One fifth of average weekly wage

Adapted from references 44 and 46.

5.3 Economic model

From these references the estimated costs of medication and the running of an acupuncture clinic have been calculated based on the assumption that the hay fever season runs for 4 months and the monthly cost of treatment (drugs) is £18. The number of acupuncture sessions in the studies in this review varied from 2-16 so these values will be used in the model. The costs of treatment will be the same in both the intervention and non-intervention arms of the model as patients were allowed to continue treatments in the trials. The study by Magnusson[41] has been chosen as it provides individual patient information on the number of patients having an improved symptom score compared to numbers not improving or getting worse. This information was used in the model as similar studies only report the mean change in symptom scores between groups. The study did not have a standard treatment alone group so commonly both the active and inactive groups have shown an improvement in symptoms. This has led to non-significance in most studies but raises the question as to whether the simple act of having acupuncture improves symptom severity. The trial showed that 75% of patients treated with acupuncture had improved symptom severity at 12 months. The question this model is attempting to address is whether giving acupuncture is of sufficiently low cost to be worth considering in patients with allergic rhinitis that doesn't respond to conventional treatments as a way of improving symptoms.

5.3.1 Economic model from the NHS perspective for the use of acupuncture in allergic rhinitis.



ICER for 2 sessions = (174-72)/(0.75) = **£136** per patient with improved symptom severity at 12 months

ICER for 16 sessions = (510-72)/(0.75) = **£584** per patient with improved symptom severity at 12 months

ICER for 12 sessions (as per study) = (414-72)/(0.75) = **£456** per patient with improved symptom severity at 12 months

Figure 7. Decision tree cost-effectiveness model for improved symptoms at 12 months.

5.3.2 Data inputs:

Intervention costs – Acupuncture costs were taken from the study by Ratcliffe[46] (see table 3). This includes an initial consultation cost and subsequent sessions at £24 per session. It is assumed a clinic would run as described in Cochrane.[44] Additional one of costs of acupuncture needles and other equipment has been costed at £20. So the cost of 2 sessions would be £24 x 2 + £34 + £20 = £102.

Standard Care costs – taken from Cochrane[44] and assumed to be £18 per month. The hay fever season is assumed to last 4 months, so the cost is £72.

Intervention effectiveness – This was taken from the study by Magnuson et al who quote actual numbers of patients who improve and not the mean percentage change as in the other studies identified.

5.3.3 Model assumption

The medication costs in the intervention group have been kept the same as the non-intervention group and it is assumed that changes would be the same in these two groups.

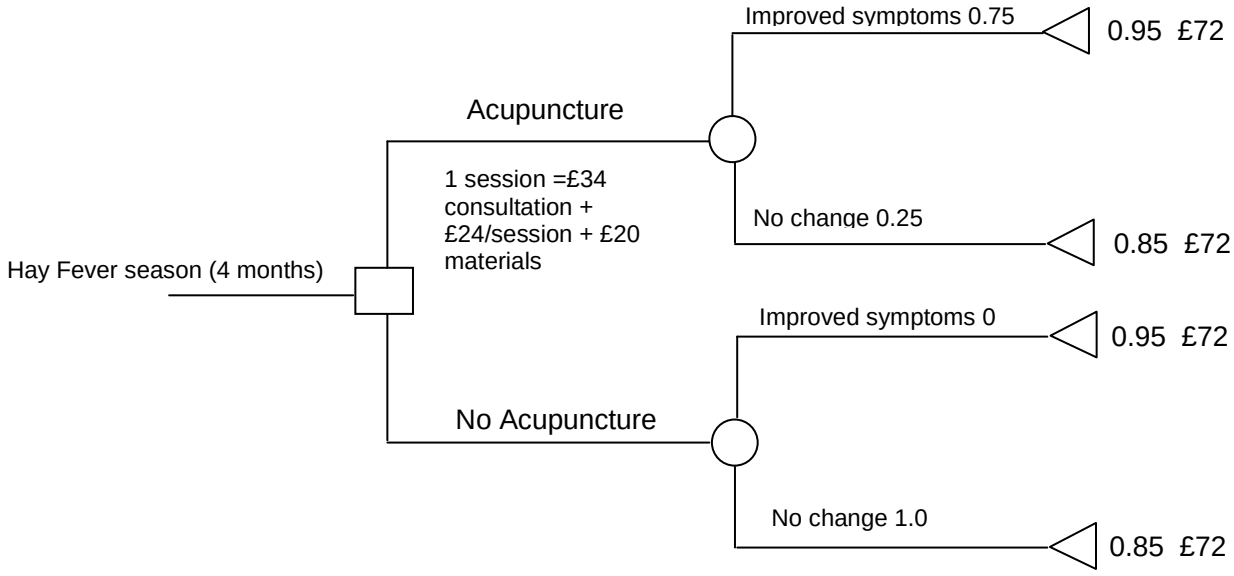
5.3.4 Sensitivity analysis

The combined effectiveness of 75% is very high. If the effectiveness is reduced to 50%, 25%, 10%, 5%, 2.5% and 1% the corresponding costs and ICER's are found. The cost per patient assumes medication use would drop proportionally to symptom severity.

Effectiveness	ICER (2 sessions)	Cost per patient including reduced medication (2 sessions)	ICER (16 sessions)	Cost per patient including reduced medication (16 sessions)
50%	£60	£138	£732	£474
25%	£120	£156	£1464	£492
10%	£300	£166.8	£3660	£502.8
5%	£600	£170.4	£7320	£506.4
2.5%	£1200	£172.2	£14640	£508.2
1.0%	£3000	£173.28	£36660	£509.28

Table 4. Sensitivity values for 2 and 16 sessions of acupuncture and associated cost per patient

5.4 Economic model using QoL utility measure.



ICER for 2 sessions = (174-72)/(0.024) = **£4250** per QALY

ICER for 16 sessions = (510-72)/(0.024) = **£18,250** per QALY

ICER for 12 sessions (as per study) = (414-72)/(0.024) = **£14,250** per QALY

Figure 8. Decision tree cost-utility model for changes in symptoms and associated utility

5.4.1 Data inputs:

Intervention costs – As above section 5.3.1

Standard Care costs – As above section 5.3.1

Utility values for QALY calculation – Utility values were not available from the studies so estimated values were used. A value of 0.85 was assumed for allergic rhinitis sufferers during the 4 months of the hay fever season. If a reduction in symptom severity was achieved, or during the remaining months of the year a value of 0.95 was assumed. The utility is therefore equal to 8 months at 0.95 and 4 months at 0.85 so was 0.66 x 0.95 + 0.33 x 0.95 x 0.75 = 0.705 in the successfully treated acupuncture arm and 0.66 x 0.95 + 0.33 x 0.85 x 0.25 = 0.227 in the unsuccessfully treated acupuncture arm. So the combined utility was 0.932 compared with 1x 0.66 x 0.95 + 0.33 x 0.85 = 0.908 in the no intervention arm. Difference in utility between intervention and no intervention is therefore equal to 0.024.

5.4.2 Sensitivity analysis

A sensitivity analysis was performed with varying levels of QALY gain between the treatment and control for 2 sessions and 16 sessions of acupuncture. It was found even with a very small improvement in utility acupuncture remains theoretically cost-effective.

Assuming two sessions of acupuncture the QALY gain would be as low as 0.0034 to still be cost effective. Using the values in the above analysis this would equate to 0.95 in the successful intervention arm and 0.946 in the untreated arm.

QALY gain	ICER (2 sessions)
0.024	£4250
0.01	£10,200
0.008	£12,750
0.005	£20,400
0.0048	£21,250
0.0034	£30,000

Table 5. Sensitivity analysis for 2 acupuncture sessions

Assuming sixteen sessions of acupuncture the QALY gain would be as low as 0.0146 to still be cost effective. Using the values in the above analysis this would equate to 0.95 in the successful intervention arm and 0.935 in the untreated arm.

QALY gain	ICER (16 sessions)
0.024	£18,250
0.020	£21,900
0.019	£23,052
0.018	£24,333
0.016	£27,375
0.0146	£30,000

Table 6. Sensitivity analysis for 16 acupuncture sessions.

5.5 Discussion of the economic models

The economic models have shown that acupuncture is highly likely to be cost effective. Due to the lack of clinical effectiveness data utility values for the hay fever season had to be estimated for the purposes of the model. However, the model has demonstrated that with the current costs for acupuncture treatment based on 2 sessions the difference in QALY gain would only need to be as low as 0.0034 to still be theoretically cost-effective. The study by Magnusson was used to estimate the number of individual who may improve given acupuncture treatment. This study had a high percentage of individuals who improved with 75%. Using these figures the model has shown again based on two sessions if only 1% were seen to improve with acupuncture treatment it would still be cost-effective. An improvement in symptom severity may be associated with a number of other utilities such as reduced medication use, improved ability to work or attend school and reduced visits to the GP. It is hoped the data contained in this model would serve as a basis for a power calculation for a clinical trial.

6 DISCUSSION

Seven RCTs were identified and included in this systematic review. The available RCT evidence does not make it possible to support or refute the use of acupuncture for allergic rhinitis for a number of reasons.

1. The trials identified are small in size

Study sizes are very small and ranged from 26 in the Xue[38] study to 102 in the Williamson[42] study. The average number of participants overall was 61. There was no mention of power calculations in any study or attempts to determine an appropriate sample size to show an effect. Allergic rhinitis is very common disorder with as many as 25% of Western populations effected.[1] Recent RCT of desensitisation treatments and nasal sprays for allergic rhinitis have recruited over 600 individuals.[47,48]

2. Some outcomes are difficult to interpret

The reported reductions in plasma IL-10 levels seen in the Petti[34] study were difficult to interpret. The reporting of the study suggests that the main function of IL-10 is pro-inflammatory in that it is involved in activating mast cells and basophils.[34] However, IL-10 can also suppress the production of prostaglandin E2, an important secondary mediator in allergy and has an effect on monocyte production of numerous pro-inflammatory cytokines, including TNF-α, IL-1, IL-6, and IL-8. Therefore the benefit of reducing IL-10 in allergic individuals could be argued. Also, normal plasma levels of IL-10 are quoted to be less than 7.8pg/ml by some manufacturers of ELISA assays. The control group in this study who were normal healthy individuals had plasma IL-10 levels of 78.97ng/ml. This is extremely high for healthy individuals, and raises concerns about the assay used in this study.

The study by Ng[40] reports a significant reduction in daily symptom score in the intervention group compared to the control group but there was no associated difference in symptom relief score. This suggests although daily symptoms were reduced, relief from them was not.

3. Blinding and placebo effect

Blinding is a difficult concept with acupuncture studies. None of the studies address participant's ability to guess which treatment they received. Sham treatment away from the active site or smaller needles was used in most studies. In the study by Magnusson,[41] 28% of the intervention group and 18% of the control group had previously received acupuncture treatment, so would have experienced the 'de qi' sensation (dull ache at needle site) associated with active acupuncture. Similarly in the cross-over trial by Xue[38] the group receiving inactive treatment second would have experienced de qi sensation in the active treatment phase. Neither of these studies addressed this in the analysis. A placebo effect was seen in some of the studies. In the Petti[34] study

both the active and inactive acupuncture groups showed improvements in symptom scores compared to the group receiving no treatment. The study by Williamson[42] reported the perceived effect of the treatment with 37% in the intervention group and 32% in the control group rating the effect as 'very good' and 25% in the intervention group and 30% in the control group stating there was 'no effect'. The study by Langer & Hauswald[39] gave details on patient judgment of effects and showed 86% of the acupuncture group, 69% of the laser acupuncture group and 53% of the placebo group considered an improvement in their overall condition.

4. Statistical versus clinical significance

The studies used a subjective measure such as a VAS to measure symptom severity. In most studies only small changes were seen between groups. Changes in symptom scores are only meaning full if an accurate diagnosis of allergic rhinitis was adequately performed. In most of the studies individuals were recruited by advertisements and not via GP practices. Bauchau & Durham reported in 2004 that from a random telephone survey of 9,646 people, 19% reported self-awareness or self diagnosis of allergic rhinitis. Of this group, on clinical examination, only 40% actually had clinically confirmable allergic rhinitis.[2]

The study by Xue[38] for example showed a statistically significant difference between intervention and control groups in symptom severity with a 0.6 unit difference on the VAS scale (range 0-5). There was no description as to whether this had a meaningful clinical significance (such as on QOL) or not.

Possibly the most useful clinical outcomes measured were medication use, symptom free days and ability to work/attend school. The Williamson[42] study showed no difference in medication use between groups. The Magnusson[41] study showed no difference between groups in medication usage or ability to work. Langer & Hauswald[39] showed a reduction in medication use, but in both the acupuncture and placebo groups. The study by Ng[40] was the only study to

show a highly significant improvement in the number of symptom free days which increased from 3.2 to 12.7 in the intervention group.

A previous systematic review by the ARIA group looked at the use of acupuncture amongst many other CAM treatments for allergic rhinitis.[31] The studies by Ng[40], Williamson[42], and Xue[38] were included in the analysis. The conclusions of this review were that studies have inadequate methodology (Jadad score less than 3) to make strong recommendations. This review has included four other trials including two in non-English language. The conclusions back-up the work by the ARIA group in that the overall quality of evidence in acupuncture trials for allergic rhinitis is poor. Further this review has highlighted the need for some clarification of the methods employed in acupuncture studies in relation to consistency with the intervention and outcome measures. The limited amount of cost information available suggests that running and acupuncture clinic would be fairly cheap and likely to be cost-effective for very small changes in utility.

6.1 Conclusions and comment

- The available evidence from RCT's is not strong enough or of high enough quality to support or refute the use of acupuncture in the treatment of allergic rhinitis.

It is worth noting that whilst a large clinical trial would answer the question of clinical effectiveness, clarification is first needed on the many variable parameters seen in acupuncture treatments. The trials identified in this review have used a number of different approaches to both the intervention and delivery of acupuncture - for example, the location of acupoints and the optimal frequency and duration of acupuncture sessions. Acupuncturists need to form some consensus on the methodology before further resources are allocated to trials. It is hoped that the type of information contained in the economic model of this report may be useful in power calculations for further trials in this area.

7 APPENDICES

7.1 Appendix 1

The following search terms were used for a literature scoping search.
1) Acupuncture
2) Rhinitis OR allergic rhinitis OR hay fever
3) 1 AND 2

The following search strategy was used based on a modified version of the Cochrane complementary medicines group search criteria, and similar search strategies contained in other Cochrane reviews. The following search strategy was used and adapted to the search engine being used.

1 Rhinitis/
2 hypersensitivity/
3 allerg*/
4 Hay Fever
5 or/1-4
6 ACUPUNCTURE/
7 Acupuncture Therapy/
8 ELECTROACUPUNCTURE/
9 acupuncture$.
10 electroacupuncture$.
11 or/6-10
12 clinical trial.
13 Randomised controlled trial
14 Trial
15 or/12-14
16 5 AND 11
17 5 AND 11 AND 15

The results were viewed with and without the clinical trial filters.

7.2 Appendix 2. Inclusion criteria check list of studies

Study (Author Publication date)	Do the patients or study population have allergic rhinitis? (not non-allergic rhinitis)	Is an Acupuncture treatment compared to a control or standard care group?	Are patients randomised to their treatment? (RCT)	Is a relevant outcome measured - symptom scores/quality of life/serum IgE/serum cytokine levels	Include?
Brinkhaus 2004 Allergy[49] 2005 Chinesische Medizin[50]	√	X all patients also given Chinese herbal remedy	√	Unable to separate herbal treatment and acupuncture	X
Chari 1988 Am J Acu[51]	√	√	? not mentioned/ unclear	√	X
Chuanjie 1990 Chinese J Acu Med[52]	√	X Cohort without control group	X	?	X
Drasnar & Palecek 1981[53]	√	X Uncontrolled case series	X	√	X
Langer & Hauswald 1989[39]	√	√	√	√	√
Magnusson 2004 Am J Chin Med [41]	√	√	√	√	√
Ng 2004[40] Pediatrics	√	√	√	√	√
Petti 2002[34] J Trad Chinese Med	√	√	√	√	√
Querfurt 1994 Dtsch.Zschr.Akup[54]	√	X Uncontrolled before and after study	X	√	X
Williamson 1996 Acupuncture in Medicine[42]	√	√ sham acupuncture	√	√	√
Wolkenstein & Horak 1993/1996/1998[35-37]	√	√	√	√	√
Xue 2002 Am J Chin Med[38]	√	√ Cross-over trial	√	√	√
Xue 2003 Hong Kong Med J[55]	√	X all patients given acupuncture Chinese herb being investigated	N/A	Efficacy of herb not acupuncture being tested	X
Zhao 2005 Shaanxi Chinese Med[56]	√	√ but unclear what control group received	? unclear	√ percentage efficacy	X

7.3 Appendix 3. Data Extraction form

Title of Study:

Reference Manager ID Number; full paper/abstract/other:

1st Author/Year/Country:

Data extracted by:

Population Characteristics

Sample source:

Setting:
(e.g. private clinic, GP, NHS clinic)

In-/Exclusion criteria for patients:

How was allergy confirmed (reference test?)

Total number of patients eligible/recruited:

Randomised patient characteristics	**Intervention**	**Control**
n=		
age		
sex (m/f)		
Allergy history:		
Co-morbidity:		
Medication:		
Other/comments:		

Intervention

Type of acupuncture under investigation:

Person performing acupuncture

Was the acupoint(s) detailed?

Duration/Frequency of acupuncture:

What is the comparator?

Outcomes

State all outcome measures:

How were outcomes assessed (e.g. symptom scores, Serum IgE) and by whom?

Results: if applicable state individual patient data and/or summary measures, SD/SE/CI, statistical significance (p-value)

Outcome measure	**Intervention**	**Control**

Losses to follow-up:

State losses to follow up for intervention and control groups:

7.4 Appendix 4. Quality Assessment Checklist

Study	Wolkenstein 1993,1996,1998	Langer & Hauswald 1989	Petti 2002	Xue 2002	Magnusson 2004	Ng 2004	Williamson 1996
A: Randomisation							
1: Was trial described as random?	Y	Y	Y	Y	Y	Y	Y
2: Was randomisation truly random? (method stated)	Y	N	N	CT	Y	Y	Y
3: If randomisation method described, was it adequate?	Y	N/A	N	CT	Y	Y	Y
Concealment							
Was there a statement regarding concealment?	N	N	N	N	N	Y	Y
Was method of concealment described?	N	N	N	N	N	N	Y
If method of concealment described, was it adequate?	N	N	N	N	N	N	Y
Blinding							
Was the trial described as blinded?	N	N	N	Y	Y	Y	Y
Was there statement regarding blinding of patients?	N	N	N	Y	Y	Y	Y
Was there statement regarding blinding of individuals administering intervention?	N	N	N	N	Y	CT	CT
Was there a statement regarding blinding of individuals recording outcomes (if different to above)?	N	Y	N	N	N	Y	CT
Was there statement regarding blinding of data analysts (if different to above)?	N	N	N	N	N	Y	CT
Was intervention indistinguishable from the placebo?	CT	Y/N No for acupuncture and yes for laser	CT	CT	CT	CT	CT
Loss to follow-up/ITT							
Was loss to follow-up stated for both groups?	Y? in one of	Y	Y	Y	Y	Y	Y

Study	Wolkenstein 1993,1996,1998 three papers	Langer & Hauswald 1989	Petti 2002	Xue 2002	Magnusson 2004	Ng 2004	Williamson 1996
If stated, was loss to follow-up < 20% in treatment group?	CT not clear which group 6 lost patients were in	Y	Y	Y	N	Y	Y
If stated, was loss to follow-up < 20% in control group?	CT	Y	Y	Y	Y	Y	Y
Was there a statement regarding intention to treat analysis?	N	N	N	N	Y	N	N
Was this confirmed by the data/results presented?	N/A	N/A	CT	CT	Y	CT	Y
Comparability of treatment groups							
Were intervention and control group characteristics comparable at entry? (in terms of : age, sex, history of allergy, any co-morbidity or medication)	N baseline VAS scores not equal in the two groups	CT? Appears to be differences in pre-treatment scores	Y	Y	N	Y	CT
Were intervention and control groups treated the same throughout the trial? (in terms of: number of repeat interventions given, number of follow-up visits etc.)	Y	N	Y	Y	Y	Y	Y
Were intervention and control groups followed-up for the same length of time?	Y	Y	Y	Y	Y	Y	Y
SCORE (Max 20)	**6**	**7**	**7**	**10**	**12**	**14**	**14**

7.5 Appendix 5. Some guidelines for administering acupuncture as a routine treatment for allergic rhinitis.

Indications
Any patient with hay fever who wishes to try acupuncture

Requirements
Gloves
Acupuncture needles
Sterile gauze swabs
Couch for patient's comfort

Procedure
The nurse should obtain and document history
The nurse should decline treatment:
A. pregnancy
B. Children <5yrs
C. Diabetes
D. Previous treatment with acupuncture where facial needles involved

The nurse should palpate the foot until the anatomical position of Liv3 is located. With full explanation to the patient the acupuncture needle should be introduced to the depth of approximately 1cm on the right foot. The nurse should then rotate the needle backwards and forwards intermittently not causing over stimulation approximately 2-3 minutes.
The nurse should remove the needle if the patient complains of pain or starts to exhibit bizarre behaviour.
On removal of the needle the area should be wiped with sterile gauze and elastoplast applied.
The nurse should inform the patient that a response should be expected within 72 hours.
The treatment may last for the season or repeated treatments may be required.

Adapted from reference 44.

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