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**Ionisers for chronic asthma (Review)**

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[Intervention Review]

# Ionisers for chronic asthma

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## ABSTRACT

### Background

Previous reports have shown that ion content in the air may have an effect on respiratory function. Results from studies which test the efficacy of air ionisers to reduce asthma symptoms are often inconclusive and their use as a treatment for asthma remains debatable.

### Objectives

We conducted a systematic review of the available evidence to determine the effectiveness of positive and negative ion generators in people with asthma.

### Search methods

We searched the Cochrane Airways Group Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL) as well as the alternative medicine database AMED. Searches were current as of June 2012.

### Selection criteria

Randomised controlled trials (parallel or crossover design studies) comparing ionisers with dummy ionisers (being negative or positive ion emitters), in children or adults with chronic asthma.

### Data collection and analysis

Two reviewers independently assessed titles and abstracts of studies and assessed trial quality. Study quality was determined using two methods: The Cochrane approach to allocation concealment and the five point Jadad scale.

### Main results

Six studies were selected for inclusion (106 participants). No results were combined as the studies were all of a crossover design.

#### EFFECTS OF NEGATIVE ION GENERATORS (five studies)

No study reported a significant difference in lung function between ionised and control air (morning Peak expiratory flow (PEF) - three studies; forced expiratory flow in one second (FEV1) - one study). There were no significant differences in symptoms or beta-2 agonist usage between ionised and control air in three studies.

#### EFFECTS OF POSITIVE ION GENERATORS (one study)

This study demonstrated that although positively ionised air was associated with a larger fall in FEV1 with exercise, this did not reach statistical significance. Baseline FEV1 was not demonstrated to be significantly different between treatment groups.

**Authors' conclusions**

Based on the evidence currently available from randomised controlled trials, a recommendation cannot be given for the use of room air ionisers to reduce symptoms in patients with chronic asthma.

**PLAIN LANGUAGE SUMMARY****Ionisers for chronic asthma**

Ion generators have been marketed for use in homes to remove dust and smoke particles in order to improve symptoms in people with asthma. Although complex laboratory studies show that ion generators alter airways function, the few studies which have been conducted in the homes of people with asthma, demonstrate no significant benefit in improving lung function or symptoms.

## BACKGROUND

Asthma is a chronic pulmonary disorder which affects an estimated 3.4 million people in the UK (ONS 1996). A recent National Asthma Campaign survey (Smith 2000) suggests that 42% of those who have asthma face significant challenges in their daily lives due to their condition. Two thirds of the asthma population are said to be receiving inhaled steroids with many expressing concerns about the long-term effects of their medication (Smith 2000). Although pharmacological interventions continue to improve, the prevalence of asthma remains high (ONS 1996). Such concerns highlight the need for further investigation into the benefits of non-pharmacological treatment in order to compliment pharmacological therapies.

Previous reports have shown that alteration of ions in the air may have an effect on respiratory function (Wehner 1969). As a result, interest has grown in the physiological effects of positive and negative air ions in people with asthma. With the development of ion generators it has become possible to artificially manipulate the ion content in air. Studies (Nogrady 1983; Lipin 1984; Warner 1993) have been carried out to test the efficacy of air ionisers in order to reduce air-borne allergens and smoke particles, with a view to alleviating asthma symptoms. Results of such studies are often inconclusive and the effectiveness of air ionisers as a treatment for asthma remains debatable. This systematic review of the available evidence was conducted in order to summarise the results of all identified randomised controlled trials comparing ionisers to placebo.

## OBJECTIVES

To determine whether air ionisers (positive or negative ion emitters) are effective in relieving symptoms and improving respiratory function in people with chronic asthma.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomised controlled trials (parallel or crossover design studies).

#### Types of participants

We included studies assessing children and adults with chronic asthma.

#### Types of interventions

Inhalation of positively or negatively ionised air, generated by an ioniser in the home or laboratory setting. The comparative group will have inhaled non-ionised air through a dummy ioniser.

#### Types of outcome measures

##### Primary outcomes

1. Respiratory physiological measures: Peak Expiratory Flow (PEF) and Forced Expiratory Volume in one second (FEV1)
2. Asthma symptom scores

##### Secondary outcomes

1. Health-related Quality of Life

2. Exacerbation
3. Provocation tests (e.g. exercise, histamine)
4. Bronchodilator usage
5. Inhaled corticosteroids usage

### Search methods for identification of studies

Trials were identified using the Cochrane Airways Group Specialised Register of trials which is derived from systematic searching of electronic databases including CENTRAL, MEDLINE, EMBASE and CINAHL, and hand-searching of respiratory journals and meeting abstracts. All records in the Specialised Register coded as 'asthma' were searched using the following terms:

(ionis\* or ioniz\* or "electrostatic precipitator\*")

The Cochrane Central Register of Controlled Trials (CENTRAL) was searched using the same terms. Additional searching was carried out on the alternative medicine database AMED (1985 - present) using the search:

```
#1 exp ASTHMA/
#2 asthma$ or wheez$
#3 1 or 2
#4 exp IONS/
#5 (ionis$ or ioniz$).tw.
#6 electrostatic$.tw.
#7 4 or 5 or 6
#8 3 and 7
```

Searches were current as of January 2010.

### Data collection and analysis

#### Selection of studies

Two reviewers (KB and SLA) independently assessed titles and abstracts of studies, identified by the database search, and selected studies for inclusion in the review. We also independently assessed the full text of all selected abstracts for suitability for inclusion in the review.

#### Data extraction and management

We extracted data independently from the eligible studies. Disagreement was resolved by consensus.

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

We independently determined study quality using two methods:

(1) The Cochrane approach to allocation concealment using the following grading system:

Grade A: Adequate concealment

Grade B: Uncertain

Grade C: Inadequate concealment

Grade D: allocation concealment not used

(2) The five point Jadad scale (Jadad 1996) according to the following criteria:

(a) Study described as randomised (yes: 1, no: 0)

(b) Method of randomisation described and appropriate (yes: 1, no: -1)

(c) Study described as double blind (yes: 1, no: 0)

(d) Method of blinding described and appropriate (yes: 1, no: -1)

(e) There was a description of withdrawals and drop outs (yes: 1, no: 0)

Data were extracted independently by both reviewers and authors of trial reports were contacted for extra or missing information. We resolved any disagreement between reviewers by discussion.

### Data synthesis

Due to the crossover design employed in the studies, we could not reliably pool data from the individual studies in RevMan, and individual study data only is shown in the Forest plots. We extracted first arm data for [Nogrady 1983](#) and analysed this based upon individual patient scores. We reported data for outcomes in the crossover trials in the text of the review.

If parallel group data are available in future versions of this review, we will report pooled analyses as weighted mean differences (WMD) and standardised mean differences (SMD) depending upon the availability of data measured on the same or different metrics. If we can obtain suitable paired data for crossover studies, we will combine this using inverse variance meta-analysis. Where a more positive outcome is favourable, (e.g. PEF) data, we entered this as positive values. In this case the titles of the horizontal axes have been reversed so that effects that favour the treatment under review move to the right. We have graphed continuous outcomes for which lower scores imply improvement (e.g. symptom scores and percentage reduction in FEV<sub>1</sub> as a measure of bronchial reactivity) according to standard Cochrane graphical convention such that effects that favour the treatment under review move to the left.

The following data were entered separately on the basis of:

1. charge of ion emission, i.e. positive versus negative ions;
2. duration of exposure to ionised air.

### Subgroup analysis and investigation of heterogeneity

We performed a subgroup analysis on the basis of age group of participants (adults versus children)

## RESULTS

### Description of studies

#### Results of the search

We identified 22 abstracts from the original search, nine of which were not trials. Thirteen full text articles were obtained. Two studies were excluded because they were not randomised ([Kirkham 1984](#); [Osterballe 1979](#)) one was excluded because it was neither randomised nor controlled ([Jones 1976](#)) and two studies were not suitably controlled ([Palti 1966](#); [Zylberberg 1960](#)) One study determined the effect of ionisers on airborne particles but recorded no patient outcomes ([Wickman 1989](#)) and one study reported previously published data ([Nogrady 1983](#)). A total of six studies were included in this review. An update search conducted in June 2012 did not identify any additional relevant studies.

#### Included studies

See [Characteristics of included studies](#) for details of individual studies.

We included six studies in this review, all of which utilised a crossover design. The review includes studies conducted between 1983 and 1994 two studies from Israel ([Ben-Dov 1983](#); [Lipin 1984](#)) and four studies conducted in Australia ([Nogrady 1983](#)), UK ([Warner 1993](#)) and Denmark ([Daugbjerg 1988](#); [Larsen 1994](#)). Two studies were published in Danish and were translated into English ([Daugbjerg 1988](#); [Larsen 1994](#)). The remaining studies were all published in English.

### Study design

All studies were randomised. One was single-blind ([Daugbjerg 1988](#)). The remaining studies were double-blind ([Ben-Dov 1983](#); [Larsen 1994](#); [Lipin 1984](#); [Nogrady 1983](#); [Warner 1993](#)). No information on methods of randomisation were reported. [Larsen 1994](#) provided details on the method of randomisation upon request.

### Participants

Sixty eight children participated in four studies ([Ben-Dov 1983](#) (n = 17); [Lipin 1984](#) (n = 12); [Daugbjerg 1988](#) (n = 19); [Warner 1993](#) (n = 20)) with an age range of eight months to 20 years. There were 40 adults who participated in two studies ([Nogrady 1983](#) (n = 20); [Larsen 1994](#) (n = 20)), with a mean age of 36 to 47 years (see [Table 1](#)).

Diagnosis and severity of asthma were not described in the studies. [Ben-Dov 1983](#) and [Lipin 1984](#) recruited participants known to have had asthma attacks provoked by exercise challenge. [Daugbjerg 1988](#) did not report how a diagnosis of asthma was reached and no baseline data on symptoms were reported. [Larsen 1994](#) recruited participants with an observed variation in peak flow of >20% or reversibility of over 15% in FEV<sub>1</sub> after inhalation of 0.2 mg of salbutamol, were treated with  $\leq$  1000 mcg inhaled steroids per day and required bronchodilators on a daily basis. [Nogrady 1983](#) made a clinical assessment for asthma at the outset of the study, including PEF and allergen sensitivity. No other details of clinical examination were reported. [Warner 1993](#) recruited children described as suffering from perennial asthma.

### Interventions

Negatively ionised air was used in four home-based studies ([Daugbjerg 1988](#); [Larsen 1994](#); [Nogrady 1983](#); [Warner 1993](#)) and one laboratory based study ([Ben-Dov 1983](#)). Positively ionised air was used in one laboratory based study ([Lipin 1984](#)).

[Nogrady 1983](#) exposed participants to 150,000 negative ions/ml at night for 10 hours during the 8 week active treatment period. [Daugbjerg 1988](#) exposed participants to 220,000 negative ions per cm<sup>3</sup> or placebo for either eight and then four weeks or four and then eight weeks treatment. In [Larsen 1994](#) and [Warner 1993](#) the ion count was not reported. In both studies participants were exposed to an ioniser during the day in the living room and at night in the bedroom for a treatment period of four weeks ([Larsen 1994](#)) and six weeks ([Warner 1993](#)).

[Ben-Dov 1983](#) exposed participants to negatively charged ions (0.5 to 1.0 x 10<sup>6</sup> ions per cm<sup>3</sup> for approximately 45 minutes) and conducted identical six minute exercise provocation tests (cycle ergometry) where each challenge was undertaken twice (3 to 24 hours apart) with active and placebo ionisers. Participants were also exposed to 4 to 5 x 10<sup>5</sup> negative ions per cm<sup>3</sup> during histamine provocation, with doubling concentrations of histamine

to a maximum of 10 mg/ml until a 20% drop in FEV1 was obtained compared to baseline values. Each challenge was undertaken twice (24 hours apart) with active and placebo ionisers.

Lipin 1984 exposed participants to positively charged ions (0.5 to 1.0 x 10<sup>6</sup> ions per cm<sup>3</sup>) and conducted identical six minute exercise provocation tests (cycle ergometry) where each challenge was undertaken twice (24 hours apart) with and without exposure to the active ioniser.

See Table 2 for a summary of the duration of the included trials.

### Outcome measures

There was variation in the overall outcomes used across the six studies.

The studies conducted under laboratory conditions measured lung function and did not assess symptoms or medication usage (Ben-Dov 1983; Lipin 1984)

Of the remaining studies, assessments were conducted of lung function in three studies (Larsen 1994; Nogrady 1983 and Warner 1993); symptoms were assessed in three studies (Daugbjerg 1988; Larsen 1994 and Warner 1993) and attempts to record medication usage were made in two studies (Daugbjerg 1988; Warner 1993).

One study (Nogrady 1983) reported data with significant differences in baseline measurements (approximately 100 ml difference in PEF) between the two comparison groups possibly due to the gender distribution which is suggestive of unsuccessful randomisation. Results were presented in the form of the two groups, according to whether participants were exposed to the active ioniser or the placebo ioniser first. Data from each group were analysed separately and intra-group comparisons were made between the active and placebo periods. A second publication of the trial contributed no extra data to the review so is listed in 'excluded studies'.

Data from another study (Daugbjerg 1988) does not appear in the table of comparisons as the data were not useable due to the use of non-validated symptom scoring.

### Risk of bias in included studies

Overall, the included papers were of strong study design. All studies were conducted double-blind, except the Daugbjerg study (Daugbjerg 1988) which was single blind. The order of the treatments within the crossover were described as randomised but randomisation methods were not stated. However, none of the studies commented on the number of participants excluded from the trials or reported a power calculation to determine sample size. Withdrawals and drop-outs were adequately described.

The sample sizes of each of the six studies were small, ranging from 12 to 20 participants. The total number of participants contributing data from all six studies was 106.

A wash-out period between treatment arms of two weeks was reported in only one study (Nogrady 1983). Although the duration of exposure in the laboratory studies was short, it is unknown whether a wash-out period of greater than 3 to 24 hours would be required.

Inclusion/exclusion criteria were not formally specified. Inclusion criteria was specified in two studies, with respect to a definition

of stable asthma (Larsen 1994), and a concentration of house dust mite allergen Der p1 (Warner 1993). The two laboratory based studies reported a general statement of inclusion of subjects as those being "known to have had asthmatic attacks provoked by physical exertion". Only one study specified exclusion criteria relating to medication use (Larsen 1994).

There was total agreement between two independent assessments of study quality using the Cochrane approach and the Jadad scale. All five studies were graded B according to the Cochrane approach to concealment of allocation as none described the method of concealment of allocation. This is not a major concern if the blinding of participants and assessors was secure. No further details were provided by the authors, about methods of concealment or randomisation, which increased the allocated scores of the included trials. All studies were given a Jadad score of 3.

## Effects of interventions

### EFFECTS OF NEGATIVE ION GENERATORS

#### Respiratory physiological measures

##### Peak Expiratory Flow

###### Morning PEF

Two studies with adult participants (Nogrady 1983; Larsen 1994) did not report significant differences between the exposure periods.

One study conducted in children (Warner 1993) reported no significant difference.

###### Evening PEF

No statistically significant differences were reported for evening PEF (Nogrady 1983; Warner 1993; Larsen 1994). No values were presented in the papers.

#### Forced Expiratory Volume in one second

##### Baseline FEV1

Only one study, which was a laboratory based study in children (Ben-Dov 1983) measured FEV1 after 10 minutes inhalation of control and negatively ionised air, but prior to exercise testing. No significant differences were demonstrated in "Baseline" FEV1 between the treatment groups.

##### (ii) Percentage fall in FEV1 after exercise provocation

Ben-Dov 1983 demonstrated no significant difference in percentage reduction in FEV1 from baseline after exercise provocation in the ionised air exposed group compared to those exposed to control air.

##### (iii) Percentage fall in FEV1 after histamine provocation

Ben-Dov 1983 demonstrated no significant difference in percentage reduction in FEV1 from baseline after histamine provocation in the ionised air exposed group compared to those exposed to control air.

##### (iv) Absolute FEV1

Only one study, which was a home based study in adults (Larsen 1994) measured FEV1 after four weeks exposure to control and negatively ionised air. This study determined there was no significant difference in absolute FEV1 (litres) between treatments.

## Asthma symptom scores

Three studies, one conducted in children (Warner 1993) and two in adults (Nogrady 1983; Larsen 1994) recorded asthma symptoms. The Warner study utilised a different symptom scale while the Nogrady and Larsen studies used the same. These measured five dimensions of symptoms and reported a mean symptom score only, not scores for the individual dimensions including the "Total" dimension. Of these three studies, only the Larsen study reported a "Total" dimension. Thus it was not possible to pool these data in an analysis using a standardised mean difference and the analyses are reported separately according to the use of Asthma Symptom Scale "1" and Asthma Symptom Scale "2".

Using the Asthma Symptom Score "1" (Warner 1993) there were no significant differences between the treatments. After six weeks exposure to both ionised air and control air, in the symptom dimensions of "nighttime wheeze"; "daytime wheeze"; "nighttime cough" and "daytime activity".

Using the Asthma Symptom Score "2" (Larsen 1994) there were no significant differences between the treatments, after four weeks exposure to both ionised and control air, in the symptom dimensions scores of: "total"; "sleep disturbance"; "wheeze"; "activity level"; "coughing" and "sputum production".

Nogrady 1983 also used this scale, however, the authors reported a mean of all five dimensions only. There was no significant difference between exposure periods in the mean symptom score.

### Bronchodilator Use

Three studies recorded participants' asthma medication use (inhaled or oral bronchodilators, corticosteroids, sodium cromoglycate and other medications) (Nogrady 1983; Warner 1993; Larsen 1994). No study reported a significant difference in favour of ionised air versus control.

### EFFECTS OF POSITIVE ION GENERATORS

Only one study measured the effects of positive ions on lung function. This study (Lipin 1984), conducted in children demonstrated that positively ionised air was associated with bronchoconstriction, measured by the maximum fall in FEV1 after exercise from baseline (after 10 minutes exposure to ionised air but before cycling) between treatment groups. The confidence interval of the effect of positive ionisation on FEV1 after exercise includes no difference and also a clinically significant deterioration, but the sample size is too small to draw any firm conclusion. Baseline FEV1 was also demonstrated not to be significantly different between treatment groups.

### DISCUSSION

The impact of weather and the resulting ionic charge of the air has been thought to have an impact on biological systems (Sulman 1984) including the respiratory system (Palti 1966). Studies of the effects of weather on morbidity have been conducted with respect to the Foehn, a dry southerly wind of central Europe (Posse 1975; Gnechi Ruscone 1985) and although asthma patients often report a worsening of symptoms with weather changes, early studies indicate no relationship (Dantzer 1983; Wagner 1983).

Ion generators have been marketed for use to reverse negative ion depletion and to remove dust and smoke particles by electrostatic

precipitation. There is a paucity of data in the literature generated from randomised controlled trials of the effects of ion generators for chronic asthma. Consequently this review has been limited by the small numbers of studies eligible for inclusion in the review and also the inconsistent use of outcome measures. It is possible that the studies lacked the statistical power to detect changes in outcomes because of the small sample sizes of these studies, ranging from 12 to 20.

The five studies of the effects of negative ion generators and the one study of the effect of a positive ion generator included in this review have failed generally to demonstrate any benefit of these instruments for the treatment of chronic asthma in children and adults. Relevant outcome measures such as PEF, FEV1 after exercise and histamine provocation, symptom scores and asthma medication showed no significant improvement after extended periods of exposure to charged ions compared to normal/control air. It is important to note however that the Ben-Dov et al study (Ben-Dov 1983), a laboratory based study in children demonstrated that during the active ionisation period, the FEV1 after exercise provocation fell 8% less than that during the control air period. This reduction in bronchial reactivity was statistically significant using the Student's paired t-test with a P value of less than 0.015. This reflects the power inherent in a paired t-test, compared to the use of a mean difference. The clinical relevance of this finding generated in a controlled laboratory setting with the concentration of ions at the mouthpiece 100 times the natural concentration in the air is unclear. Furthermore, a statistically significant reduction in bronchial reactivity after histamine challenge did not occur. Interestingly, four of nine participants demonstrated greater histamine sensitivity during inhalation of negative ions compared to control air.

The study by Lipin et al (Lipin 1984) also demonstrated a statistically significant increase in bronchial reactivity after exercise in participants during inhalation of positive ions ( $P = 0.04$ ). In this study, eight of twelve children experienced a greater reduction in FEV1 when the active ioniser was used compared to the placebo ioniser. Two showed no change and two showed a reduction in reactivity. All other outcomes in this review were statistically consistent with those reported by authors of the studies.

Asthma symptoms were not demonstrably improved as a consequence of active ionisation. The two studies, however, which recorded or reported this outcome used two apparently unvalidated symptom scales; the Nogrady study (Nogrady 1983) which utilised the same scale as the Larsen study (Larsen 1994) reported a mean symptom score of the five dimensions rather than the "Total" dimension score. The frequency of "nighttime cough" recorded in the Warner study (Warner 1993) increased during the ionisation period (exposure to negative ions for six weeks) to a level which approached statistical significance [Wilcoxon signed rank sum test  $P = 0.055$ ]. If the use of room air ionisers is to be pursued then this finding requires further investigation.

Asthma medication use was not demonstrated to be significantly reduced during active ionisation compared to when the placebo ioniser was in use. Beta-2 agonist use was an outcome measure in only one of three studies which recorded medication use. The amount of rescue medication used is more likely to reflect a change in condition as compared to other asthma medications.



One study (Larsen 1994) provoked some interesting correspondence (Jonassen 1996) which suggests the need to carry out initial trials on the efficiency of the ioniser before using it in a trial. The ioniser is an instrumental component in the trial and could potentially influence the trial outcome. Another point about the length of time an ioniser should be turned on in order to 'clean' the air in a room is also worthy of consideration. Any trials implemented to test an improvement of symptoms in asthma patients should consider these points.

In conclusion, individual studies in a laboratory setting suggest that positively ionised air may aggravate exercise induced asthma and negatively ionised air may attenuate exercise induced asthma during exposure to these charged ions at 100 fold the concentration found naturally in the air. No other significant benefit or harm in terms of lung function (baseline and absolute FEV<sub>1</sub>, PEF), asthma symptoms or medication use were demonstrated and none occurred in the home setting.

## AUTHORS' CONCLUSIONS

### Implications for practice

Based on the evidence currently available from randomised controlled trials, a recommendation cannot be given for the use of room air ionisers in the homes of patients with chronic asthma.

### Implications for research

The strength of evidence from six randomised controlled trials does not suggest that air ionisers are significantly beneficial for patients with chronic asthma. There are no further data to provide additional evidence to support their use and the absence of such data in the medical literature since 1993 suggests a declining interest. The review does suggest, however, that further trials would need to incorporate issues on compliance, efficiency of the ioniser and the environment in which the trial takes place.

## ACKNOWLEDGEMENTS

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\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies [ordered by study ID]

**Ben-Dov 1983**

Methods	Crossover study Randomisation method: unclear Blinding: Double-Blind Excluded: not described Withdrawals: None stated Baseline characteristics: comparable Power calculation: not given Jadad Score: 3
Participants	Total = 17 children with asthma (17 completing trial) Gender-11M:6F. Age range 10-20 years, mean age 12.5 years All patients had exercise-induced asthma Inclusion/exclusion criteria-not stated 11 exercised challenged 10 histamine challenged (4 participated in both)  No details of severity reported
Interventions	Laboratory-based study: Negatively ionised air (4x10 <sup>5</sup> -10x10 <sup>5</sup> ions /cm <sup>3</sup> ) versus Control room or non-ionised air. 10 minutes pre-challenge (exercise and histamine) exposure, 6 minutes exercise test 3-24 hours apart. 3 minutes post-histamine challenge measurement. Histamine provocative dose = PD <sub>20</sub>
Outcomes	FEV <sub>1</sub> measurement pre-challenge, during challenge and post-challenge
Notes	
<b>Risk of bias</b>	
<b>Bias</b>	<b>Authors' judgement</b> <b>Support for judgement</b>

**Ionisers for chronic asthma (Review)**

**Ben-Dov 1983** (Continued)

Allocation concealment (selection bias)	Unclear risk	Information not available
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**Daugbjerg 1988**

Methods	Crossover study Randomisation method: unclear Blinding: single blind Excluded: not described Withdrawals: 3 No baseline statistics given Power calculation: not given Jadad score: 3
Participants	Total = 19 children (16 completing trial) Gender: 12m:7F (9m:7F completing) Average age 63 months No baseline measurements taken All patients had asthma or 'Wheezy Bronchitis' Inclusion/exclusion criteria-not stated  No details of severity reported.
Interventions	Home-based study: negatively ionised air versus control/non-ionised air 3 x 4-week periods
Outcomes	In house developed four point symptom score; medication usage; parent reported school absence/days of sickness
Notes	Results not usable

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

**Larsen 1994**

Methods	Crossover study Randomisation method: Third party drew 'active' or 'placebo' labels out of an envelope (personal communication from trialist). Blinding: Double-blind Excluded: not stated Withdrawals: 1 Baseline characteristics: comparable Power calculation: not given Jadad score: 5
Participants	Total = 20 adults (19 completing trial) Gender: 9M:10F (one dropout), Age range 18-60 years, mean age 47 All patients had asthma

**Ionisers for chronic asthma (Review)**

**Larsen 1994** (Continued)

Inclusion criteria-stable asthma defined by oral steroid use  
 Variation in PEF of > 20% or > 15% FEV1 reversibility after 0.2mg salbutamol delivered by spacer  
 Inhaled steroid use < 1000mcg/day ipratropium bromide/sodium cromoglycate

Interventions	Home-based Ionised air versus control/ non-ionised air 24hours per day, Positive or negative not stated Ionised air for 4 weeks then control air for 4 weeks
Outcomes	Morning/evening PEF, FEV1, FVC, VC, Symptom scores
Notes	Jadad score: 5 Higher scoring due to extra information provided by author through personal communication

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Low risk	Sealed envelope; investigators unaware as to treatment group assignment

**Lipin 1984**

Methods	Crossover study Randomisation method: unclear Blinding: double-blind Withdrawals: none stated Baseline statistics: comparable Power calculation: not given Jadad score: 3
Participants	Total = 12 (12 completing trial) Gender: 7M:5F, Age range 9-15 years, mean age 12 years All patients were asthmatic Inclusion/exclusion criteria-not stated  No details of severity were reported.
Interventions	Laboratory-based study: Positively ionised air versus control/non-ionised air 10 minutes exposure and exposure during 6 minute exercise test. Tests carried out 24 hours apart
Outcomes	Bronchial reactivity- measuring the effect on FEV1
Notes	

**Risk of bias**

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	Information not available

**Nogrady 1983**

Methods	Crossover study Randomisation method: unclear Blinding: double-blind Excluded: not stated Withdrawals: 1 Power calculation: not given Jadad score: 3
Participants	Original version of study had a total no. = 20 adult (19 completing trial). Gender: 10M:9F Mean age 36 years Original study group of 20 separated into groups (a) and (b) because of gender distribution between groups and baseline lung function higher probably due to gender distribution All patients had asthma Inclusion/exclusion criteria-not stated Group (a) consists of 10 subjects: 8 males and 2 females, which started study on the active ioniser and whose mean (SD) baseline characteristics were: am PEF: 399(132) pm PEF: 442(103) symptom score: 1.8(1.85) medication: 5.9(2.9) See Nogrady (b)
Interventions	Home-based Negatively ionised air or control/ non-ionised air. 2 x 8 week treatment arms with 4 weeks washout. Total length of trial 6 months
Outcomes	Morning PEF measurement; Sympton scores
Notes	
<b>Risk of bias</b>	
<b>Bias</b>	<b>Authors' judgement</b> <b>Support for judgement</b>
Allocation concealment (selection bias)	Unclear risk                      Information not available

**Warner 1993**

Methods	Crossover study Randomisation method: unclear Blinding: double-blind Excluded: not stated Withdrawals: not described Baseline characteristics: comparable Power calculation: not given Jadad score: 3
Participants	Total = 20 (20 completing the trial) No gender ration given. Age range 3-11 years, median age 9 years All patients had asthma Inclusion criteria-Der p1 concentration in the living room and child's bedroom > 2mg/m3 air  No details of severity reported.

**Ionisers for chronic asthma (Review)**

**Warner 1993** *(Continued)*

Interventions	Home-based Negatively ionised air versus non-ionised air/ control air. 6 weeks ionised, 6 weeks non-ionised/control. Air sampling performed at beginning, middle and end of each period	
Outcomes	Morning/evening PEF, nighttime wheeze, daytime wheeze, nighttime cough, daytime cough, daytime activity, medication	
Notes		
<b>Risk of bias</b>		
<b>Bias</b>	<b>Authors' judgement</b>	<b>Support for judgement</b>
Allocation concealment (selection bias)	Unclear risk	Information not available

**Characteristics of excluded studies** *[ordered by study ID]*

Study	Reason for exclusion
<a href="#">Jones 1976</a>	Not randomised No control group
<a href="#">Kirkham 1984</a>	Not randomised
<a href="#">Mitchell 1980</a>	No placebo treatment Not blinded
<a href="#">Nogrady 1983b</a>	Secondary report of included study [Nogrady(a) and Nogrady(b)] No extra data extracted
<a href="#">Osterballe 1979</a>	Not randomised
<a href="#">Palti 1966</a>	Groups not comparable. One group of 13 suffering from asthmatic bronchitis. One group of 6 with no respiratory problems.
<a href="#">Ponomarenko 2003</a>	Study inadequately described to determine whether it was randomised or not.
<a href="#">Wickman 1989</a>	Randomised control trial measuring the ionisers effect on the reduction of airborne particles. Correspondence with author revealed no patient data as none was originally recorded.
<a href="#">Zylberberg 1960</a>	No placebo group Compared negative ionisation with positive ionisation

**DATA AND ANALYSES**

**Comparison 1. Negative ionised air versus non-ionised air**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 FEV1 (Fall %) after exercise test	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Adults	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Baseline FEV1(litres) (after inhalation of negative ions prior to exercise testing)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Adults	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Morning Peak Expiratory Flow (Litres/min)	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Adults	2		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 FEV1 (Litres/min) > 4 weeks	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Adults	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 Children	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Evening Peak Expiratory Flow (Litres/min)	3		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Adults	2		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 FEV1 (Fall %) after histamine challenge	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Adults	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Asthma Symptom Score 1	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 nighttime wheeze	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.2 daytime wheeze	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.3 nighttime cough	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7.4 daytime activity	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Asthma Symptom Score 2	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected



Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 sleep disturbance	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 wheeze	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.3 activity level	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.4 coughing	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.5 sputum production	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.6 TOTAL	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8.7 mean score of all five dimensions	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
<b>9 Bronchodilator use</b>	3		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 Adults	2		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9.2 Children	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
<b>10 Morning PEFr (First arm change score)</b>	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

**Analysis 1.1. Comparison 1 Negative ionised air versus non-ionised air, Outcome 1 FEV1 (Fall %) after exercise test.**

Study or subgroup	Ionised air		Non-ionised air		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
<b>1.1.1 Adults</b>						
<b>1.1.2 Children</b>						
Ben-Dov 1983	11	21 (9.9)	11	29 (16.6)	-8	[-19.42, 3.42]

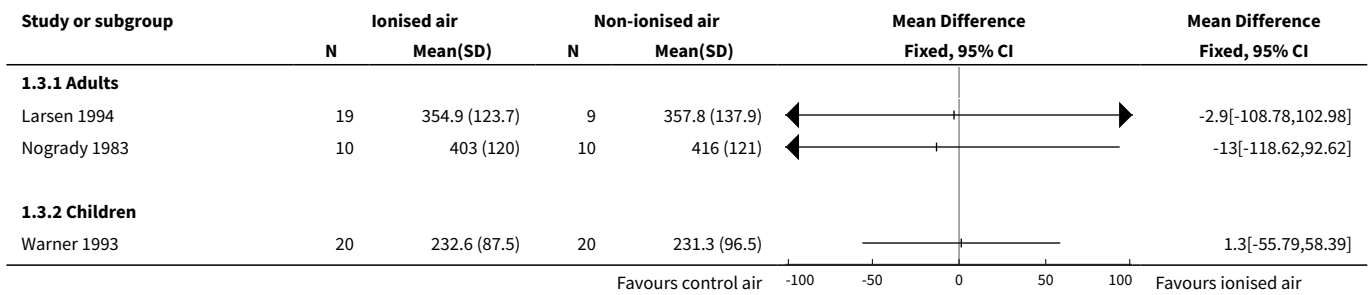
Favours ionised air    -100    -50    0    50    100    Favours control air

**Analysis 1.2. Comparison 1 Negative ionised air versus non-ionised air, Outcome 2 Baseline FEV1(litres) (after inhalation of negative ions prior to exercise testing).**

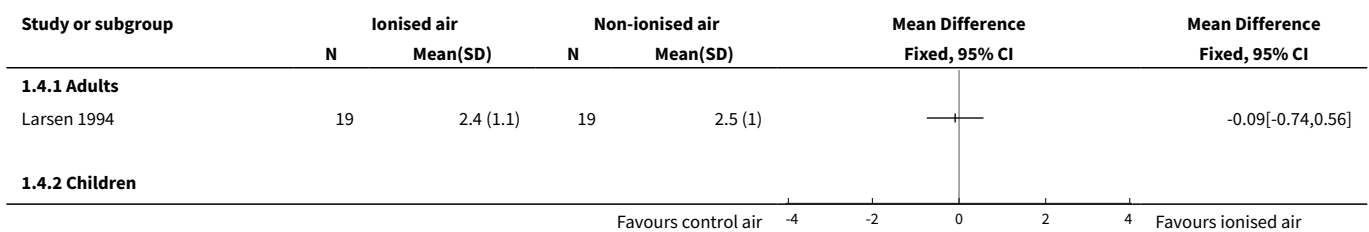
Study or subgroup	Ionised air		Control air		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
<b>1.2.1 Adults</b>						
<b>1.2.2 Children</b>						
Ben-Dov 1983	11	1.4 (0.3)	11	1.4 (0.2)	-0.02	[-0.23, 0.19]

Favours control air    -4    -2    0    2    4    Favours ionised air

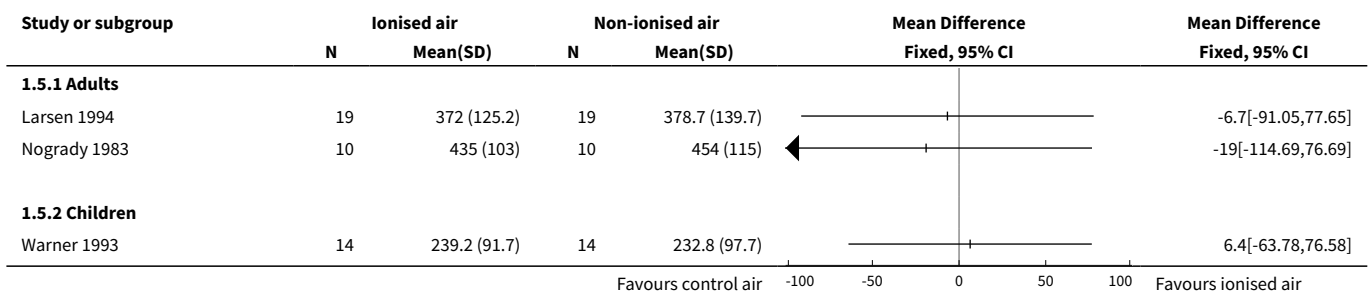
**Analysis 1.3. Comparison 1 Negative ionised air versus non-ionised air, Outcome 3 Morning Peak Expiratory Flow (Litres/min).**



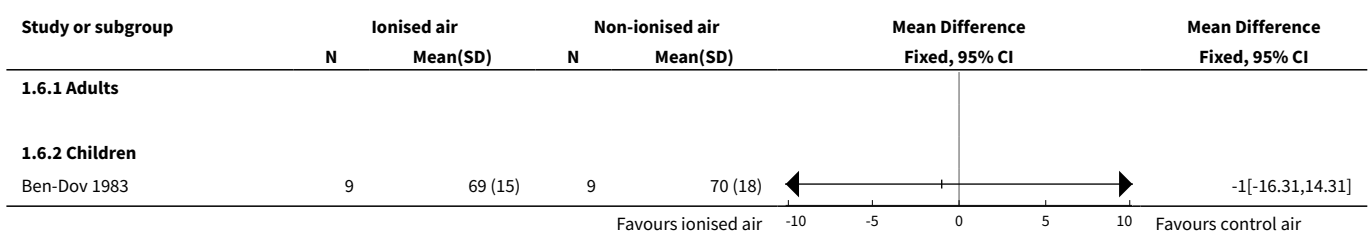
**Analysis 1.4. Comparison 1 Negative ionised air versus non-ionised air, Outcome 4 FEV1 (Litres/min) > 4 weeks.**



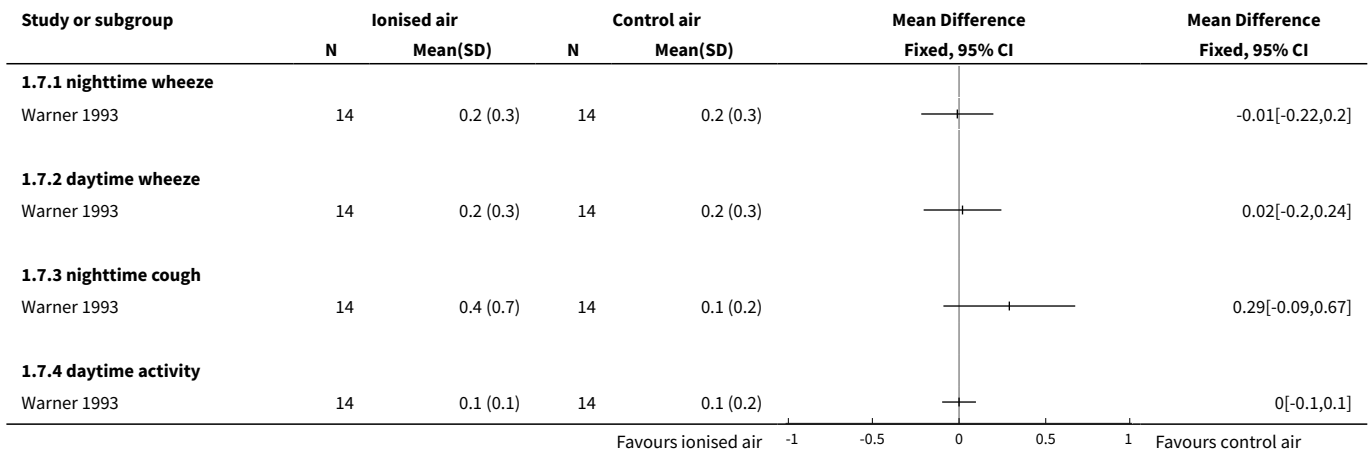
**Analysis 1.5. Comparison 1 Negative ionised air versus non-ionised air, Outcome 5 Evening Peak Expiratory Flow (Litres/min).**



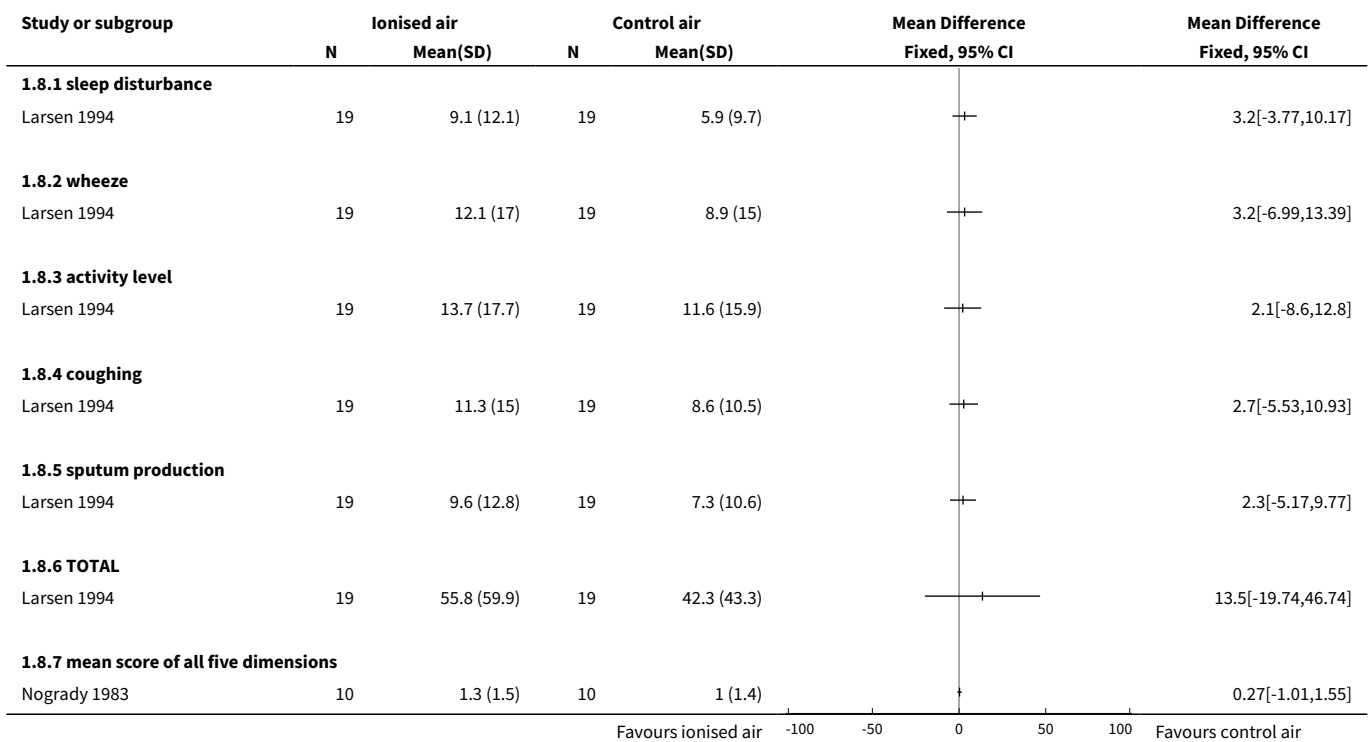
**Analysis 1.6. Comparison 1 Negative ionised air versus non-ionised air, Outcome 6 FEV1 (Fall %) after histamine challenge.**



**Analysis 1.7. Comparison 1 Negative ionised air versus non-ionised air, Outcome 7 Asthma Symptom Score 1.**



**Analysis 1.8. Comparison 1 Negative ionised air versus non-ionised air, Outcome 8 Asthma Symptom Score 2.**



**Analysis 1.9. Comparison 1 Negative ionised air versus non-ionised air, Outcome 9 Bronchodilator use.**

Study or subgroup	Ionised air		Non-ionised air		Std. Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Std. Mean Difference Fixed, 95% CI
<b>1.9.1 Adults</b>						
Larsen 1994	19	56.4 (45.7)	19	55.2 (43.9)		0.03[-0.61,0.66]
Nogrady 1983	10	6 (3)	10	5.2 (3.1)		0.25[-0.63,1.13]
<b>1.9.2 Children</b>						
Warner 1993	14	0.5 (0.7)	14	0.5 (0.9)		-0.06[-0.8,0.68]

Favours ionised air    -100    -50    0    50    100    Favours control air

**Analysis 1.10. Comparison 1 Negative ionised air versus non-ionised air, Outcome 10 Morning PEFR (First arm change score).**

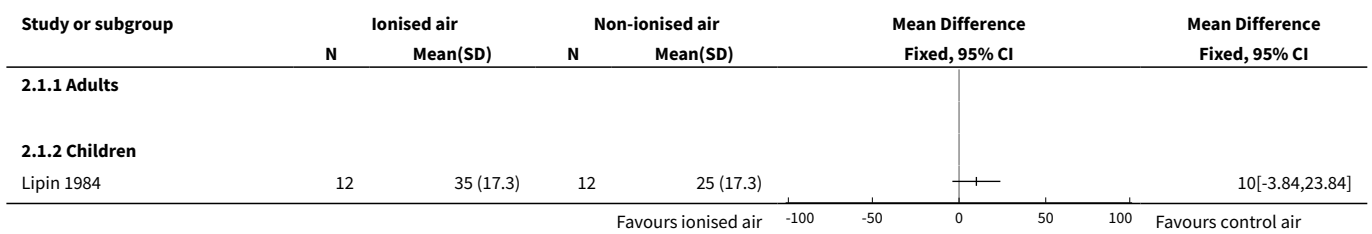
Study or subgroup	Treatment		Control		Mean Difference	
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Mean Difference Fixed, 95% CI
Nogrady 1983	10	3.4 (23.8)	9	-0.8 (24.9)		4.18[-17.78,26.14]

Favours control air    -10    -5    0    5    10    Favours ionised air

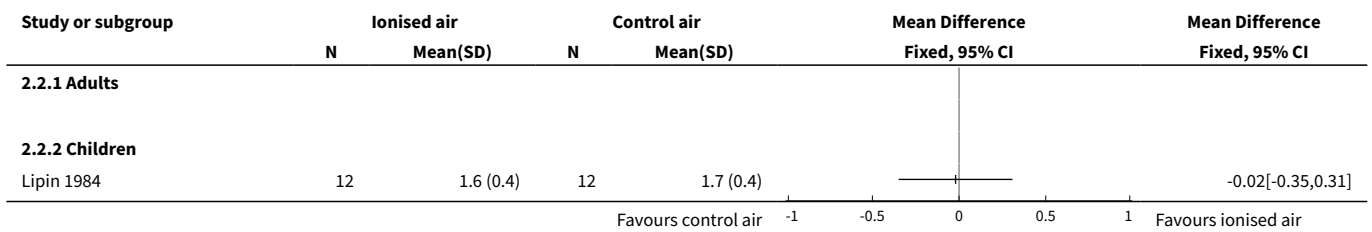
**Comparison 2. Positive ionised air versus non-ionised air**

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 FEV1 (Fall %) after exercise test	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Adults	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Baseline FEV1(litres) (after inhalation of positive ions prior to exercise testing)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Adults	0		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2.2 Children	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

**Analysis 2.1. Comparison 2 Positive ionised air versus non-ionised air, Outcome 1 FEV1 (Fall %) after exercise test.**



**Analysis 2.2. Comparison 2 Positive ionised air versus non-ionised air, Outcome 2 Baseline FEV1(litres) (after inhalation of positive ions prior to exercise testing).**



**ADDITIONAL TABLES**

**Table 1. Age groups of participants**

Study	No of patients	Average age	Age range
<a href="#">Ben-Dov 1983</a>	17	12.5 years	10-20 years
<a href="#">Daugbjerg 1988</a>	19	63 months	8-47 months
<a href="#">Larsen 1994</a>	19	47 years	18-60 years
<a href="#">Lipin 1984</a>	12	12 years	9-15 years
<a href="#">Nogrady 1983</a>	19	36 years	No range given
<a href="#">Warner 1993</a>	20	9 years	9-14

**Table 2. Duration of trial**

Study	Intervention	Between intervention	Total duration
<a href="#">Ben-Dov 1983</a>	10 minute exercise/histamine test	24 hours	Unclear
<a href="#">Daugbjerg 1988</a>	1 week treatment/placebo	1 week	4 weeks

**Table 2. Duration of trial** (Continued)

Larsen 1994	4 weeks treatment/placebo	None	8 weeks
Lipin 1984	6 minute exercise test	24 hours	Unclear
Nogrady 1983	8 weeks treatment/placebo	4 weeks (washout)	6 months
Warner 1993	6 weeks	None	12 weeks

## WHAT'S NEW

Date	Event	Description
4 September 2017	Amended	New literature search run (7 February 2017) to assess the need to update this review. One potentially eligible study identified and added to <a href="#">Studies awaiting classification</a> .

## HISTORY

Protocol first published: Issue 4, 2000

Review first published: Issue 3, 2003

Date	Event	Description
22 June 2012	New search has been performed	New literature search run, no new eligible studies identified.  There have been no new studies published on this topic in the past 18 years and therefore we have moved this topic to a longer search cycle. We plan to update the literature search in Feb 2017. If you are aware of the publication of any potentially eligible trials in the interim period, please let us know using the "submit comments" button for this review on The Cochrane Library.
22 June 2012	New citation required but conclusions have not changed	New literature search run.
19 January 2010	New search has been performed	Literature search re-run; no new studies.
1 August 2008	Amended	Converted to new review format.
1 February 2003	New citation required and conclusions have changed	Substantive amendment

## CONTRIBUTIONS OF AUTHORS

KB and SLA developed the protocol with suggested changes from CJC

KB carried out searches and KB and SLA reviewed abstracts for inclusion

KB and SLA extracted data with advice on data entry from CJC

SLA conducted the meta-analysis and reported results

KB wrote the abstract. SLA and KB developed the discussion and conclusion section with CJC.

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## DECLARATIONS OF INTEREST

None known.

## SOURCES OF SUPPORT

### Internal sources

- None, UK.

### External sources

- None, UK.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Air Ionization; Anions [therapeutic use]; Asthma [\*therapy]; Cations [therapeutic use]; Cross-Over Studies; Ions [therapeutic use]; Randomized Controlled Trials as Topic

### MeSH check words

Adolescent; Adult; Child; Child, Preschool; Humans; Infant; Young Adult