

Caffeine for asthma (Review)

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[Intervention Review]

Caffeine for asthma

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ABSTRACT

Background

Caffeine has a variety of pharmacological effects; it is a weak bronchodilator and it also reduces respiratory muscle fatigue. It is chemically related to the drug theophylline which is used to treat asthma. It has been suggested that caffeine may reduce asthma symptoms and interest has been expressed in its potential role as an asthma treatment. A number of studies have explored the effects of caffeine in asthma, this is the first review to systematically examine and summarise the evidence.

Objectives

To assess the effects of caffeine on lung function and identify whether there is a need to control for caffeine consumption prior to either lung function or exhaled nitric oxide testing.

Search strategy

We searched the Cochrane Airways Group trials register and the reference lists of articles (August 2009). We also contacted study authors.

Selection criteria

Randomised clinical trials of oral caffeine compared to placebo or coffee compared to decaffeinated coffee in adults with asthma.

Data collection and analysis

Trial selection, quality assessment and data extraction were done independently by two reviewers.

Main results

Seven trials involving a total of 75 people with mild to moderate asthma were included. The studies were all of cross-over design.

Six trials involving 55 people showed that in comparison with placebo, caffeine, even at a 'low dose' (< 5mg/kg body weight), appears to improve lung function for up to two hours after consumption. Forced expiratory volume in one minute showed a small improvement up to two hours after caffeine ingestion (SMD 0.72; 95% CI 0.25 to 1.20), which translates into a 5% mean difference in FEV1. However in two studies the mean differences in FEV1 were 12% and 18% after caffeine. Mid-expiratory flow rates also showed a small improvement with caffeine and this was sustained up to four hours.

One trial involving 20 people examined the effect of drinking coffee versus a decaffeinated variety on the exhaled nitric oxide levels in patients with asthma and concluded that there was no significant effect on this outcome.

Caffeine for asthma (Review)

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Authors' conclusions

Caffeine appears to improve airways function modestly, for up to four hours, in people with asthma. People may need to avoid caffeine for at least four hours prior to lung function testing, as caffeine ingestion could cause misinterpretation of the results. Drinking caffeinated coffee before taking exhaled nitric oxide measurements does not appear to affect the results of the test, but more studies are needed to confirm this.

PLAIN LANGUAGE SUMMARY

The effect of caffeine in asthma

Caffeine is found in coffee, tea, cola drinks and cocoa. Caffeine is a drug that is very similar to theophylline. Theophylline is a bronchodilator drug that is taken to open up the airways in the lungs and therefore relieve the symptoms of asthma, such as wheezing, coughing and breathlessness. Scientists are interested in finding out whether caffeine has the same effect on the lungs as theophylline.

There are two major reasons why it is important to know if caffeine is a bronchodilator. The first is because it may be beneficial for asthmatics to take caffeine in order to relieve the symptoms of asthma. The second is because consuming caffeine may affect the results of important tests that determine how bad someone's asthma is.

If caffeine acts as a bronchodilator and widens the airways, then a patient who has consumed caffeine before taking the test would show a better result in a lung function test than they would have if they had not consumed any caffeine. The potential problem with this is that if the test results are better than expected doctors may prescribe a lower dose or a weaker drug than is really necessary, which can lead to problems with asthma management.

This review carefully examines all the available high-quality clinical trials on caffeine in asthma. This review was conducted to discover if people should avoid consuming caffeine before taking lung function tests.

This review found that even small amounts of caffeine can improve lung function for up to four hours. Therefore caffeine can affect the result of a lung function test (e.g. spirometry) and so caffeine should be avoided before taking a lung function test if possible, and previous caffeine consumption should be recorded.

It is not known if taking caffeine leads to improvements in symptoms. It may be that in order to improve the symptoms of asthma, caffeine is needed in such large amounts that the drug's adverse effects would become a problem, so more research is needed.

Another clinical trial looked at the effect of caffeine on exhaled nitric oxide levels and found that there is no significant effect so it appear unlikely that patients would need to avoid caffeine before taking this type of test. However, this is the result of just a single study so more research is needed to clarify this.

BACKGROUND

Caffeine has been widely consumed throughout the world for centuries. It is used for both non-medical and medical purposes. It is ubiquitous, being found in coffee, tea, cola flavoured soft drinks and compounds containing cocoa. Caffeine and its derivatives have therapeutic uses, and are contained in medicines such as analgesics and cold remedies.

The general pharmacological effects of caffeine have been extensively investigated and are described in several reviews (e.g. [Curatolo 1983](#), [Stephenson 1977](#)). Early studies reported that caffeine improved mental performance and increased motor activity

([Cheney 1935](#)) and this has been confirmed in other studies. Caffeine ingestion has also been shown to elevate oxygen consumption ([Grollman 1930](#)), increase respiratory rates in disease-free patients ([Robertson 1978](#)), and increase ventilation in patients with coronary obstructive pulmonary disease (COPD) ([Woodcock 1981](#)).

Caffeine belongs to a group of chemicals called methylxanthines, along with the bronchodilator drug theophylline. As a class, these drugs have a history of use in respiratory disorders. The mechanism of action of the methylxanthines is uncertain, but is possibly due to their inhibition of the enzyme phosphodiesterase. Phospho-

diesterase hydrolyses cyclic adenosine monophosphate (cAMP) which is a messenger within the cell that regulates many functions including the contraction and relaxation of smooth muscle. Methylxanthines are also competitive antagonists for adenosine receptors. One of the effects of adenosine, a chemical regulator, is that of bronchoconstriction. Methylxanthines are known to be weak bronchodilators, and they also interact with respiratory muscles to reduce respiratory muscle fatigue. Some believe the latter to be more important than the former in the treatment of respiratory diseases.

Thus, interest has been expressed in the potential role of caffeine as a treatment in respiratory disease (Pagano 1988). As early as 1859, Salter (in Becker 1984) recommended coffee as one of the best remedies for asthma. A study of the general Italian population in 1983 by Pagano 1988 found an inverse relationship between the prevalence of bronchial asthma and the amount of coffee consumed. From this, the authors suggested that caffeine may reduce asthma symptoms.

Why it is important to do this review

Despite the amount of information regarding caffeine and its potential effectiveness in obstructive airways diseases, no reviews have been conducted that examine the evidence in a systematic fashion. The results from such a review could have important implications for research and clinical practice.

OBJECTIVES

1. To identify all published randomized controlled trials of caffeine in the management of asthma.
2. To assess the methodological quality of these randomized controlled trials.
3. To estimate the overall effect of caffeine upon lung function and exhaled nitric oxide (FeNO).
4. To test whether there is a need to control for caffeine consumption prior to lung function testing and testing exhaled nitric oxide (FeNO).
5. To examine the need for further research into the effects of caffeine in asthma.

METHODS

Criteria for considering studies for this review

Types of studies

Studies must be randomized controlled trials.

Types of participants

Adults with previously documented asthma of any level of severity.

Types of interventions

Oral caffeine versus placebo or coffee versus decaffeinated coffee.

Types of outcome measures

Outcome measures were not used to decide if a study was eligible for consideration in the study.

Challenge test data were not included in this review.

Primary outcomes

1. Lung function outcomes used were: forced expiratory volume in 1 second (FEV1), maximum mid-expiratory flow (FEF25-75) and specific airway conductance (Gaw/VL).
2. Exhaled nitric oxide concentration (FeNO).

Secondary outcomes

1. Forced vital capacity (FVC)
2. Maximal expiratory flow rates at 25 and 50% of vital capacity (Vmax50 and Vmax25 respectively)
3. Exercise-induced bronchoconstriction
4. PC20
5. Carbachol challenge
6. Pulse
7. Blood pressure
8. Symptoms
9. Side effects and adverse effects.

Search methods for identification of studies

The search was updated using the following methods.

Electronic searches

Trials were identified using the Cochrane Airways Group Specialised Register of trials, which is derived from systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, AMED and PsycINFO, and handsearching of respiratory journals and meeting abstracts. All records in the Specialised Register coded as 'AST' were searched using the following terms: caffeine* or *caffein or coffee or tea or chocolate or cola. Trials were not excluded on the basis of language.

Searching other resources

Reference lists of all primary studies and review articles were reviewed for additional references.

Authors of identified trials were contacted and asked to identify other published and unpublished studies.

Searches were current as of August 2009.

Data collection and analysis

Selection of studies

The title, abstract and key words of the references obtained from the literature search were independently reviewed by the two reviewers (AB, EB). For the 2009 update this was done by EW and CC. All studies that were not randomized controlled trials or that clearly did not fit the inclusion criteria were excluded. All other citations were reviewed independently in full text by two review authors to assess eligibility. Complete agreement was achieved at all stages.

Data extraction and management

Authors were contacted in an effort to obtain raw and missing data for the original review. Means and standard deviations or standard errors were independently extracted by both reviewers (AB, EB). Standard errors were converted to standard deviations. Graphically presented data were extracted visually by the two reviewers and two research staff from the Division of Physiological Medicine, St. George's Hospital Medical School (Sally Spencer and Catherine O'Leary). There was little variation in the data extracted by the four reviewers. The mean figures from the four independently extracted sets were used in this review.

Only data from cross-over studies were available for inclusion in this review. Since caffeine is a short acting agent, and most studies reported washout periods, 'carryover' and 'period' effects were not considered to affect the results in an important way. They were treated as parallel designs in the analyses for the original review, but for the 2009 update paired t-test results have been used with Generic Inverse Variance pooling. In addition, since no results were reported from parallel group studies, there was no need to provide subgroup analyses on the basis of design.

Extracted data were entered on to the Cochrane Collaboration software program (Review Manager 5.0).

In one paper (Bukowskyj 1987) the mean value provided in the table and that in the corresponding figure were inconsistent (value for %change FEF25-75 at 0.5 hours), this was assumed to be a misprint and therefore omitted from the meta-analysis.

Assessment of risk of bias in included studies

For this 2009 update the risk of bias was assessed by two authors (EW and CC) according to four domains:

1. Allocation generation & concealment
2. Blinding
3. Handling of missing data
4. Selective reporting bias

For each domain we judged the risk of bias as being low ('Yes'), unclear ('Unclear'), and high ('No'), in line with recommendations from the Cochrane Handbook.

Measures of treatment effect

The individual and pooled statistics are reported as odds ratios (OR) with 95% confidence intervals (95% CI). Weighted mean difference (MD) was used when identical units of measurement were reported. To allow the combination of studies where different units (e.g. actual values, change scores, % predicted values) were reported for a particular pulmonary function test (e.g. FEV1 or FEF25-75), analyses were performed using the standardised mean difference (SMD).

Unit of analysis issues

Outcomes were measured and reported at a variety of different time points and following different doses of caffeine. For the purposes of this review and meta-analysis, data were grouped for each outcome according to time of measurement. Data were divided into three time frames labelled as follows: 'short' (less than or equal to two hours); 'medium' (greater than two hours and less than or equal to four hours); 'long' (greater than four hours). In the 2009 review a comparison of all doses at two hours was included; where no data at two hours was given we used the nearest data point and recorded the time in Table 1.

Table 1. Characteristics of studies used in meta-analysis

Study	Dose of caffeine	Formulation of dose	Mean baseline % predicted FEV1	Time of reading used in meta-analysis
Bukowskyj 1987	5 mg/kg	Aqueous solution	48	2 h
Colacone 1990	5 mg/kg	Aqueous solution	84	2h

Table 1. Characteristics of studies used in meta-analysis (Continued)

Crivelli 1986	6 mg/kg	Aqueous solution	--	45 min
Duffy 1991	5 mg/kg ('low') 10 mg/kg ('high')	Capsules	92.9	90 min
Gong 1986	7.2 mg/kg	Decaffeinated coffee plus caffeine	56	2 h
Kivity 1990	3.5 mg/kg ('low') 7 mg/kg ('high')	Capsules	78.8	2 h
Taylor 2004	15 g Coffee	Coffee of decaffeinated coffee	94	--

Dealing with missing data

Since the trials were run over a few hours there were few dropouts. Out of a total of 75 patients only six dropped out.

Data synthesis

Continuous data were analysed using the inverse-variance fixed-effect method in Review Manager.

Subgroup analysis and investigation of heterogeneity

For each outcome in each time frame, sub-group analyses were performed to test for differences between 'high' and 'low' doses of caffeine. Using the median value to divide the data, doses were defined as: 'high' (greater than 5 mg/kg [mg per kg of body weight]); 'low' (lower than 5 mg/kg).

RESULTS**Description of studies**

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Results of the search

An all years' literature search returned 22 references to 2009. Twelve were discarded on the basis of the title, abstract or title

and abstract. Full papers were obtained for the remaining 10 references. Seventeen additional references were identified by searching the bibliographies of the retrieved studies.

Seven trials fulfilled the inclusion criteria and were included in this review. Complete agreement was achieved between the reviewers.

Included studies

Six studies were included in the original review and an update search conducted in August 2009 identified one additional study which met the inclusion criteria ([Taylor 2004](#)). All studies are outlined in the [Characteristics of included studies](#) table.

Six studies tested for the effects of caffeine on pulmonary function, although the main aim of these studies differed. Three studies of these six additionally tested the influence of caffeine on bronchial provocation challenge tests, one using histamine ([Colacone 1990](#)), one carbachol ([Crivelli 1986](#)) and one using eucapnic voluntary hyperventilation (EVH) ([Duffy 1991](#)). Challenge test data were not included in this review. One study also tested the effect of caffeine on exercise-induced bronchoconstriction ([Kivity 1990](#)). One study also compared caffeine to aminophylline ([Gong 1986](#)), but this data was not analysed as it was considered to be beyond the scope of this review.

One study [Taylor 2004](#) assessed the effects of coffee on exhaled nitric oxide (FeNO).

Participants

There were 55 (39 male) adult participants in the six included studies testing for pulmonary function in the original review. These patients were all described as having stable, mild to moderate asthma. Further details of baseline lung function are found in [Table 1](#).

There were 20 adult participants (gender not specified) in the study testing for exhaled nitric oxide included in the 2009 update. The severity of their asthma was not described, but there were 10 steroid naive and 10 steroid-treated patients.

Interventions

Caffeine and matched placebos were administered orally, (as a solution = three studies, capsule = two studies, decaffeinated coffee plus caffeine = one study, caffeine versus decaffeinated coffee = one study). Two studies contributed to the 'low' dose comparison; [Bukowskyj 1987](#) (5 mg/kg) and [Colacone 1990](#) (5 mg/kg). Four studies contributed to the 'high' dose comparison; [Crivelli 1986](#) (6 mg/kg), [Duffy 1991](#) (10 mg/kg), [Gong 1986](#) (7.2 mg/kg) and [Kivity 1990](#) (7 mg/kg).

One study, [Taylor 2004](#), assessed drinking a cup of coffee (intervention group) versus decaffeinated coffee (placebo group) prepared using a standard quantity (15 g) of either caffeine-containing coffee or decaffeinated coffee.

Outcomes

Pulmonary function tests were the only outcomes suitable for entry into the meta-analysis.

See [Characteristics of included studies](#) for details of secondary outcomes of trials.

Excluded studies

From examination of the full papers of the of the potentially eligible references, two studies ([Becker 1984](#) and [Henderson 1993](#)) were excluded. One potentially eligible reference was returned from the bibliographic search and this was excluded on retrieval of the full paper ([Simmons 1983](#)). See [Characteristics of excluded studies](#).

Risk of bias in included studies

Complete agreement was reached by the reviewers for both assessments. See [Characteristics of included studies](#) for risk of bias tables for individual studies and [Figure 1](#) for an overview.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Adequate sequence generation?	Allocation concealment?	Blinding?	Incomplete outcome data addressed?
Bukowskyj 1987	?	+	+	+
Colacone 1990	?	+	+	+
Crivelli 1986	?	?	?	+
Duffy 1991	?	?	+	+
Gong 1986	+	?	+	+
Kivity 1990	?	?	+	+
Taylor 2004	?	?	?	+

Allocation

In the original review (2001) and update (2005) three of the six studies were graded A (Bukowskyj 1987; Colacone 1990; Gong 1986) and three B (Crivelli 1986; Duffy 1991; Kivity 1990) and all six studies were given Jadad's score of four as a result of communication with the authors.

For this update (2009) allocation bias was assessed according to the new Cochrane guidelines. All the papers stated that the trials were randomised. One trial reported computerised sequence generation which was judged to have a low risk of bias (Gong 1986), while the remaining six trials were unclear. Two trials reported adequate allocation concealment (Bukowskyj 1987; Colacone 1990) while the remaining five were unclear.

Blinding

All the studies were described as double blind. Blinding of the patient is important so that they put the same effort in to lung function testing regardless of intervention, however they would presumably be able to detect if they had ingested any caffeine due to side effects. Five studies were judged to have a low risk of bias with respect to blinding (Bukowskyj 1987; Colacone 1990; Duffy 1991; Gong 1986; Kivity 1990). None of the papers described blinding of the investigator administering the caffeine or placebo to the patient or the investigator taking the outcome readings.

Incomplete outcome data

Since the trials took place over relatively short time frames there were few drop outs and only one missing data point throughout all the studies. All trials were judged to be of low risk of bias with respect to dealing with incomplete data.

Other potential sources of bias

All the included studies used a cross-over design. In all cases the cross-over rule was time. The time period between study days was not always stated, but where details were provided, ranged from consecutive days to within two weeks. To control for the effects of circadian rhythms, tests took place at the same time on each day in all studies. Few studies comment on the existence or effect of outlying values.

Effects of interventions

Outcomes relating to lung function

Pooling all results related to lung function testing, 61 subjects were randomized to receive oral caffeine and placebo, however six

patients did not complete their study protocol. The description of the analysis will follow the list of comparisons used in this Cochrane review and will concentrate on caffeine versus placebo results. Subgroup analyses will highlight the 'low' dose versus 'high' dose and time of final assessment comparisons.

Six studies reported FEV1 outcomes, however data were available for the meta-analyses from only four. Some provided data for more than one time frame comparison as follows: 'short' = four studies, 'medium' = two studies, 'long' = one study. Two studies provided FEF25-75 outcomes, both at the 'short' and 'medium' time frames, but only one at the 'long' time frame. One study provided specific airway conductance (Gaw/VL) data for the 'short' comparison only.

An improvement was seen for all outcomes after ingesting caffeine compared to placebo at all recorded time frames. This effect was statistically significant in all cases except for FEV1 at the 'medium' and 'long' time frames where the confidence intervals crossed the line of no effect.

Results:

FEV1: 'short' (SMD 0.72; 95% CI 0.25 to 1.20), 'medium' (MD 12.66; 95% CI -0.34 to 25.67), 'long' (MD 11.00; 95% CI -6.49 to 28.49).

FEF25-75: 'short' (MD 25.14; 95% CI 11.92 to 38.37), 'medium' (MD 32.72; 95% CI 16.26 to 49.17), 'long' (MD 26.00; 95% CI 5.02 to 46.98).

Gaw/VL: 'short' (MD 30.30; 95% CI 1.08 to 59.52).

Sub-group analysis: 'low' dose

Two studies reported FEV1 outcomes at 'low' dose. Data for the three time frame comparisons came from the following number of studies: 'short' = two studies, 'medium' = one study, 'long' = one study. For FEF25-75 only one study contributed data at all time frames. There were no data for Gaw/VL at this dose.

All lung function parameters tended to improve post caffeine ingestion compared to placebo. For FEV1, this effect was clear only at the 'short' time frame. For FEF25-75, the difference was clear at all times.

Sub-group analysis: 'high' dose

Four studies reported FEV1 outcomes at 'high' dose. Data were available for the meta-analysis from two studies at the 'short' and one study at the 'medium' time frame. No FEV1 data were reported at the 'long' time frame. For FEF25-75, one study only contributed data at the 'short' and 'medium' time frames. One study provided data for Gaw/VL at the 'short' time frame only.

Lung function was found to improve following a 'high' dose of caffeine compared to placebo for all measured outcomes. This

effect was clear at the 'short' time frame only for FEV1 and FEF25-75. A clear improvement in Gaw/VL was also seen at the 'short' time frame.

Two other studies (Duffy 1991; Crivelli 1986) tested the effect of 'high' dose caffeine at the 'short' time frame on FEV1, but no data were extracted for inclusion into the meta-analysis in the original review. However, in correspondence, both authors reported no significant difference in bronchodilation between caffeine and placebo ingestion. For the 2009 update, data were extracted from Crivelli 1986 from the original patient data provided into FEV1 outcomes at 2 hours.

Sub-group analysis: FEV1 outcomes at two hours

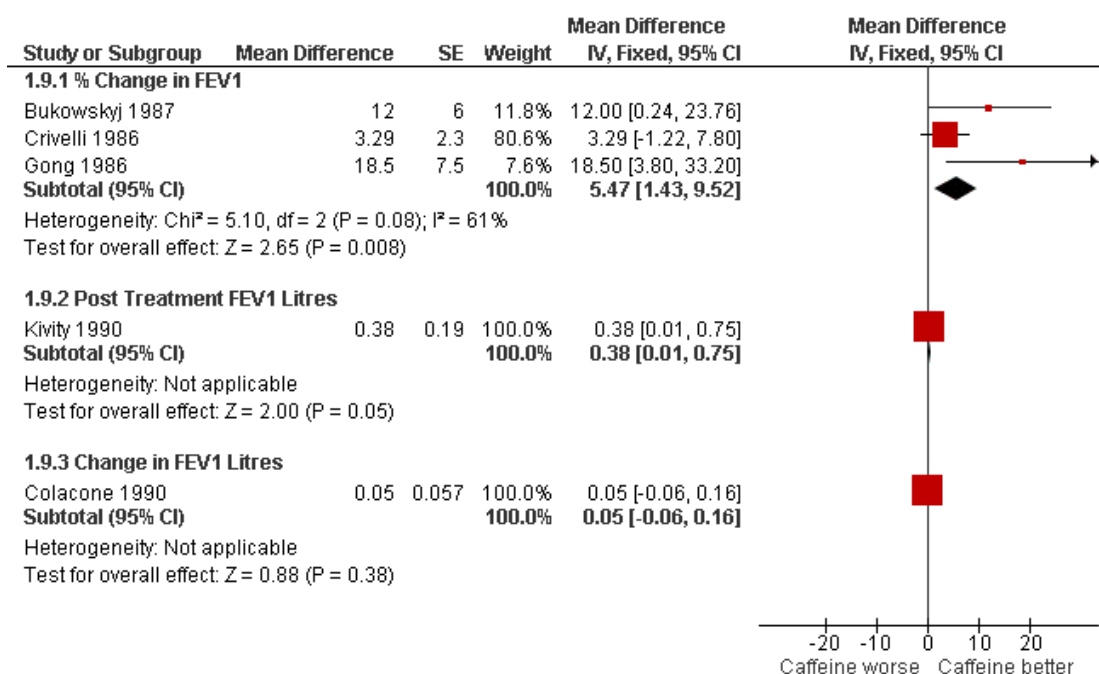
In order to draw an overall conclusion we felt that it would be helpful to have a comparison with as many studies side by side as possible (2009 update). Peak FEV1 readings were recorded at around two hours, so this was chosen as the best time point, see Table 1. Crivelli 1986 reported a reading of FEV1 at 45 min rather than two hours and this data was included in the meta analysis. Data were extracted from the patient data provided in Crivelli 1986. Five studies gave FEV1 readings at 'high' doses

and one gave an additional reading at 'low' dose. The forest plot shows improved FEV1 when patients had consumed caffeine prior to testing, (SMD 0.76; 95% CI 0.32 to 1.20). There was no heterogeneity in the result ($I^2 = 0$) indicating a good agreement in the outcome data between studies.

For this update the paired t-test results were entered into the review using Generic Inverse Variance pooling for the two hour FEV1 outcome. The confidence intervals for each trial were fairly similar to those found previously, when the results had not been analysed with paired t-tests. This provides reassurance that the previous conclusions of the review are valid.

When analysed as % change in FEV1 the pooled result of three trials showed a significant benefit with caffeine at higher dose (MD 5.47%; 95% CI 1.43 to 9.52) see Figure 2. There was significant heterogeneity in this result ($I^2 = 61\%$), but this appears to come from Crivelli 1986; the participants in this trial were asymptomatic and on no treatment for asthma, so would have little potential to increase their FEV1 following caffeine. If the results of the two other trials (Bukowskyj 1987; Gong 1986) are combined this gives a larger mean difference with caffeine of around 15% difference in FEV1 (MD 14.54%; 95% CI 5.35 to 23.72).

Figure 2. Forest plot of comparison: 1 All caffeine doses (highest dose from each study) vs placebo, outcome: 1.10 FEV1 outcomes at 2 hours (High dose).



Serum caffeine levels

The papers differed in their reporting of serum caffeine levels. After a dose of caffeine (5 mg/kg), [Bukowskyj 1987](#) reported a peak serum level of 8.7 (SD = 1.7) µg/mL one hour after ingestion. [Colacone 1990](#) used the same dose, and reported a mean (but not peak) level at 1 hour 45 min of 5.4 (SD = 1.23) µg/mL. [Duffy 1991](#) reported that peak serum levels of caffeine (mean 18.8; 95% CI 12.4 to 25.2 mg/L at 45 min) were observed 45 to 60 min after ingestion of caffeine (10 mg/kg).

Side effects

Five of the studies commented on side effects, including heart rate and blood pressure changes although none contributed data that could be entered in a meta-analysis. No side effects were reported after 'low' doses of caffeine. After ingestion of a 'high' dose of caffeine two patients reported mild tremor ([Kivity 1990](#)), three patients reported nervousness and gastrointestinal upset ([Gong 1986](#)), and one patient withdrew from the study because of nervousness and agitation ([Duffy 1991](#)), which was presumed to be due to the caffeine. Only one study ([Gong 1986](#)) reported significant changes in heart rate (a decrease up to 9%) and blood pressure (an increase up to 12%).

Outcomes relating to exhaled nitric oxide

The impact of caffeine on FeNO was assessed in [Taylor 2004](#). This small study reported no significant difference in exhaled nitric oxide (data reported in the text as non-significant (P = 0.38), and presented graphically). Findings were not significantly different in subgroups for those treated with inhaled steroids and those not treated with steroids.

[Taylor 2004](#) reported that at 60 minutes, serum caffeine levels were higher after ingesting regular caffeine-containing coffee than after decaffeinated coffee at 60 minutes (3.9 versus 0.4 mg/mL respectively). Statistical tests of significance were only reported for within-group differences.

DISCUSSION

The available evidence of the effect of caffeine compared to placebo on lung function and exhaled nitric oxide from randomized controlled trials are summarised in this systematic review.

Summary of main results

For all dose strengths, caffeine compared to placebo was found to significantly improve lung function measured in terms of FEV1, FEF25-75 and Gaw/VL for up to two hours post ingestion. This

effect was sustained for FEF25-75 for over four hours. Improvement was also seen in FEV1 up to this time, however this effect did not reach statistical significance. No data were available for Gaw/VL after two hours. Bronchodilation was also seen after ingesting caffeine even following a 'low' dose (5 mg/kg). For FEV1, the difference between the caffeine and placebo groups was not significant after two hours. In contrast, for FEF25-75 the effect was clear at all times, even over four hours. A clear increase following a 'high' dose of caffeine (>5 mg/kg) compared to placebo was seen in FEV1, FEF25-75 and Gaw/VL at up to two hours only. Gaw/VL outcomes were not recorded beyond two hours. At two hours at all doses, there was an improvement in lung function after ingesting caffeine, and when reported as % increase in FEV1 this showed an average difference of 5% change: (MD 5.47%; 95% CI 1.43 to 9.52). However when the study on patients who were asymptomatic and on no treatment ([Crivelli 1986](#)) was excluded, the change in FEV1 was higher after caffeine (MD 14.54%; 95% CI 5.35 to 23.72).

The size of improvements in lung function were small and at the margins of what would normally be considered clinical significance, (FEV1: maximum 13.7% change from baseline ([Gong 1986](#)), or maximum 330 mL absolute change for caffeine versus placebo ([Kivity 1990](#))). Only one study ([Gong 1986](#)) explicitly recorded the patients' perception; four of the nine participants reported improved breathing following ingestion of a 'high' dose of caffeine, the same information was not provided for the placebo group.

Concerns have been raised as to whether caffeine interferes with the measurement of exhaled nitric oxide levels, based on a randomized study in non-asthmatic healthy volunteers ([Bruce 2002](#)). The only randomized study to date in a small sample of people with mild asthma did not identify a significant difference between a cup of coffee made with 15 g of grounds and a similar cup made with decaffeinated coffee ([Taylor 2004](#)). Additional studies would help to determine whether this finding is valid.

Overall completeness and applicability of evidence

Comparison of the findings across studies was complicated by the use of five different doses of caffeine, different outcome measures recorded at different times, and different methods of reporting outcomes. To permit the aggregation of data the trials were grouped according to dose and time. Similarly, analyses were made using the SMD where the combined trials used different units of measurement for the same variable. Despite this, few data were available to be combined in the meta-analysis.

The dose of caffeine tested varied greatly between studies, from 5 to 10 mg/kg. In an effort to make this more meaningful in dietary terms, most authors related doses to cups of coffee. However, the average amount of caffeine per cup is quoted as between 30 to 150 mg, although 150 mg was most commonly stated. Consequently,

the number of cups of coffee required to produce bronchodilation is reported from one to five cups.

One method of standardising the dose ingested between studies would be to examine the peak serum levels. The reported peak serum levels vary greatly; from 5.4 mg/L (Colacone 1990) to 18.8 mg/L (Duffy 1991). Interestingly, the study reporting serum caffeine level of 18.8 mg/L after a dose of caffeine (10 mg/kg), found no increase in FEV1, although a later protective effect against bronchoconstriction post broncho provocation challenge test was found (Duffy 1991). These data were not presented in a way that would enable extraction for entry into the meta-analysis. Peak serum levels of caffeine tended to occur at 45 or 60 minutes post caffeine intake. However, a clear difference between caffeine and placebo was seen even four hours post ingestion (Bukowskyj 1987). Few studies reported measurements beyond four hours post-dosing. However, serum caffeine was detected in some patients at baseline. It is not known whether this would affect the potential for bronchodilation, especially where lung function outcomes were reported in terms of change from baseline. Even consideration of the peak serum levels would not fully compensate for this.

The findings of any review are only applicable to the characteristics of the participants taking part in the included studies. Although a standardised definition was not used across the studies, participants were described as having mild or moderate asthma, therefore results may not be generalisable to those with more severe asthma. Most subjects were described as having stable or asymptomatic asthma, but how this was assessed was not described. Similarly, patients' treatment regimens varied greatly across the trials and the effect of this was not studied.

It could be argued that insufficient data was presented on side effects resulting from caffeine, however the studies were designed not to assess the long term effects of caffeine, but instead to assess the short term impact of ingesting caffeine on lung function and exhaled nitric oxide tests. The side effects of caffeine are similar to those of theophylline (tachycardia, palpitation, nausea and other gastro-intestinal disturbances, headache, CNS stimulation, insomnia).

The issue arising from this review is not whether caffeine should or should not be used as a bronchodilator in preference for theophylline or whether the side effects are sufficient to override this benefit. Instead the issue is whether or not the amount of caffeine ingested in a cup of coffee (or two) is sufficient to alter the result of a lung function test. This may be important in coffee drinkers who may show a better results in lung function tests than they would achieve if they did not drink coffee. The evidence presented here shows that taking a "normal" amount of caffeine, equivalent to one to five cups of coffee, is enough to alter the results of a lung function test. Therefore patients should be advised not to drink coffee for four hours before taking a lung function test. Drinking coffee before taking a FeNO test does not affect the results according to the single-study data presented here, although further data

is necessary to clarify. The long term impact of drinking coffee was not studied in these trials or reviewed here.

Quality of the evidence

Interpretation of the results of this overview must include consideration of methodological limitations. All of the studies employed a cross-over design. Although the method of allocation was in all cases reported to be randomized, none of the authors assessed order effects, and only two authors explicitly stated that the patients could not discern which treatment they had received (Bukowskyj 1987; Gong 1986). Sample sizes were small and the existence or effect of outlying values were rarely discussed. Outlying values are important in small studies using cross-over designs, as each subject provides a large proportion of the data.

This review was restricted to an analysis of clinically relevant data in terms of a patient response and excluded the scientific issue of whether caffeine affects airway response to bronchoconstricting agents.

Potential biases in the review process

The possibility of publication bias (non-publication of negative studies) should be considered given that only small differences in bronchodilator effect were found between caffeine and placebo. However, we used a comprehensive search strategy and searched for unpublished trials in an attempt to minimise this bias.

Agreements and disagreements with other studies or reviews

No other published reviews.

AUTHORS' CONCLUSIONS

Implications for practice

Caffeine, even at 'low' doses, has been found to improve lung function for at least four hours after ingestion. One trial using the most sensitive outcome measurements (FEF25-75) showed that effects are sustained for over four hours post ingestion. It is therefore recommended that patients be advised to withhold caffeine for at least four hours prior to lung function testing. Alternatively lung function tests results should be considered in light of caffeine ingested within four hours of the start of the test as coffee drinkers may present with a better lung function test result than if they had not consumed so much caffeine. Caffeine does not appear to have a significant effect on exhaled nitric oxide levels.

With regard to advice to patients, caffeine ingestion may improve lung function in the short term. However, these trial data do not

indicate whether the effect reaches a threshold for clinical significance in terms of an improvement of symptoms or quality of life. This was not the purpose of trials examined in this review. It is not known if tolerance to the bronchodilatory effects of caffeine develops in habitual consumers, which is a concern given that tolerance has been found in studies of sleep and renal function (Curatolo 1983). The amount of dietary caffeine required and the true benefit of dietary caffeine intake would be difficult to calculate due to the varying levels of caffeine within different foods and beverages. It appears that a substantial intake of caffeinated products would be needed to achieve a beneficial bronchodilatory effect and that possible undesirable side-effects may outweigh the benefits.

Implications for research

That caffeine has a bronchodilatory effect in asthma is clear from existing research. Future studies could address:

1. Patients' perception of the effect of caffeine on their asthma and quality of life, as this has not been systematically studied.
2. The maximum length of time at which bronchodilation is sustained, as this cannot be determined from existing trials.

3. Effects on patients with different levels of asthma severity, since existing trials have only studied people with mild to moderate asthma.

4. The response to caffeine of well-controlled asthmatics on anti-inflammatory agents. Asthmatics using inhaled steroids may be less responsive and this needs further evaluation.

5. Differences in the bronchodilator effects of caffeine between habitual consumers and non-consumers.

6. Whether caffeine ingestion alters management decision in asthma (based on lung function measurements).

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Bukowskyj 1987

Methods	Randomised controlled trial. Crossover design - double-blinded, run = time (1 week).
Participants	Ten patients admitted, eight (four male) completed the study. Mean age 64.8 (SD = 8) years. Severity of asthma: Inclusion criteria: reversible obstructive airway disease, clinically stable, FEV1 < 75% predicted value. Exclusion criteria: congestive heart failure, hepatic disease, ingestion of cimetidine, ingestion of oral contraceptives. Prescribed medication: Seven patients took oral theophylline and salbutamol; three patients took inhaled beclomethasone dipropionate; one patient took inhaled beclomethasone dipropionate and prednisolone. Control measure: Refrained from caffeine, other methylxanthine-containing substances and orally administered beta-agonists for 12 h prior to and throughout eight h study. Refrained from inhaling beta-agonists for six h prior to and throughout the eight h study period.
Interventions	5 mg/kg caffeine vs placebo as a solution in a juice drink.
Outcomes	% change FEV1, % change FVC, % change FEF25-75, % change Vmax50, % change Vmax25, FEV1 % predicted, pulse, blood pressure.
Notes	Administration of corticosteroids was continued unchanged in those patients receiving long-term therapy with these drugs.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Yes	Allocated by pharmacist.
Blinding? All outcomes	Yes	Quote: Double-blinded Quote: The medication code was known only to the hospital pharmacists.
Incomplete outcome data addressed? All outcomes	Yes	Quote: The two patients who withdrew did so because they found the repeated spirometric tests unacceptably tiring. There was one patient who completed the study except for the last four h of the placebo day

Bukowskyj 1987 (Continued)

		when she developed dyspnea. No data used from these patients
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Colacone 1990

Methods	Randomised controlled trial. Crossover design, run = time (variable, within two weeks).
Participants	Ten adults (seven male) completed the study. Mean age 46 (SD = 17) years. Asthma severity: Mild. Nine patients had previously documented increased airways reactivity, and one had seasonal asthma. Symptom free. Prescribed medication: Seven patients took inhaled beta-agonist, five patients took theophylline, four patients took inhaled corticosteroid and two required no medication. Control measures: No caffeine 48 h before study. Fasted for eight h. Withheld antiasthmatic medications according to standard guidelines for histamine bronchoprovocation testing. Beta-agonists and anticholinergic drugs withheld for 8 to 12 h and theophylline for 12 h before testing. Slow release theophylline and antihistamines withheld 48 h before testing. Steroids continued as normal.
Interventions	5 mg/kg caffeine vs placebo in a juice drink solution indistinguishable in taste and smell. Histamine bronchoprovocation challenge.
Outcomes	change in FEV1, PC20.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Yes	Allocated by pharmacist.
Blinding? All outcomes	Yes	Quote: Caffeine and corresponding placebo were prepared in solution and coded by the hospital pharmacy. Quote: Both solutions were indistinguishable by taste, colour and smell.
Incomplete outcome data addressed? All outcomes	Yes	No dropouts.

Crivelli 1986

Methods	Randomised controlled trial. Crossover design rule = time (two consecutive days).
Participants	Seven adults (six male) completed the study. Age range 27 to 40 years. Asthma severity: Asymptomatic. Included: patients with documented asthmatic airway obstruction. Excluded: Pregnant women asthmatic patients with concomitant liver and/or cardiovascular diseases, and patients treated with drugs affecting the hepatic microsomal enzyme system (barbiturates, phenytoin, rifampicin etc). Prescribed medication: no bronchodilators, sodium cromoglycate, or steroids for at least two weeks before the investigation. Control measures: Withheld all caffeine and methyl xanthine-containing foods and beverages at least 12 h prior to the experiment.
Interventions	6 mg/kg caffeine vs placebo. Orange juice drink containing caffeine or a placebo drink containing solvent i.e. saline. Carbachol challenge.
Outcomes	FEV1, SGaw.
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Unclear	Method of allocation unknown.
Blinding? All outcomes	Unclear	Described as "double-blind" but caffeine or saline given in orange juice so may not have tasted the same
Incomplete outcome data addressed? All outcomes	Yes	No dropouts

Duffy 1991

Methods	Randomised controlled trial. Crossover design - double-blinded, rule = time (not stated).
Participants	12 adults (11 male) admitted, 11 males completed the study. Age range 18 to 42 years. Inclusion criteria: FVC and FEV1 > 80% predicted, and at least 10 % fall in FEV1 in response to EVH (eucapnic voluntary hyperventilation) broncho provocation. Non-smokers. Exclusion criteria: Upper respiratory tract infection or influenza vaccination within six

Duffy 1991 (Continued)

	<p>weeks before testing, an episode of asthma requiring hospitalisation or steroids within the previous six weeks before testing, pregnancy, or other cardiovascular disease apart from asthma.</p> <p>Prescribed medication: no daily asthma medication.</p> <p>Control measures: Refrain from caffeine and methylxanthine-containing substances for 12 hours, and food and cigarettes for four hours before testing.</p>
Interventions	<p>5 mg/kg, 10 mg/kg, placebo.</p> <p>EVH broncho provocation.</p>
Outcomes	<p>FEV1, FVC, %dFEV (the percentage fall in FEV1, after EVH).</p>
Notes	<p>Quote: 8 of 11 subjects had detectable caffeine levels on the day placebo was given, despite explicit instructions for avoidance of xanthine-containing products.</p>

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Unclear	Quote: on three separate test days, each individual received, in random order, either placebo, 5 mg/kg caffeine or 10 mg/kg caffeine.
Blinding? All outcomes	Yes	Quote: After baseline pulmonary function tests, caffeine was given in a randomized, crossover, double blind fashion. Gelatin capsules were administered which contained either 0 mg, 5 mg/kg, or 10 mg/kg caffeine.
Incomplete outcome data addressed? All outcomes	Yes	Dropout = One (female). Due to side effects of nervousness and agitation presumably from the caffeine.

Gong 1986

Methods	<p>Randomised controlled trial. Method of allocation computer program.</p> <p>Crossover design - double-blinded, rule = time (at least three days).</p>
Participants	<p>Nine, (four male).</p> <p>Mean age = 35 (SD = 17) years</p> <p>Inclusion criteria: Stable asthma (ATS criteria), 12 years of mild to moderately severe asthma, allergic in nature for seven subjects, no other clinically evident disorders including hepatic disease or hypertension.</p> <p>Exclusion criteria: No subject was receiving immunotherapy</p>

Gong 1986 (Continued)

	<p>Prescribed medication: seven = theophylline, eight = sympathomimetic agents, three = inhaled corticosteroids, one = oral corticosteroids, one = cromolyn sodium.</p> <p>Control measures: fasted for four hours prior to study and withheld the following prior to each day of study: theophylline compounds (48 h); adrenergic agents, oral (12 h) and inhaled (8 h); corticosteroids, oral (24 h) and inhaled (12 h); cromolyn sodium (24 h); antihistamines (48 h); caffeine-containing beverages and medications (12 h).</p>
Interventions	<p>Decaffeinated coffee (containing ~13 mg caffeine) plus a capsule containing aminophylline (200 mg).</p> <p>Decaffeinated coffee (containing ~13 mg caffeine) plus a placebo (lactose) capsule.</p> <p>Decaffeinated coffee with additional 150 mg caffeine plus a placebo (lactose) capsule.</p> <p>Decaffeinated coffee with additional 300 mg caffeine plus a placebo (lactose) capsule.</p> <p>Decaffeinated coffee with additional 450 mg caffeine plus a placebo (lactose) capsule.</p>
Outcomes	<p>% change FEV1, FVC, FEF25-75, Gaw/VL (results given only for 7.2 mg/kg caffeine vs placebo + 200mg aminophylline). Sampling of venous blood, whole body plethysmography, spirometry, respiratory rate, heart rate, sitting blood pressure, and symptoms.</p>

Notes

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Randomized by computer program.
Allocation concealment?	Unclear	No details
Blinding? All outcomes	Yes	Although they went to lengths to blind the patients, there was no indication of method for blinding investigators.
Incomplete outcome data addressed? All outcomes	Yes	No dropouts

Kivity 1990

Methods	<p>Randomised controlled trial.</p> <p>Crossover design - double-blinded, run = time (within two weeks).</p>
Participants	<p>13 admitted, 10 adults (seven male) completed the study</p> <p>Mean age = 19.5 (SD = 1.1) years.</p> <p>Inclusion criteria: documented reversible obstructive airway disease with a 20% improvement in either FVC or FEV1 after bronchodilator therapy, exercise-induced drop in FEV1 of ≥15% from baseline, all patients clinically stable.</p> <p>Exclusion criteria: any other chronic illness or receiving medication other than for bronchial asthma.</p> <p>Prescribed medication: Two = slow release theophylline, ten = inhaled salbutamol. None</p>

Kivity 1990 (Continued)

	of the patients were receiving corticosteroids, cromolyn sodium, or ketotifen.
Interventions	Opaque placebo capsule or opaque 3.5 mg/kg caffeine capsule or opaque 7 mg/kg caffeine capsule taken with 100 mL water. Exercise-induced bronchoconstriction.
Outcomes	FEV1, pulse, blood pressure.
Notes	Patients refrained from caffeine for 12 h, from theophylline containing drugs for 48 h, and from inhaled beta-agonists eight hours prior to the study. The patient did not have caffeinated drinks 24 h prior to the study day (conflicting information in paper). The patients did not eat during the study.

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Unclear	No details
Blinding? All outcomes	Yes	Quote: Caffeine and placebo were given through an opaque capsule together with 100 mL of water. Stated double-blind
Incomplete outcome data addressed? All outcomes	Yes	Quote: three patients who withdrew from the study could not comply with multiple visits to the clinic. No data used from these patients.

Taylor 2004

Methods	Randomised, double-blind, crossover trial.
Participants	20 adults (gender not specified) completed the study. Mean age: 37 (range 16 to 73) years. Inclusion criteria: regular coffee drinkers; FeNO >10 PPB. 10 steroid naive and 10 treated with ICS (mean dose 980 µg/d). Exclusion criteria: oral prednisone, oral theophylline, or inhaled long-acting beta-agonist for one month prior to study. Control measures: caffeine withheld for 24 hours. Inhaled bronchodilators withheld six hours.
Interventions	Intervention: 15 g caffeine-containing coffee (Illy Espresso Caffè Macinato) prepared in an espresso coffee maker as a 200 mL cup of coffee. Placebo: 15 g decaffeinated coffee (Illy Espresso Decaffeinated Macinato) prepared in an espresso coffee maker as a 200 mL cup of coffee.

Taylor 2004 (Continued)

Outcomes	FeNO.	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	No details
Allocation concealment?	Unclear	Stated randomized, no information given on method used.
Blinding? All outcomes	Unclear	Stated double-blind, but patient blinding depends on regular and decaffeinated coffee being indistinguishable by taste. No mention of researcher blinding.
Incomplete outcome data addressed? All outcomes	Yes	No dropouts.

Characteristics of excluded studies [ordered by study ID]

Becker 1984	Participants are children. Interventions are caffeine vs theophylline.
Henderson 1993	Histamine broncho provocation challenge, (FEV1 measured after challenge).
Simmons 1983	Not RCT

DATA AND ANALYSES

Comparison 1. All caffeine doses vs placebo

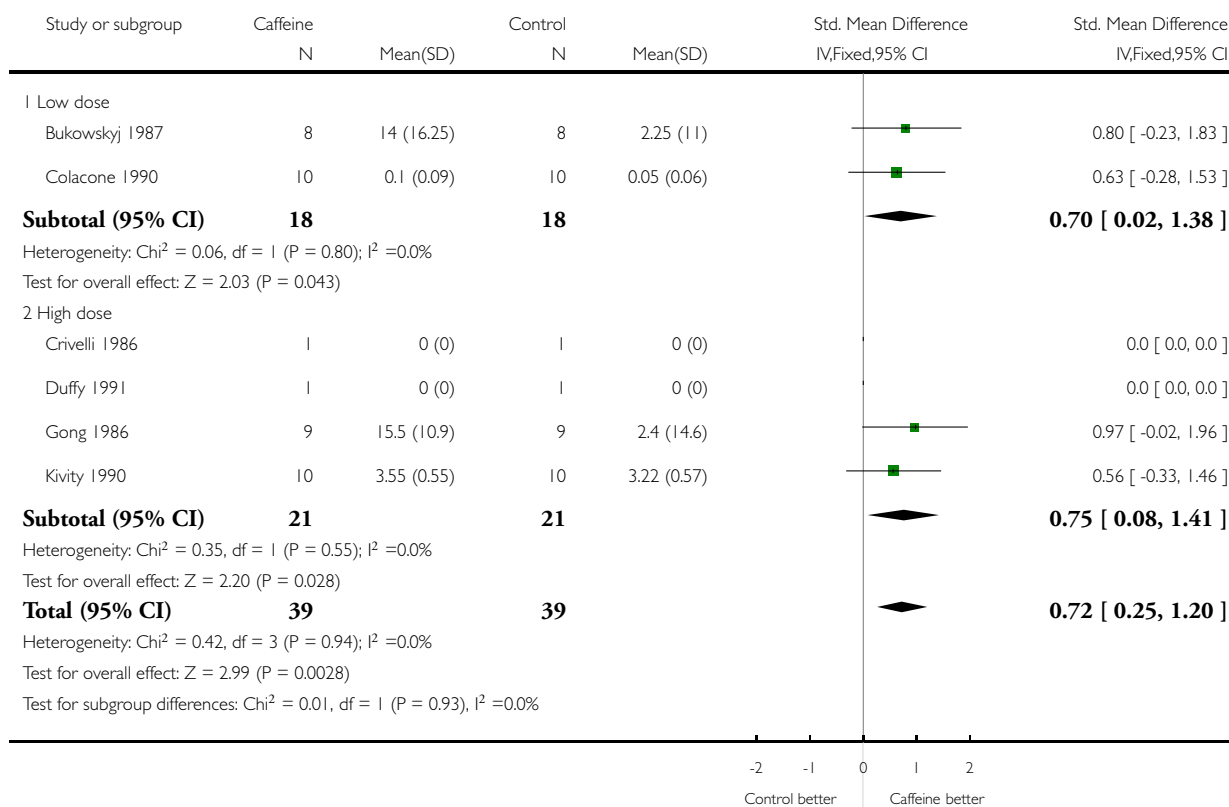
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 FEV1 outcomes at 'short' time frame	6	78	Std. Mean Difference (IV, Fixed, 95% CI)	0.72 [0.25, 1.20]
1.1 Low dose	2	36	Std. Mean Difference (IV, Fixed, 95% CI)	0.70 [0.02, 1.38]
1.2 High dose	4	42	Std. Mean Difference (IV, Fixed, 95% CI)	0.75 [0.08, 1.41]
2 FEV1 outcomes at 'medium' time frame	2	34	Mean Difference (IV, Fixed, 95% CI)	12.66 [-0.34, 25.67]
2.1 Low dose	1	16	Mean Difference (IV, Fixed, 95% CI)	11.5 [-7.44, 30.44]
2.2 High dose	1	18	Mean Difference (IV, Fixed, 95% CI)	13.7 [-4.18, 31.58]
3 FEV1 outcomes at 'long' time frame	1	16	Mean Difference (IV, Fixed, 95% CI)	11.0 [-6.49, 28.49]
3.1 Low dose	1	16	Mean Difference (IV, Fixed, 95% CI)	11.0 [-6.49, 28.49]
3.2 High dose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
4 FEF 25-75 outcomes at 'short' time frame	2	34	Mean Difference (IV, Fixed, 95% CI)	25.14 [11.92, 38.37]
4.1 Low dose	1	16	Mean Difference (IV, Fixed, 95% CI)	23.33 [6.18, 40.48]
4.2 High dose	1	18	Mean Difference (IV, Fixed, 95% CI)	27.8 [7.03, 48.57]
5 FEF 25-75 outcomes at 'medium' time frame	2	34	Mean Difference (IV, Fixed, 95% CI)	32.72 [16.26, 49.17]
5.1 Low dose	1	16	Mean Difference (IV, Fixed, 95% CI)	35.5 [15.85, 55.15]
5.2 High dose	1	18	Mean Difference (IV, Fixed, 95% CI)	26.20 [-3.89, 56.29]
6 FEF 25-75 outcomes at 'long' time frame	1	16	Mean Difference (IV, Fixed, 95% CI)	26.0 [5.02, 46.98]
6.1 Low dose	1	16	Mean Difference (IV, Fixed, 95% CI)	26.0 [5.02, 46.98]
6.2 High dose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
7 Gaw/VL outcomes at 'short' time frame	1	18	Mean Difference (IV, Fixed, 95% CI)	30.30 [1.08, 59.52]
7.1 Low dose	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable
7.2 High dose	1	18	Mean Difference (IV, Fixed, 95% CI)	30.30 [1.08, 59.52]
8 FEV1 outcomes at 2 hours	5		Std. Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Low dose	1	20	Std. Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.49, 1.29]
8.2 High dose	5	88	Std. Mean Difference (IV, Fixed, 95% CI)	0.76 [0.32, 1.20]
9 FEV1 outcomes at 2 hours (High dose)	5		Mean Difference (Fixed, 95% CI)	Subtotals only
9.1 % Change in FEV1	3		Mean Difference (Fixed, 95% CI)	5.47 [1.43, 9.52]
9.2 Post Treatment FEV1 Litres	1		Mean Difference (Fixed, 95% CI)	0.38 [0.01, 0.75]
9.3 Change in FEV1 Litres	1		Mean Difference (Fixed, 95% CI)	0.05 [-0.06, 0.16]

Analysis 1.1. Comparison 1 All caffeine doses vs placebo, Outcome 1 FEV1 outcomes at 'short' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 1 FEV1 outcomes at 'short' time frame

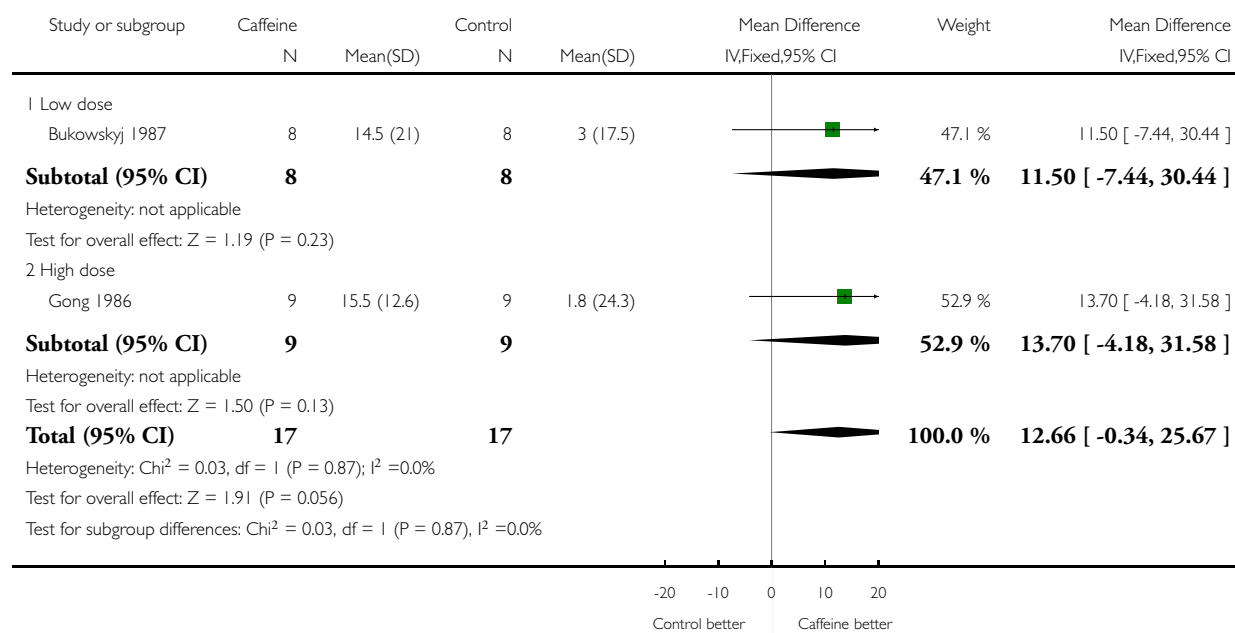


Analysis 1.2. Comparison 1 All caffeine doses vs placebo, Outcome 2 FEV1 outcomes at 'medium' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 2 FEV1 outcomes at 'medium' time frame

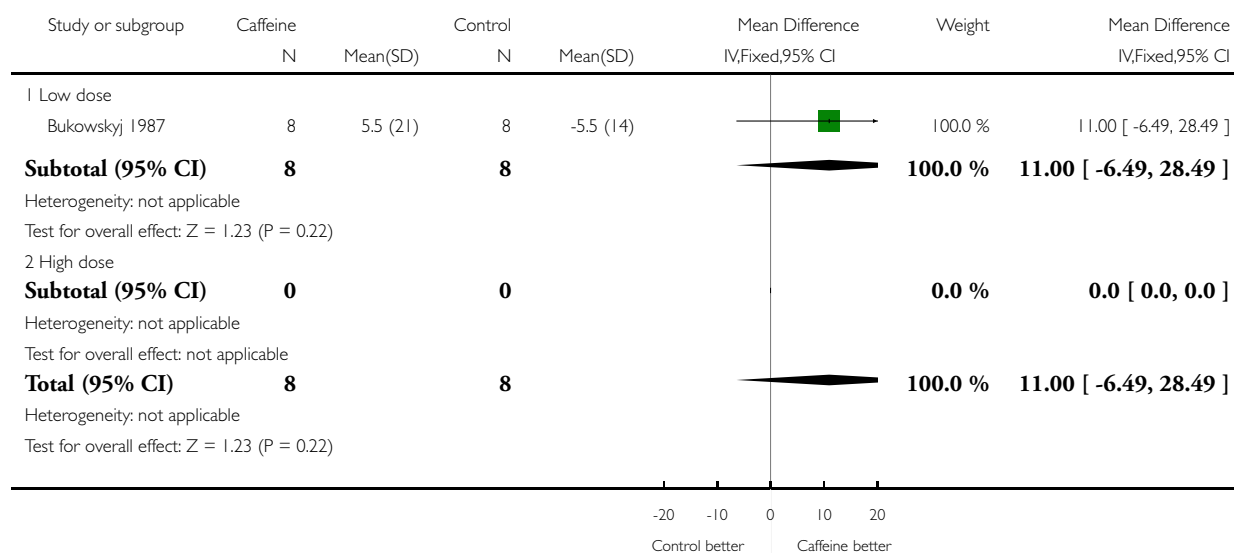


Analysis 1.3. Comparison 1 All caffeine doses vs placebo, Outcome 3 FEV1 outcomes at 'long' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 3 FEV1 outcomes at 'long' time frame

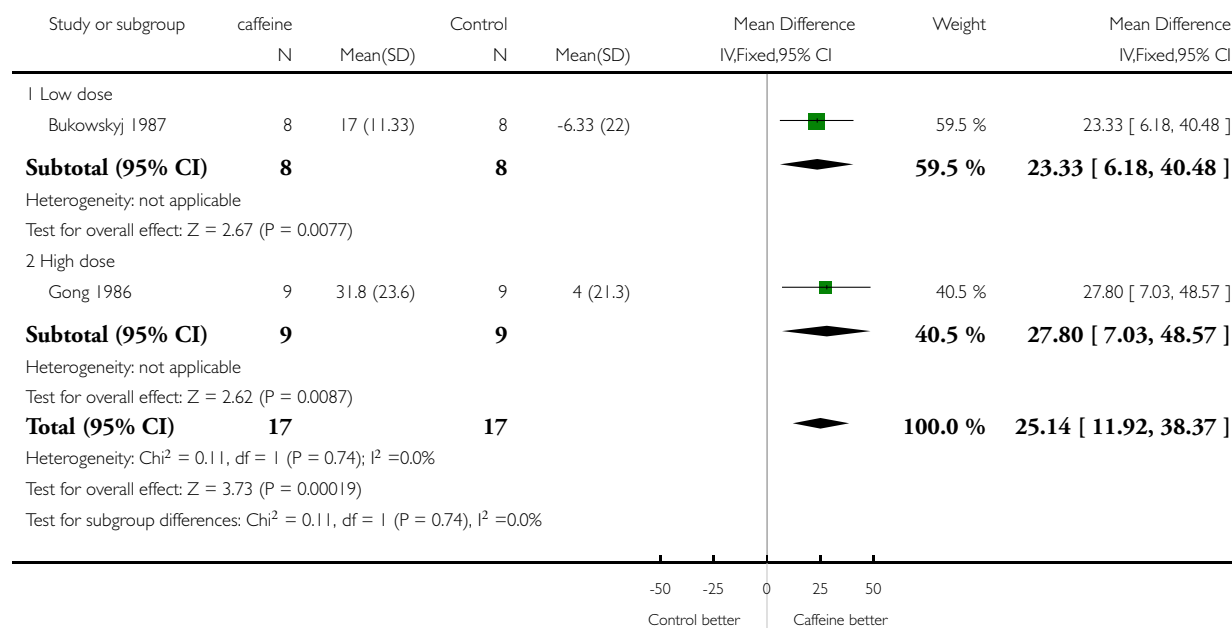


Analysis 1.4. Comparison 1 All caffeine doses vs placebo, Outcome 4 FEF 25-75 outcomes at 'short' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 4 FEF 25-75 outcomes at 'short' time frame

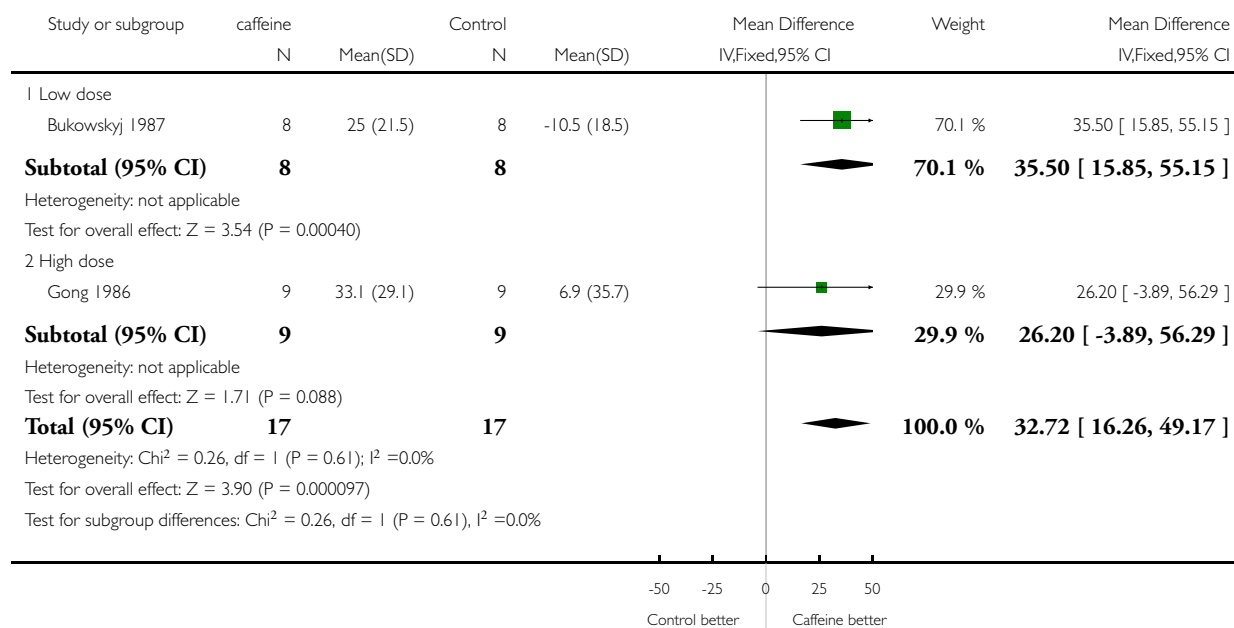


Analysis 1.5. Comparison 1 All caffeine doses vs placebo, Outcome 5 FEF 25-75 outcomes at 'medium' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 5 FEF 25-75 outcomes at 'medium' time frame

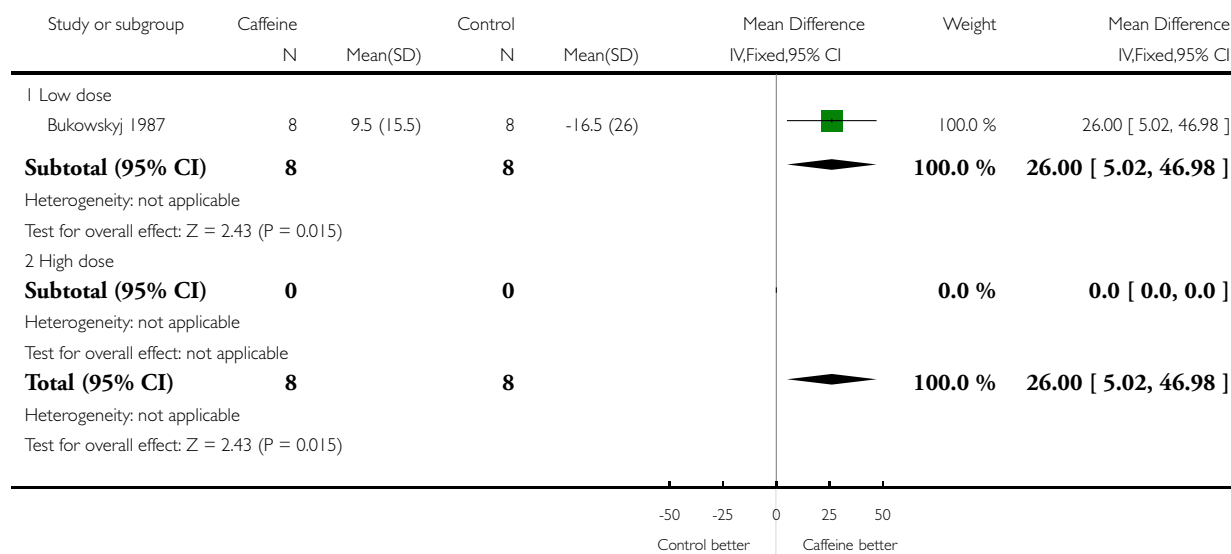


Analysis 1.6. Comparison 1 All caffeine doses vs placebo, Outcome 6 FEF 25-75 outcomes at 'long' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 6 FEF 25-75 outcomes at 'long' time frame

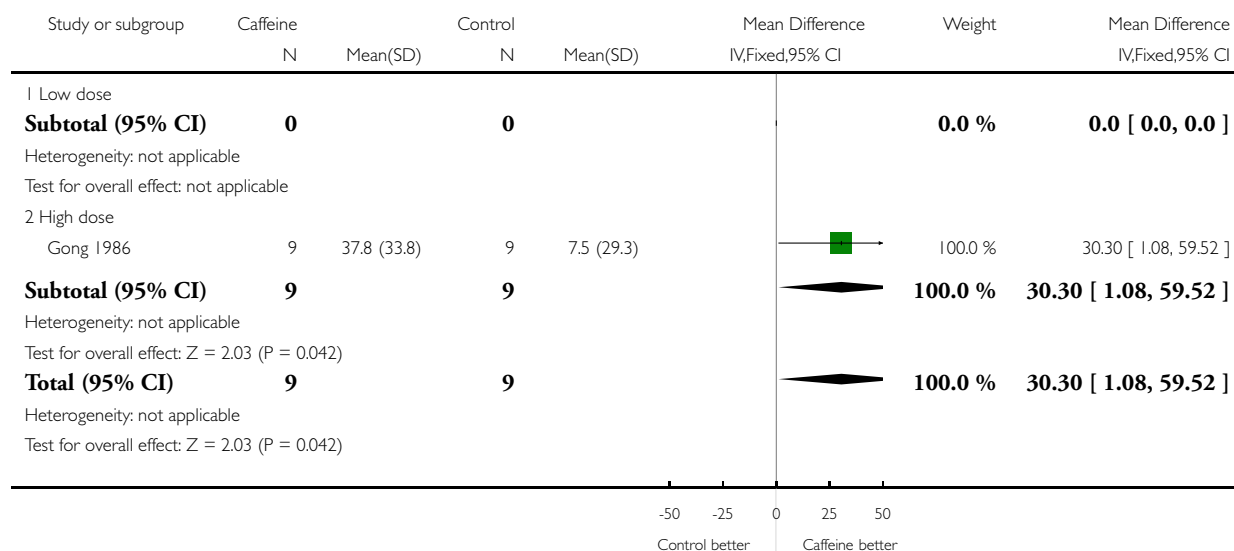


Analysis 1.7. Comparison 1 All caffeine doses vs placebo, Outcome 7 Gaw/VL outcomes at 'short' time frame.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 7 Gaw/VL outcomes at 'short' time frame

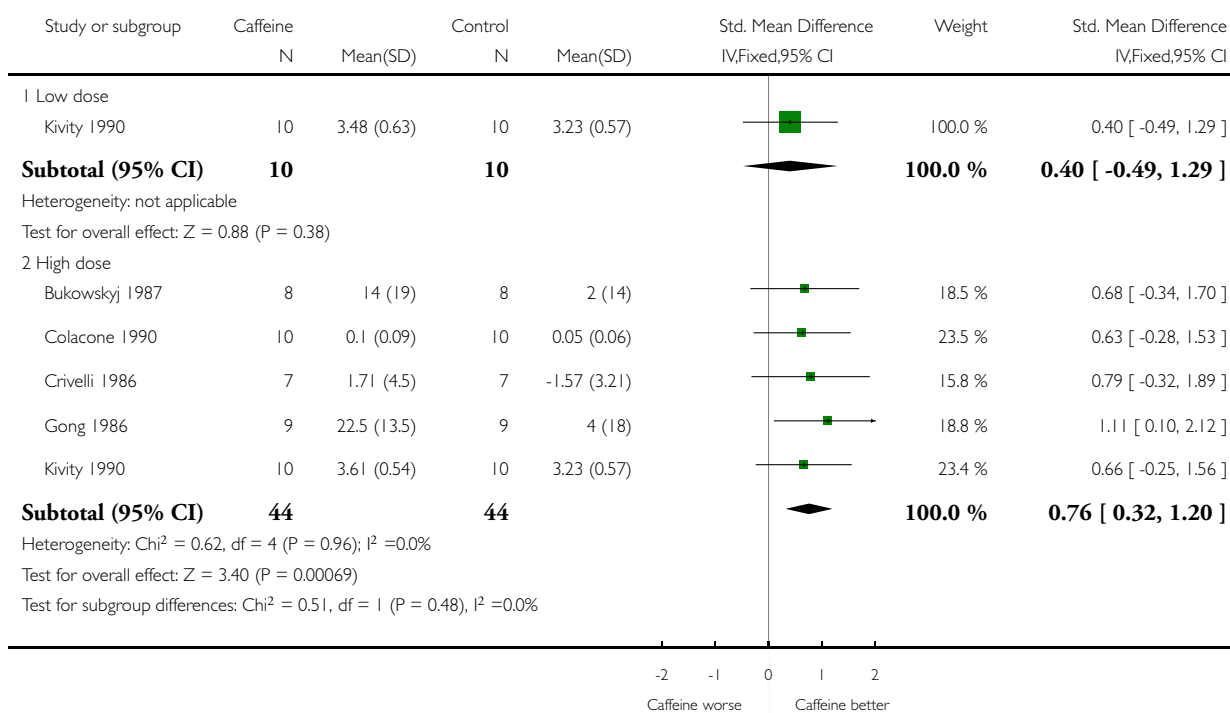


Analysis 1.8. Comparison 1 All caffeine doses vs placebo, Outcome 8 FEV1 outcomes at 2 hours.

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 8 FEV1 outcomes at 2 hours

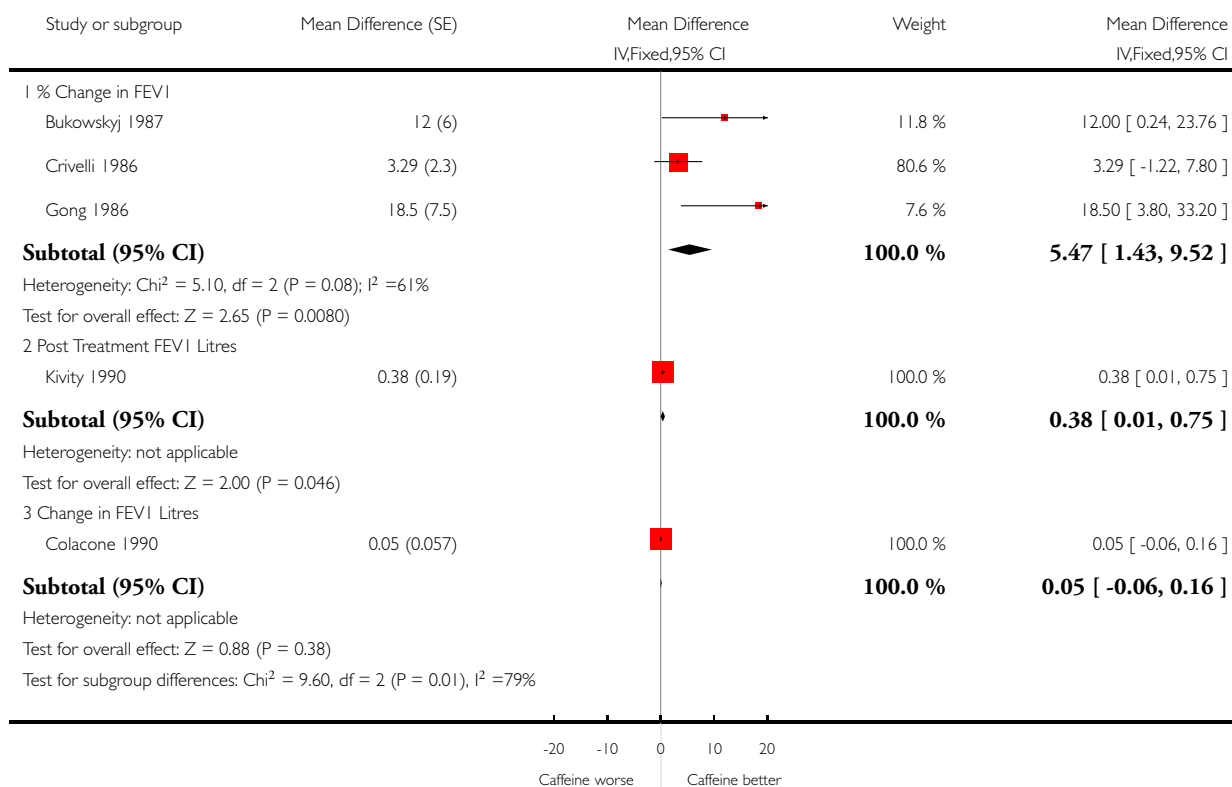


Analysis 1.9. Comparison 1 All caffeine doses vs placebo, Outcome 9 FEV1 outcomes at 2 hours (High dose).

Review: Caffeine for asthma

Comparison: 1 All caffeine doses vs placebo

Outcome: 9 FEV1 outcomes at 2 hours (High dose)



FEEDBACK

Historical use of caffeine

Summary

Reading the “Background” in the Abstract, it seems that the interest by caffeine as a bronchodilator is new. As a matter of fact, caffeine is used for asthma since, at least, the last decades of 1800. We can find reference to this drug in Marcel Proust’s “A l’Ombre de Jeunes Filles en Fleur”. This author, an asthmatic, refers that when he was very young (he was born in 1871) he used caffeine “that was prescribed for help me breathing”.

Reply

Thank you for this comment.

Contributors

Roni Marques, chest physician.

WHAT'S NEW

Last assessed as up-to-date: 5 August 2009.

29 September 2009	New citation required but conclusions have not changed	New authorship of the review.
27 August 2009	New search has been performed	New search conducted, added new included study (Taylor 2004), amendments made to plain language summary, reformatted results and discussion and added risk of bias and summary of findings table. Conclusions unchanged.

HISTORY

Protocol first published: Issue 3, 1996

Review first published: Issue 2, 1998

21 July 2008	Amended	Converted to new review format.
7 January 2005	New search has been performed	New studies found and included or excluded: 8/1/05
8 January 2003	New search has been performed	New studies sought but none found: 8/1/03
18 June 2001	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Anna Bara and Elizabeth Barley extracted the data, did the meta-analyses and drafted the original review.

Emma Welsh updated the review, reformatted and redrafted it, added a new included study ([Taylor 2004](#)), added risk of bias and summary of findings table. Chris Cates extracted data for the risk of bias table, carried out the GIV analyses and edited the review update.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- NHS Research and Development, UK.

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The 2009 update included regular caffeine-containing coffee versus decaffeinated coffee as a comparison type. The 2009 review also compared lung function at all doses at 2 hours.

INDEX TERMS

Medical Subject Headings (MeSH)

*Respiratory Function Tests; Asthma [diagnosis; *drug therapy]; Bronchi [drug effects]; Bronchodilator Agents [*pharmacology]; Caffeine [*pharmacology]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans