OSAHS

Study	**Kennedy 2019[110]**
Study type	Systematic Review
Number of studies (number of participants)	N=48 studies Studies that were randomised and controlled, either parallel group or cross-over design, including those that were single-blind.
Countries and setting	Conducted in Multiple countries; Setting: Hospital
Line of therapy	Mixed line
Duration of study	Intervention + follow up: 2 weeks to 2 years
Method of assessment of guideline condition	Yes
Stratum	-Moderate -severe
Subgroup analysis within study	Not applicable
Inclusion criteria	Randomised parallel group or crossover trials in people with OSA. studies that compared auto-titrating CPAP (auto-CPAP), Bi-level PAP (non-invasive ventilation), or the addition of heated humidification to CPAP with fixed pressure CPAP alone
Exclusion criteria	Trials assessing interventions in people with central sleep apnoea and where sleep apnoea was related to sleeping position. Excluded studies that were conducted as short-term laboratory based interventions, since

	they did not intend to capture the effects of interventions administered on a nightly basis at home. Excluded studies that were less than two weeks in duration because we were primarily interested in the effects of pressure modification in the context of ongoing use of CPAP.
Recruitment/selection of patients	Participants had to be randomised in trials assessing one of the following comparisons: 1. Automatically adjusted-CPAP (auto-CPAP including forced oscillation technique) versus fixed CPAP (fixed pressure setting); 2. Bi-level PAP (non-invasive ventilation) versus fixed CPAP; 3. Humidification plus CPAP versus fixed CPAP;
Age, gender and ethnicity	Average age of the study populations ranged between 49 and 55 and average body mass index was between 32 and 35 kg/m2. Baseline sleep disruption as measured by AHI was severe and ESS scores indicated that the study populations had excessive daytime sleepiness (11 to 16). One study recruited people with co-existing sleep apnoea and obesity hypoventilation syndrome (Masa 2015).
Further population details	Participants were adults of either sex with a diagnosis of OSA, based on history and results of sleep studies. The sleep studies were either oximetry studies showing desaturation index (DI) of at least 5 per hour or of respiratory movements and airflow to give an apnoea hypopnoea index (AHI) of at least 5 per hour.
Extra comments	The majority of studies excluded participants who had previously used CPAP. Most studies were conducted in Europe and North America. A smaller number of trials were conducted in Australia, Hong Kong ,New Zealand and Thailand. The median study sample size is 40 (range 10 to 322). Average study duration was between 12 and 16 weeks in studies comparing auto-CPAP or Bi-level PAP with fixed pressure CPAP. Studies comparing additional humidification with fixed pressure CPAP had shorter average durations (6 weeks respectively). The use of standard CPAP titration protocols was common across the studies. Most were conducted over one or two nights, with the exception of Pépin 2016 where home based pressure titration occurred over eight nights

Indirectness of population	No indirectness
Interventions	Intervention 1 :Automatically adjusted CPAP (auto-CPAP) compared with fixed CPAP (n=36 studies; 2135 participants): Duration between 12 and 16 weeks Indirectness: No indirectness Intervention 2 Non-invasive ventilation with fixed pressure CPAP (n= 6 studies ; 325 participants) Duration between 12 and 16 weeks Indirectness: No indirectness Intervention 3 addition of humidification to fixed pressure CPAP (n= 6 studies ; 359 participants) Duration 6 weeks. Indirectness: No indirectness
Funding	The majority of the included studies were funded by industry

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Auto-CPAP versus fixed CPAP

Protocol outcome 1: Machine usage (hours/night)
- Actual outcome: Machine usage (hours/night); MD 0.21 [95% CI 0.11 to 0.31];

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Number of participants who used CPAP therapy > 4 hours per night
- Actual outcome: Number of participants who used CPAP therapy > 4 hours per night; RR; 1.06 [95% CI 0.90, 1.24]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Machine usage (frequency of usage as % of days)
- Actual outcome: Machine usage (frequency of usage as % of days); MD; 1.60 [95% CI -0.83 to 4.03]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Machine usage (% of nights of > 4 hours of use) - crossover studies
- Actual outcome: Machine usage (% of nights of > 4 hours of use) - crossover studies; MD; 6.25 [95% CI -0.05 to12.54]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 5: Symptoms (Epworth Sleepiness Scale)
- Actual outcome: Symptoms (Epworth Sleepiness Scale); MD; -0.44 [95% CI -0.72, to -0.16]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 6: Withdrawals (parallel group trials/first arm crossover trials)
- Actual outcome: Withdrawals (parallel group trials/first arm crossover trials); RR 0.91 [95% CI 0.67, 1.24]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 7: Quality of life (Functional Outcome of Sleep Questionnaire)
- Actual outcome: Quality of life (Functional Outcome of Sleep Questionnaire); MD 0.12 [95% CI -0.21, 0.46]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness.

Protocol outcome 8: Quality of life (Sleep Association Quality of Life Index)
- Actual outcome: Quality of life (Sleep Association Quality of Life Index); MD -0.14 [95% CI -0.54, 0.27]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 9: Quality of life (SF-36 questionnaire) physical
- Actual outcome: 0.76 [-3.50, 5.01]; MD 0.76 [-3.50, 5.01]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 10: QOL (SF-36)
- Actual outcome: Role physical ; MD -3.73 [95% CI -13.46, 6.01]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 11: QOL SF-36
- Actual outcome: bodily pain ; MD 4.21 [95% CI -4.23, 12.64]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 12: QOL SF-36
- Actual outcome: general health; MD 2.49 [955 CI -4.99, 9.97]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 13: QOL SF-36
- Actual outcome: vitality ; MD 1.32 [-1.25, 3.88]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 14: QOL SF-36
- Actual outcome: social functioning ; MD 3.31 [-4.29, 10.92]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 15: QOL SF-36
- Actual outcome: role emotional ; MD 0.70 [-4.19, 5.59]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 16: QOL SF-36
- Actual outcome: mental health ; MD; 0.20 [95% CI -1.88 to 2.27]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 17: Apnoea Hypopnoea Index (events/hr)
- Actual outcome: Apnoea Hypopnoea Index (events/hr); MD 0.48 [95% CI 0.16, 0.80]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 18: Arousals (events/hr)
- Actual outcome: Arousals (events/hr); MD -0.66 [955 CI -2.90, 1.58]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 19: Pressure of CPAP treatment (cm H_2O)
- Actual outcome: Pressure of CPAP treatment (cm H_2O); MD -1.49 [-2.12, -0.85]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 20: Systolic blood pressure [mmHg]
- Actual outcome: Systolic blood pressure [mmHg]; MD ; 1.87 [-1.08, 4.82]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 21: Diastolic blood pressure [mmHg]
- Actual outcome: Diastolic blood pressure [mmHg]; MD 4.01 [-1.46, 9.49]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 22: 24 hour mean BP
- Actual outcome: 24 hour mean BP; MD 0.59 [95% CI -1.05, 2.22]

Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 23: 24 hour systolic BP
- Actual outcome: 24 hour systolic BP; MD -0.15 [95% CI -2.21, 1.91]

Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 24: 24 hour diastolic BP
- Actual outcome: 24 hour diastolic BP; MD 0.90 [-0.65, 2.44]

Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 25: Tolerability outcomes
- Actual outcome Intolerable treatment pressure; RR 0.90 (0.66 , 1.23);
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 26: Tolerability outcomes
- Actual outcome: mask leak ;RR 1.11 (0.74, 1.66)
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 27: Tolerability outcomes
- Actual outcome: dry mouth ; RR 0.82 (0.61, 1.10); ;
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 28: Tolerability outcomes
- Actual outcome: stufyf nose; RR 0.98 (0.63, 1.54);
Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 29: Patient preference (auto-CPAP/not auto-CPAP)
- Actual outcome: Patient preference (auto-CPAP/not auto-CPAP); RR 0.99 [0.64, 1.56] ;
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Non-invasive ventilation versus fixed CPAP
Protocol outcome 1: Machine usage (hours/night)
-Actual outcome: Machine usage (hours/night); MD 0.14 [-0.17, 0.45]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Symptoms (Epworth Sleepiness Scale)
- Actual outcome: Symptoms (Epworth Sleepiness Scale); MD -0.49 [-1.46, 0.48]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Withdrawals (parallel group trials/first arm cross-over trials)
- Actual outcome: Withdrawals (parallel group trials/first arm cross-over trials); RR 0.61 [0.33, 1.15]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Quality of life (Functional Outcome of Sleep Questionnaire)
- Actual outcome: Quality of life (Functional Outcome of Sleep Questionnaire); MD 1.00 (0.56, 1.79);
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 5: Quality of life (Sleep Association Quality of Life Index)
- Actual outcome: Quality of life (Sleep Association Quality of Life Index); MD 0.40 (-0.34, 1.14);
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 6: Quality of life (SF-36 questionnaire

- Actual outcome: Quality of life (SF-36 questionnaire) Physical ; MD 0.60 (-2.21, 3.41); ;
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 7: Quality of life (SF-36 questionnaire)
- Actual outcome: Quality of life (SF-36 questionnaire) Mental; MD -2.90 (-7.09, 1.29); ;
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 8: Apnoea Hypopnoea Index (events/hr)
- Actual outcome: Apnoea Hypopnoea Index (events/hr); MD 1.36 [95% CI -6.92, 9.63]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 9: Patient preference - BiPAP/no preference or CPAP
- Actual outcome: Patient preference - BiPAP/no preference or CPAP; RR 0.88 [0.47, 1.65]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 10: Tolerability outcomes
- Actual outcome: dry mouth; RR; 0.56 (0.15, 2.17)
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 11: Tolerability outcomes
- Actual outcome: mask intolerance ; RR; 1.1.3 (0.45, 2.85)
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 12: Treatment comfort score
- Actual outcome Treatment comfort score; MD; ; 9 (-3.54, 21.54)

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: Heated humidification + fixed pressure CPAP versus fixed pressure CPAP alone

Protocol outcome 1: Machine usage (hours/night)
- Actual outcome: Machine usage (hours/night); MD 0.37 [0.10, 0.64]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 2: Symptoms (Epworth Sleepiness Scale)
- Actual outcome: Symptoms (Epworth Sleepiness Scale); MD; -0.34 [-0.93, 0.26]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 3: Withdrawals (parallel group trials/first arm cross-over trials)
- Actual outcome: Withdrawals (parallel group trials/first arm cross-over trials); RR 1.00 [0.56, 1.79]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 4: Apnoea Hypopnoea Index (events/hr)
- Actual outcome: Apnoea Hypopnoea Index (events/hr); MD 0.30 (-0.95, 1.55) ;
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 5: Quality of life (SF-36 questionnaire) [SF-36]
- Actual outcome: Quality of life (SF-36 questionnaire) [SF-36]; MD 0.11 [-6.97, 7.18]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 6: Nasal symptoms (parallel group trials)
- Actual outcome: runny nose; RR 0.39 [0.13, 1.15]

Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 7: Nasal symptoms (parallel group trials)

- Actual outcome: blocked nose ;RR 0.37 [0.20, 0.70]

Risk of bias: All domain - low, Selection - low, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 8: Nasal symptoms (parallel group trials)
- Actual outcome: dry nose; MD; -0.38 [-0.78, 0.01]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 9: Nasal symptoms (parallel group trials)
- Actual outcome runny nose:; MD ; -0.30 [-0.69, 0.09]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 10: Nasal symptoms (parallel group trials)
- Actual outcome: blocked nose; MD -0.38 [-0.78, 0.01]

Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 11: Nasal symptoms (parallel group trials)
- Actual outcome: bleeding nose; MD; -0.45 [-0.99, 0.10]
Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness

Protocol outcome 12: Preference

- Actual outcome: Preference; RR; 1.06 (0.67, 1.67) Risk of bias: All domain - high, Selection - high, Blinding - Low, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low, Subgroups - Low, Other 1 - Low, Other 2 - Low, Other 3 - Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	None